Many studies have investigated sex differences in language lateralization. Despite the large number of investigations, controversy about the presence of sex differences in lateralization remains. This study aims to provide a complete overview of sex differences in several reflections of language lateralization: handedness, asymmetry of the Planum Temporale (PT) and functional lateralization of language, measured by asymmetric performance on dichotic listening tests (Right Ear Advantage) and asymmetry of language activation as measured with functional imaging techniques. Meta-analysis of studies that assessed handedness in males and females yielded more left-handedness in males (mean weighted odds ratio: 1.25, \( p < 0.001 \)). Meta-analysis of studies on PT asymmetry yielded no sex difference (Hedges' \( g = -0.11, p = 0.68 \)). Results of the meta-analysis on dichotic listening studies also retrieved no sex difference in lateralization (Hedges' \( g = 0.09, p = 0.18 \)). When the studies were subdivided according to the paradigm they applied, studies that used the consonant–vowel task yielded a sex difference favouring males, while studies that applied other paradigms yielded no sex difference. The subdivision into applied paradigm largely overlapped with the subdivision into studies that did or did not focus on sex differences as their main topic. The observed sex effect may therefore be caused by publication bias. Meta-analysis of functional imaging studies yielded no sex difference (Hedges' \( g = 0.01, p = 0.73 \)) in language lateralization. Sub-analyses of studies that applied different paradigms all yielded no sex difference. In conclusion, males are more frequently non-right handed than females, but there is no sex difference in asymmetries of the Planum Temporale, dichotic listening or functional imaging findings during language tasks.

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**Keywords:** Sex difference, Language lateralization, Handedness, Asymmetry

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1. **Introduction**

In 1978 Harris wrote the first review on sex differences in lateralization, in which he concluded that females are less lateralized than men (Harris, 1980). Reviews conducted in the years since then have generally agreed with Harris’ conclusion that females have lower degrees of language lateralization than males (Bryden, 1982; McClone, 1980). Boles (1984), however, failed to find a sex difference in lateralization in a meta-analysis on studies that applied visual half-field paradigms.
Another review by Hiscock and Mackay (1985) also failed to find a sex difference in lateralization assessed with dichotic listening. In line with these findings, a more recent meta-analysis on functional imaging studies applying language tasks yielded no sex difference (Sommer et al., 2004). Thirty years after the first review on this topic, there is still no consensus about sex differences in lateralization and it remains a much debated topic (Clements et al., 2006; Plante et al., 2006).

There are several reasons why this topic remains in the centre of attention for so many years. First, there are considerable differences between girls and boys in the development of language abilities. When speaking first begins, girls generally articulate better than boys and produce longer sentences (Maccoby and Konrad, 1966). Perhaps as a consequence of this advantage, girls tend to have larger working vocabularies and better use of grammar than boys. Some years later, girls typically have superior reading abilities than boys. Part of this verbal advantage for females survives into adult age, especially in the domain of verbal fluency and the use of grammar. Furthermore, language disabilities, both of severe and mild type, affect boys more frequently than girls, with reported sex ratios between 3:1 and 7:1 (reviewed by Liederman et al., 2005). Psychiatric disorders, such as autism, Attention Deficit Hyperactivity Disorder (ADHD) and schizophrenia all have higher prevalences.

**Sex differences in handedness**

<table>
<thead>
<tr>
<th>Study name</th>
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<th>p-Value</th>
</tr>
</thead>
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</tr>
<tr>
<td>Clark 1957</td>
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<td>0.00</td>
</tr>
<tr>
<td>Falik 1959</td>
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<tr>
<td>Crovitz and Zener 1962</td>
<td>1.11</td>
<td>0.52</td>
</tr>
<tr>
<td>Pelecanos 1969</td>
<td>1.23</td>
<td>0.15</td>
</tr>
<tr>
<td>Beckman and Elston 1962</td>
<td>0.89</td>
<td>0.68</td>
</tr>
<tr>
<td>Oldfield 1971</td>
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<td>0.01</td>
</tr>
<tr>
<td>Dawson 1972</td>
<td>9.10</td>
<td>0.14</td>
</tr>
<tr>
<td>Annett 1972</td>
<td>1.03</td>
<td>0.76</td>
</tr>
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<td>Hardyck et al. 1976</td>
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<td>0.01</td>
</tr>
<tr>
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<td>Heim and Watts 1976</td>
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<td>Gur and Gur 1977</td>
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<td>Silverberg et al. 1979</td>
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<td>Teng et al. 1979</td>
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<td>Porac and Coren 1981</td>
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<tr>
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</tr>
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<td>Ellis et al. 1988</td>
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</tr>
<tr>
<td>Levander and Schalling 1988</td>
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<td>0.29</td>
</tr>
<tr>
<td>Singh Bryden 1994</td>
<td>1.17</td>
<td>0.45</td>
</tr>
<tr>
<td>Singh Bryden 1994 II</td>
<td>2.84</td>
<td>0.00</td>
</tr>
<tr>
<td>Iwasei et al. 1995</td>
<td>0.45</td>
<td>0.05</td>
</tr>
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<td>Davis and Annett 1994</td>
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<td>0.00</td>
</tr>
<tr>
<td>Singh et al. 2001</td>
<td>4.15</td>
<td>0.03</td>
</tr>
<tr>
<td>Yim et al. 2003</td>
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<td>0.53</td>
</tr>
<tr>
<td>Annett 2004</td>
<td>1.05</td>
<td>0.74</td>
</tr>
<tr>
<td>Medland et al. 2004</td>
<td>1.26</td>
<td>0.00</td>
</tr>
<tr>
<td>Elamis and Tan 2005</td>
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<td>0.00</td>
</tr>
<tr>
<td>Demura et al. 2006</td>
<td>1.69</td>
<td>0.00</td>
</tr>
<tr>
<td></td>
<td>1.25</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Fig. 1 – Meta-analysis of sex differences in handedness.
in males as compared to females (reviewed by Afifi, 2007). These psychiatric disorders may be associated with deviations in standard cerebral dominance (Bradshaw and Sheppard 2000; Sommer et al., 2007). Finally, women appear to recover better from aphasia than males after left cerebral stroke (Pedersen et al., 1995). If women indeed have more bilateral language lateralization than men, this could provide an explanation for all these observed sex differences.

