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Morphological derivation overflow as a result of disruption of the left frontal aslant white matter tract

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ABSTRACT

The frontal aslant tract (FAT) is a recently described major connection between the preSMA and Broca's area, whose functional role remains undefined. In this study we examined a patient presenting a morphological overregularization strategy in a verb generation task during awake surgery. This specific language deficit coincided with brain tumor resection at the level of the left FAT. During the task execution the patient formed the non-existent verbs by applying a morphological derivation rule to the given nouns, instead of retrieving the appropriate verbs. DTI results confirmed left FAT damage. Neuropsychological follow-up showed that this morphological derivation impairment partially persisted after surgery, whereas the results on a wide spectrum of other language-related tasks remained satisfactory. Additionally, we compared the pre- and the post-operational fMRI activation maps for the same verb generation task. We discuss the potential role of the left FAT in the morphological derivation process and in lexical retrieval.

1. Introduction

The frontal aslant white-matter tract (FAT) has recently been described in detail using diffusion tensor imaging (DTI) in humans (Catani et al., 2012; Ford, McGregor, Case, Crosson, & White, 2010; Lawes et al., 2008; Oishi et al., 2008) and monkeys (Thiebaut de Schotten, Dell'Acqua, Valabregue, & Catani, 2012) but is one of the fasciculi whose functional role continues to be unresolved. The FAT is formed by the white-matter fiber bundles descending from the anterior cingulate cortex and the pre-supplementary motor area (preSMA) to Broca's area (pars opercularis of the inferior frontal gyrus, BA 44). Considering its anatomical relation to these gray matter areas, it was hypothesized that this tract could be part of an extended network involved in initiating and coordinating complex eye, head and arm movements in reaching actions (Catani et al., 2012). In line with this proposal that the FAT is involved in specific motor functions, a recent ESM-case study by Martino and colleagues (Martino, de Lucas, Ibáñez-Plágaro, Valle-Folgueral, & Vázquez-Barquero, 2012) revealed that electrical stimulation of the right FAT caused Foix-Chavany-Marie syndrome, a rare type of suprabulbar palsy affecting the orofacial musculature.

When we consider the possible functional role of the FAT in language processing it is the left hemisphere that should draw our focus. The main reason that suggests an important role of this white-matter pathway in language processing is the anatomical connectivity with regions involved in controlled lexical retrieval, syntactic processing, language production and monitoring.

Broca's area is known to be crucial for word production (Grodzinsky & Santi, 2008), controlled lexical retrieval (Novick, Trueswell, & Thompson-Schill, 2005; Schnur et al., 2009;

Abbreviations: FAT, frontal aslant tract; DTI, diffusion tensor imaging; ESM, Electrical Stimulation Mapping; fMRI, Functional Magnetic Resonance Imaging; TMS, Transcraneal Magnetic Stimulation; SMA, supplementary motor area; AF, arcuate fasciculus; CST, cortical spinal tract; ILF, inferior longitudinal fasciculus; IFOF, inferior fronto-occipital fasciculus; UF, uncinate fasciculus; ROI, region of interest.

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Thompson-Schill, D'Esposito, Aguirre, & Farah, 1997), grammatical and morphological processing (Bozic, Szlachta, & Marslen-Wilson, 2013; Bozic, Tyler, Ives, Randall, & Marslen-Wilson, 2010; Shapiro & Caramazza, 2003), whereas the SMA is related to speech initiation, coordination, performance and speech monitoring (Alario, Chainay, Lehericy, & Cohen, 2006; Chauvel, Rey, Buser, & Bancaud, 1996; Crosson et al., 2001; Fried et al., 1991; Gabarrós et al., 2011; Indefrey, 2011; Indefrey & Levelt, 2004; Krainik et al., 2003; Laplane, Talairach, Meininger, Bancaud, & Orgogozo, 1977; Pai, 1999). Therefore, more posterior connections with SMA are related to motor aspects of articulation. Loss of integrity of the left FAT is associated with a decline in verbal fluency (Catani et al., 2013; Kinoshita et al., 2014; Mandelli et al., 2014), and its electrical intraoperative stimulation results in disturbance of speech initiation (Kinoshita et al., 2014). In contrast, connections to preSMA are more related to linguistic processing (Catani et al., 2013). In a handful of studies (Alexander, Naeser, & Palumbo, 1987; Hogan, Vargha-Khadem, Saunders, Kirkham, & Baldeweg, 2006; Naeser, Palumbo, Helm-Estabrooks, Stiassny-Eder, & Albert, 1989) it has been reported that patients suffering from deep lesions in the periventricular white matter of the frontal lobe presented impaired fluency, agrammatism (i.e., impaired syntactic processing) and reduced performance monitoring, which could be explained by a disconnection of the frontal aslant and fronto-striatal tracts. Finally, more anterior connections to medial prefrontal cortex are likely to be involved in social cognition and theory of mind (Catani & Bambini, 2014). Moreover, this tract is left lateralized in right-handed subjects (Catani et al., 2012) which gives further weight to its possible role in language processing.

In our study we mainly focused on derivational morphology – one of the most important mechanisms of word formation based on the combination between word stems (e.g. *happy*, *speak*) and derivational morphemes (e.g. *-un*, *-ness*, *-er* in English). This mechanism may be used to form words from both the same (e.g. *happy*, *unhappy*-adjectives) and distinct grammatical categories (e.g. *happy*, *happiness*-adjective to noun; *speak*-*speaker*-verb to noun) in contrast to inflection, the product of which always represents the same grammatical category (e.g. *speak*, *speaks*, *speaking*, *spoken*-verb); (Bozic et al., 2010; Marangolo et al., 2003). In the present work, we used distinct tasks to study derivation and inflection. We used noun-based verb generation and verb-based noun generation tasks to assess derivational morphology and we used the morphological transformation task to evaluate inflection (see Table 1).

Importantly, derivational patterns differ in their level of productivity with some being more commonly used for word formation than others. We investigated a case of a patient who presented an unusual strategy of overregularization, applying a very frequent Spanish morphological derivation rule. This rule is highly productive serving to generate verbs from nouns by attaching the suffix –*ear* to the noun to create an infinitive verb (e.g., from the loan word "chat", the derived verb is created by attaching the suffix –*ear* to the stem, "chat*ear*"). In a noun-based verb generation task we clearly observed a strong tendency for the patient to apply this particular rule and create new non-existing verbs in Spanish (e.g., from the noun "libro" – meaning *book*, the verb "libr*ear*" was created instead of retrieving the correct associated verb "leer", to *read*). Given that this phenomenon occurred during the removal of a tumor at the level of the left FAT, we hypothesized that the disruption of this white-matter pathway affected the communication between cortical regions used to correctly retrieve the verbs associated to a specific noun however preserving the morphological derivation processes involved in creating new verb forms. Electrical Stimulation Mapping (ESM) combined with refined neuropsychological testing allowed us to control the noun-based verb generation task performance during surgery.

Even if speech disturbances were previously observed during the course of intraoperative stimulation of the left FAT (Kinoshita, 2014), to our knowledge, this is a first report showing word retrieval deficits in a noun–verb morphological derivation task related to the intraoperative stimulation of this tract.

2. Methods

2.1. Participant

The patient is a 39-year old right-handed Spanish monolingual woman, who underwent an asleep–awake–asleep brain surgery for tumor removal. According to the histological analysis, she harbored an anaplastic aligogastrocytoma (grade III WHO) with neither necrosis nor miscrovascular proliferation. This lesion was localized in the left premotor-frontal area encompassing Brodmann areas (BA) 6 and 8 (middle and superior frontal gyri) and indirectly affecting BA 9. Pre-surgery clinical fMRI neuroradiological assessment showed that the patient's language functions were distributed predominantly in the left hemisphere. This left lateralization for language allowed the patient to be included in the asleep–awake–asleep brain surgery procedure (electrical stimulation mapping for language is reliable only if performed in the dominant hemisphere).

2.2. Neuropsychological assessment

2.2.1. Standard protocol

Neuropsychological assessment carried out before and after surgery in the Neurology Ward of Hospital Universitari de Bellvitge involved a standard protocol designed to explore supplementary motor area functions. This protocol included the *Informative content of language task* (a subtest of the Barcelona test) (Pena-Casanova, 2004), *picture description* (the *Cookie Theft* from the *Boston Naming test*) (Kaplan, Goodglass, & Weintraub, 2001), *semantic (animals)* and *phonological (letters: "p", "m", "r") verbal fluency* (Goodglass & Kaplan, 1983), motor execution - *Purdue Pegboard test* (Tiffin & Asher, 1948), processing speed-*WAIS III (digit-symbol coding and symbol search)* and working memory-*WAIS III (Digit span, letter-number sequencing and arithmetic*) (Wechsler, 1997), (see Tables 1 and 2). In addition, the handedness was assessed with the Handedness Edinburgh Inventory (Oldfield, 1971). This standard questionnaire assesses the habits to use right, left or both hands in everyday life activities. It assigns a score of "10" for right-handedness, "50" for left-handedness and the intermediate values indicate ambidexterity.

