Original article

Epileptic Disord 2011; 13 (4): 368-74

Lessons learned from a comparison of language localisation using fMRI and electrocortical mapping: case studies of neocortical epilepsy patients

Kwang Ki Kim [1,2], Michael D Privitera [2,3], Jerzy P Szaflarski [2,3,4]

[1] Department of Neurology, Dongguk University International Hospital, Gooyang-shi, Kyeonggi-do, Korea
[2] Department of Neurology, University of Cincinnati,
[3] Cincinnati Epilepsy Center, University of Cincinnati,
[4] Center for Imaging Research, University of Cincinnati, Cincinnati, OH, USA

Received May 10, 2010; Accepted November 13, 2011

ABSTRACT – Electrocortical mapping (ECM) is recognised as an established method for localisation of eloquent cortex in patients undergoing resective surgery for epilepsy management. Functional MRI (fMRI) has been utilised for language and other cortical function localisation. We describe language localisation in two patients using both ECM and fMRI. Co-registration of fMRI and ECM revealed that although two fMRI tasks localised multiple language areas, the verb generation task had an advantage over the semantic decision/tone decision task in that there was a clear overlap between the language areas identified by the verb generation task and ECM. In addition to the language areas detected by ECM, fMRI showed other language-related areas that may be important for post-operative language outcome. Therefore, fMRI may provide additional and complementary information to ECM in presurgical evaluation of patients with epilepsy. The correlation between fMRI and ECM may depend on the language testing methods utilised during the procedures.

Key words: functional MRI (fMRI), electrocortical mapping (ECM), language, outcomes, epilepsy, surgery

Correspondence:
Kwang Ki Kim
Department of Neurology,
University of Cincinnati Academic Health Center,
260 Stetson Street,
Cincinnati, OH 45267-0525, USA
<neukim@duih.org>

Patients considered for dominant fronto-temporal neocortical resections usually undergo cortical mapping in order to avoid removal of the eloquent areas *e.g.* language cortices. Classically, two invasive methods have been used for the purpose of language lateralisation and localisation; the intracarotid amobarbital procedure (IAP) and electrocortical mapping (ECM). While IAP is a reliable tool for language lateralisation, its main limitation is the inability to localise

doi:10.1684/epd.2011.0473

the language area. It is also invasive and may cause complications including stroke, infection, or bleeding and may falsely lateralise (Loddenkemper *et al.*, 2004; Schulze-Bonhage *et al.*, 2004). ECM is considered to be the gold standard but is invasive and limited by the location of the monitoring electrodes.

Recently, functional neuroimaging methods have undergone substantial development and are now performed routinely in patients undergoing presurgical evaluation for epilepsy surgery. Several studies have addressed the issues of language lateralisation in epilepsy patients; in some, language lateralisation using IAP and fMRI was compared and in others the similarity between fMRI and ECM was studied (Binder *et al.*, 1996; FitzGerald *et al.*, 1997; Lurito *et al.*, 2000; Ruge *et al.* 1999; Rutten *et al.*, 2002; Szaflarski *et al.*, 2008). Comparisons between direct electrocortical mapping and fMRI are reported infrequently because of the relative difficulty in obtaining both types of studies in the same patient, as well as the relative difficulty in co-registering the various imaging procedures (*e.g.* MRI, fMRI, and ECM electrode localisation based on X-ray and computed tomography data). Studies have already shown a fair degree of concordance between these modalities (FitzGerald *et al.*, 1997; Lurito *et al.*, 2000; Ruge *et al.*, 1999; Rutten *et al.*, 2002).

The goal of reporting the following cases was to illustrate possible advantages of fMRI over other methods of cognitive function mapping in presurgical evaluation of patients and to address some of the pitfalls related to fMRI task design.

