## Letter to the Editor

## Reply to 'Time-resolved sex differences in language lateralization'

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In response to our meta-analysis on sex differences in language lateralization (Sommer *et al.*, 2004), Ortigue and colleagues point out the limited time resolution of functional MRI (fMRI), PET and echo Doppler as a possible cause for failing to find a significant sex difference in the meta-analysis. The activation pattern of fMRI and PET studies, they argue, is composed of language components, but also of non-specific cerebral activity, especially when the control task consists of passive rest.

Ortigue and colleagues explain that the functionally relevant time for language is between 170 and 400 ms poststimulus. They present data of an event-related potential (ERP) study in 13 right-handed women and 13 right-handed men. In their study, the period between 170 and 400 ms indeed was the period when signal intensity over the left hemisphere was higher than that over the right hemisphere. In this period, laterality in male subjects was higher than in female subjects, though exact levels of significance were not reported. In the earlier and later periods, the signal was not significantly higher in either hemisphere, nor was there a sex difference.

We agree that time resolution is limited in fMRI, PET and Doppler studies. However, we do not agree with their opinion that this should be a problem in detecting subtle differences in language lateralization. The studies we included in the metaanalysis showed clear lateralization for the whole sample (males and females). Studies that have used fMRI to study language show significant activation of language-related areas, such as Broca's and Wernicke's areas. Both facts (lateralized activation pattern and activation in Broca's and Wernicke's areas) indicate that the language component contributed significantly to the results of the included studies.

In addition, there is other proof to show that fMRI and Doppler are valid techniques to investigate language lateralization. Wada testing (the gold standard in determining language dominance) demonstrated 95% left cerebral dominance in right-handed subjects and 70% left dominance in left-handed subjects (Rasmussen and Milner, 1977). The difference in language lateralization between right- and left-handers can thus be regarded as rather subtle. Nevertheless, large-scale studies using both fMRI (Pujol et al., 1999) and Doppler (Knecht et al., 2000) were able to detect significant differences in language lateralization between right- and left-handed volunteers. The same largescale studies also analysed sex influences and found no significant difference. This indicates that fMRI and Doppler are adequate techniques to detect subtle differences in language lateralization. The failure to find a sex difference therefore implies that there is no sex difference language lateralization at the population level. in Nevertheless, we agree with Ortigue and colleagues that taking into account temporal characteristics deserves a closer look, and may possibly reveal more consistent evidence for sex differences, although this question remains open to investigation.

## References

- Knecht S, Drager B, Deppe M, Bobe L, Lohmann H, Floel A, et al. Handedness and hemispheric language dominance in healthy humans. Brain 2000; 12: 2512–8.
- Pujol J, Deus J, Losilla JM, Capdevila A. Cerebral lateralization of language in normal left-handed people studied by functional MRI. Neurology 1999; 52: 1038–43.
- Rasmussen T, Milner B. The role of early left-brain injury in determining lateralization of cerebral speech functions. Ann NY Acad Sci 1977; 299: 355–69.
- Sommer IEC, Aleman A, Bouma A, Kahn RS. Do women really have more bilateral language representation than men? A meta-analysis of functional imaging studies. Brain 2004; 127: 1845–52.