The aim of this meta-analysis is to provide an overview of the current literature on sex differences in cerebral dominance, as reflected in handedness, asymmetry of the Planum Temporale (PT) and functional language lateralization. The current review is not only an update of earlier reviews on sex differences in lateralization, but it also provides a broader scope, since it includes meta-analyses of four different reflections of cerebral dominance for language.

2. Results

2.1. Sex differences in handedness

We included 43 studies on handedness providing information on 241,573 subjects. Fig. 1 shows the included studies assessing handedness for males and females from several countries. The mean weighted odds ratio was 1.25 ($p < 0.0001$), indicating a 25% higher prevalence of non-right handedness in males. The $I^2$-value for heterogeneity was 78%, indicating large variability among studies that cannot be explained by chance alone. Since culture or race may be involved in this sex difference in handedness, studies that assessed handedness in Western countries (European countries, Australia, Canada and USA) were compared to those assessing handedness in non-Western countries (Asia, Africa, Near East). The mean weighted odds ratio of 31 studies assessing Western populations was 1.19 ($p < 0.0001$), while the mean odds ratio of 12 studies assessing non-Western populations was 1.5 ($p < 0.0001$). The difference in odds ratios for sex differences between Western and non-Western countries was significant ($Q = 5.0, p = 0.03$).

2.2. Sex differences in asymmetry of the temporal plane

Thirteen studies could be included that provided data of right and left PT size per sex (Fig. 2). Twelve studies applied MRI measurements and one study measured post-mortem brains. All studies included only adult right-handed subjects. Meta-analyses of the PT asymmetry per sex showed that there was significant leftward asymmetry of the PT, both in males ($Hedges' g = 0.98, p < 0.001$) and in females ($Hedges' g = 0.98, p < 0.001$). The meta-analysis comparing asymmetry between males and females included 807 subjects and yielded no significant sex difference: $Hedges' g = -0.11, p = 0.68$. The $I^2$-value for heterogeneity was high: 92%. The same analysis was repeated after exclusion of the post-mortem study in an attempt to reduce heterogeneity, but the results were rather similar: $Hedges' g = -0.16, p = 0.6, I^2 = 92%$. Separate analyses were ran for studies measuring surface of the PT ($n=5$) and those measuring volume of the PT ($n=3$). Hedges' $g$ for the surface measurements was $-0.19, p = 0.25$ and 0.19, $p = 0.14$ for the volume measurements. However, heterogeneity in the separate analyses remained high: 94% for the surface measurements and 81% for the volume measurements.

In order to assess the possible influence of publication bias, studies that focussed on sex differences were compared to studies that reported sex differences as a by-product. Five studies reported sex differences as their main topic, including a total of 184 subjects. $Hedges' g$ of these studies was 0.35, $p = 0.64$. The $I^2$-value for heterogeneity increased to 93%, indicating that the studies of this sub-analysis are even more heterogeneous. Eight studies provided the sex differences in PT asymmetry as a by-product. These studies included a total of 623 subjects and $Hedges' g$ was $-0.32, p = 0.28$. Again, studies remained highly heterogeneous ($I^2 = 91\%$).