Case reports

Case 1

A 33-year-old right-handed female developed complex partial seizures at the age of 19. At the time of the evaluation she was treated with oxcarbazepine and levetiracetam; previous treatment with phenytoin and valproic acid was stopped due to side effects. Her seizure log reported 12-60 seizures per month. Video-EEG monitoring recorded two complex partial and six simple partial seizures. Clinically, the two complex partial seizures were characterised by inability to speak and confusion without loss of consciousness; the patient repeated incomprehensible sounds. Postictal language delay was approximately five minutes (Privitera and Kim, 2010). EEG showed onset of left temporal T1 maximum discharge at less than 5 Hz with characteristics of neocortical temporal onset. Other testing included normal 3T brain MRI with thin cuts through the temporal lobes; left lateral-temporal hypometabolism on PET and bilateral (left > right) language representation on IAP (*table 3*; Subject 10 in Szaflarski *et al.* [2008]). Presurgical neuropsychological testing revealed average intelligence (FSIQ = 93, VIQ = 97, PIQ = 89) and normal or low average memory, spatial orientation, complex problem solving and language functions. Intracranial EEG with a 64-electrode grid over the left fronto-parieto-temporal regions (*figure 1A*; a four-contact subtemporal strip was also placed; data not shown) localised ictal onset zone to the left lateral temporal area. ECM was performed for eloquent cortex localisation (*figure 1A*). Before the ECM, the patient received a loading dose of phenytoin to achieve therapeutic blood level. Stimulation of four electrodes over the left posterior superior temporal gyrus elicited speech arrest (*figure 1A*; yellow dots); there was an overlap between the ictal onset zone and the language area identified by ECM and fMRI (*figure 1A and B*). The patient underwent cortical excision of non-speech areas of lateral temporal cortex (*figure 1A*, yellow solid line) and multiple subpial transections over the speech area (*figure 1A*, yellow interrupted line). Post-surgically, the patient experienced aphasia that recovered gradually; at one year after surgery she continued to have mild difficulty in reading and comprehension but was able to return to nursing work in full capacity; she continues to be seizure-free at five years after surgery.

Case 2

A right-handed patient was referred for epilepsy surgery at the age of 31. She underwent shunt placement at the age of 16 for increased intracranial pressure due to a left frontal arachnoid cyst. First seizure occurred one week after the surgery. At the time of EEG monitoring she was experiencing three to four seizures per week. The patient reported sudden inability to hear and speak without loss of consciousness. She also reported occasional right upper extremity automatisms and secondary generalisation. At the time of surgery, she was treated with levetiracetam and lamotrigine; previous treatment with oxcarbazepine, levetiracetam and phenytoin was unsuccessful. Brain MRI at 3T revealed left frontal encephalomalacia. Video-EEG monitoring captured two secondary generalised tonic-clonic seizures with ictal onset over the left frontal area (*figure 1C*). IAP showed bilateral language representation (left > right) (*table 3*; Subject 20 in Szaflarski *et al.* [2008]). Her intellectual ability was within average range (FSIQ = 102, VIQ = 98, PIQ = 106) with mildly impaired memory retention, naming difficulty on the Boston Naming Test (BNT, 10th percentile), and defective word fluency (1st percentile). Spatial orientation and complex novel problem solving ability were within normal range. Intracranial electrodes were

