## Handedness and language lateralization in partial epilepsies

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**Background:** Epilepsy may influence hemispheric specialization. Previous studies have reported an increased incidence of left-handedness and atypical language lateralization in epilepsy patients, compared to controls (1, 2). Several factors have been proposed to affect atypical language lateralization. However, the interplay between language lateralization, handedness, and seizure focus localization has not been well studied in the epilepsy population. We investigate this relationship in patients with unilateral partial epilepsy using functional MRI of language and a validated handedness inventory.

**Methods:** We retrospectively evaluated 181 subjects (83 controls, 98 patients) that underwent fMRI language investigation between 1/7/2000 and 30/6/2004 at our institute. All patients had refractory partial epilepsy, based on diagnosis obtained from participation in a comprehensive epilepsy program. Imaging was performed on a 3-tesla GE scanner (General Electric, Milwaukee, WI), including whole brain fMRI (multi-slice GR-EPI, TR = 3.6 seconds, TE = 40 msec, flip = 60deg, 128 X 128 matrix or TR = 3.2 seconds, TE = 40 msec, flip = 75 degrees, 64 X 64 matrix). The language paradigm was a noun-verb generation task, performed in a block design (4). The fMRI data were processed using SPM02 (Wellcome Department of Imaging Neuroscience, London, UK) and iBrain® (3). A language laterality index (LI) was calculated using the equation (left – right)/(left + right), based on the number of activated voxels in left- and right-sided language-associated regions. Language lateralization was considered atypical if the LI was  $\leq 0.2$  (4). The LI was obtained in 154 subjects. Handedness was assessed using the 12-item Edinburgh Handedness Inventory (5) to calculate a handedness quotient (HQ). The HQ was obtained in 148 subjects. The groups were compared using chi-square, bivariate regression and MANOVA tests, with a level of significance set at 5%.

**Results:** Patients had a higher incidence of atypical language (22%, table) than controls (12%), patients were also more frequently left-handed (20%), compared to controls (8%). Similarly, mean LI scores were lower in patients (0.43, table) than controls (0.57), and mean HQ scores were also lower in patients (51) than controls (71). The relationship between HQ and LI was assessed using bivariate regression analysis. A significant model emerged only in patients; F(1,69) = 18.77, p < .05, whereby LI accounted for 20.2% of the variance in HQ scores, but not in controls F(1,57) = 0.35, p > .05. Language LI and HQ were not different between patients with a right- or left-sided seizure focus (table).

|                                  | Patients                     | Controls                    | р     |
|----------------------------------|------------------------------|-----------------------------|-------|
| Language lateralization          | n = 86                       | n = 68                      |       |
| Atypical language lateralization | 20 (22%)                     | 8 (12%)                     | < .05 |
| Laterality index (LI)            | $0.43 \pm 0.43$              | $0.57 \pm 0.33$             | < .05 |
| Seizure focus                    | <b>Right</b> ( <i>n</i> =22) | <b>Left</b> ( <i>n</i> =49) |       |
| Laterality index (LI)            | $0.52 \pm 0.24$              | $0.45 \pm 0.48$             | > .05 |
| Handedness                       | n = 72                       | n = 67                      |       |
| Left-handedness                  | 16 (20%)                     | 5 (8%)                      | < .05 |
| Handedness quotient (HQ)         | $51 \pm 63$                  | $71 \pm 42$                 | < .05 |
| Seizure focus                    | <b>Right</b> $(n=22)$        | <b>Left</b> ( <i>n</i> =49) |       |
| Laterality index (LI)            | $40 \pm 78$                  | $57 \pm 55$                 | > .05 |

Table 1: Language lateralization and handedness in epilepsy patients compared to controls

Values expressed as number ( $\sqrt[6]{}$  overall number), and as mean  $\pm$  standard deviation

**Discussion:** Patients with epilepsy show an increased degree of left-handedness and atypical language lateralization compared to controls, confirming previous reports (1, 2). Interestingly, handedness and language lateralization were linked in patients, but not in controls. This supports the concept of 'pathological left handedness', where an underlying abnormality is causing both left-handedness and atypical language lateralization. The hemispheric localization of the seizure focus had no major influence on handedness or language lateralization, indicating that the disturbance of hemispheric specialisation, caused by the epilepsy, is not restricted to the hemisphere harbouring the seizure focus.

## **References:**

1. Rasmussen, T., Milner, B. (1977). Annals of the New York Academy of Science, 299, 355-369.

2.Springer, J. A., Binder, J. R. et al. (1999). Brain, 122, 2033-2045.

- 3. Abbott, D., Jackson, G. D. (2001). Neuroimage, 13, 59.
- 4.Briellmann, R. S., Saling, M. M., et al (2004). Brain and Language, 89, 531-542.
- 5.Oldfield, R. C. (1971). Neuropsychologia, 9, 97-113.