2.2.2. Extended language protocol (morphological, semantic and phonological processing)

The standard neuropsychological assessment was extended post-surgery to the tasks concerning morphological aspects of language-Morphological transformation task (De Diego-Balaguer Costa, Sebastián-Galles, Juncadella, & Caramazza, 2004), semantic processing-Pyramids and Palm trees test (Howard, 1992), the Spanish version of 96-trial synonym judgment task (Jefferies, Patterson, Jones, & Lambon Ralph, 2009), phonological processing-words and nonwords repetition task, verbs and nouns generation-image-based verbs generation task and noun-based verb generation (this particular task was also carried out in the pre-surgical assessment) (Havas et al., in press) and verb-based noun generation task. The two aforementioned tasks are of particular interest in this study (see Table 2). In the noun-based verb generation task the patient was presented with a list of 33 nouns read aloud and was instructed to create the relevant verb based on the name of the object. In Spanish, when a noun and a verb

Table 1
Neuropsychological language assessment results (please notice that due to screening purposes and ESM requirements the number of items per task may vary over the time points).

Task	Time point			
	Before surgery	ESM mapping	2 days after-surgery	1 month after surgery
Noun-based verb generation task (from object to action)	Set 1: 32/33 (26 of non-phonologically overlapping stem, 1 error: percha-armador)	At the cortical level: 23 trials[a], 27 items[b] each (23 of non-phonologically overlapping stem); all correct At the level of left FAT: 2 trials, (20 items first trial, 16 items second trial); errors for all the verbs of non-phonologically overlapping stem (11 in the 1st set and 9 in 2nd set), error type: oreja-orejar, libro-librear, pistola-pistolear, pincel-pincelar, regadora-regatear, cama-camejar o comer, llave-llavetear, vaso-vacíar o vasear, cuchara-cucharrerar, perro-perreaer, coche-cochear, nube-nubear)	Set 1: 17/33 (26 of non-phonologically overlapping stem) 3 missings, 4 delays, 1 phonological paraphasia, 8 errors in verb creation (libro-librear, lápiz-lapicear, luz-lucear, pistola-pistolear, regadora-regatear, cuchara-cucharear)	Set 1: 32/33 (26 of non-phonologically overlapping stem, 1 missing) Set 2[c]: 31/33 (13 of non-phonologically overlapping stem, 2 missings)
Noun generation task (from action to object)	–	–	–	Set 1: 30/33 (error type: 3 inflections; escribir-escribo, matar-mato, limpiar-limpio) Set 2: 16/33 (error type: 18 inflections; aclarar-aclaro, sonar-sonajero, soplar-sopla, costar-cuesta, cavar-cava, equivocarse-equivocar, atornillar-atornillo, traducir-traduzco, ordenar-ordeno, saborear-saboreo, copiar-copio, buscar-busco, subrayar-subrayo, escoger-escojo, acusar-acuso, calcular-calculo, pesar-peso)
Verb generation visual	–	–	–	30/30
Verb naming	–	39/64 (error type: 3 circumlocutions, 7 inflections; soplar-sopla, saltar-saltando, 10 missings, 5 semantic paraphasias)[d]	51/64 (error type: 5 delays, 1 phonological and 3 semantic paraphasias, 3 missings, cavar-pisotear, perseverations, significant slowness and delay in responses)	60/64 (1 phonological and 3 semantic paraphasias)
Object naming	–	6/11[e]	55/60	57/60
Non-words repetition		126/135	–	40/40
Words repetition	–	133/135	–	40/40
Semantic task 1[f]	–	–	–	85/96
Semantic task 2[g]	–	–	–	48/52
Morphological transformation task	–	–	47/48 (short form)	136/136
Cookie Theft test	Normal	–	–	Normal
Spontaneous speech	Fluent	–	–	Fluent
Verbal Fluency		–	–	
Semantic (animals)	RS = 27, Pe = 12			RS = 12, Pe = 12
Phonological (letters)				
p	RS = 13, Pe = 8			RS = 9, Pe = 5
m	RS = 15, Pe = 10			RS = 10, Pe = 8
r	RS = 9, Pe = 7			RS = 6, Pe = 2

RS, raw score; Pe, Percentile.
[a] Trial refers to the procedure of testing with the same task using all the items that compose the latter.
[b] Item refers to each single word or image forming the test.
[c] The second set of tasks was added in the follow-up.
[d] The task was not screened for the correct answers before surgery.
[e] The task was not screened for the correct answers before surgery and its performance was stopped due to patient's fatigue after 11 items.
[f] 96 synonym Judgment Task.
[g] Pyramids and Palm Trees.

share a phonologically overlapping stem the speaker may simply apply a grammatical rule adding a suitable suffix while deriving a verb (e.g. peine–peinar, English: "comb-to comb"). If not, they are forced to retrieve the verb corresponding to the given noun from the lexicon (e.g. lápiz-escribir, English: pencil- to write). The task was composed of 29 nouns, 26 of which did not share the stem with the verb to be derived (non-phonologically overlapping stems). The verb-based noun generation task was based on the same principle, but the patient was instructed to make an inverse operation i.e. derive nouns from its corresponding verbs. During the surgery we mainly used the verb generation task (25 trials) permitting us to control for verb processing (which is of particular interest in patients with lesions involving SMA). We also performed some additional tasks: words and non-words repetition verb naming task and the classical naming task, but very soon in the operation course we abandoned the latter naming task's administration due to the patient's fatigue.

In this study we considered a verb to be "overregularized" when this derivational rule was applied to the "stem" and the final derived verb does not exist in Spanish. For example, for the noun "lápiz" (meaning "pencil"), the semantically associated verb correctly retrieved might have been "dibujar", "pintar" o "escribir"; meaning "to draw", "to paint" or "to write". However, if the patient failed to retrieve any of these possible verb candidates and generated the novel verb "lapicear" (lápiz + "ear"), overregularization was noted. It is important to mention that the final derived new verb, although incorrect, might be easy to understand, being semantically transparent.

Table 2
Standard neuropsychological assessment results.

Task	Time point	
	Before surgery	1 month after surgery
WAIS III processing speed		
Number key	RS = 49, Pe = 8	RS = 38, Pe = 7
Symbols	RS = 37, Pe = 13	RS = 28, Pe = 10
WAIS III working memory		
Digits	RS = 12, Pe = 8	RS = 10, Pe = 7
Numbers and Letters	RS = 8, Pe = 8	RS = 6, Pe = 7
Arithmetic	RS = 12, Pe = 10	RS = 10, Pe = 9
Fist/Edge/Palm Right/Left		
Right	1/2	2/2
Left	2/2	1/2
Tapping		
Right	2/2	2/2
Left	2/2	2/2
Graphic alternation Right/Left		
Right	1/2	2/2
Left	1/2	2/2
Graphic loops Right/Left		
Right	2/2	2/2
Left	2/2	2/2
Reciprocal coordination	1/2	1/2
Purdue pegboard test 1		
Preferred hand	30″: 17	30″: 17
Nonpreferred hand	30″: 14	30″: 15
Both hands	30″: 12 (1 line)	30″: 13
Assemblies	60″: 41	60″: 30

WAIS, Wechsler Adult Intelligence Scale; RS, raw score; Pe, Percentile; 1, normative data: Preferred hand: mean = 15.94 and SD = 1.61; Nonpreferred hand: mean = 13.63 and SD = 1.89; Both hands: mean = 13.13 and SD = 1.31; Assemblies: mean = 41.44 and SD = 5.75.

2.3. fMRI

2.3.1. Data acquisition

MR imaging was performed on a Philips Intera 1.5 T system with a maximum field gradient strength of 76 mT/m FMRI scans were acquired before and after surgery in order to check language lateralization and localize the brain network associated with the patient's performance of the task. Functional images were acquired in the axial plane using a single-shot T2*-weighted gradient-echo EPI sequence (slice thickness = 3.5 mm; gap = 0.1 mm; number of slices = 35, repetition time (TR) = 3000 ms; echo time (TE) = 50 ms; flip angle = 90°; matrix = 64 × 64; field of view FOV = 230 mm; voxel size = 3.59 × 3.59 × 3.5 mm). In addition to the functional runs a high-resolution T1-weighted image (slice thickness = 1 mm; number of slices = 160; repetition time (TR) = 8.4 ms; echo time (TE) = 3.9 ms; flip angle = 8°; matrix = 248 × 173; field of view FOV = 246 × 163 mm; voxel size = 1 × 1 × 1 mm) was also acquired.

2.3.2. FMRI task

For the noun-based verb generation task the patient listened to an auditorily presented list of nouns and was instructed to covertly name a relevant verb based on the name of the object. This task was the same as the one used intraoperatively and in the neuropsychological assessment, but this time using a larger set of items. In the pre-operative and post-operative fMRI session we also employed exactly the same protocol.

For the fMRI verb generation condition a standard block design task was developed. Two conditions, active task and baseline, were defined. Each of 7 active blocks of the verbs generation task took 30 s (3 s for 10 different actions to be named, with all nouns used only once) and was followed by 30 s of rest yielding a total run time of 7 min and 30 s (adding 30 s of initial rest).

