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Electrical stimulation mapping of nouns and verbs in Broca's area

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ABSTRACT

Electric stimulation mapping (ESM) is frequently used during brain surgery to localise higher cognitive functions to avoid post-chirurgical disabilities. Experiments with brain imaging techniques and neuropsychological studies showed differences in the cortical representation and processing of nouns and verbs. The goal of the present study was to investigate whether electric stimulation in specific sites in the frontal cortex disrupted noun and verb production selectively. We found that most of the stimulated areas showed disruption of both verbs and nouns at the inferior frontal gyrus. However, when selective effects were obtained, verbs were more prone to disruption than nouns with important individual differences. The overall results indicate that selective impairments can be observed at inferior and middle frontal regions and the action naming task seems to be more suitable to avoid post-chirurgical language disabilities, as it shows a greater sensitivity to disruption with ESM than the classical object naming task.
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1. Introduction

The importance of the left inferior frontal gyrus (IFG) in language processing has been described as early as the XIXth century when Paul Broca presented the case of a 51-year-old patient with extensive damage at the left middle and inferior frontal gyri and other adjacent regions, who had severe difficulties in spoken language, meanwhile, his other cognitive faculties remained intact (Broca, 1861). Follow-up models such as the Wernicke–Geschwind model (Geschwind, 1972) proposed that the main role of Broca's area (BA 44, 45) was the elaboration and storage of motor programs for speech production. However, since then numerous studies have been conducted to map the neural networks underlying the language faculty with different techniques like functional magnetic resonance imaging (fMRI), repeated transcranial magnetic stimulation (rTMS), or electric stimulation mapping (ESM). These studies gave more precise specifications linking this area to a broader range of language processes including phonology, morphology and syntax as well as semantics both in the modalities of language production and comprehension (Amunts et al., 2004; Ben-Shachar, Hendler, Kahn, Ben-Bashat, & Grodzinsky, 2003; Friederici & Kotz, 2003; Friederici, Rüschemeyer, Hahne, & Fiebach, 2003; Heim, Opitz, & Friederici, 2003; De Diego Balaguer et al., 2006; Salmelin, Hari, Lounasmaa, & Sams, 1994; Tyler & Marslen-Wilson, 2008; see Bookheimer, 2002 for review).

The role and function of this specific brain region is of crucial importance in the case of patients who have to undergo brain surgery because language deficits can lead to profound limitations to their quality of life. To avoid damage to brain regions relevant in language processing ESM is frequently applied during surgery to map the most important language related areas. For this aim the naming task is used routinely (Ojemann, Ojemann, Lettich, & Berger, 1989; Ojemann, Berger, Lettich, & Ojemann, 2003; Sanai, Mirzadeh, & Berger, 2008). In the naming task, patients are presented with pictures of everyday objects and are asked to name them. At the moment of the presentation of the picture an electric pulse is applied to the different brain regions. Whenever speech arrest, latency or language errors are observed as a consequence of the brain stimulation, the brain region is marked as relevant for language processing. Although the naming task has been established as a useful way of mapping language function during surgery, a different task – verb generation – has been used experimentally to evaluate whether there is dissociation between the language areas

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identified by the two tasks. The verb generation task is similar to the object-naming task but instead of naming the object in the picture, the patient has to produce the verb that describes the action the agent on the picture is performing.

This new line of research using ESM emerged because dissociation between the brain regions that underlie verb and noun processing has been seen in cases of patients with aphasia after focal and progressive brain damage (Aggujaro, Crepaldi, Pistarini, Taricco, & Luzzatti, 2006; Bastiaanse & Jonkers, 1998; Berndt, Haendiges, Mitchum, & Sandson, 1997; Breedin, 1996; Caramazza & Hillis, 1991; Damasio & Tranel, 1993; Shapiro & Caramazza, 2003a,b) as well as in studies with healthy controls using the fMRI technique, rTMS and positron emission tomography (PET) (Mestres-Missé, Rodriguez-Fornells, & Münte, 2010; Shapiro, Pascual-Leone, Mottaghy, Gangitano, & Caramazza, 2001; Shapiro et al., 2005; see for review Vigliocco, Vinson, Druks, Barber, & Cappa, 2011). If differences using ESM were found the use of both tasks would be necessary for an accurate mapping to avoid language deficits after surgery.

Even after decades of research, a clear-cut dichotomy in terms of the specific brain regions associated to either noun or verb processing is still lacking because results are highly controversial. Evidence from stroke patients supports a fronto-temporal dichotomy hypothesis where verbs are more impaired by left prefrontal lesions, whereas problems with noun processing emerge in case of patients with left anterior temporal damage (Caramazza & Hillis, 1991; Damasio & Tranel, 1993; Daniele, Giustolisi, Silveri, Colosimo, & Gainotti, 1994). However, De Renzi and di Pellegrino (1995) reported a case where the lesion and symptoms were not consistent with this pattern. The 35-year-old patient with fronto-temporal lesion described in this work had a severe impairment in the production of nouns but not verbs. In another case study Silveri, Perri, and Cappa (2003) reported a patient with a left parietal lesion with mild difficulties in object naming and severe impairment in verb generation. Yet other studies revealed that even though damage of the inferior frontal regions and the underlying structures usually impairs the morphosyntactic processing, this impairment is not necessarily specific for verb production or comprehension but can lead to problems of certain kind of morphological operations for words of different categories (Faroqi-Shah & Thompson, 2004; Marslen-Wilson & Tyler, 1997; Miceli, Silveri, Romani, & Caramazza, 1989; Ullman et al., 1997). Several fMRI studies showed a greater activation for verbs relative to nouns in the left posterior middle temporal gyrus and/or the left inferior frontal gyrus (Davis, Meunier, & Marslen-Wilson, 2004; Mestres-Missé et al., 2010; Shapiro et al., 2005; Yokoyama et al., 2006). On the other hand, the results of other fMRI studies (Berlingeri et al., 2008; Sahin, Pinker, & Halgren, 2006) demonstrated that nouns compared to verbs can show a greater activation in the left inferior frontal gyrus (IFG) (BA 44, 45 and 47) when the task is morphologically more demanding. One possible explanation for these results suggests that a common circuit supporting inflectional morphology across different grammatical categories exists and that this could explain the larger activation observed in the left IFG for verbs, mostly because verbs in most languages are morphologically more complex. Using the technique of electric stimulation mapping, Ojemann, Ojemann, and Lettich (2002) found distinct sites where verb generation and object naming was disrupted suggesting the existence of a separate system for these grammatical categories. Nevertheless, in this study, the authors also found that both tasks could be disrupted at any given anatomical region within the perisylvian cortex and the exact site could vary largely from patient to patient.