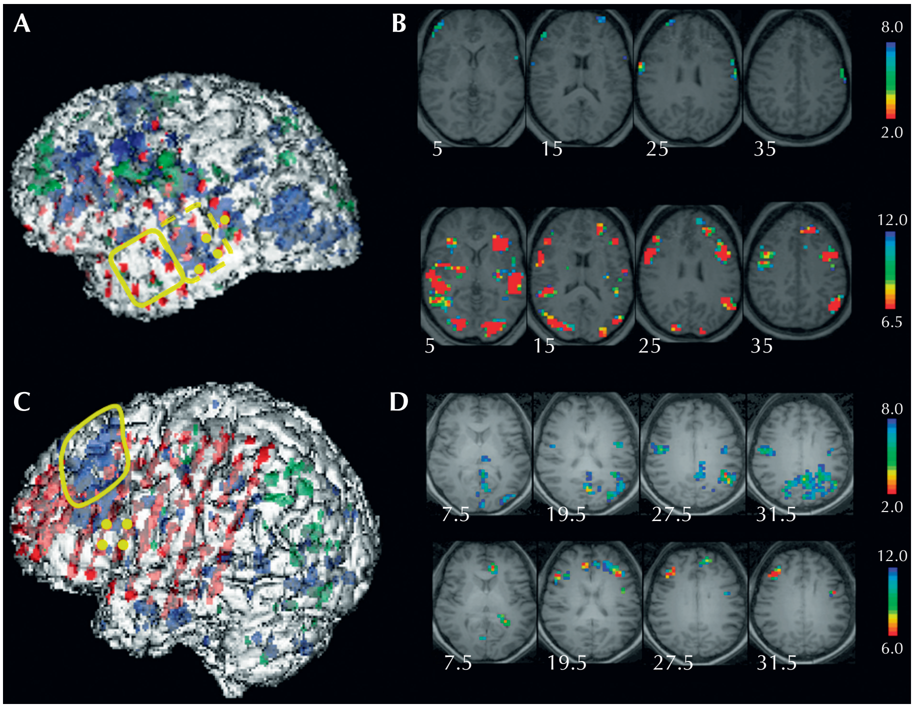

Figure 1. (A) Co-registered fMRI, CT and MRI images of patient 1. A 64-channel electrode grid covered frontal, parietal and temporal cortex. Ictal discharges were detected in eight electrodes covering the lateral temporal cortex. The area of ECM speech arrest overlapped with ictal onset zone in the posterior temporal region and with brain areas activated by verb generation task (threshold (T): SDTD task = 2.0, VG task = 6.5). Blue colour: areas activated by VG task; green colour: areas activated by SDTD task, yellow line (solid: resection; interrupted: subpial transections); yellow dots: speech arrest by ECM; electrodes are seen as red dots. The patient underwent cortical excision of non-speech areas of lateral temporal cortex and multiple subpial transections over the speech area.
(B) Axial Z-map images of the activations with the SDTD (top) and VG (bottom) tasks in patient 1 (all images are in radiological convention [right on the picture is left in the brain]).
(C) Co-registered image of patient 2 A 20-channel electrode grid was placed over the left anterior frontal region and another 64-channel electrode grid covered the posterior part of the frontal, parietal and superior part of the temporal cortex. Speech arrest occurred with stimulation of four inferior frontal electrodes; this area overlapped with language areas identified by the verb generation task (threshold [T]; SDTD task = 2.0, VG task = 6.0). Cortical resection (1 cm thickness) was performed over the left dorso-lateral prefrontal cortex (DLPFC) including medial frontal area (not shown) and was overlapped with the brain area that was activated by the VG task (yellow line: resection margin over left DLPFC).
(D) Axial Z-map images of the activations with the SDTD (top) and VG (bottom) tasks in patient 2 (all images are in radiological convention [right on the picture is left in the brain]).

placed over the left anterior frontal region (20 contacts) and over the posterior part of the frontal, parietal and superior parts of the temporal cortex (64 contacts; *figure 1C*). Additionally, an eight-contact medial frontal strip, a four-contact orbital frontal strip, and a four-contact subtemporal strip were implanted (data not shown). Ictal onset zone was identified at the dorso-lateral and medial frontal region with anterior frontal region spread (data not shown). ECM identified language (yellow dots) and motor areas (data not shown). Excision of the dorso-lateral and medial frontal region was performed (*figure 1C*; yellow solid line). Post-surgically, she remained seizure-free and has been maintained on stable doses of carbamazepine and lamotrigine; she reported worsening of the pre-surgical word finding difficulties but these did not interfere with her functioning. Postoperative neuropsychological testing showed overall improvement in spatial orientation and memory functions, although word fluency remained defective (1st percentile).