2.3.3. fMRI data analysis

The analysis of fMRI was performed using SPM8 (The Wellcome Institute of Neurology, London, UK). The pre-processing included realignment, segmentation, normalization and smoothing with an 8 mm Gaussian kernel. Unified Segmentation (Ashburner & Friston, 2005) with medium regularization and cost function masking (CFM) was applied (Andersen, Rapcsak, & Beeson, 2010; Brett, Leff, Rorden, & Ashburner, 2001; Ripolles et al., 2012). The cost function masks were defined for the patient by applying a binary mask of the lesioned tissue using the MRIcron software package (Rorden & Brett, 2000) (http://www.cabiatl.com/mricro/mricron/index.html). For the first level analysis, a general lineal model was created using task and rest conditions. The translational and rotational motion parameters extracted from the realignment phase were also included in the model. Finally, after model estimation, statistical parametrical maps were created for the noun-based verb generation task comparing active versus rest blocks. The pre-surgical and post-surgical activations, both compared to rest baseline, are reported at an uncorrected level of $p < 0.001$ (Table 3 and Fig. 3).

2.4. DTI

2.4.1. Data acquisition

Diffusion tensor imaging (DTI) was performed both pre and post surgery. Pre-surgery DTI was performed on a Philips Intera 1.5 T system with a maximum field gradient strength of 76 mT/m. Data were obtained using a single-shot echo planar imaging (EPI) sequence. Diffusion gradients were applied along 16 directions using a b-value of 0 and 800 s/mm^2. DTI sequences were acquired in the axial plane with 60 contiguous sections, a 2 mm section thickness (voxel size of 1.63 × 1.63 × 2 mm), no intersection gap, TR/TE: 15,600/79, FOV = 170 × 234 mm^2, and with an 84 × 117 matrix size. Post-surgery, the medical team decided to improve the quality of the diffusion tensor images doubling the number of directions along which the diffusion gradients were applied (from 16 to 32). In order to do so, the patient was redirected to

Table 3
Brain regions activated during verb generation contrasted with the baseline, $P < 0.01$, minimum cluster size $n = 20$. Coordinates use the MNI system.

Activations						
Area	BA	Clustersize (mm^3)	*T* value	Peak coordinates		
				x	*y*	*z*
Pre-surgery						
LEFT HEMISPHERE						
Middle frontal gyrus	46	4582	7.11	−46	42	20
Inferior frontal gyrus	–	201	6.46	−54	14	0
Inferior parietal lobe	7	429	4.69	−32	−48	40
Superior temporal gyrus	42	485	4.45	−64	−32	8
Thalamus	–	116	4.23	−20	−24	0
Orbitofrontal gyrus	11	95	3.65	−34	40	−18
Middle occipital gyrus	37	131	3.43	−54	−66	−12
Superior frontal gyrus	10	61	3.28	−30	64	4
Caudate	–	111	2.99	−6	8	20
RIGHT HEMISPHERE						
Inferior frontal gyrus	45	1042	5.59	48	18	6
Middle frontal gyrus	11	866	5.38	24	40	−10
	9	122	5.15	36	42	34
Superior temporal gyrus	22	343	5.18	70	−34	6
Putamen	–	266	4.00	24	−6	26
Hippocampus	–	99	4.10	28	−18	−20
Precuneus	–	35	3.49	22	−82	26
Inferior temporal gyrus	37	43	3.22	50	−56	−8
Supplementary motor area	–	25	3.19	2	6	66
Inferior parietal lobe	40	23	2.91	42	−48	44
Caudate	–	42	2.77	18	2	14
Cerebellum	–	98	3.15	4	−82	−26
Post-surgery						
LEFT HEMISPHERE						
Inferior temporal gyrus	37	4669	7.76	−54	−60	−14
Middle/Inferior frontal gyrus	9	2494	7.26	−48	12	30
Orbitofrontal gyrus	11	764	6.24	−30	46	−18
Cerebellum	–	219	4.23	−10	−60	−30
Precentral gyrus	6	87	3.97	−42	−6	56
Parahippocampal gyrus	36	39	3.51	−30	−30	−24
Supramarginal gyrus	40	29	3.34	−62	−24	30
RIGHT HEMISPHERE						
Superior temporal gyrus	22	5382	10.95	68	−40	4
Cerebellum	–	977	6.69	30	−70	−26
Middle frontal gyrus	8	484	5.24	2	34	42
Inferior parietal lobe	39	339	5.04	34	−62	40
Inferior frontal gyrus	44	82	4.58	58	14	14
Superior frontal gyrus	10	286	4.51	12	70	2
Precentral gyrus	6	48	4.06	44	−50	−8
Cerebellum	–	80	3.65	34	−66	−44
Putamen	–	63	3.65	32	−24	0
Inferior temporal gyrus	20	37	3.59	60	−8	−24
Supramarginal gyrus	40	126	3.36	46	−46	48
Caudate	–	24	2.99	12	8	10
Postcentral gyrus	4	36	2.95	24	−30	−56
Supplementary motor area	6	623	4.67	8	4	72
Cingulate	–	101	3.87	−2	−60	8
Gyrus rectus	11	102	4.14	0	56	−16

BA, Brodmann area; R, right; L, left.

the associated hospital (Hospital Duran i Reynals). There, the post-surgical imaging was performed on a Philips Ingenia 1.5 T using a single-shot echo planar imaging (EPI) sequence, as in the presurgical scanning session. However, in this acquisition, diffusion gradients were applied along 32 directions. DTI sequences were acquired in the axial plane with 48 contiguous sections with no intersection gap. FOV was of 224×224 mm^2, the matrix size of 92×88 and the voxel size of $1.75 \times 1.75 \times 2.5$ mm. The rest of the parameters were the same as in the presurgical scanning.

2.4.2. Preprocessing of DTI data

Data were first corrected for eddy current distortions using FMRIB's Diffusion Toolbox (FDT), part of the FMRIB Software Library (FSL www.fmrib.ox.ac.uk/fsl/) (Smith et al., 2004; Woolrich et al., 2009). The gradient matrix was then rotated and the structural image was fully-stripped using FSL's Brain Extraction Tool (Smith et al., 2002). Diffusion tensors were reconstructed using the linear least-squares method provided in the Diffusion Toolkit (Ruopeng Wang, Van J. Wedeen, TrackVis.org, Martinos Center for Biomedical Imaging, Massachusetts General Hospital). Tractography was carried out in all brain voxels with FA > 0.2. Tractography was stopped when the angle between two consecutive tractography steps was larger than 35°. This whole-brain approach ensured that tractography reconstruction was less dependent on the regions of interest (ROI) delineation. Finally, tractography data and diffusion tensor maps were exported into Trackvis for manual dissection of the tracts.

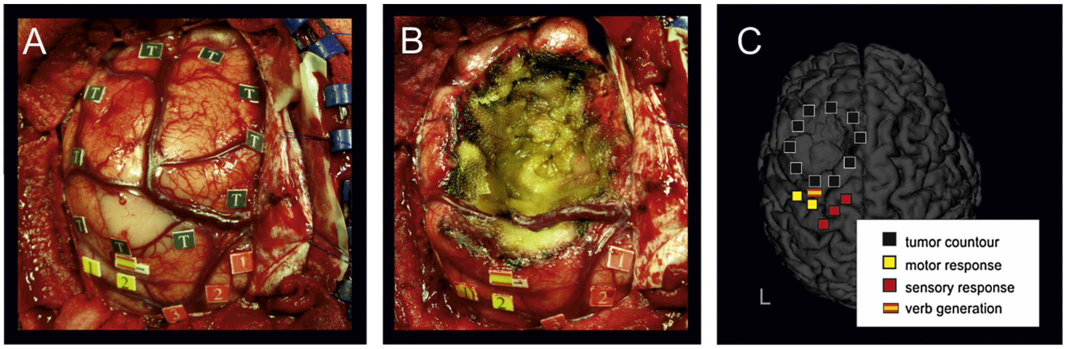

Fig. 1. Electrical Stimulation Mapping (ESM) results. A and B – the intraoperative photographs of patient taken after the ESM procedure and after tumor removal, respectively; C – points of ESM located using the arbitrary two-dimensional grid superimposed on the 3D image of the Patient's cortex reconstruction.