<table>
<thead>
<tr>
<th>Study name</th>
<th>Hedges's $g$</th>
<th>Hedges's $g$ and 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wada et al. 1975</td>
<td>0.42</td>
<td>$0.04$ $0.47$</td>
</tr>
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<td>Delisi et al. 1994</td>
<td>-0.23</td>
<td>0.00 $0.00$</td>
</tr>
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<td>Kulyntych et al. 1994</td>
<td>3.13</td>
<td>0.00 $0.00$</td>
</tr>
<tr>
<td>Preis et al. 1999</td>
<td>-3.04</td>
<td>0.00 $0.00$</td>
</tr>
<tr>
<td>Watkins et al. 2001</td>
<td>0.56</td>
<td>0.00 $0.00$</td>
</tr>
<tr>
<td>Foundas et al. 2002</td>
<td>0.19</td>
<td>0.44 $0.00$</td>
</tr>
<tr>
<td>Knaus et al. 2004</td>
<td>-2.47</td>
<td>0.00 $0.00$</td>
</tr>
<tr>
<td>Chance et al. 2006</td>
<td>0.89</td>
<td>0.07 $0.07$</td>
</tr>
<tr>
<td>Eckert et al. 2006</td>
<td>-0.22</td>
<td>0.27 $0.27$</td>
</tr>
<tr>
<td>Dos Santos Sequeira et al. 2006</td>
<td>-0.48</td>
<td>0.02 $0.02$</td>
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<td>Takahashi et al. 2006</td>
<td>-0.13</td>
<td>0.56 $0.56$</td>
</tr>
<tr>
<td>Vadlamudi et al. 2006</td>
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<td>0.15 $0.15$</td>
</tr>
<tr>
<td>Walder et al. 2007</td>
<td>0.83</td>
<td>0.11 $0.11$</td>
</tr>
<tr>
<td></td>
<td>-0.11</td>
<td>0.68 $0.68$</td>
</tr>
</tbody>
</table>

Fig. 2 – Meta-analysis of sex differences in asymmetry of the Planum Temporale.
2.3. **Sex differences in language lateralization measured with verbal dichotic listening tests**

For the meta-analysis on language lateralization measured with dichotic listening techniques, 12 studies could be included that provided mean and standard deviations of the Right Ear Advantage (REA) for both sexes separately (Fig. 3). All studies included adult subjects. Several studies included both right and non-right handed subjects. Data were available from a total of 3822 subjects. The mean weighted effect size for a sex difference in lateralization was 0.09 (p = 0.18), indicating no significant difference. The heterogeneity value $I^2$ was 35%. Several potential moderators were assessed. First, a correlation was calculated between the percentage of non-right handed subjects per study and the effect size for sex, which was not significant (Pearson’s rho = -0.07, N = 12, p = 0.82). This indicates that the inclusion of non-right handed subjects has no major influence on the sex difference in language lateralization measured with dichotic listening techniques. We also assessed type of paradigm as a possible moderator. Studies were divided into three categories: those using Consonant–Vowel (–Consonant) (CV(C) tasks), studies applying rhyme words or fused words and studies using sets of digits or words (including triad tasks). Seven studies applied a digit or word task, including a total of 1762 subjects. The sex difference was not significant (Hedges $g = -0.02$, p = 0.72) and studies were homogeneous ($I^2$-value = 6%). Four studies applied the CV(C) task including 506 subjects. A significant sex difference was observed favouring larger asymmetry in males (Hedges $g = 0.30$, p = 0.05) but studies were more heterogeneous than in the total analysis ($I^2 = 45$%). Only one study applied the fused word task (n = 48), which yielded no significant sex difference (Hedges $g = -0.07$, p = 0.8). This implicates that paradigm is a moderator of the sex difference in language lateralization assessed with the dichotic listening paradigm. However, the subdivision into studies applying different paradigms largely overlaps with the division into studies that either focus on sex differences or report sex differences as a by-product. None of the studies that reported a sex difference as a by-product applied the CV(C) task, while the majority of studies that focus on sex differences did apply the CV(C) task. To assess the potential influence of publication bias, studies were divided on the basis of their main topic (sex difference or otherwise). Seven studies focussed on sex differences, including a total of 1076 subjects. Meta-analysis of these studies yielded a significant mean weighted effect size (Hedges $g = 0.25$, p = 0.01) and heterogeneity increased ($I^2 = 39$%). Four studies did not focus on sex differences, including 1240 subjects. Meta-analysis of these studies yielded no significant sex difference (Hedges $g = -0.04$, p = 0.56), while these studies were homogeneous ($I^2 = 15$%). It appears that the main topic of a study (focus on sex differences or not) is a confounder for paradigm, which also is a significant moderator. To assess the potential influence of publication bias, we compared the sub-analysis of the published studies applying the CV(C) task to a large database (Kenneth Hugdahl, University of Bergen, unpublished data) consisting of 1506 subjects that also performed the CV(C) task. The effect size of the sex difference in this database was 0.07 (p = 0.17), indicating no significant sex difference in asymmetry.