Electrocortical mapping protocol

Stimulation consisted of 3-5 seconds of 40 Hz, 0.3 msec monophasic square pulses delivered through the subdural electrodes spaced 1 cm apart with a constant current stimulator (model S-88, Grass Medical Instruments, Quincy, MA). Initial stimulation established motor threshold and the motor threshold for testing was used for all stimulation for language. An electrode that showed no motor response from stimulation was used as the reference for a bipolar stimulation. All electrodes were tested for language (speech arrest, paraphasic errors or motor activity). We increased current intensity by 2 mA to reveal speech arrest, paraphasic errors or motor activity, or until 12-14 mA current intensity was reached. Patients were asked to perform picture naming, read short paragraphs, and follow two-step commands during stimulation.

Functional MRI (fMRI)

The fMRI language tasks used are utilised by our group for studies of language in children and adults and a detailed description is available elsewhere (Szaflarski *et al.*, 2008; Jacola *et al.*, 2006; Szaflarski *et al.*, 2006a; Szaflarski *et al.*, 2006b; Yuan *et al.*, 2006). Briefly, in the verb generation task (VGT), subjects performed silent verb generation in response to a noun presented binaurally every five seconds; in the control condition, subjects performed sequential, bilateral finger tapping starting with the thumb and fifth opposing digits in response to each frequency-modulated tone presented every five seconds. Each block lasted for 30 seconds with control condition repeated six times and active condition repeated five times; the first run of the control condition was discarded. The semantic decision/tone decision (SDTD) task consisted of two blocked intervening conditions, each lasting 30 seconds; the control condition (tone recognition, performed eight times) and the active condition (semantic recognition, performed seven times) (Binder *et al.*, 1996; Szaflarski *et al.*, 2008; Szaflarski *et al.*, 2002). In the tone condition, subjects heard brief sequences of four to seven tones of 500 and 750 Hz every 3.75 seconds (eight times per block) and responded with a non-dominant hand button press for any sequence containing either two 750-Hz tones ("1") or anything other than two 750-Hz tones ("2"). In the active condition, subjects heard spoken English nouns designating animals every 3.75 seconds (eight times per block) and responded by pressing "1" with a non-dominant hand button press to stimuli which met two criteria: "native to the United States" and "commonly used by humans". In all other cases, they responded by pressing "2". The first five volumes were discarded (control condition). Both subjects underwent fMRI using VGT and SDTD at 4T (Varian Unity Inova scanner; Oxford Magnet Technology, Oxford, UK). This procedure was described previously in detail (Szaflarski *et al.*, 2008; Vannest *et al.*, 2008). Briefly, from the initial scout images, 30 axial planes to be imaged in the fMRI procedures were identified. The specific protocol for the gradient-echo EPI scans was: TR/TE = 3000/25 ms, FOV = 25.6 × 25.6 cm, matrix = 64 × 64 pixels, slice thickness = 4 mm, and flip angle array = 85/180/180/90. For the anatomical scans, the protocol was: TR = 13 ms, TE = 6 ms, FOV = 25.6 × 19.2 × 15.0, and flip angle array of 3: 22/90/180 with voxel size of 1 × 1 × 1 mm. The fMRI image post-processing was performed with CCHIPS (Cincinnati Children's Hospital Image Processing System) software that runs in the IDL software environment (IDL 7.1; Research Systems, Boulder, CO). Additionally, a high-resolution T1-weighted 3D anatomical scan was obtained using a modified driven equilibrium Fourier transform (MDEFT) protocol: TR = 15 ms, TI = 550 ms, TE = 4.3 ms, FOV = 25.6 × 19.2 × 16.2, with flip angle = 20 to provide images for anatomical localisation of the activation maps. This acquisition took approximately 9 minutes and yielded spatial resolution of 1 × 1.5 × 1.5 mm. A Hamming filter was applied to raw EPI data prior to reconstruction to reduce the truncation artefacts at the edges of *k*-space and to reduce high-frequency noise in the images; geometric distortion was corrected *via* the multi-echo reference method. Data were then co-registered to further reduce the effects of motion artefact using a previously developed pyramid co-registration algorithm; individual subject data for each task were analysed using a general linear model to identify voxels with a time course similar to the time course of stimulus presentation. Z-score maps were computed from the results of this analysis.