In an attempt to solve this controversy, Shapiro and Caramazza (2003a) proposed that because nouns and verbs differ along different dimensions as morphology, syntax and semantics, the heterogeneity in the location of brain lesions leading to functional dissociations might stem from different lesions to each of these dimensions. For example, at the semantic level, nouns usually designate objects whereas verbs refer to actions, therefore a semantic deficit may lead to noun–verb dissociations. However, nouns and verbs show dissociations even when semantic variables are controlled for (Laiacona, Capitani, & Caramazza, 2003) and they may also differ when nouns and verbs need to be used in an appropriate syntactic context because each of them requires specific computations. Therefore lesions affecting either of those levels may lead to noun–verb dissociations but will be caused by lesions at different sites (Shapiro & Caramazza, 2003a). Following this idea, a recent study investigated noun–verb mapping distinctions within the temporal cortex using ESM (Corina et al., 2005). Corina and colleagues used a noun and verb naming task and recorded the type of errors the patients displayed during stimulation. Related errors maintaining the same grammatical category (e.g. *table* instead of *chair* when naming a picture of a chair) were considered semantic errors whereas errors involving a speech arrest or a change in the grammatical category (i.e. a verb for a noun or a noun for a verb) were coded as category specific errors.

Similarly, Corina et al. (2005) and Ojemann et al. (2002) found a double dissociation between verb and noun-specific points in the parieto-temporal region. Nevertheless, they could not corroborate the classical model of anatomical division between verb and noun processing based on the lesion studies, as specific points for either grammatical category were found along the perisylvian region, and the results were greatly variable across patients. This fact led them to conclude that there is a high individual specialization of these processes. On the other hand, the authors found that sites in the left superior temporal lobe related to impairment in noun naming were more anterior to those related to verb generation errors in the same patient. In addition, stimulations in the left supramarginal gyrus led to a specific impairment for verb generation.

Up to now this issue remains less clear for the representation of verbs and nouns in the frontal lobe. While noun–verb dissociations have been found in the temporal lobe, no noun–verb distinction within Broca's area have been reported in lesion and TMS studies. However, more recent reports with TMS (Cappelletti, Fregni, Shapiro, Pascual-Leone, & Caramazza, 2008; Shapiro et al., 2001) and fMRI (Shapiro, Moo, & Caramazza, 2012) point to functional dissociations between the left middle frontal gyrus at the superior border with Broca's region and the ventral frontal regions within Broca's area. In that study, stimulation in Broca's area disrupted both verb and noun production, whereas middle frontal stimulation produced a specific disruption of verb processing.

Most of the studies looked for specific regions responsible for either the processing of certain grammatical categories, or other linguistic features that influence verbs and nouns differently, but there is an alternative explanation for the inconsistencies found in the data. Crepaldi, Berlingeri, Paulesu, and Luzzatti (2011) reviewed the most relevant studies looking at the dissociation between verbs and nouns using different techniques and paradigms. They found that even taking into account such variables as differences in task and methods used, results are still unclear, and the fronto-temporal dichotomy hypothesis cannot be supported by an important part of the findings. Equally, most brain areas found specific for one grammatical category in one study might be found specific for another grammatical category in a different study. As a solution for this problem they suggest that grammatical-class specific circuits are not clustered into separate brain areas, but they are dispersed in different parts of the brain and are interleaved with neural structures that are shared by nouns and verbs.

The objective of our study was, thus, to learn about noun and verb representation within the frontal lobe. In particular our aim was to test whether a noun–verb dissociation is found within Broca's area or, as it has been recently suggested using other techniques, both nouns and verbs are disrupted in Broca's area but only verbs are disrupted in the left middle frontal gyrus. To have a broader view, we have also studied the functional verb–noun dissociations in the temporal lobe when possible (depending on the location and size of the craniotomy). Aside from our better understanding of the grammatical distinction between nouns and verbs within the frontal lobe, this information is crucial to avoid specific aphasic grammatical deficits after resection (cf. Rapp & Caramazza, 2002).

2. Methods

2.1. Participants

Ten patients [5 men, 5 women; age range 26–65 years, mean age 45 ± 13 (SD)] who had to undergo respective surgery took part in this experiment. A functional MRI evaluation administered previous to surgery showed that their affected brain hemisphere was the dominant for language. A brief description of the tasks used in the fMRI session to determine language lateralisation is provided in point 2.2.3. One of the patients was excluded from the analysis because he had right hemisphere language dominance. The other nine patients had left hemisphere language dominance. All patients were right-handed. See Table 2 for details of the patients' clinical history and properties of their tumor.

Neuropsychological evaluation including also the object and action naming tasks that were used later on in surgery, semantic verbal fluency and repetition of non-words subscales of a standard neuropsychological test battery – Programa integrado de exploración neuropsicológica: test Barcelona (Peña-Casanova, 2005)-, and spontaneous language, revealed normal or close to normal language functions in all patients (see Table 1. for the results of the neuropsychological evaluation). Two patients (patients 2 and 9) presented mild anomia. Short-term memory and working memory were assessed using the digit span subscale (direct and reverse) of the Test of Barcelona and revealed normal levels of cognitive function of these domains. Patients were evaluated in their native language either Spanish or Catalan.

The location and size of the craniotomy varied from patient to patient depending on the characteristics of the tumour (Fig. 1 shows the stimulated area of each patient). The craniotomy of all of the patients extended to the inferior precentral gyrus, posterior portions of the inferior frontal gyrus including most parts of the pars opercularis, pars triangularis and posterior dorsal parts of the pars orbitalis, and the most anterior portion of the lateral fissure and a small part of the superior temporal pole (Brodmann's area 38, 22, 52). Seven out of the nine patients had craniotomy in larger portions of the anterior part of the STG (Brodmann's area 38, 22, 52, 41, 42), six of the nine in the most posterior parts of the STG and anterior portion of the middle temporal gyrus (MTG) and four of the nine patients had craniotomy in parts of the posterior portion of the MTG (see Figs. 1 and 2C).

2.2. Material and methods

2.2.1. fMRI tasks to determine language lateralization

Three tasks were used to locate language function in patients: (i) noun-based verb generation, (ii) noun and verb picture naming and (iii) verbal fluency. For the noun-based verb generation task patients listened to an auditorily presented list of nouns and were asked to covertly name a relevant verb based on the name of the object. Finally, in the fluency task participants were asked to generate words that started with a certain letter predetermined by the experimenter. All three tasks had a standard block design with two conditions, active task and baseline resting state. We used the contrast of these two conditions to uncover the location of language regions in each patient.

2.2.2. Language task materials and procedure for ESM

During surgery, after the identification of the rolandic cortex, a series of back and white line drawing images depicting objects and actions (see examples in Appendix A) were presented to the patients who were asked to verbalize the names of the objects or the verbs represented by the action pictures respectively in blocks. Patients were instructed to produce the verbs in infinitive form to avoid greater morpho-syntactic complexity in verb production compared to object naming. Images were presented on a computer screen one by one, manually controlled to be synchronized with the electric stimulation approximately every 3 seconds. Patients were acquainted with the task during the pre-surgical neuropsychological evaluation. For each patient, pictures that were incorrectly named or were not correctly identified were deleted from the set of images that were shown during surgery. In this way we ensured that speech arrests or language errors were produced due to electric stimulation and not to previous word retrieval difficulties for these items.