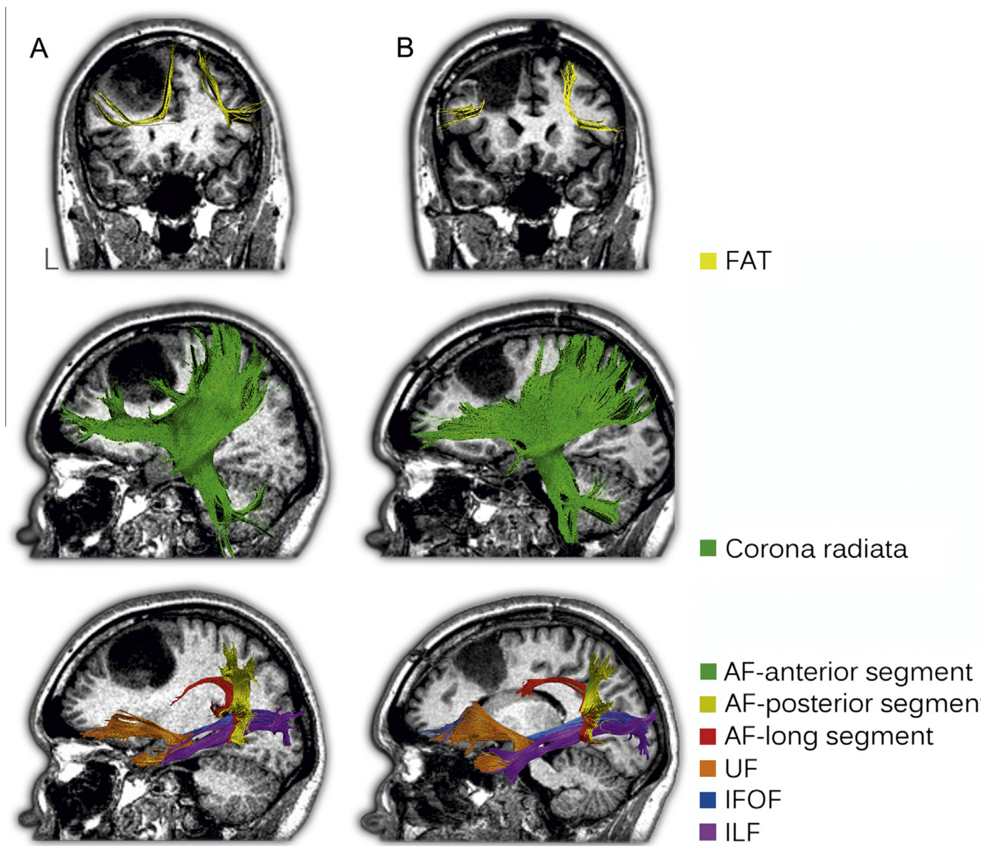

Fig. 2. Diffusion tensor imaging (DTI) results. Virtual *in vivo* dissections before (A) and after surgery (B); FAT, frontal aslant tract; AF, arcuate fasciculus; UF, uncinate fasciculus; ILF, inferior longitudinal fasciculus; IFOF inferior fronto-occipital fasciculus.

2.4.3. Tractography dissections

In order to give further validity to our case study, we dissected not only the frontal aslant tract (FAT) but also: the arcuate fasciculus (AF), cortical spinal tract (CST), inferior longitudinal fasciculus (ILF), inferior fronto-occipital fasciculus (IFOF), uncinate fasciculus (UF) and the corona radiate in both hemispheres. In the left hemisphere, the criteria that we used while choosing the tracts to dissect were the proximity to the lesion and/or previously reported involvement in language processing. We also dissected the right analogues of these tracts as the control tracts. Virtual dissections of these tracts were carried out in the native space, in accordance with previous studies (Catani & Thiebaut de Schotten, 2008; Catani et al., 2007, 2012, 2013; Catani, Jones, & ffytche, 2005; Catani & Thiebaut de Schotten, 2008; López-Barroso et al., 2013; Tuomiranta et al., 2014; Yu et al., 2007) and using Trackvis software (Ruopeng Wang, Van J. Wedeen, TrackVis.org, Martinos Center for Biomedical Imaging, Massachusetts General Hospital) (for more detailed description of the virtual dissections see supplementary material). In the post-surgical dataset, we also calculated the lateralization indices for the tracts of interest following the formula previously employed by Catani et al. (2007; see supplementary material; Table 4).

2.5. Electrical Stimulation Mapping (ESM)

On the cortical level, the ESM was performed according to previously reported methodology (Lucas, Drane, Dodrill, & Ojemann, 2008; Ojemann, Ojemann, Lettich, & Berger, 2008,; Roux et al., 2004; Sierpowska et al., 2013). At the level of white matter, the tumor and its adjacent structures were stimulated during all the time of tumor resection. This was achieved using CUSA (cavitron ultrasonic surgical aspirator), which enabled not only simultaneous fragmentation, suction, and irrigation of tissue, but also its continuous stimulation (a transient inhibition of axonal conduction was proposed as a possible mechanism of this phenomena; Carrabba et al., 2008). Simultaneously to the tumor removal, language tasks were carried out by the neuropsychologist. Once the repeated alteration of language processing was observed, the resection was stopped and the classical (non-continuous) electrical stimulation mapping was repeated at the subcortical level (for this methodology description see Duffau, 2007). Following the standard procedure, when the patient started to commit the verb generation errors, but there was still a part of tumor left, maximization of tumor resection (grade III WHO) and prevention of post-surgical loss was considered to decide the extension of tumor removal. In the current case, the surgeon proceeded to complete removal of tumoural tissue based on the commonly observed good spontaneous recovery in SMA damage (Desmurget, Bonnetblanc, & Duffau, 2007; Gabarrós et al., 2011; Martino et al., 2011) and the preserved patient's ability to repeat words and non-words and generate verbs overlapping phonologically (indeed, our patient remarkably improved her performance on language processing tasks one month after surgery).

During all the time of surgery, the surgeons were equipped with the neuronavigation system (BrainLab vector Vision compact). The anatomical T1 weighted 3D images were corregistered with the Patient's head and consulted during the surgery in order to control the tumor resection anatomical accuracy and also in these moments, when the neuropsychologists observed disturbances in language tasks performance.

3. Results

3.1. Electrical stimulation mapping

The exact localization of the ESM points on the cortical level was reproduced based on intraoperative photographs. An arbitrary, two-dimensional grid was placed on the picture and the exact localization of points was transferred to a patient's 3D cortex reconstruction. The ESM cortical mapping revealed that the stimulation of the motor cortex induced involuntary movements and the stimulation of the premotor cortex altered the alternate hands movement (in this motor task the patient continuously opened her right fist while closing the left one and then the other way round). The only cortical point mapped as subservient to verb generation was found at the level of the supplementary motor area (Fig. 1). In order to control morphological language processing, the noun-based verb generation task execution was continued during tumor removal. Throughout the most part of the tumor extraction procedure the patient was generating the verbs correctly (23 trials). However, as the resection reached the level of the left FAT the patient started to produce accurate verbs only for the nouns which shared the stem with their derived verbs (e.g.: peine–peinar, English: comb-to comb). When she had to generate the verbs from nouns with no phonological overlap (e.g.: Spanish: lápiz-escribir, English: pencil-to write), she overregularized these forms (see Table 1). During tumor removal the patient used the same strategy of overregularization for 1 trial of 20 items and incorrectly derived verbs for all of the 11 nouns with no phonological overlap. After having observed the recurrent alterations in verb formation, surgeons suspended the resection and continued the electrical stimulation at the subcortical level. During this procedure, the task was repeated again using 16 items (9 with non-phonologically overlapping stem) and the patient continued to use overregularization, irrespective of whether the stimulation was applied or not. This observation permitted us to conclude that, not the subcortical ESM, but the stimulation associated with the usage of CUSA in the tumor resection and the removal itself, both provoked the language disturbance.

3.2. Neuropsychological assessment

3.2.1. Before surgery

Standard neuropsychological assessment carried out before surgery revealed right-handedness (Edinburgh Inventory score: 10), good language skills, normal processing speed and normal working memory. Before surgery the patient was able to correctly generate verbs from nouns. The only impairment observed before surgery concerned the motor functions of upper extremities (see Tables 1 and 2).

3.2.2. After surgery

3.2.2.1. Acute. Two days after surgery the patient's speech was characterized by motor impairment, overall slowness of the

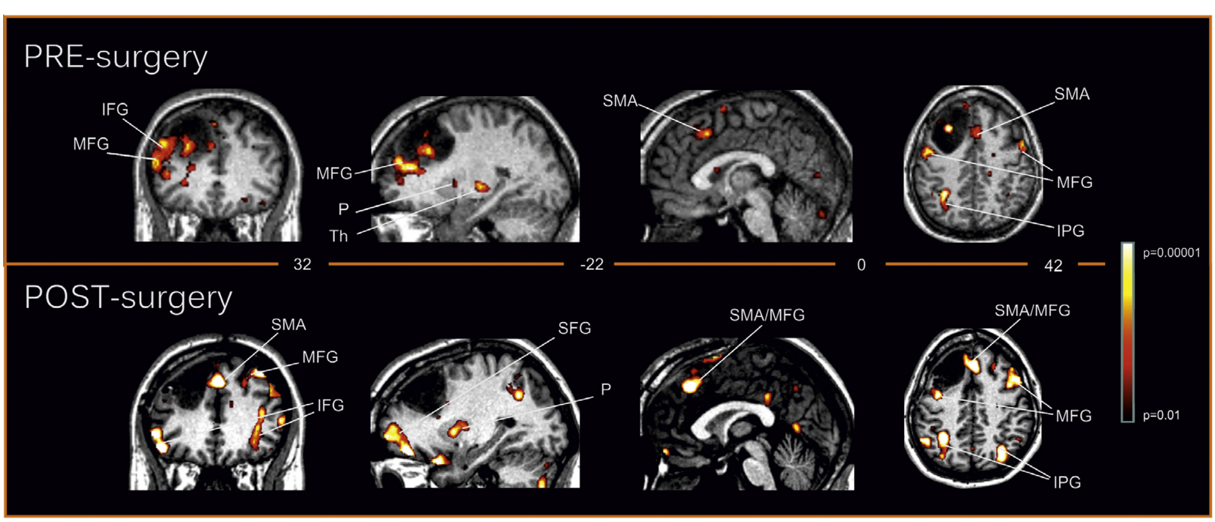

Fig. 3. Functional Magnetic Resonance Imaging (fMRI) results. Activations related to the noun-based verb generation task (active task condition versus baseline) represented on the coronal, sagittal and axial view; IFG, inferior frontal gyrus; MFG, middle frontal gyrus; P, Putamen; Th, Thalamus; SMA, supplementary motor area; IPG, inferior parietal gyrus.

discourse, delays in the naming and verb generation tasks, perseverations, need for phonological cues and word finding difficulties. The extended neuropsychological assessment revealed a good capacity for verb and object naming. Importantly, the patient improved in the noun-based verb generation task compared to the intraoperative session, although the impairment and overregularization strategy both persisted (compare 8 errors in the acute phase to the complete inability in the tasks performance during the surgery, see Tables 1 and 2). Given the overregularization strategy used in the verb from noun generation task, the morphological transformation task was also used to explore more general morphological capacities in the patient (past and present tense forms of Spanish verbs; from: de Diego-Balaguer et al., 2004). The performance in this test was virtually perfect (see Table 2).