Functional MRI and ECM co-registration

We utilised a 3D surface registration method (ANALYZE version 8.1; Biomedical Imaging Resource, Mayo Foundation, Rochester MN) to co-register the post-implantation CT image with high resolution T1-weighted 3D anatomical scans and with Z-maps of subjects' fMRI results (all in native space). For the purpose of co-registration, we converted the post-implantation CT images in DICOM format and Z-maps of each fMRI task in CCHIPS format into ANALYZE format. We then applied the linear interpolation method in ANALYZE to co-register the Z map of each fMRI study onto the anatomical images.

Results

Functional MRI and ECM co-registration results

The co-registered images and fMRI activation maps of both patients are illustrated in *figure 1A-D*. In *figure 1B*, fMRI activations are shown superimposed on an anatomical scan before fMRI/CT fusion. Review of the neuroimaging data of patient 1 indicated an overlap between speech area defined by ECM and activation maps of the VGT. Activations related to the SDTD were in close proximity to the ECM-identified language area but there was no direct overlap (*figure 1A*).

In patient 2, ECM produced speech arrest in four electrodes over the left inferior frontal area (*figure 1C*). These four electrodes were directly over the area activated by VGT (*figure 1D* shows fMRI activation patterns with both fMRI tasks superimposed on an anatomical scan). Again, there is no direct overlap between the language area identified by the SDTD task and ECM but the fMRI changes were in close proximity to the language cortex.

Discussion

Using these two cases, we have focused on a comparison of language localisation with fMRI and electrocortical mapping in the presurgical evaluation of epilepsy patients and add to the already existing, albeit relatively small body, of literature. We show an overlap of language areas detected by fMRI and ECM; fMRI showed additional areas that were not detected by ECM with many of these areas outside the region of ECM electrode coverage. Therefore, fMRI has an advantage over ECM in detecting not only the ECM-identified language areas but also those not identified by ECM. Although areas outside of the ECM are not necessarily in danger of being removed during the surgical procedure, the advantage of identifying all areas involved in language processing outside of the ictal onset zone is that these areas may potentially take over the functions that are lost due to resection or subpial transections *via* cortical plasticity, as seen in other brain injury models e.g. stroke (Tillema *et al.*, 2008).

Previously, we noted a higher correlation between language lateralisation with IAP and the SDTD task *vs* the VGT (Szaflarski *et al.*, 2008). The SDTD task activates, among many sites, the prefrontal cortex of the inferior, middle, and superior frontal gyri, anterior/superior temporal sulcus and middle temporal gyrus, and posterior/inferior temporal gyri (Szaflarski *et al.*, 2002). The VGT-activated areas involved in lexical processing include the inferior frontal gyrus, dorsolateral prefrontal cortex, superior and middle temporal gyri, and anterior cingulate gyrus (Szaflarski *et al.* 2006a) with very little overlap between the cortical language areas identified by these tasks, but with overall greater reliability for activation of frontal rather than temporo-parietal regions (Eaton *et al.*, 2008). Since the tasks utilised for ECM (reading, naming and counting to elicit speech) were more similar to verb generation rather than to the more complicated SDTD task utilised for fMRI, it was not surprising to find better overlap between fMRI/VGT and ECM, while language areas identified by the SDTD task were somewhat remote from the language sites identified by ECM. Our results are in agreement with a previous report in which temporo-parietal language areas were identified by ECM and a verb generation task (Ojemann *et al.*, 2002). These authors argued that language distribution should be similar when either ECM or fMRI is conducted with the VGT. Therefore, based on the available literature and the results of this study, we suggest that the fMRI language tasks, utilised for comparison with ECM, identify similar language functions and may be useful to validate the results of one technique with the other.