Verb (64 items) and noun pictures (60 items) (see the list of verbs and nouns in Appendix B) did not differ in frequency for Spanish (M_{verb} = 28.86, SD = 78.94; M_{noun} = 26.00, SD = 59.73; $t(122) = -0.26$, $p > .7$), orthographical neighbourhood (M_{verb} = 2.11,

Table 1
Results of the neuropsychological evaluation. The first number refers to the performance of the test conducted before the surgical intervention, the second one refers to the performance after intervention for each test. In the columns of nouns and verbs the per cent of correct word production of the experimental tasks (results of the neuropsychological evaluation before and after surgery) is reported. In the rest of the columns we report the results of standardized tests where the age and educational background of the patients were taken into account. The scores are reported in percentiles. '–': – data not available; * – excluded patient.

Case number	Nouns (% correct)		Verbs (% correct)		Semantic fluency (percentile)		Non-word repetition (percentile)		Digit span (percentile)			
									Direct		Reverse	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
1	97	98	91	86	15–19	15–19	95<	95<	5>	5>	5>	5>
2	72	93	73	78	30–39	5>	95<	5>	50–59	80–89	40–49	75–79
3	98	88	80	89	25–29	5>	–	–	50–59	50–59	50–59	20–24
4	90	–	94	–	20–24	15–19	95<	95<	5>	5>	20–24	–
5	97	97	77	83	25–29	75–79	–	–	20–24	20–24	50–59	50–59
6	93	–	95	–	70–74	–	95<	95<	30–39	–	95<	–
7	98	98	98	98	25–29	20–24	95<	95<	75–79	50–59	95<	95<
8	92	75	77	58	50–59	5>	95<	95<	80–89	15–19	75–79	5>
9*	40	40	58	56	15–19	5>	95<	–	90–94	10–14	95<	70–74
10	95	95	83	83	50–59	5>	95<	95<	50–59	50–59	40–49	40–49

Table 2
Patients' characteristics and clinical history are summarized here.

Case number	Age	Sex	Handedness	Dominant hemisphere	Medical history					
					Tumour attributes			Epileptic seizures (presence of seizures)		
					Type	Location	Maximum diameter size	Pre-surgery	Intra-surgery	Post-surgery
1	29	F	R	L	Grade III astrocytoma with PNET component	Parietal	5.5	Yes	No	No
2	65	F	R	L	Grade IV glioblastoma	Frontal	2.5 cm	Yes	No	No
3	39	M	R	L	Cavernous angioma	Temporal	2 cm	Yes	No	No
4	30	M	R	L	Grade III astrocytoma	Fronto-temporo-insular	11 cm	Yes	No	No
5	33	F	R	L	Grade II oligodendroglioma	Frontal	5 cm	Yes	No	No
6	53	M	R	L	Grade II astrocytoma	Temporal	3.2 cm	Yes	No	No
7	40	F	R	L	Grade III astrocytoma	Fronto-temporo-insular	9.3 cm	Yes	No	No
8	56	F	R	L	Grade III oligodendroglioma	Frontal	7.4 cm	No	No	No
9	51	M	R	R	Gemistocytic astrocytoma	Temporal	5 cm	Yes	No	Yes
10	53	M	R	L	Grade II oligodendroglioma	Frontal	2.5 cm	Yes	No	No

SD = 2.54; M_{noun} = 2.81, SD = 3.84; $t(122) = -1.19$, $p > .24$) or phonological neighbourhood (M_{verb} = 3.81, SD = 4.06; M_{noun} = 4.44, SD = 5.94; $t(120) = -0.69$, $p > .49$). As it is often the case when comparing different grammatical categories, nouns were significantly more imageable than verbs (M_{verb} = 3.43, SD = 2.98; M_{noun} = 4.77, SD = 2.79; $t(122) = -2.70$, $p < .01$).

2.2.3. Electric stimulation mapping

Electric stimulation mapping (ESM) technique was used for localising the language function within the dominant hemisphere (left hemisphere for nine patients and right hemisphere for the one patient removed from the analysis). Mapping techniques were performed according to the methodology described by Berger and Ojemann (1992). Local anaesthesia with svedocaine 0.25% and lidocaine 2% was used for scalp and temporal muscle. After the opening of the duramater, patients were stimulated in fully awake conditions. An Ojemann cortical stimulator (OCS Radionics, Inc., Burlington, MA, USA) was used to stimulate the brain cortex. The inter-electrode distance of the bipolar forceps was 5 mm. This constant current generator was set to deliver biphasic square wave pulses of 4-ms duration with a pulse frequency of 60 Hz. The duration of each stimulation train was 3 seconds. The current intensity started at 1.5 mA and was progressively increased by 0.5 mA until the desired responses were observed.

Electrical cortical stimulation was initiated in the motor strip. The current intensity needed to obtain motor responses was then used as a reference during language mapping. Sites for stimulation were selected following the anatomy of the gyri. Stimulated points were at a distance of 0.5 cm in order to cover the totality of the exposed cortical surface. The current was applied as the image appeared on the screen. Each site was stimulated at least 3 times both for verbs and nouns. A site was considered to be essential for language production and coded as one speech error in the frequency count if at least two out of three stimulations caused error in the word production of one or the other grammatical category. If the stimulation of a point caused an error in both noun and verb production (non-specific site) it was considered to be essential for language production, but not specific for a certain grammatical category. If the stimulation of a certain point caused language error only for one of the two grammatical categories that point was considered noun or verb-specific. Once a verb/noun-related point was identified, a numbered label was placed on that site. These labels were recorded photographically after the experiment (see Fig. 2A). The frequency of errors was then calculated in each site. To illustrate the process consider the following example: 10 points were stimulated in Broca's area in patient "*n*". Each point was stimulated three times for both tasks. We found that two stimulations out of three at points 1–5 produced speech arrest during the naming task, and two stimulation out of three produced speech arrest during the verb generation task at points 3–8. Furthermore, stimulation did not cause speech alteration at points 9 and 10. In this case we counted the following frequency for the patient – 2 noun-specific points (points 1 and 2), 3 verb-specific points (points 6,7 and 8), 3 non-specific language points (points 3,4 and 5) and 2 points not related to language (points 9 and 10) in Broca's area.

2.3. Data analysis

The location of the points of the stimulation in relation to the central sulcus, sylvian fissure and sulci separating the major gyri was determined from the intraoperative photographs. In order to normalize this information, an arbitrary grid [similar to the one used by Ojemann et al. (1989)] was placed on the individual photographs. As illustrated in Fig. 2B, in the frontal cortex the grid included 1.5-cm segments in each gyrus, beginning with the most anterior evoked motor response on the vertical axis. On the horizontal axis, the grid was determined by the major sulci dividing the superior, middle and inferior frontal gyri. Furthermore the inferior and middle gyri were divided into halves (inferior and superior) by a line parallel to the sylvian fissure. After the identification of the zones where each point belonged to, the data was transferred to a model based on the same landmarks (e.g. Fig. 2B). This way boxes one through four contain pars opercularis and pars triangularis (and parts of pars orbitalis) and were named Broca's area, boxes 5–6 contain the anterior portion of the inferior frontal gyrus, and boxes 7–9 represent the ventral part of the middle frontal gyrus. For the temporal cortex on the horizontal axis, the grid was delimited by the sylvian fissure and the major sulci dividing the superior, middle and inferior temporal gyri. On the vertical axis the line between the foot of the central sulcus and the posterior end of the sylvian fissure was divided into fourths. Counting the area anterior to the line of the central sulcus and the area posterior to the posterior end of the sylvian fissure both superior and middle temporal gyri were divided into six regions (see Fig. 2B).