2.4. **Sex differences in language lateralization measured with functional imaging**

Twenty six functional imaging studies could be included that provided data on language lateralization from males and females separately (Fig. 4). A total of 2151 subjects could be included in the meta-analysis. All studies included only right-handed subjects, both children and adults. The difference in language lateralization between males and females was not significant (Hedges $g = 0.09$, p = 0.24) and there was heterogeneity among studies ($I^2 = 44$%). We assessed several potential moderators. First, we compared sex differences in lateralization

<table>
<thead>
<tr>
<th>Study name</th>
<th>Hedges's g</th>
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<th>Hedges's g and 95% CI</th>
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<tr>
<td>Kraft 1982</td>
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<td></td>
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<td>0.21</td>
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<td></td>
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<td>Lewis et al. 1988</td>
<td>0.04</td>
<td>0.62</td>
<td></td>
</tr>
<tr>
<td>Munro and Govier 1993</td>
<td>-0.09</td>
<td>0.76</td>
<td></td>
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<td>Govier and Bobby 1994</td>
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<td>Rahman et al. 2007</td>
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</table>

Fig. 3 – Meta-analysis of sex differences in the Right Ear Advantage.
between children and adults. Twenty studies assessed language lateralization in 1098 adult subjects. Meta-analysis of these studies yielded no sex difference (Hedges’ $g=0.12$, $p=0.24$) and heterogeneity remained ($I^2=40$%). Five studies assessed language lateralization in children. Again, no significant sex difference emerged (Hedges’ $g=0.01$, $p=0.96$), but these studies were homogeneous ($I^2=0$%).

To assess the possible influence of the applied language paradigm on sex differences in lateralization, separate analyses were performed for word generation tasks, such as verbal fluency and verb generation, for semantic decision tasks and for listening tasks (either to speech, stories or single words). Twelve studies applied a word generation task and included a total of 1075 subjects. No sex difference was found in this analysis (Hedges’ $g=-0.12$, $p=0.15$) and studies were homogeneous ($I^2=0$%). Eight studies on 510 subjects applied a semantic decision task. Again, no sex difference emerged (Hedges’ $g=0.01$, $p=0.95$) and studies were homogeneous ($I^2=0$%). Five studies applied a listening task and included 293 subjects in total. Analysis of these studies retrieved no sex difference (Hedges’ $g=0.24$, $p=0.36$), but these studies were heterogeneous ($I^2=82$%).

Finally, we compared studies that focussed on sex differences to studies that reported sex differences as a by-product. Sixteen studies including a total of 1036 subjects had a different main topic and reported sex differences as a by-product. Meta-analysis of these studies yielded no sex difference (Hedges’ $g=0.06$, $p=0.37$) and these studies were homogeneous ($I^2=0$%). Ten studies did focus on sex differences and included 1115 subjects. Analysis of these studies found no sex difference (Hedges’ $g=-0.02$, $p=0.69$), but these studies remained heterogeneous ($I^2=76$%).

### 3. Discussion

This study aimed to provide an overview of possible sex differences in relation to cerebral language lateralization. Meta-analyses were performed of studies on handedness, asymmetry of the PT, dichotic listening tests and functional imaging paradigms.
A significant sex difference was observed for handedness, with more right-handedness in females. We observed no sex difference in PT asymmetry, language lateralization as measured with dichotic listening or language lateralization as assessed with functional imaging. Sub-analyses of dichotic listening studies applying a CV(C) task did reveal a significant sex difference with lower degrees of language lateralization in females. This sex difference could not be replicated in a large unpublished database applying the same task and could be the result of publication bias.

3.1. Handedness

Males were found to have a 25% higher prevalence of non-right handedness than females. Though the higher prevalence of non-right handedness in males was a rather consistent finding, there was considerable variation in the extent of the sex difference, producing heterogeneous results. Heterogeneity may in part be caused by the variety in culture, or possibly in race, of the included subjects. The sex difference in non-Western samples was higher than in Western studies, indicating that cultural (or possibly racial) differences are a moderator of the sex difference in handedness.

3.2. PT asymmetry

Males, having a higher prevalence of non-right handedness, may be expected to have a lower degree of asymmetry of the PT as well, since non-right handedness is associated with decreased PT asymmetry (Herve et al., 2006). This expectation was not met, since no sex difference emerged from the meta-analysis. It remains, however, possible that a sex difference is present in other asymmetric brain structures. Since results were heterogeneous, sub-analyses of studies were performed for studies measuring surface or volume of the PT, but heterogeneity remained high in both sub-analyses. Sub-analyses were also performed on studies that focussed on sex differences and studies that had another main topic. The studies differed in the direction of their mean sex difference (more asymmetry in men in studies that focussed on sex differences and more asymmetry in women in studies with another main topic) but significance was not reached in either analysis and heterogeneity remained high in both sub-analyses. This indicates that publication bias may be a moderator of the retrieved sex differences in PT asymmetry.