3.2.2.2. Follow-up. 1 month after surgery the patient continued presenting motor deficits. Moreover, we detected a more multifaceted impairment. The most significant loss was observed in verbal fluency, processing speed and working memory (Tables 1 and 2). The patient presented a good level of semantic (semantic decisions), morphological (the past and present tense forms) and phonological (non-words repetition) processing. The only remarkable alteration was related to noun-based verb-generation and verb-based noun generation. In order to further explore the strategy of overregularization and minimize the possible effect of learning, we created a second set of nouns and an inverse task (verbs to nouns generation). The patient continued improving creating verbs from nouns (only 1 missing/27 items with no phonological overlap on the first task set and 2 missings in the second set) but had difficulties generating nouns from verbs (19 errors/66 verbs; see Table 1). While comparing the selected language processing measures collected one month after surgery to the acute post-surgical phase, we can observe that the patient substantially improved in verb generation and naming (Table 1).

3.3. Functional magnetic resonance imaging

The pre-surgical and post-surgical activation maps using the noun-based verb generation task versus baseline were very similar with both exhibiting activations at the level of: the right putamen, the frontal and temporal lobes bilaterally and also in the supplementary motor area and the cerebellum. Nevertheless, they slightly differ in their lateralization for the basal ganglia networks. While pre-surgery the patient showed enhanced activations in the left thalamus and in the caudate bilaterally, a right caudate activation for the post-surgical scanning emerged. Moreover, the post-surgical evaluation also showed enhanced activation of the cingulate cortex, gyrus rectus and the precentral and postecentral gyri. Finally, the hippocampus and parahippocampal cortex were activated during this task in both scanning sessions, however before surgery the activation was right-lateralized and after surgery left-lateralized (see Table 3 and Fig. 3).

3.4. Diffusion tensor imaging

We performed the virtual *in vivo* dissections depicting the white matter organization of the patient in both, presurgical and postsurgical datasets. Our analysis revealed that the ventral pathways (ILF, IFOF and UF) associated with the semantic processing of language (Hickok & Poeppel, 2007; Rauschecker, 2012; Saur et al., 2010; Weiller, Bormann, Saur, Musso, & Rijntjes, 2011), long and posterior segments of AF and cortico-spinal tract (CST), were spared equally before and after surgery. The anterior segment of the arcuate fasciculus was not detected in our dataset before surgery and scant post-surgically. Upon visual inspection of presurgical data, we observed the displacement of fibers due to the mass effect in the left corona radiata and in the left FAT. Post-surgical acquisition revealed that the operation damaged these two tracts (see Fig. 2). In the post-surgical dataset, we compared the left language related tracts to their right hemispheric analogues (see supplementary material, Table 4). Considering volume and number of streamlines of the selected tracts, we observed rightward asymmetry for the anterior and long segments of AF and leftward asymmetry for the UF and posterior segment of AF. These values for the left versus right IFOF and ILF tracts were very similar. (Please note that after surgery the anatomical imaging data acquisition was performed in different equipment, which although improved the quality of data, impeded pre-versus post-surgical comparison of DTI parameters). In any case, we should be very careful while interpreting these lateralization indices, since the observed results may reflect the plastic changes due to tumor progressive growth having different effects on distinct microstructural measures.

4. Discussion

This case study examines a 39 year-old woman who underwent the asleep–awake–asleep brain surgery for left premotor-frontal tumor removal. When presented with a noun-based verb-generation task during the surgery, the patient failed to correctly generate verbs from nouns, repetitively using an overregularization strategy: in order to produce a verb, she was attaching a very productive suffix in Spanish morphological derivation *–ear* to the noun stem. This observation coincided with the stimulation and tumor resection at the level of the pre-SMA and extending to the left FAT. The deficit partially persisted after surgery with a similar pattern of compensatory strategy in the inverse task (i.e. verb based noun generation). The post-surgical *in vivo* tractography outcome confirmed that although the surgical intervention left Broca's area intact (at the cortical level only the SMA/preSMA region was damaged; see Fig. 1), the fibers ascending from Broca's area to the pre-SMA (FAT) were nevertheless damaged.

Broca's area and SMA are widely considered to be related to verb processing (Ben-Shachar, Hendler, Kahn, Ben-Bashat, & Grodzinsky, 2003; Davis, Meunier, & Marslen-Wilson, 2004; Friederici & Kotz, 2003; Heim, Opitz, & Friederici, 2003; Mestres-Missé, Rodriguez-Fornells, & Münte, 2010; Shapiro et al., 2005; Vigliocco, Vinson, Druks, Barber, & Cappa, 2011; Willms et al., 2011; Yokoyama et al., 2006). Hence, the structural and functional connectivity between these areas should also be very important for verb processing. Indeed, the pre and post-surgical fMRI analyses of the verb generation task revealed Broca's area and preSMA activations, both of these areas being cortical terminations of the FAT tract (see Fig. 1). This idea is consistent with the proposal that white-matter lesions could interfere with language or other cognitive processes through interruptions in the connections among cortical centers (Catani & ffytche, 2005; Catani & Mesulam, 2008; Lichtheim, 1885; Wernicke, 1874).

Although little is still known about the FAT white matter bundle function itself, previous studies have reported to be associated to speech initiation difficulties (Duffau et al., 2002 and Kinoshita et al., 2014), speech fluency (Kronfeld-Duenias, Amir, Ezrati-Vinacour, Civier, & Ben-Shachar, 2014) and verbal fluency dysfunctions (Catani et al., 2013; Kinoshita et al., 2014; Mandelli et al., 2014). In a very recent model proposed by Catani & Bambini (A model for Social Communication And Language Evolution and Development –SCALED; 2014), the authors hypothesized that the FAT may "constitute the neural underpinning of the expression and recognition of communicative intentions". Our patient did not display speech and verbal fluency dysfunctions and we did not assess theory of mind deficits. Thus we cannot conclude on possible communicative intentions concerning this latter function.

Nevertheless, the overall picture from the reports available reflects the heterogeneity of functions of the anterior posterior connections of the FAT. Lesions to fibers connecting with SMA connections appear related to articulation, lesions to pre-SMA connections have a more linguistic function such as the case reported here, and connections with medial prefrontal cortex may have an implication with social cognition as proposed by the SCALED model.

From a cognitive point of view, the pattern of deficits observed in the current report fit well with dual route models for morphological processing. These models are based on the distinction between grammar and lexicon (Baayen, Dijkstra, & Schreuder, 1997; Clahsen, Aveledo, & Roca, 2002; Marslen-Wilson & Tyler, 1997; Pinker & Ullman, 2002, 2004; Ullman et al., 1997). According to the aforementioned dual route model, both rule-production and lexical retrieval of irregular forms are activated in parallel during morphological processing. In normal circumstances, the existence of a lexical form associated to a morphological transformation blocks the default rule application. In the case of our patient, the failure to block the rule-production route by the lexical retrieval process might allow the rule application to "win the race" leading to overregularized verb forms. Even if these assumptions were developed and applied mainly to the English past tense, the difference between regular (rule-based) versus irregular inflection (lexical retrieval) may be analogous to the distinction between derivation/retrieval of words with phonologically overlapping versus non-overlapping stems. In this work we focused on the difference between compositional derivation (grammar) versus full form retrieval (lexicon). The left inferior frontal region (including Broca's area) was previously related to the control of lexical retrieval and/or selection of semantic knowledge (Alario et al., 2006; de Diego-Balaguer et al., 2006; Novick et al. 2005; Thompson-Schill, D'Esposito, Aguirre, & Farah, 1997), which is an operation necessary for the production of the correct verb form during the verb generation task. The surgical intervention impaired the correct functioning of the left inferior frontal cortex by lesioning its FAT connection which prevented the access to the verbs forms stored in the mental lexicon associated to the derivation of the nouns. It is possible then to assume that by injuring this connection the surgical manipulation might have affected the capacity to control lexical retrieval (Schnur et al., 2009; Thompson-Schill, D'Esposito, Aguirre, & Farah, 1997) and the access to the target full form.