Sites related with language production were found in the middle and inferior frontal gyri and perisylvian areas (superior and middle temporal gyri and the supramarginal gyrus). Frequency of the points where speech arrest during language production occurred for nouns and verbs in each area delimited by the grid was calculated. Because speech arrest is a categorical variable with

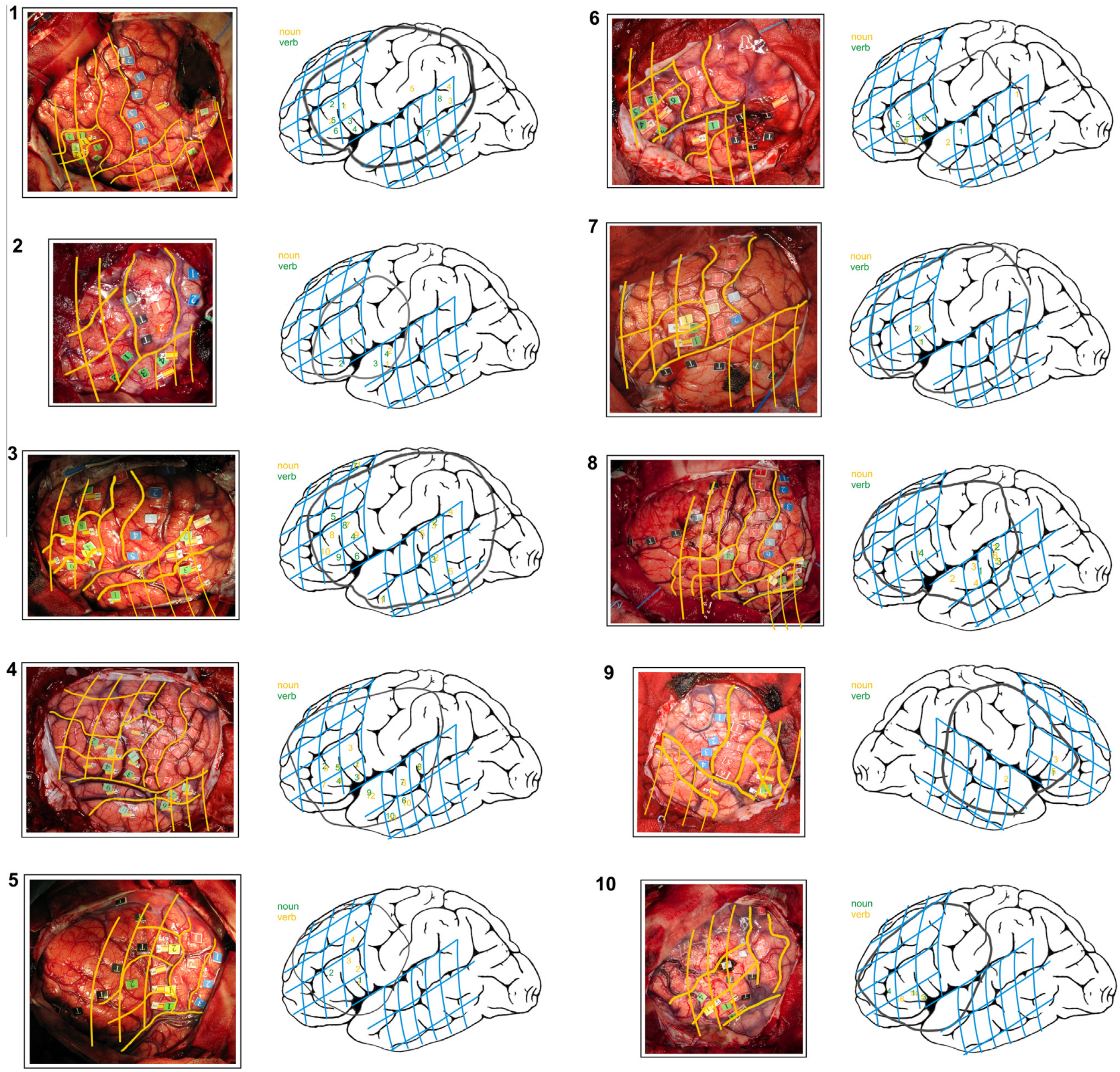

Fig. 1. This figure shows the intra-operative photographs of each patient and the data transferred to the schematic model. The labels on the photos are codified as follows: Red labels: areas with evoked motor response, blue labels: evoked sensory response, green labels: speech arrest produced during verb or noun production, Spanish flags: speech arrest evoked during verb or noun production (noun–verb labels vary from patient to patient), yellow label shows sights of an unrelated motor task. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

two possible values (presence or absence of speech arrest), we chose the generalized linear models approach with a binomial probability function and a logit link function to carry out the repeated measures analyses (ANOVA) (Agresti, 1990; Jaeger, 2008). SPSS software uses Wald test to determine statistical significance, which is distributed following the χ^2 function. Therefore, we report significance using χ^2 statistic. In some cases, we did not find a solution for the coefficients of the regression model because we encountered a singularity in the Hessian matrix during the process of convergence. When this problem arose, we used alternative analyses described in detail in the results section. On the other hand, we used the Wilcoxon signed-rank non-parametric test on the data of the temporal sites due to the smaller number of patients with temporal lobe craniotomy.

3. Results

23% of the electric stimulation in the middle and inferior frontal gyri caused speech arrest across patients. 93% of these language related points were localised within Broca's area [with higher frequency at the pars opercularis (49%) and pars triangularis (41%) and lower frequency at the pars orbitalis (10%)], and were situated in adjacent areas with rare exceptions (see Fig. 3). 45% of the language related points in the inferior frontal and middle frontal gyri were verb-specific, 14% were noun-specific and were always situated at a distance of 1 cm or less from a verb-specific site or a site where stimulation produced speech arrest during both tasks. 41% were points common for verbs and nouns, thus more points essential in the production of verbs than nouns were present in the