3.3. Language lateralization, dichotic listening

The meta-analysis on dichotic listening studies showed that there is no sex difference in language lateralization. Handedness of the included subjects showed no correlation with the sex difference, which implies that restricting the sample to right-handed subjects has no major impact on the sex difference in lateralization. When sub-analyses were performed on the basis of the paradigm applied, a significant sex difference was retrieved by studies that used the CV(C) task, while meta-analysis of studies that applied digit or word tasks yielded no sex difference. However, studies applying a CV(C) task largely overlap with studies that had a main focus on sex differences. Sub-analyses of studies that focussed on sex differences yielded a significant sex difference, while studies that focussed on another topic found no sex difference. To distinguish between the influence of paradigm and that of publication bias, the effect size of the sex difference in lateralization was calculated from a large dataset (Bergen Dichotic Listening Database; courtesy of Prof. Hugdahl, see also Hugdahl, 2003; Hugdahl et al., 2001) that also applied the CV(C) task. This database has been accomplished by merging data from several studies that all applied the same paradigm. The sample size of the database was three times larger (1506 subjects) than the sample size of our sub-analysis on published studies applying the CV(C) task (506 subjects). In the Bergen Dichotic Listening Database, no sex difference was present, indicating that publication bias is probably the most powerful moderator of the results.

Earlier reviews on sex differences in dichotic listening studies came to similar conclusions. For example, Hiscock et al. (1994) reviewed 114 studies that reported on sex differences in dichotic listening. Of these, 49 studies (34.8%) found at least one significant effect involving the factor sex. Most of these effects, however, involved an interaction between sex and another factor, such as age or task performance. Only 11 studies (10%) reported a main effect for sex. From these, 9 studies found higher degrees of language lateralization in males and 2 studies found higher lateralization in females. Hiscock’s review did not include a quantitative analysis, since many studies did not provided enough exact data. Voyer (1996) performed a meta-analysis on perceptual half-field studies in the auditory, visual and tactile domain. He concluded that there is a modest, but significant sex difference in laterality. Voyer’s results were, however, not resistant to the file drawer problem, indicating that the results may have been caused by a publication bias for studies that report a positive effect for sex.

3.4. Language lateralization, functional imaging studies

In parallel to the results of the (overall) meta-analysis on dichotic listening studies, the analysis on functional imaging studies yielded no sex difference in language lateralization. Sub-analyses of studies applying word generation tasks, semantic decision tasks and listening tasks all produced no sex difference in language lateralization. Sub-analyses of studies on language lateralization in adults versus children also produced no sex differences. Finally, sub-analyses of studies that did or did not focus on sex difference did not produce a sex difference in either of the analyses. Thus, in contrast to dichotic listening studies, publication bias favouring studies with positive findings may not be a major factor in explaining heterogeneity among functional imaging studies. These findings are in accordance with our earlier meta-analysis on 12 functional imaging studies (Sommer et al., 2004).

The absence of a sex difference in PT asymmetry and language lateralization observed in all three meta-analyses appears to be a quite consistent finding. Three hypotheses may be considered in the light of these findings. Firstly, there may be a sex difference at the population level, but it is relatively small so that it is only sporadically observed. Were this to be true, studies with larger sample sizes would be expected to report a sex difference in lateralization more frequently than studies with smaller sample sizes, since they have more power to detect
subtle differences. On inspection of our data, this appears not to be the case. Furthermore, all three meta-analyses included more than 400 males and females, which makes the chance for three false negative findings very small. Thus, the hypothesis of a true, but subtle sex difference in cerebral asymmetry and language lateralization at the population level is not supported by our data. A second hypothesis to explain the absence of a main sex difference in language lateralization is that sex differences may be task dependent. Indeed, there was significant heterogeneity among the studies in our meta-analyses on dichotic listening and functional imaging studies, which may be congruent with this hypothesis. The results of our moderator analysis on dichotic listening studies appeared to support this idea, since a significant sex effect was retrieved only in a sub-analysis of studies using the CV(C) task. However, a much larger (unpublished) database applying the same task showed no sex difference in lateralization, which weakens the argument for a task-specific sex difference. Sub-analyses of functional imaging studies according to task did not produce a sex difference in lateralization. Thus, the argument for a task-specific sex difference is not supported by our meta-analysis.

The third hypothesis is the null-hypothesis; that there is no sex difference in cerebral asymmetry and language lateralization at the population level. If this hypothesis were to be true, the sex differences reported in the small sample studies may reflect biased reporting of chance findings, i.e. the “file drawer problem” (Rosenthal, 1991). This hypothesis is consistent with the absence of a sex difference in the large unpublished database (Hugdahl). In addition, this hypothesis offers an explanation for the different results from sub-analyses on PT asymmetry and dichotic listening studies that did or did not have sex differences in lateralization as their main topic.