The evidence from neuropsychological studies (e.g. Bozic et al., 2010; Marangolo et al., 2003) suggests that distinct subtypes of inflection and derivation may work independently being subserved by slightly different variants of the same network. Marangolo et al. (2003), Marangolo et al. (2006), for instance, observed selective impairment for derivation of nouns from verbs and preservation of other forms of the derivation and inflection in patients with right-hemisphere lesions. Miozzo (2003) reported also on a patient accurately producing regular forms of verbs and nouns while impaired with irregular forms and another patient (Miozzo, Fischer-Baum, & Postman, 2010) with the inverse pattern in nouns inflections. In line with observations by Shapiro and Caramazza (2003), these authors suggested that distinct grammatical categories may be subserved by separate neural systems. Similarly, our patient was impaired in the verb generation task from nouns but was able to correctly inflect both regular and irregular verbs. The lack of presurgical and particularly intraoperative measures of past tense inflection prevents us to discern whether the intraoperative impairment also included inflection.

A second possibility explaining the observed impairment could be related to cognitive control deficits (e.g., inhibition and error monitoring) and may therefore not derive from a purely linguistic deficit. Verb and noun generation tasks require a selection of responses among competing alternatives. The patient may have been unable to successfully suppress the noun cue or the default rule application leading to the generation of the final "overregularized" verb (stimulus-bound behavior; Archibald, Mateer, & Kerns, 2001). Previous authors have indeed proposed that selection deficits may underlie the control of lexical retrieval (Thompson-Schill, D'Esposito, Aguirre, & Farah, 1997; Schnur et al., 2009). This hypothesis may also be supported by the presurgical fMRI scan results revealing activations of areas traditionally involved in cognitive control and error monitoring, such as: middle, inferior frontal and anterior cingulate cortices (Aron, Robbins, & Poldrack, 2004; Botvinick, Cohen, & Carter, 2004; Buchsbaum, Greer, Chang, & Berman, 2005; Carter et al., 1998; Chikazoe, 2010). Additionally, the cortical projection of the FAT reached not only the IFG, but also the MFG (Catani et al., 2012; see Fig. 2). Moreover, the neuropsychological assessment of our patient revealed a slight decline in executive function tests after surgery (i.e. processing speed and working memory indices) (see Table 2). Interestingly, this interpretation goes in line with the one of Marangolo et al. (2006), who associated the deficit in derivation with impairment of inhibitory mechanisms. However, these authors suggested that this operation might have been subserved by the right basal ganglia. Our activation map for verb generation also revealed basal ganglia activation in addition to the prefrontal network described. This data confirms the right hemispheric pattern post-surgically, although being more lateralized at left before surgery (see Table 3 and Fig. 2). Given this activation map and lesion location it would have been interesting to test the integrity of the subcallosal (fronto-stratial) connection. Unfortunately the parameters of our DTI acquisition sequence (see Section 2) did not allow us to perform this analysis.

It should also be noticed that according to the post-surgical *in vivo* DTI dissections, not only the FAT but also the corona radiata was partially damaged. Interestingly, this tract was previously associated with derivational processing (nouns from verbs generation; Marangolo & Piras, 2008), but those results referred to the right hemisphere, which in our patient was spared. On the left hemisphere, the corona radiata has been previously associated to verbal fluency (Yogarajah et al., 2010), nonetheless this ability is not directly related to the impairment observed in our patient during the surgery. Moreover, this tract was relatively less injured during the surgery than the left FAT (see Fig. 2). In addition, the surgery did not disrupt the CST integrity and the patient did not present any articulatory problem. Therefore, the language impairment presented by our patient could not be explained by a motor disturbance. Similarly, the uncinate fasciculus was preserved, being this fasciculus associated to naming ability (Catani et al., 2013), which was not disrupted in the present case. Our results also confirmed the previously reported relation between FAT and verbal fluency (Catani et al., 2013; Kinoshita et al., 2014), taking into account that in our patient the post-surgical decline on this measure co-occurred with the disruption of FAT fibers (see Table 1 and Fig. 2).

Finally, an alternative explanation to the deficits observed would be that the rule-based verb generation is, to a certain extent, less demanding than the effort required for lexical retrieval of the forms that do not overlap phonologically (de Diego-Balaguer et al., 2006). Thus, the patient could be simply tired or resource depleted during task execution during surgery and chose to respond employing the more automatic route (the default morphological derivation rule application). Nevertheless this account would not explain why both greater impairment of lexical retrieval forms and also greater rule-based impairments have been reported after brain lesions (de Diego-Balaguer, 2004; Miozzo, 2003; Miozzo et al., 2010), and in our patient, would not account for the spared irregular inflection despite the lexical retrieval deficit in derivation.

To conclude, to the best of our knowledge, this is the first study reporting relation between verb generation and intraoperative stimulation of the left FAT. We believe that selection of well-adjusted and individualized neuropsychological tasks may enable developing each time more efficient brain mapping protocols. In this manner, the surgeons may target the electric stimulation procedures on brain functions strictly related to the lesion's location. In our opinion, the verb generation task should be further explored as a good candidate for neuropsychological control in surgeries involving preSMA, Broca's area and left FAT.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.bandl.2015.01.005.