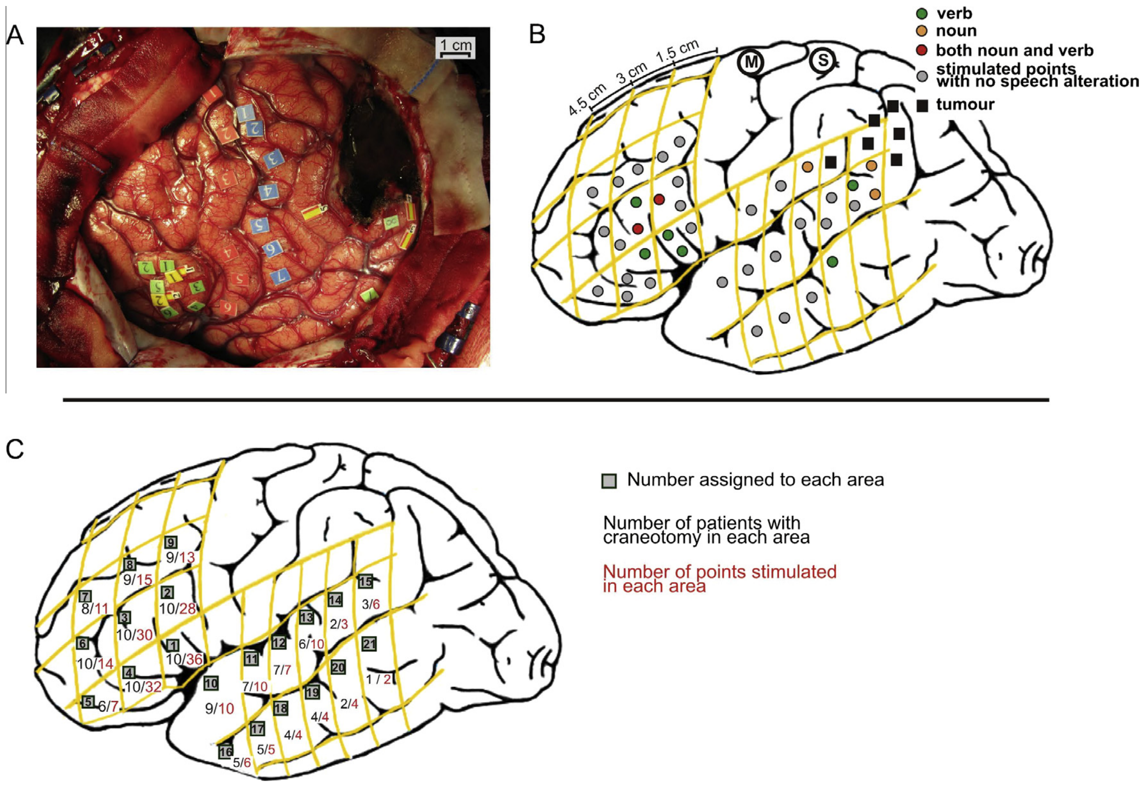

Fig. 2. A. An example of the intraoperative photograph of a patient with fronto-temporo-parietal craniotomy recorded after the experiment was concluded and the labels were placed. Red labels: areas with evoked motor response, blue labels: evoked sensory response, green labels: speech arrest produced during verb production, Spanish flags: speech arrest evoked during naming, yellow label shows sights of an unrelated motor task. B. Model used to transfer for the normalization of data where all stimulated sites were transferred taking Sylvian fissure and the motor cortex as landmarks. C. In this figure the number in the grey square denotes the arbitrary number we assigned to each grid area (grid number), numbers in black on the left under the square informs about the number of patients that had a craniotomy in that particular area, and numbers in red on the right stand for the number of points stimulated within each area across participants (absolute frequency). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

inferior and middle frontal cortex (see Fig. 4, for the proportion of evoked speech arrest in each area and for each condition).

First, to assess the distribution of the language related areas in the frontal cortex, a repeated measures ANOVA of one factor – location – was performed for the following areas of stimulation: Broca's area (1–4 grid sites), anterior inferior frontal gyrus (aIFG) (grid sites 5–6) and ventral middle frontal gyrus (vMFG) (grid sites 7–9). This analysis showed a significant difference between these areas [$\chi^2(2) = 10.134$, $p = .006$]. The post-hoc test with Bonferroni correction revealed differences between Broca's area and the aIFG ($p = .001$) and between Broca's area and the vMFG ($p = .001$), but no difference between the aIFG and vMFG ($p = .99$) showing that Broca's area has significantly more language related points than the other parts of the middle and inferior frontal gyri.

Second, the distribution of verb-specific, noun-specific and non-specific sites in Broca's area (grid areas 1–4) and the vMFG was explored through a repeated measures ANOVA of 2 factors: (i) Grammatical category – 3 levels (verb-specific, noun-specific, and non-specific)-, and (ii) Brain region – 2 levels (Broca's area, vMFG). We found a statistically significant difference for both factors [Grammatical category: $\chi^2(2) = 9.071$, $p = .011$; Brain region: $\chi^2(1) = 6.903$, $p = .009$]. We could not observe the interaction because of the singularity of the Hessian matrix. To address this issue, we conducted further analyses with Bonferroni correction. We transformed the categorical frequency data into Gaussian distributed data by calculating the proportion of each level of grammatical category respectively to the total number of stimulated points in each area (see Table 3 for a detailed look of the observed frequencies and transformed data), and conducted a 2 × 3 repeated measures ANOVA analysis with the factors: location (Broca's area, vMFG) and grammatical category (verb-specific, noun-specific, non-specific). Results showed a significant main effect of both factors – location: $F(1,8) = 28.579$, $p = .001$, partial $\eta^2 = .781$, grammatical category: $F(2,16) = 5.090$, $p = .019$, partial $\eta^2 = .389$. There was no significant interaction between the two factors: $F(2,16) = 2.108$, $p = 154$, partial $\eta^2 = .209$. Post-hoc analysis showed that there were significantly more verb-specific points in both areas compared to noun-specific points ($p = .012$), but there were no significant difference between verb-specific and non-specific, or noun specific and non-specific categories ($p > .1$).

For a more fine-grained analyses of Broca's area where most of the language related points were found, two 2-way repeated measures ANOVAs were performed. First we compared the anterior and the posterior sites with the within-factors (i) Grammatical category [3 levels, verb-specific and noun-specific, and non-specific] and ii) location [2 levels, anterior (grid areas 3 and 4) and posterior (grid areas 1 and 2)] with the percentage of the speech arrest caused by electric stimulation during verb and/or noun generation task as the dependent variable. We found a significant difference between the grammatical categories [$F(2,14) = 21.58$, $p < .0001$], locations [$F(1,7) = 30.354$, $p = .001$] and a significant grammatical category by location interaction [$F(2,14) = 20.821$, $p = .001$] Post-hoc analysis with Bonferroni correction indicated that there were more non-specific language points in the posterior part of Broca's area compared to verb-specific ($p = .006$) and noun-specific points ($p = .002$). We also found a marginally significant difference between the verb and noun-specific conditions in the same region ($p = .073$) with more verb related points. We found no difference