Our data appear to be most consistent with a sex difference in handedness without an associated sex difference in cerebral asymmetry and language lateralization. The increased prevalence of non-right handedness in males, in the absence of sex differences in asymmetry and lateralization is not easily explained. Several differences between men and women may account for the increased non-right handedness in males, such as genetic, hormonal or social influences. It could reflect sex-linked inheritance of the genetic predisposition to develop right-handedness. For example, a gene associated with handedness could be located on the X-chromosome (Corballis et al., 1996). Another possibility could be the different imprinting in males and females of a gene related to handedness. Indeed, an imprinted gene (LRRTM1, on chromosome 2p12) was recently found to be associated to handedness (Francis et al., 2007). The suggestion of a genetic cause for the sex difference in handedness is supported by studies that found a higher chance for non-right handed women to have non-right handed offspring as compared to non-right handed men (reviewed by Annett, 1999). However, handedness is associated to brain asymmetry and to language lateralization and the genetic basis for handedness is supposed to overlap, at least in part, with the genetics of asymmetry and lateralization (McManus 1991; Annett 2004). A genetic cause for increased non-right handedness in males would therefore be expected to be paired with decreased asymmetry and language lateralization in males, which is not supported by our meta-analyses.

Higher prenatal and postnatal levels of testosterone may be another factor to cause more non-right handedness in males. Studies in patients with abnormal levels of sex hormones appear to support this hypothesis. Schachter (1994) investigated the prevalence of non-right handedness in a group of women whose mothers had been administered diethyl-stilbestrol (DES) during their pregnancies. DES is a synthetic estrogen, administered to prevent miscarriage, which affects the foetal brain in a similar fashion as testosterone. The DES exposed women had a higher prevalence of non-right handedness than controls. This finding was replicated by Scheirs and Vingerhoets (1995). Another example of the influence of testosterone on handedness is provided by females with the Congenital Adrenal Hyperplasia (CAH) syndrome, whose adrenal glands produce abnormally high levels of testosterone as a by-product of dysfunctional cortisol synthesis. Women with CAH were found to have a higher prevalence of non-right handedness than their sisters with normal levels of testosterone (Nass et al., 1987). The increased non-right handedness in women with CAH was replicated by Smith and Hines (2000), but not by Helleday et al. (1994). Though inconsistent and rather anecdotic, these studies lend some support to the idea that higher prenatal testosterone could cause an increased prevalence of non-right handedness, which may account for the higher prevalence of non-right handedness in males as compared to females. The same argument as we made for a genetic cause can also be made against this explanation; why should differences in testosterone cause a sex difference in handedness but not in PT asymmetry or language lateralization? There is indeed some evidence that prenatal testosterone levels do affect language lateralization as well (Grimshaw et al., 1995).

Social influences may be a better candidate to explain the retrieved sex difference in handedness only. It can be hypothesized that social pressure to use the right hand for unimanual tasks, such as writing and eating, is higher for females than for males. Alternatively, females may be more apt to meet social preferences for using the right hand than males. In support of this hypothesis, Porac et al. (1986, 1990) found that women reported significantly more frequent than men to be forced to change handedness from left to right. Porac et al. (1986) suggested that this could explain the overall difference in handedness between the sexes. Interestingly, Annett (2004) noted in her large samples of handedness data that right-handed females more frequently use the left hand for one or two items of a handedness scale, while right-handed males were more frequently consistently right-handed for all items. This may reflect a higher percentage of natural left-handers who have switched to right hand writing in the female group. In our meta-analysis we found that the sex difference in handedness was larger in non-Western samples, which may be indicative of more sex-specific social pressure in non-Western cultures. These findings strengthen the idea that females who are innate left or mixed-handed more frequently switch to right-hand use for social activities such as writing and eating than left or mixed-handed males.

4. Experimental procedure

Handedness is associated with language lateralization in that non-right handed subjects have a higher chance of having
bilateral or right cerebral dominance than right-handed subjects, though the majority of left-handers have left cerebral dominance (Pujol et al., 1999). Handedness therefore provides a weak reflection of language lateralization. Though this reflection is not very accurate, it can be observed easily and has been assessed in large samples of males and females. We have selected three other measurement methods that correlate to language lateralization and have frequently been applied in the study of healthy males and females, which are:

1. Asymmetry of the PT, measured with MRI or directly in post-mortem brains,
2. the REA measured with dichotic presentation of verbal stimuli, and

4.1. Search criteria

The literature on handedness and language lateralization comprises more than forty years of research and is estimated to consist of over 10,000 studies. This meta-analysis cannot, therefore, provide a complete review of all studies reporting sex differences in handedness or lateralization. Only English publications from international journals and book chapters were selected. Explored databases were Embase, PsychLit, PubMed and Science Direct, using combinations of the following search terms: “handedness”, “sex”, “left-handed”, “gender”, “Planum Temporale”, “REA”, “dichotic listening”, “fMRI”, “language lateralization”, “FTCD” and “PET”. Reference lists from retrieved articles were also assessed for cross-references. In addition, the last five volumes of three journals (Brain and Language, NeuroImage and Human Brain Mapping) were searched manually to check for other suitable studies.