References

Alario, F.-X., Chainay, H., Lehericy, S., & Cohen, L. (2006). The role of the supplementary motor area (SMA) in word production. *Brain Research, 1076*(1), 129–143.
Alexander, M. P., Naeser, M. A., & Palumbo, C. L. (1987). Correlations of subcortical CT lesion sites and aphasia profiles. *Brain: A Journal of Neurology, 110*(Pt 4), 961–991.
Andersen, S. M., Rapcsak, S. Z., & Beeson, P. M. (2010). Cost function masking during normalization of brains with focal lesions: Still a necessity? *NeuroImage, 53*(1), 78–84.
Archibald, S. J., Mateer, C. A., & Kerns, K. A. (2001). Utilization behavior: Clinical manifestations and neurological mechanisms. *Neuropsychology Review, 11*(3), 117–130.
Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2004). Inhibition and the right inferior frontal cortex. *Trends in Cognitive Sciences, 8*(4), 170–177.
Ashburner, J., & Friston, K. J. (2005). Unified segmentation. *NeuroImage, 26*(3), 839–851.
Baayen, R. H., Dijkstra, T., & Schreuder, R. (1997). Singulars and plurals in Dutch: Evidence for a parallel dual-route model. *Journal of Memory and Language, 37*(1), 94–117.
Ben-Shachar, M., Hendler, T., Kahn, I., Ben-Bashat, D., & Grodzinsky, Y. (2003). The neural reality of syntactic transformations: Evidence from functional magnetic resonance imaging. *Psychological Science, 14*(5), 433–440.
Botvinick, M. M., Cohen, J. D., & Carter, C. S. (2004). Conflict monitoring and anterior cingulate cortex: An update. *Trends in Cognitive Sciences, 8*(12), 539–546.
Bozic, M., Szlachta, Z., & Marslen-Wilson, W. D. (2013). Cross-linguistic parallels in processing derivational morphology: Evidence from Polish. *Brain and Language, 127*(3), 533–538.
Bozic, M., Tyler, L. K., Ives, D. T., Randall, B., & Marslen-Wilson, W. D. (2010). Bihemispheric foundations for human speech comprehension. *Proceedings of the National Academy of Sciences of the United States of America, 107*(40), 17439–17444.
Brett, M., Leff, A. P., Rorden, C., & Ashburner, J. (2001). Spatial normalization of brain images with focal lesions using cost function masking. *NeuroImage, 14*(2), 486–500.
Buchsbaum, B. R., Greer, S., Chang, W.-L., & Berman, K. F. (2005). Meta-analysis of neuroimaging studies of the Wisconsin card-sorting task and component processes. *Human Brain Mapping, 25*(1), 35–45.
Carrabba, G., Mandonnet, E., Fava, E., Capelle, L., Gaini, S. M., Duffau, H., & Bello, L. (2008). Transient inhibition of motor function induced by the Cavitron ultrasonic surgical aspirator during brain mapping. *Neurosurgery, 63*(1), E178–E179.
Carter, C. S., Braver, T. S., Barch, D. M., Botvinick, M. M., Noll, D., & Cohen, J. D. (1998). Anterior cingulate cortex, error detection, and the online monitoring of performance. *Science (New York, N.Y.), 280*(5364), 747–749.
Catani, M., Allin, M. P. G., Husain, M., Pugliese, L., Mesulam, M. M., Murray, R. M., et al. (2007). Symmetries in human brain language pathways correlate with verbal recall. *Proceedings of the National Academy of Sciences, 104*(43), 17163–17168.
Catani, M., & Bambini, V. (2014). A model for Social Communication And Language Evolution and Development (SCALED). *Current Opinion in Neurobiology, 28*, 165–171.
Catani, M., Dell'acqua, F., Vergani, F., Malik, F., Hodge, H., Roy, P., et al. (2012). Short frontal lobe connections of the human brain. *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior, 48*(2), 273–291.
Catani, M., & ffytche, D. H. (2005). The rises and falls of disconnection syndromes. *Brain: A Journal of Neurology, 128*(Pt 10), 2224–2239.
Catani, M., Jones, D. K., & ffytche, D. H. (2005). Perisylvian language networks of the human brain. *Annals of Neurology, 57*(1), 8–16.
Catani, M., & Mesulam, M. (2008). What is a disconnection syndrome? *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior, 44*(8), 911–913.
Catani, M., Mesulam, M. M., Jakobsen, E., Malik, F., Martersteck, A., Wieneke, C., et al. (2013). A novel frontal pathway underlies verbal fluency in primary progressive aphasia. *Brain: A Journal of Neurology, 136*(Pt 8), 2619–2628.
Catani, M., & Thiebaut de schotten, M. (2008). A diffusion tensor imaging tractography atlas for virtual in vivo dissections. *Cortex, 44*(8), 1105–1132.
Chauvel, P. Y., Rey, M., Buser, P., & Bancaud, J. (1996). What stimulation of the supplementary motor area in humans tells about its functional organization. *Advances in Neurology, 70*, 199–209.
Chikazoe, J. (2010). Localizing performance of go/no-go tasks to prefrontal cortical subregions. *Current Opinion in Psychiatry, 23*(3), 267–272.
Clahsen, H., Aveledo, F., & Roca, I. (2002). The development of regular and irregular verb inflection in Spanish child language. *Journal of Child Language, 29*(3), 591–622.
Crosson, B., Sadek, J. R., Maron, L., Gökçay, D., Mohr, C. M., Auerbach, E. J., et al. (2001). Relative shift in activity from medial to lateral frontal cortex during internally versus externally guided word generation. *Journal of Cognitive Neuroscience, 13*(2), 272–283.
Davis, M. H., Meunier, F., & Marslen-Wilson, W. D. (2004). Neural responses to morphological, syntactic, and semantic properties of single words: An fMRI study. *Brain and Language, 89*(3), 439–449.
De Diego Balaguer, R., Costa, A., Sebastián-Galles, N., Juncadella, M., & Caramazza, A. (2004). Regular and irregular morphology and its relationship with agrammatism: Evidence from two Spanish–Catalan bilinguals. *Brain and Language, 91*(2), 212–222.
De Diego Balaguer, R., Rodríguez-Fornells, A., Rotte, M., Bahlmann, J., Heinze, H.-J., & Münte, T. F. (2006). Neural circuits subserving the retrieval of stems and grammatical features in regular and irregular verbs. *Human Brain Mapping, 27*(11), 874–888.
Desmurget, M., Bonnetblanc, F., & Duffau, H. (2007). Contrasting acute and slow-growing lesions: A new door to brain plasticity. *Brain: A Journal of Neurology, 130*(Pt 4), 898–914.
Duffau, H. (2007). Contribution of cortical and subcortical electrostimulation in brain glioma surgery: Methodological and functional considerations. *Neurophysiologie Clinique = Clinical Neurophysiology, 37*(6), 373–382.
Duffau, H., Capelle, L., Sichez, N., Denvil, D., Lopes, M., Sichez, J.-P., et al. (2002). Intraoperative mapping of the subcortical language pathways using direct stimulations. An anatomo-functional study. *Brain: A Journal of Neurology, 125*(Pt 1), 199–214.
Ford, A., McGregor, K. M., Case, K., Crosson, B., & White, K. D. (2010). Structural connectivity of Broca's area and medial frontal cortex. *NeuroImage, 52*(4), 1230–1237.
Fried, I., Katz, A., McCarthy, G., Sass, K. J., Williamson, P., Spencer, S. S., et al. (1991). Functional organization of human supplementary motor cortex studied by electrical stimulation. *The Journal of Neuroscience. The Official Journal of the Society for Neuroscience, 11*(11), 3656–3666.
Friederici, A. D., & Kotz, S. A. (2003). The brain basis of syntactic processes: Functional imaging and lesion studies. *NeuroImage, 20*(Suppl 1), S8–S17.
Gabarrós, A., Martino, J., Juncadella, M., Plans, G., Pujol, R., Deus, J., et al. (2011). [Intraoperative identification of the supplementary motor area in neurooncological surgery]. *Neurocirugía (Asturias, Spain), 22*(2), 123–132.
Goodglass, H., & Kaplan, E. (1983). *The assessment of aphasia and related disorders*. Philadelphia: Lea & Febiger.
Grodzinsky, Y., & Santi, A. (2008). The battle for Broca's region. *Trends in Cognitive Sciences, 12*(12), 474–480.
Havas, V., Gabarrós, A., Juncadella, M., Plans G., Acebes, J. J., de Diego-Balaguer, R. Electrical stimulation mapping of nouns and verbs in Broca's area. *Brain and Language* (in press).
Heim, S., Opitz, B., & Friederici, A. (2003). Distributed cortical networks for syntax processing: Broca's area as the common denominator. *Brain and Language, 85*(3), 402–408.
Hickok, G., & Poeppel, D. (2007). The cortical organization of speech processing. *Nature Reviews. Neuroscience, 8*(5), 393–402.
Hogan, A. M., Vargha-Khadem, F., Saunders, D. E., Kirkham, F. J., & Baldeweg, T. (2006). Impact of frontal white matter lesions on performance monitoring: ERP evidence for cortical disconnection. *Brain: A Journal of Neurology, 129*(Pt 8), 2177–2188.
Howard, D. P. K. (1992). *The pyramids and palm trees test. A test of semantic access from words and pictures*. Bury St. Edmunds, UK: Thames Valley Company.
Indefrey, P. (2011). The spatial and temporal signatures of word production components: A critical update. *Frontiers in Psychology, 2*, 25.
Indefrey, P., & Levelt, W. J. M. (2004). The spatial and temporal signatures of word production components. *Cognition, 92*(1–2), 101–144. http://dx.doi.org/10.1016/j.cognition.2002.06.001.
Jefferies, E., Patterson, K., Jones, R. W., & Lambon Ralph, M. A. (2009). Comprehension of concrete and abstract words in semantic dementia. *Neuropsychology, 23*, 492–499.