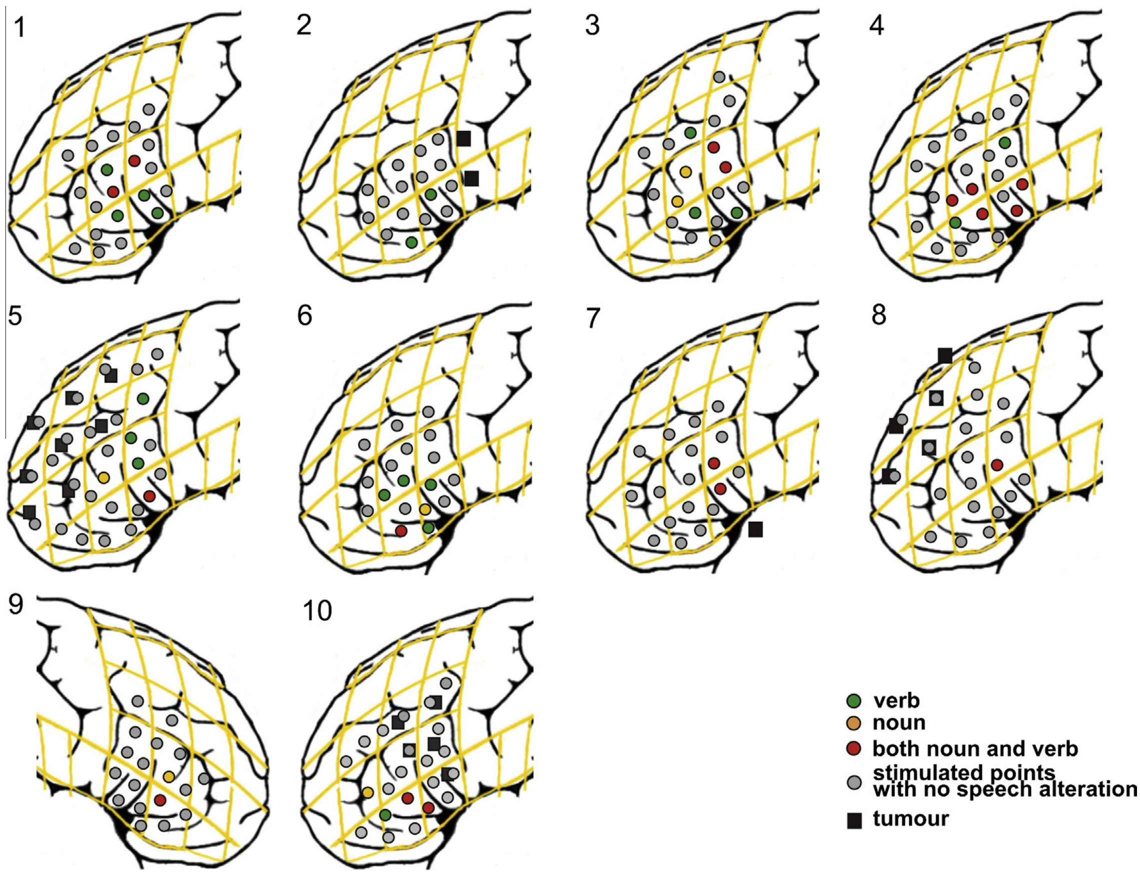

Fig. 3. Schematic representation of the stimulated brain areas in the prefrontal cortex after normalization for each patient. Green dots represent areas where speech arrest was evoked only in the verb production condition, yellow dots represent areas where speech arrest was evoked only in the noun production condition, red dots represent areas where stimulation caused speech arrest during both tasks, grey dots represent areas where no speech arrest had occurred during stimulation, and black squares represent the location of the tumour on the cortical surface. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

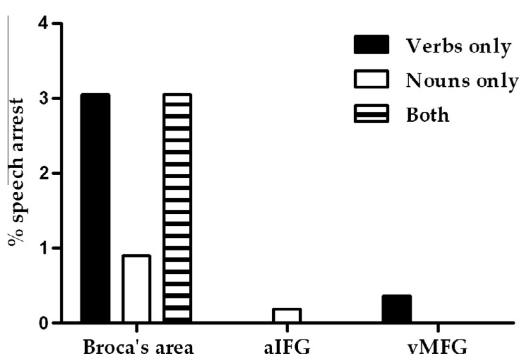

Fig. 4. This figure shows the percentage of points where electric stimulation caused speech arrest with respect to all the stimulated points in the frontal lobe on a group level.

between the grammatical categories in the anterior region ($p > .9$). Then, we compared the dorsal and ventral sites with the within-factors (i) Grammatical category [3 levels, verb-specific and noun-specific, and non-specific] and ii) location [2 levels, ventral (grid areas 1 and 4) and dorsal (grid areas 2 and 3)] with the percentage of the speech arrest caused by electric stimulation during verb and/or noun generation task as the dependent variable. We found no significant effect of grammatical categories [$F(2,18) = 3.24$ $p = .105$] or location [$F < 1$]. We did not find a significant interaction either [$F < 1$].

Finally, even though we focused our attention in the present study on the inferior frontal cortex as there were not enough patients with temporal lobe craniotomy to compare frontal and temporal regions, percentages of verb and noun-specific points were calculated for the anterior and posterior, superior and middle temporal gyri (aSTG – grid areas 10, 11, 12; pSTG – grid areas 13, 14, 15; aMTG – grid areas 16, 17, 18, and pMTG – grid areas 19, 20, 21). The Wilcoxon signed-rank non-parametric test was applied to assess the differences between verb and noun production in each of these four temporal lobe areas. The statistical analysis showed a marginally significant difference between grammatical categories in the pSTG [$Z(7) = -1.83$, $p = .068$] in favour of more noun errors. No further differences were found.

Inhomogeneity in patient population is always a factor that complicates statistical analyses and makes generalization of the results and reaching conclusions about the whole of the sample difficult. To address this issue we conducted an exploratory analysis of the data to see how the pre-surgery language impairment affected the dependent variable, speech arrest upon electric stimulation during resective surgery. First, we compared the results of the pre-surgical evaluation of the verb and noun task to see if there were pre-existing differences between the two tasks. Paired-sample t-test revealed a difference between the patients' ability to produce nouns and verbs [$t(8) = -2.289$, $p = .051$], due to the difficulty some of the patients had to produce verbs. We computed then the correlations between these factors [accuracy of the verb and noun generation tasks (pre-surgical results)] and the outcome of the experimental tasks (percentages of the verb-

Table 3
A summery of the raw data describing our findings in the IFG for the categories: verb-specific (V), noun-specific (N) and non-specific (B; points where both verbs and nouns were interrupted by electric stimulation); observed frequencies are presented on the left, and the percentage of each category with respect to the total number of stimulated points per patient per brain region is presented on the right. * indicates the patient with right hemisphere craniotomy.

Patient	Frequencies							Percentages					
	Broca's area			vMFG				Broca's area			vMFG		
	V	N	B	V	N	B		V	N	B	V	N	B
1	4	0	2	0	0	0		31	0	15	0	0	0
2	2	0	0	–	–	–		14	0	0	–	–	–
3	2	2	2	1	0	0		17	17	17	20	0	0
4	2	0	5	0	0	0		14	0	36	0	0	0
5	2	1	1	1	0	0		18	9	9	20	0	0
6	4	1	1	0	0	0		31	8	8	0	0	0
7	0	0	2	0	0	0		0	0	18	0	0	0
8	0	0	1	0	0	0		0	0	10	0	0	0
9*	0	1	1	0	0	0		0	7	7	0	0	0
10	1	0	2	0	0	0		7	0	14	0	0	0
Total frequency	17	5	17	2	0	0	Total percentage	13	4	13	5	0	0

and noun-specific points in Broca's area and the vMFG). We did not find a statistically significant correlation between any of these factors ($p > .1$), which suggests the ability of producing verbs and nouns did not have an impact on the experimental tasks.