Studies were included if they met the following criteria:

I. The study used the same measurement method in males and females (either a handedness questionnaire, asymmetry of the PT, functional language lateralization as measured either with dichotic listening or with functional imaging).  
II. The study included individuals who were not selected on the basis of a special condition that may be related to language lateralization (such as dyslexia, schizophrenia, epilepsy, professional mathematicians, homosexuals or subjects with a history of birth trauma). The unsolicited control groups for specific population subsets were, however, included.  
III. Twin studies were excluded, since there is reason to assume that handedness and lateralization in twins is different from that in singletons (Sicotte et al., 1999).  
IV. Sufficient exact data were available in the paper to calculate effect sizes for the sex difference, or could be provided post hoc by the corresponding author.

More than 1000 studies were selected and screened for suitability. Approximately half of these articles did not assess sex differences in their sample. From the studies that did mention a sex effect, the majority reported that there were no significant sex differences. These studies could have been included by presuming that the main effect of sex would have an F-value of zero. This would have been a quite conservative approach and may have led to an underestimation of the sex effect. We therefore preferred to exclude these studies, at the disadvantage of overestimating the true sex effect. Only studies that provided percentages (for handedness) or means and standard deviations per sex (PT asymmetry, language lateralization) or exact F, t or p-values for the main effect for sex were included. If the study provided insufficient statistical data, contact was sought with the corresponding author. Additional data was requested from 64 studies and obtained from 16 of them.

4.2. Combination of measurement methods

4.2.1. Handedness

Studies that assessed handedness have used a variety of handedness scales. A large unpublished, but frequently cited, meta-analysis by Beatrice M. Seddon and I.C. McManus (1993, unpublished) found that the incidence of non-right handedness was not related to the method of measurement, or the length or number of response items included in handedness inventories. Whether handedness is assessed by a questionnaire, a performance measurement or a simple question (such as “writing hand” or “handedness of the subject”) appears not to affect the observed incidence of non-right handedness. We therefore felt confident to combine percentages of right-handedness obtained with different methods. When several handedness criteria were provided, we selected data based on writing hand in order to increase uniformity among studies. The percentage right-handedness per sex was entered in the meta-analysis. The non-right handed group therefore consists of both mixed and left-handers.

4.2.2. Planum Temporale

Studies assessing asymmetry of the PT also applied different methods of measurement. Some studies measured the surface of the PT, while others measured PT volume. Determination of the borders of the PT also showed minor differences between studies. However, in all studies right and left PT were measured in a similar fashion. The effect size for asymmetry that was calculated from PT sizes may therefore be better comparable between studies than the absolute data of the size of right and left PT. In addition, effect sizes for asymmetry were compared between men and women from the same study before combining them with other studies to calculate a mean weighted effect size.

4.2.3. Dichotic listening

Studies that measured language lateralization with the dichotic listening paradigm applied several different stimuli. Studies were included that used either a Consonant–Vowel(–Consonant) (CV or CVC) task, a fused word or a rhyme word task or binaural presentation of different digits or words (tridat task and other recall tasks), to elicit a REA. The type of paradigm applied to elicit a REA may affect the degree of language lateralization. It is therefore possible that the paradigm also affects the sex difference in perceptual asymmetry. In order to assess this possibility, paradigm was entered in the analysis.
as a potential moderator. One study (Lamm and Epstein, 1997) provided data on two different paradigms. Mean values of the two paradigm were used for the main analysis. For sub-analyses per paradigm, data sets from the two paradigms were entered as separate studies.

4.2.4. Functional imaging
In parallel to dichotic listening studies, studies applying functional imaging to assess language laterализation have used several different language paradigms, such as verb generation, story listening, picture naming and semantic decision making. Again, the type of language paradigm was entered as a potential moderator. One study (Plante et al., 2006) provided data on four different paradigms. Mean values of the four tasks were used for the main analysis. For sub-analyses per paradigm, data sets from these paradigms were entered as separate studies.

4.3. Children and adults
Handedness is a rather stable individual characteristic, from about 7 years of age (Michel and Harkins 1986). We have therefore included handedness data from both children (above age 7) and adults. Subject’s age may however be a factor to affect language laterализation (Holland et al., 2001) and possibly asymmetry of the PT. A significant interaction between age and sex has been described in studies on language laterализation (Plante et al., 2006; Gaillard et al., 2001). We therefore marked whether data were obtained from children, from adults, or from a mixed group. An additional analysis was performed to assess possible differences in the sex difference in laterализation between children and adults.