Kaplan, E., Goodglass, H., & Weintraub, S. (2001). *Boston naming test*. Philadelphia.: Lippincott, Williams, & Wilkins.
Kinoshita, M., de Champfleur, N. M., Deverdun, J., Moritz-Gasser, S., Herbet, G., & Duffau, H. (2014). Role of fronto-striatal tract and frontal aslant tract in movement and speech: An axonal mapping study. *Brain Structure and Function*, 1–14.
Krainik, A., Lehéricy, S., Duffau, H., Capelle, L., Chainay, H., Cornu, P., et al. (2003). Postoperative speech disorder after medial frontal surgery: Role of the supplementary motor area. *Neurology, 60*(4), 587–594.
Kronfeld-Duenias, V., Amir, O., Ezrati-Vinacour, R., Civier, O., & Ben-Shachar, M. (2014). The frontal aslant tract underlies speech fluency in persistent developmental stuttering. *Brain Structure and Function*, 1–17.
Laplane, D., Talairach, J., Meininger, V., Bancaud, J., & Orgogozo, J. M. (1977). Clinical consequences of corticectomies involving the supplementary motor area in man. *Journal of the Neurological Sciences, 34*(3), 301–314.
Lawes, I. N. C., Barrick, T. R., Murugam, V., Spierings, N., Evans, D. R., Song, M., et al. (2008). Atlas-based segmentation of white matter tracts of the human brain using diffusion tensor tractography and comparison with classical dissection. *NeuroImage, 39*(1), 62–79.
Lichtheim, L. (1885). Ueber Aphasie. Aus der medicinischen Klinik in Bern. *Deutsches Archiv für klinische Medicin, 36*, 204–268.
López-Barroso, D., Catani, M., Ripollés, P., Dell'acqua, F., Rodríguez-Fornells, A., & de Diego-Balaguer, R. (2013). Word learning is mediated by the left arcuate fasciculus. *Proceedings of the National Academy of Sciences of the United States of America, 110*(32), 13168–13173.
Lucas, T. H., 2nd, Drane, D. L., Dodrill, C. B., & Ojemann, G. A. (2008). Language reorganization in aphasics: An electrical stimulation mapping investigation. *Neurosurgery, 63*(3), 487–497.
Mandelli, M. L., Caverzasi, E., Binney, R. J., Henry, M. L., Lobach, I., Block, N., et al. (2014). Frontal white matter tracts sustaining speech production in primary progressive aphasia. *The Journal of Neuroscience. The Official Journal of the Society for Neuroscience, 34*(29), 9754–9767.
Marangolo, P., Incoccia, C., Pizzamiglio, L., Sabatini, U., Castriota-Scanderbeg, A., & Burani, C. (2003). The right hemisphere involvement in the processing of morphologically derived words. *Journal of Cognitive Neuroscience, 15*(3), 364–371.
Marangolo, P., & Piras, F. (2008). Dissociations in processing derivational morphology: The right basal ganglia involvement. *Neuropsychologia, 46*(1), 196–205.
Marangolo, P., Piras, F., Galati, G., & Burani, C. (2006). Functional anatomy of derivational morphology. *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior, 42*(8), 1093–1106.
Marslen-Wilson, W. D., & Tyler, L. K. (1997). Dissociating types of mental computation. *Nature, 387*(6633), 592–594.
Martino, J., de Lucas, E. M., Ibáñez-Plágaro, F. J., Valle-Folgueral, J. M., & Vázquez-Barquero, A. (2012). Foix-Chavany-Marie syndrome caused by a disconnection between the right pars opercularis of the inferior frontal gyrus and the supplementary motor area. *Journal of Neurosurgery, 117*(5), 844–850.
Martino, J., Gabarrós, A., Deus, J., Juncadella, M., Acebes, J. J., Torres, A., et al. (2011). Intrasurgical mapping of complex motor function in the superior frontal gyrus. *Neuroscience, 179*, 131–142. http://dx.doi.org/10.1016/j.neuroscience.2011.01.047.
Mestres-Missé, A., Rodriguez-Fornells, A., & Münte, T. F. (2010). Neural differences in the mapping of verb and noun concepts onto novel words. *NeuroImage, 49*(3), 2826–2835.
Miozzo, M. (2003). On the processing of regular and irregular forms of verbs and nouns: Evidence from neuropsychology. *Cognition, 87*(2), 101–127.
Miozzo, M., Fischer-Baum, S., & Postman, J. (2010). A selective deficit for inflection production. *Neuropsychologia, 48*(9), 2427–2436.
Naeser, M. A., Palumbo, C. L., Helm-Estabrooks, N., Stiassny-Eder, D., & Albert, M. L. (1989). Severe nonfluency in aphasia. Role of the medial subcallosal fasciculus and other white matter pathways in recovery of spontaneous speech. *Brain: A Journal of Neurology, 112*(Pt 1), 1–38.
Novick, J. M., Trueswell, J. C., & Thompson-Schill, S. L. (2005). Cognitive control and parsing: Reexamining the role of Broca's area in sentence comprehension. *Cognitive, Affective and Behavioral Neuroscience, 5*(3), 263–281.
Oishi, K., Zilles, K., Amunts, K., Faria, A., Jiang, H., Li, X., et al. (2008). Human brain white matter atlas: Identification and assignment of common anatomical structures in superficial white matter. *NeuroImage, 43*(3), 447–457.
Ojemann, G., Ojemann, J., Lettich, E., & Berger, M. (2008). Cortical language localization in left, dominant hemisphere. An electrical stimulation mapping investigation in 117 patients. 1989. *Journal of Neurosurgery, 108*(2), 411–421. http://dx.doi.org/10.3171/JNS/2008/108/2/0411.
Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia, 9*, 97–113.
Pai, M. C. (1999). Supplementary motor area aphasia: A case report. *Clinical Neurology and Neurosurgery, 101*(1), 29–32.
Pena-Casanova, J. (2004). *Programa Integrado de Exploración Neuropsicológica: Test Barcelona Revisado TBR*. Barcelona, Spain: Masson.
Pinker, S., & Ullman, M. T. (2002). The past and future of the past tense. *Trends in Cognitive Sciences, 6*(11), 456–463.
Rauschecker, J. P. (2012). Ventral and dorsal streams in the evolution of speech and language. *Frontiers in Evolutionary Neuroscience, 4*, 7.
Ripolles, P., Marco-Pallarés, J., de Diego-Balaguer, R., Miró, J., Falip, M., Juncadella, M., et al. (2012). Analysis of automated methods for spatial normalization of lesioned brains. *NeuroImage, 60*(2), 1296–1306.
Rorden, C., & Brett, M. (2000). Stereotaxic display of brain lesions. *Behavioural Neurology, 12*(4), 191–200.
Roux, F.-E., Lubrano, V., Lauwers-Cances, V., Trémoulet, M., Mascott, C. R., & Démonet, J.-F. (2004). Intra-operative mapping of cortical areas involved in reading in mono- and bilingual patients. *Brain: A Journal of Neurology, 127*(Pt 8), 1796–1810.
Saur, D., Schelter, B., Schnell, S., Kratochvil, D., Küpper, H., Kellmeyer, P., et al. (2010). Combining functional and anatomical connectivity reveals brain networks for auditory language comprehension. *NeuroImage, 49*(4), 3187–3197.
Schnur, T. T., Schwartz, M. F., Kimberg, D. Y., Hirshorn, E., Coslett, H. B., & Thompson-Schill, S. L. (2009). Localizing interference during naming: Convergent neuroimaging and neuropsychological evidence for the function of Broca's area. *Proceedings of the National Academy of Sciences of the United States of America, 106*(1), 322–327.
Shapiro, K., & Caramazza, A. (2003). Grammatical processing of nouns and verbs in left frontal cortex? *Neuropsychologia, 41*(9), 1189–1198.
Shapiro, K. A., Mottaghy, F. M., Schiller, N. O., Poeppel, T. D., Flüß, M. O., Müller, H.-W., et al. (2005). Dissociating neural correlates for nouns and verbs. *NeuroImage, 24*(4), 1058–1067.
Sierpowska, J., Gabarrós, A., Ripollés, P., Juncadella, M., Castañer, S., Camins, Á., et al. (2013). Intraoperative electrical stimulation of language switching in two bilingual patients. *Neuropsychologia, 51*(13), 2882–2892.
Smith, S. M., Jenkinson, M., Woolrich, M. W., Beckmann, C. F., Behrens, T. E. J., Johansen-Berg, H., et al. (2004). Advances in functional and structural MR image analysis and implementation as FSL. *NeuroImage, 23*(Suppl 1), S208–S219.
Smith, S. M., Zhang, Y., Jenkinson, M., Chen, J., Matthews, P. M., Federico, A., et al. (2002). Accurate, robust, and automated longitudinal and cross-sectional brain change analysis. *NeuroImage, 17*(1), 479–489.
Thiebaut de Schotten, M., Dell'Acqua, F., Valabregue, R., & Catani, M. (2012). Monkey to human comparative anatomy of the frontal lobe association tracts. *Cortex; a Journal Devoted to the Study of the Nervous System and Behavior, 48*(1), 82–96.
Thompson-Schill, S. L., D'Esposito, M., Aguirre, G. K., & Farah, M. J. (1997). Role of left inferior prefrontal cortex in retrieval of semantic knowledge: A reevaluation. *Proceedings of the National Academy of Sciences of the United States of America, 94*(26), 14792–14797.
Tiffin, J., & Asher, E. J. (1948). The Purdue pegboard; norms and studies of reliability and validity. *Journal of Applied Psychology, 32*, 234–247.
Tuomiranta, L. M., Càmara, E., Froudist Walsh, S., Ripollés, P., Saunavaara, J. P., Parkkola, R., et al. (2014). Hidden word learning capacity through orthography in aphasia. *Cortex, 50*, 174–191.
Ullman, M. T. (2004). Contributions of memory circuits to language: The declarative/procedural model. *Cognition, 92*(1–2), 231–270.
Ullman, M. T., Corkin, S., Coppola, M., Hickok, G., Growdon, J. H., Koroshetz, W. J., et al. (1997). A neural dissociation within language: Evidence that the Mental dictionary is part of declarative memory, and that grammatical rules are processed by the procedural system. *Journal of Cognitive Neuroscience, 9*(2), 266–276.
Vigliocco, G., Vinson, D. P., Druks, J., Barber, H., & Cappa, S. F. (2011). Nouns and verbs in the brain: A review of behavioural, electrophysiological, neuropsychological and imaging studies. *Neuroscience and Biobehavioral Reviews, 35*(3), 407–426.
Wechsler, D. (1997). *Wechsler Adult Intelligence Scale – Third Edition (WAIS-III): Administration and scoring manual*. San Antonio, TX, USA: The Psychological Corp.
Weiller, C., Bormann, T., Saur, D., Musso, M., & Rijntjes, M. (2011). How the ventral pathway got lost: And what its recovery might mean. *Brain and Language, 118*(1–2), 29–39.
Wernicke, C. (1874). *Der aphasiche Symptomenkomplex*. Breslau: Cohn und Weigert.
Willms, J. L., Shapiro, K. A., Peelen, M. V., Pajtas, P. E., Costa, A., Moo, L. R., et al. (2011). Language-invariant verb processing regions in Spanish–English bilinguals. *NeuroImage, 57*(1), 251–261.
Woolrich, M. W., Jbabdi, S., Patenaude, B., Chappell, M., Makni, S., Behrens, T., et al. (2009). Bayesian analysis of neuroimaging data in FSL. *NeuroImage, 45*(1 Suppl), S173–186.
Yogarajah, M., Focke, N. K., Bonelli, S. B., Thompson, P., Vollmar, C., McEvoy, A. W., et al. (2010). The structural plasticity of white matter networks following anterior temporal lobe resection. *Brain: A Journal of Neurology, 133*(Pt 8), 2348–2364.
Yokoyama, S., Miyamoto, T., Riera, J., Kim, J., Akitsuki, Y., Iwata, K., et al. (2006). Cortical mechanisms involved in the processing of verbs: An fMRI study. *Journal of Cognitive Neuroscience, 18*(8), 1304–1313.
Yu, C., Shu, N., Li, J., Qin, W., Jiang, T., & Li, K. (2007). Plasticity of the corticospinal tract in early blindness revealed by quantitative analysis of fractional anisotropy based on diffusion tensor tractography. *NeuroImage, 36*(2), 411–417.