4. Discussion

We investigated the representation of object and action naming in the prefrontal and temporal cortices of the left hemisphere using electrical stimulation mapping (ESM) with patients who had to undergo surgery. In the inferior and middle frontal lobes, 93% of the language related points were located in Broca's area [pars opercularis (46%), pars triangularis (39%) and pars orbitalis (8%)]. Even though the vast majority of the language related points in the prefrontal cortex were situated in Broca's area, the number and extension of the language areas, their distribution in the cytoarchitectonically different parts of Broca's area and their connection to the two experimental tasks used were highly variable from patient to patient. Nonetheless, despite this variability, the present results show convergence with previous ESM studies (Corina et al., 2005; Ojemann et al., 2002) and add new and valuable information about the fine-grained involvement of the different regions in the inferior and middle frontal cortices in language production, both from cognitive and clinical perspectives.

4.1. Cognitive and neural differences between noun and verb production

With regard to the noun–verb dissociation hypothesized to exist in the middle and inferior frontal cortex, our results showed that overall 45% of the language related points disrupted selectively verb naming while 14% were selective for noun naming. However, 41% of the language related points identified in these prefrontal regions were non-specific and caused disruption in both tasks. Directly comparing the posterior part of the IFG (Broca's area) and the posterior portion of the ventral MFG we found the same distribution of noun–verb disruption with more verb than noun-specific points in both brain regions. Further analyses also showed more verb-specific points present in the whole of Broca's region, both in the anterior to posterior portions, and ventral and dorsal locations. It is important however to remark that, in Broca's area there were also significantly more specific points for both categories than in other regions.

Despite of the limited number of patients with temporal craniotomy we found that, in contrast to what is observed in the frontal cortex, there were more noun than verb-specific points in the posterior part of the superior temporal gyrus. Both noun and verb-specific points were found in each patient with a marginally significant difference between the two tasks in the posterior superior temporal gyrus with more noun-specific points. No further differences between tasks were found in the temporal lobe.

Neuropsychological data from studies with aphasic patients who had difficulties in processing either verbs or nouns depending on the localisation of their lesion (e.g. Damasio & Tranel, 1993) gave birth to the idea that words from different grammatical classes are stored and processed separately and use different neural substrates. Based on the findings of these studies it has been proposed that the inferior frontal gyrus supports the processing of verbs and the posterior superior and middle temporal gyri are responsible for noun processing and storage, however furthered studies showed evidence against this hypothesis (Aggujaro et al., 2006; Crepaldi et al., 2011; Silveri & Di Betta, 1997). Results from fMRI studies (see Vigliocco et al., 2011 for review) were more ambiguous. Even though they showed the importance of the brain areas before mentioned they were unable to establish a clear relationship between brain regions and linguistic functions. While our results show a higher number of verb related points in the prefrontal cortex, due to the important number of points specific for noun production, we cannot corroborate this model. This conclusion is similar to the one reached in the only study that previously assessed the same idea in the prefrontal region (Ojemann et al., 2002). The ambiguity of the results of the studies mentioned before could have been caused by the difference in the material and paradigms used as well as the differences in not only grammatical aspects but also the morphological and semantic properties of verbs and nouns or the high individual variability (Corina et al., 2005).

Similarly to the previous two studies on this issue (Corina et al., 2005; Ojemann et al., 2002) we found selective disruption during both the verb generation and naming tasks in the frontal and temporal lobes with a high individual variability across patients, which might be an indication of separate systems underlying verb and noun processing. Despite these similarities with the aforementioned studies we also found differences in the results, which might shed light on the differences underlying the processing of verbs and nouns. Even though Ojemann et al. (2002) found points in the prefrontal cortex of the dominant hemisphere where electric stimulation disrupted verb and noun production selectively, a higher number of verb-specific points was not reported in this brain region. We found, however, that a larger area of the prefrontal cortex led to speech arrest selectively in response to stimulation during the verb generation task.

Our data as well as the findings of Corina et al. (2005) and Ojemann et al. (2002) indicate that task specific points are found in every patient, i.e. every patient has at least one point that is related to verb but not noun production and/or the reverse showing that a partially distinct network for the processing of the two grammatical categories existed in each patient. On the other hand, all three studies show that neither of these tasks is clearly associated to one specific cytoarchitectonic brain structure as the map of the noun and verb-specific points differ from patient to patient. This is consistent with the model proposed by Crepaldi et al. (2011) according to which the grammatical-class specific circuits may be segregated across several brain regions, but might be situated nearby within one anatomical structure. A reason for the high individual variability and the difference found between the two language groups could be that the development of the specific circuits depends highly on the linguistic experience of each individual. These individual differences could have also led to the inconsistency in the findings of the different fMRI studies, where the statistical analysis is done over the average of the BOLD-signal across participants. Moreover, in patients who had double dissociation in both our (4 patients) and Corina et al. (2005) study the verb and noun-specific points were in a distance of 1 cm or less. These small differences could have been difficult to detect for past fMRI studies because of lower spatial resolution compared to ESM, giving therefore some important advantages to the procedure of ESM applied in the present study.

Several rTMS (Cappelletti et al., 2008; Shapiro et al., 2001) and fMRI studies (Shapiro et al., 2012) found no difference between verb and noun processing in the inferior frontal regions but did find a greater involvement of the middle frontal gyrus in tasks involving morpho-syntactic processing of verbs as compared to nouns. This led to the proposal of a model according to which the posterior parts of the IFG is involved in the processing of both grammatical categories, probably in the phonological aspects of the morpho-syntactic processes, meanwhile the MFG is more involved specifically in verb processing. Given that we found more verb than noun-specific points in both inferior and middle frontal gyri with no interaction between these conditions and brain region, our results cannot definitively validate the hypothesis regarding the specific representation of verbs in the middle frontal gyrus. Notwithstanding it is important to bear in mind that we did find both noun- and verb-specific language points in Broca's area but we only observed verb-specific disruption points in the vMFG. Thus to a certain extent, we cannot rule out the possibility of the specific relationship between vMFG and verb processing. In any case, as we only found language related points in the vMFG in two patients, it is difficult to generalize our findings and further research is needed to understand the specific role of the MFG in verb processing.

4.2. Clinical perspective

Our data suggests that there is a better chance to identify most of the language related areas with the use of the action naming task than object naming when mapping takes place in the prefrontal cortex as 86% of the language related points were disrupted during verb production [verb-specific (45%) and verb–noun common points (41%)] and only a 14% of the language related points were noun-specific. These results differ from the findings by Ojemann et al. (2002) suggesting that both object naming and verb generation can be disrupted at any given anatomical region within the perisylvian cortex. These differences could be attributed to the differences between English and Romance languages in verb morphology. Previous studies described the important role of the left IFG in morphological processing (de Diego Balaguer et al., 2006; Heim et al., 2003; Sahin et al., 2006) and therefore it is possible to expect more language related sites when using a more morphologically demanding task. As in English the base verbs do not carry any type of suffixes, the processing of verbs and nouns has a similar level of difficulty, however the infinitive form of Spanish and Catalan verbs do need a suffix to be added to the lexeme even in the infinitive form therefore this form of the verbs is more morphologically complex in Spanish than in English (de Diego Balaguer et al., 2006).