4.4. Percentage non-right handed subjects
Many studies on PT asymmetry and on language laterализation restricted their analyses to right-handed subject. Selection of only right-handed subjects may affect the sex differences in PT asymmetry or in language laterализation. To assess the potential influence of this factor, the percentage non-right handed subjects per study was correlated to the effect size for the sex difference.

4.5. File drawer problem
One of the main pitfalls of meta-analyses is the “file drawer problem” (Rosenthal, 1991), i.e. the possibility that published studies are a biased sample of the studies that are actually carried out, as it is presumed that only experiments with significant results are published. This problem is associated with the inclusion of only published studies in a meta-analysis, since exclusive use of published studies is likely to result in an overestimation of the effects under study. To overcome this problem, the present meta-analysis emphasized the inclusion of studies that did not focus on sex differences, but rather reported information on sex differences as a by-product. For example, studies that examined the effect of age or occupation were included as well as data from control groups of studies examining the effects of schizophrenia or epilepsy on laterализation. It was noted whether or not sex differences were the main objective of a study and this variable was entered as a potential moderator to obtain a reflection of the influence of publication bias. Furthermore, for the meta-analysis on dichotic listening studies, we could compare the published data to the sex difference in the Bergen Dichotic Listening Database (courtesy of Prof. K. Hugdahl), which has not been published. Comparing the results of our meta-analysis on published dichotic listening studies to the large data base of Professor Hugdahl, provides a reflection of the impact of the file drawer problem.

4.6. Meta-analytic techniques
4.6.1. Handedness
From the handedness studies, odds ratios were calculated from the percentage right-handed women compared to the percentage right-handed men. Odds ratios of all studies were combined to calculate a mean weighted odds ratio and a corresponding p-value using the program Comprehensive Meta-analysis (http://www.meta-analysis.com/). We used random effects, since handedness assessment and study population differed between studies. In addition, a homogeneity statistic (I²) was calculated, to assess the heterogeneity of results across studies. I² quantifies the effect of heterogeneity, providing a measure of the degree of inconsistency in the studies’ results (Higgins et al., 2003). Negative values of I² are put equal to zero so that I² lies between 0% and 100%. I² describes the percentage of total variation across studies that is due to heterogeneity rather than chance; a value of 0% indicates no observed heterogeneity, and larger values show increasing heterogeneity (Higgins et al., 2003). Since the nationality of the study sample may influence the sex difference in handedness, this factor was entered as a potential moderator.

4.6.2. Planum Temporale
From studies on PT asymmetry, a mean weighted effect size for asymmetry was first calculated from the right and left PT size for males and females separately. In a third meta-analysis, effect sizes of females’ asymmetry were compared to those of males. If means and standard deviations were not provided per sex in the study, exact F, t or p-values were transformed into effect sizes using Rosenthal’s (1991) formula. Effect sizes for sex differences in asymmetry of all studies were combined and weighted for sample size of the studies to obtain a mean weighted effect size “Hedges g” (Hedges and Olkin 1985) and p-values using the random effects module of Comprehensive Meta-analysis software. Homogeneity statistic (I²) was calculated, to assess the heterogeneity of results across studies (Higgins et al., 2003).

4.6.3. Dichotic listening
From each study an effect size was calculated “Hedges g” (Hedges and Olkin 1985). When means and standard deviations were not available, effect sizes were computed from exact p-values, t-values or F-values (cf. Lipeys and Wilson, 2003). After computing effect sizes for each study, the meta-analytic method was applied to obtain a combined effect size (Hedges g), which indicated the magnitude of the association across all studies. Effect sizes were weighted for sample size, in order to correct for upwardly biased estimation of the effect in small sample sizes using the random effects module of Comprehensive Meta-analysis software. A homogeneity statistic (I²) was
calculated, to assess the heterogeneity of results across studies (Higgins et al., 2003).

4.6.4. Functional imaging

From studies on language lateralization measured with functional imaging, the mean and standard deviation of the lateralization index was compared between the sexes. The lateralization index is defined as language activity in the left hemisphere minus language activity in the right hemisphere, divided by the total activity in both hemispheres. Language activity was measured as the number of “active” voxels in brain regions involved in language processing. If means and standard deviations of the lateralization indices were not provided per sex, exact F, t, or p-values for the main effect of sex on asymmetry were transformed into effect sizes using Rosenthal’s (1991) formula. Effect sizes of all studies were combined and weighted for sample size to obtain a mean weighted effect size (Hedges g) using the random effects module of Comprehensive Meta-analysis software. A homogeneity statistic ($I^2$) was calculated, to assess the heterogeneity of results across studies (Higgins et al., 2003).

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References


Further-Reading