Although we found overlapping areas using ECM and fMRI with the VGT, there were many activated areas outside the coverage of electrode grids. This confirms the limitation of ECM as it is not possible to evaluate the areas outside the grid or stimulate all brain areas detected by fMRI because some of them may be located in deeper sulci (Faro *et al.*, 2006). As an example of such limitation of ECM, the surgical resection in patient 2 did not include any of the ECM-identified language areas but the patient still had increased word finding difficulties (in retrospect, the presence of an overlap between the area identified by fMRI and the resection area predicted the possibility of post-surgical language deficits). Therefore, fMRI may have an advantage over ECM in identifying areas that are not accessible by standard cortical stimulation.

An advantage of our case studies over the previously reported fMRI/ECM correlation studies is that the majority of previous studies used camera images for co-registration in order to compare between ECM and fMRI results. This may have increased the spatial mismatch between fMRI and ECM results and affected the results of co-registration. Here, we co-registered fMRI results and post-implantation CT images into the same T1-weighted high-resolution brain MRI scans using ANALYZE software (version 8.1; Biomedical Imaging Resource, Mayo Foundation, Rochester MN). With this approach, we increased the chance of accurate co-registration which is an important surgical consideration. Another advantage in this report is that we included patients with bilateral language representation as determined by fMRI and IAP and showed that even in patients with atypical language representation the correlation between fMRI VGT and ECM is accurate and that fMRI may provide incremental information that may affect the surgical approach and outcomes.

A careful discussion of the potential shortcomings of this study is needed. One potential drawback of individual fMRI studies is the need for arbitrary thresholding and clustering which may lead to inclusion of random activations without plausible biological explanation or exclusion of activations that may be of importance for presurgical planning and subsequent resection (Loring *et al.*, 2002; Swanson *et al.*, 2007; Wilke and Lidzba, 2007). While novel methods of fMRI data analysis may obviate the need for thresholding (Suarez *et al.*, 2009), these methods have not been implemented in presurgical mapping to date. Another weakness is the fact that the fMRI tasks used by us are known to provide much more reliable activations in the frontal than in temporo-parietal regions (Eaton *et al.*, 2008). In future studies to assess the correlation between fMRI language paradigms and ECM, a range of fMRI and behavioural tasks should be used to assess the concordance between the methods (Swanson *et al.*, 2007; Binder *et al.*, 2011; Hamberger, 2007). Finally, of importance for the correlation between pre-surgically obtained fMRI data and post-implantation electrode localisation assessments, is the fact that surgical procedure may lead to a change in the anatomy of the underlying structures due to surgical shifts. While not specifically performed in this study, corrections for swelling and shifts can be performed in order to minimise the potential discrepancies in localisation between these measures of cortical activation.

To summarise, we show successful cortical mapping of language functions in two patients using fMRI and ECM. While both fMRI tasks identified numerous language areas, better correlation between fMRI and ECM was observed with the VGT. This is likely related to the nature of the language testing utilised in ECM. □

Disclosure.
This study was in part supported by The Neuroscience Institute in Cincinnati and in part by Cincinnati Epilepsy Center funds. Dr. Kim is currently supported by a fellowship from Dongguk University and by funds from the Charles and Pamela Shor Foundation. The authors do not report any conflicts of interest.

References

Binder JR, Swanson SJ, Hammeke TA, *et al*. Determination of language dominance using functional MRI: a comparison with the Wada test. *Neurology* 1996; 46: 978-84.

Binder JR, Gross WL, Allendorfer JB, *et al*. Mapping anterior temporal lobe language areas with fMRI: a multicenter normative study. *Neuroimage* 2011; 54: 1465-75.

Eaton KP, Szaflarski JP, Altaye M, *et al*. Reliability of fMRI for studies of language in post-stroke aphasia subjects. *Neuroimage* 2008; 41: 311-22.

Faro SH, Mohamed FB, MyiLibrary. *Functional MRI basic principles and clinical applications*. New York (NY): Springer, 2006: xiii: 533.

FitzGerald DB, Cosgrove GR, Ronner S, *et al*. Location of language in the cortex: a comparison between functional MR imaging and electrocortical stimulation. *AJNR Am J Neuroradiol* 1997; 18: 1529-39.

Hamberger MJ. Cortical language mapping in epilepsy: a critical review. *Neuropsychol Rev* 2007; 17: 477-89.