In our study all noun-specific areas were situated at a distance of 1 cm or less from the verb related areas. Therefore, resections located no closer than 1 cm from the sites associated with verbs in the frontal cortex of the dominant hemisphere could be predictive of a good outcome for language function postoperatively. Also, as BA 45 and 46 supports other important cognitive functions as memory retrieval, manipulation of information and the selection of correct response based on internal and external representations (Badre & Wagner, 2002; Christoff et al., 2001; Curtis & D'Esposito, 2003; Petrides, 2000; Wagner, Maril, Bjork, & Schacter, 2001) the more complex and demanding the task used the more likely it is to identify areas of these cognitive functions, which is crucial for the preservation of these important faculties and the better and faster recovery of the patient.

Even though this technique can contribute useful information for the study of the language processes it has two important limitations. The craniotomy needs to be determined by the location and properties of the tumour or lesion of the patient, therefore the control of experimental design in terms of the specific locations studied is difficult. Moreover, depending on the growth rate of the tumour or the appearance and development of the lesions in time, neural plasticity processes can take place as a reaction to the dysfunction of the damaged area. These processes can partially reorganise cognitive functions in the affected brain regions. This gives place to higher individual variability. Hence, interpretations in terms of specific functional localisation for normal brain function based on ESM in tumour patients should be cautious. However, we found cortical locations that responded selectively to nouns or to verbs; we argue that it is highly unlikely that this dissociation between nouns and verbs is a product of brain plasticity induced by tumour growth, thus, even though we ought to be careful at reaching conclusions about specific cortical areas, we can address the issue of a partially separate networks that processes nouns and verbs.

Despite these limitations, thus, it is unlikely that the brain reorganisation in those patients leads to a functional reorganisation where dissociation between elements that would be processed as the same type of representation in healthy individuals would be observed. It is therefore safer to conclude that despite we cannot associate them to a specific brain localisation, in functional terms verbs and nouns have both common and dissociable representations. This conclusion is supported the reported specific deficits for verb production only and for nouns only in different brain areas leading to a double dissociation. In addition, the overall results obtained in this study suggest that the use of the action naming paradigm is a better approach than the classically used object naming task to perform language mapping in the frontal cortex of the dominant hemisphere, as it allows the identification of the frontal portion of the language network as completely as possible.

Acknowledgments

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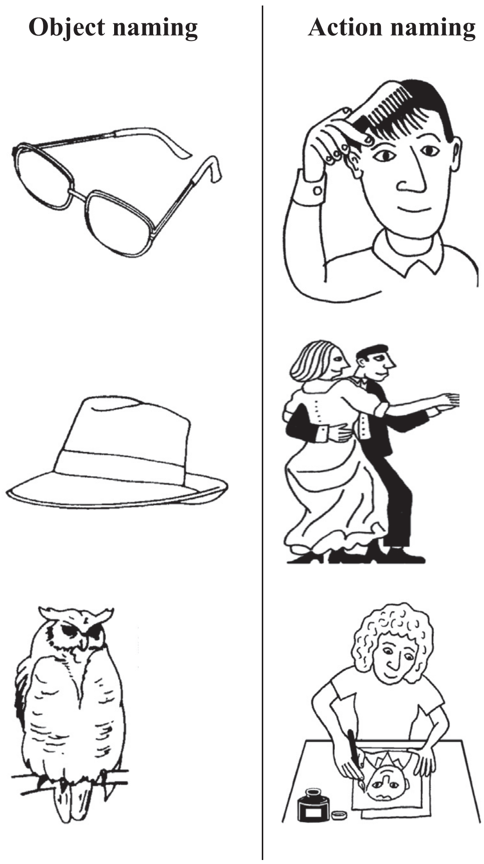
Appendix A

Examples of the line drawings used in the naming and verb generation tasks. Correct naming for the objects is from top to bottom in Spanish/Catalan (English translation): gafas/ulleres (glasses), sombrero/barret (hat), buho/mussol (owl) for object naming; peinar/pentinar (to comb), bailar/ballar (to dance), dibujar/dibuixar (to draw) for action naming.



Appendix B

List of nouns and verbs used as experimental stimuli in Spanish (English translation).

NOUNS: gafas (glasses)/mano (hand)/chaleco (west)/cañón (cannon)/zueco (clog)/volcán (volcano)/botella (bottle)/cruz (cross)/oso (bear)/cuchillo (knife)/gusano (worm)/mujer (woman)/pluma (feather)/árbol (tree)/pelota (ball)/mariposa (butterfly)/sombrero (hat)/búho (owl)/seta (mushroom)/bocadillo (sándwich)/violin (violin)/calcetín (sock)/espada (sword)/pinza (clothes peg)/cubo (cube)/mancha (stain)/bicicleta (bicycle)/ángel (angel)/peonza (spinning top)/pierna (leg)/caracol (snail)/manzana (apple)/rueda (wheel)/hoz (sickle)/martillo (hammer)/cocodrilo (crocodile)/taza (cup)/canguro (cangoroo)/pez (fish)/ardilla (squirrel)/embudo (funnel)/cepillo (brush)/candado (padlock)/zanahoria (carrot)/campana (bell)/uva (grape)/conejo (rabbit)/tijera (scissors)/flor (flower)/percha (hanger)/vaso (glass)/sierra (saw)/brazo (arm)/castillo (castle)/pañuelo (handkerchief)/avión (airplane)/oreja (ear)/casco (helmet)/luna (moon)/sartén (frying pan).

VERBS: pedir (to ask)/sangrar (to bleed)/morder (to bite)/soplar (to blow)/botar (to bounce)/construir (to construct)/llevar (to carry)/coger (to catch)/subir (to go up, to rise)/peinar (to comb)/cocinar (to cook)/cruzar (to cross)/llorar (to cry)/cortar (to cut)/bailar (to dance)/cavar (to dig)/dibujar (to draw)/soñar (to dream)/beber (to drink)/gotear (to drip)/conducir (to drive)/comer (to eat)/pescar (to fish)/flotar (to float)/volar (to fly)/planchar (to iron)/saltar (to jump)/llamar (to call)/lamer (to lick)/encender (to light)/derretir (to melt)/abrir (to open)/pintar (to paint)/pelar (to fight)/plantar (to plant)/jugar (to play)/señalar (to point)/rezar (to pray)/empujar (to push)/llover (to rain)/correr (to run)/navegar (to sail)/coser (to sew)/afeitar (to shave)/hundir (to sink)/patinar (to skate)/esquiar (to ski)/dormir (to sleep)/fumar (to smoke)/nevar (to snow)/remover (to remove)/parar (to stop)/nadar (to swim)/columpiar (to swing)/atar (to tie)/teclear (to type)/caminar (to walk)/lavar (to wash)/ver (to see)/regar (to water)/pesar (to weigh)/escribir (to write)/bostezar (to yawn)/cantar (to sing).

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