Jacola LM, Schapiro MB, Schmithorst VJ, *et al*. Functional magnetic resonance imaging reveals atypical language organization in children following perinatal left middle cerebral artery stroke. *Neuropediatrics* 2006; 37: 46-52.

Loddenkemper T, Dinner DS, Kubu C, *et al*. Aphasia after hemispherectomy in an adult with early onset epilepsy and hemiplegia. *J Neurol Neurosurg Psychiatry* 2004; 75: 149-51.

Loring DW, Meador KJ, Allison JD, *et al*. Now you see it, now you don't: statistical and methodological considerations in fMRI. *Epilepsy Behav* 2002; 3: 539-47.

Lurito JT, Lowe MJ, Sartorius C, Mathews VP. Comparison of fMRI and intraoperative direct cortical stimulation in localization of receptive language areas. *J Comput Assist Tomogr* 2000; 24: 99-105.

Ojemann JG, Ojemann GA, Lettich E. Cortical stimulation mapping of language cortex by using a verb generation task: effects of learning and comparison to mapping based on object naming. *J Neurosurg* 2002; 97: 33-8.

Privitera M, Kim KK. Postictal language function. *Epilepsy Behav* 2010; 19: 140-5.

Ruge MI, Victor J, Hosain S, *et al*. Concordance between functional magnetic resonance imaging and intraoperative language mapping. *Stereotact Funct Neurosurg* 1999; 72: 95-102.

Rutten GJ, Ramsey NF, van Rijen PC, Noordmans HJ, van Veelen CW. Development of a functional magnetic resonance imaging protocol for intraoperative localization of critical temporoparietal language areas. *Ann Neurol* 2002; 51: 350-60.

Schulze-Bonhage A, Quiske A, Loddenkemper T, Dinner DS, Wyllie E. Validity of language lateralisation by unilateral intracarotid Wada test. *J Neurol Neurosurg Psychiatry* 2004; 75: 1367-8.

Suarez RO, Whalen S, Nelson AP, *et al*. Threshold-independent functional MRI determination of language dominance: a validation study against clinical gold standards. *Epilepsy Behav* 2009; 16: 288-97.

Swanson SJ, Sabsevitz DS, Hammeke TA, Binder JR. Functional magnetic resonance imaging of language in epilepsy. *Neuropsychol Rev* 2007; 17: 491-504.

Szaflarski JP, Binder JR, Possing ET, McKiernan KA, Ward BD, Hammeke TA. Language lateralization in left-handed and ambidextrous people: fMRI data. *Neurology* 2002; 59: 238-44.

Szaflarski JP, Holland SK, Schmithorst VJ, Byars AW. fMRI study of language lateralization in children and adults. *Hum Brain Mapp* 2006a; 27: 202-12.

Szaflarski JP, Schmithorst VJ, Altaye M, *et al*. A longitudinal functional magnetic resonance imaging study of language development in children 5 to 11 years old. *Ann Neurol* 2006b; 59: 796-807.

Szaflarski JP, Holland SK, Jacola LM, Lindsell C, Privitera MD, Szaflarski M. Comprehensive presurgical functional MRI language evaluation in adult patients with epilepsy. *Epilepsy Behav* 2008; 12: 74-83.

Tillema JM, Byars AW, Jacola LM, *et al*. Cortical reorganization of language functioning following perinatal left MCA stroke. *Brain Lang* 2008; 105: 99-111.

Vannest J, Szaflarski JP, Privitera MD, Schefft BK, Holland SK. Medial temporal fMRI activation reflects memory lateralization and memory performance in patients with epilepsy. *Epilepsy Behav* 2008; 12: 410-8.

Wilke M, Lidzba K. LI-tool: a new toolbox to assess lateralization in functional MR-data. *J Neurosci Methods* 2007; 163: 128-36.

Yuan W, Szaflarski JP, Schmithorst VJ, *et al*. fMRI shows atypical language lateralization in pediatric epilepsy patients. *Epilepsia* 2006; 47: 593-600.