Semantic Interference and Its Control: A Functional Neuroimaging and Connectivity Study

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Abstract: During picture naming, the ease with which humans generate words is dependent upon the context in which they are named. For instances, naming previously presented items results in facilitation. Instead, naming a picture semantically related to previous items displays persistent interference effects (i.e., cumulative semantic interference, CSI). The neural correlates of CSI are still unclear and it is a matter of debate whether semantic control, or cognitive control more in general, is necessary for the resolution of CSI. We carried out an event-related fMRI experiment to assess the neural underpinnings of the CSI effect and the involvement and nature of semantic control. Both left inferior frontal gyrus (LIFG) and the left caudate nucleus (LCN) showed a linear increase of BOLD response positively associated with the consecutive number of presentations of semantically related pictures independently of task-load. The generalized psychophysiological interaction analysis showed that LIFG demonstrated a quantitative neural connectivity difference with the left supramarginal and angular gyri for increases of task-load and with the fusiform gyri for linear CSI increases. Furthermore, seed-to-voxel functional connectivity showed that LIFG activity coupled with different regions involved in cognitive control and lexicosemantic processing when semantic interference was elicited to a minimum or maximum degree. Our results are consistent with the lexical-competitive nature of the CSI effect, and we provide novel evidence that semantic control lies upon a more general cognitive control network (i.e., LIFG and LCN) responsible for resolving interference between competing semantically related items through connectivity with different brain areas in order to guarantee the correct response. *Hum Brain Mapp 37:4179–4196, 2016.* © 2016 Wiley Periodicals, Inc.

Key words: cognitive control; cumulative semantic interference; fMRI; semantic control

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INTRODUCTION

A crucial phenomenon for constraining models of speech production is the semantic interference (SI) effect in object naming. This phenomenon concerns the relative slowing of naming latencies for target pictures presented in the context of semantically (categorical) related information compared to unrelated information (e.g., Brown, 1981; Costa et al., 2005; Damian and Bowers, 2003; Glaser and Glaser, 1989; Howard et al., 2006; Levelt et al., 1991; Schriefers et al., 1990). For example, when naming the picture of a "DOG," reaction times will be slower when the primed context concerns categorically related items such as "CAT" compared to unrelated items such as "HAT." At the very least, SI indicates that in the course of speech planning when the intended words for production are prepared, also closely related semantic knowledge becomes activated in the system (e.g., Caramazza and Miozzo, 1997; Dell, 1986; Goldrick and Blumstein, 2006; Levelt, 1999).

Howard et al. (2006) introduced a paradigm demonstrating the presence of SI also during object naming when speakers were presented with a stream of pictures belonging to various semantic categories. Crucially, Howard et al. (2006) manipulated the ordinal position in which items of the same semantic category appeared in the stream of object naming, which were interspersed by a lag from 2 to 8 unrelated items (e.g., pliers, saw, and hammer). The authors observed that naming latencies increased about 20 ms in a cumulative and linear fashion in function of ordinal position. The more semantically related items the speaker previously uttered, the slower the naming latencies for a subsequent item of the same semantic category (see also Alario and del Prado Martin, 2010; Runnqvist and Costa, 2012). The authors suggested that the cognitive mechanism responsible for SI stems from three different components, a shared activation of semantically related items, a priming effect and a competition mechanism arising between representations of the target picture and those previously accessed for producing the name of a semantically related object. In other words, the production of a given item (DOG) would strengthen its lexical representation hereby becoming stronger coactivated when a semantically related item has to be named later on (CAT), inflicting stronger interference and slowing down the lexical selection process.

These results provided evidence for a long lasting and cumulative[1] lexical competition between semantically related items during language production. However, the precise nature of the mechanism behind this effect is largely unknown (Damian et al., 2001; Vitkovitch et al., 2001) and the level at which this potential competition occurs (i.e., semantic and lexical) still remains to be fully detailed.

[1]This competition is "cumulative" in the sense that the more semantically related items one has named the higher the total amount of competition within the lexical system for a subsequent item will be.

As previously hinted, in fact, competition can arise between semantic representations prior to lexical selection (e.g., Navarrete et al., 2010) or by the reactivation of lexical items of the same semantic category that have been selected previously and can be resolved by suppression of activation of any potential representation other than the target or by increasing levels of activation of the target itself (e.g., Howard et al., 2006). In the attempt to elucidate the level at which SI occurs, Costa et al. (2009) for instance found that with each ordinal position the ERP amplitudes were more positive between roughly 200 and 380 ms after picture onset. Given the time course and especially the ERP morphology elicited by the CSI, which has been linked to processes involved in lexical processing (e.g., Strijkers et al., 2009, 2011), the authors also concluded that this phenomenon could highlight lexical competition.

Notwithstanding the nature of competition or the level at which SI occurs in the language production system, lexical selection invokes the intervention of some sort of control to successfully resolve the competition or retrieval interference from the categorically related item previously named. In other words, cognitive control mechanisms are likely to be at play in the process of resolving competition between representations at any level of processing. Hence, to the extent that semantic overlap between representations increases competition between them, we may hypothesize that the more information overlaps, the higher is the demand for cognitive control in order to single out on the intended item.

In terms of neural activations and connectivity, these effects should be observable in some of the regions of the cognitive control network. Both cortical and subcortical brain structures are responsible to different degrees for specific cognitive control subprocesses ranging from conflict monitoring, competition resolution and response selection, all necessary in order to fulfill task objectives. Neuroimaging evidence has identified the anterior cingulate, the caudate nucleus and lateral prefrontal areas, such as the dorsolateral and inferior frontal cortex (Badre and Wagner, 2004; Carter et al., 1998; Wagner et al., 2001a) as the crucial neural components of this network responsible for subtending more general cognitive control processes.

The inhibitory or excitatory control mechanisms hypothesized to underlie lexicosemantic control processes seem to be at least partially mediated by this same network of areas. Specifically, the left inferior frontal gyrus (LIFG) seems to be linked to the selection or retrieval of semantic information in tasks involving significant executive control demands (Noonan et al., 2013; Whitney et al., 2012). Namely, an increase in activity has been observed in the LIFG when weak associations need to be inferred between words or the number of viable responses raises, paralleled with the amount of competition among potential target items (Badre et al., 2005; Thompson-Schill et al., 1997). The amount of activity in LIFG is also positively associated with increases in naming latencies induced by semantic

blocking or semantically related manipulations (Moss et al., 2005; Schnur et al., 2009). In accord with these findings, some neuropsychological evidence highlights the crucial role of the LIFG in processes related to SI. For example, Schnur et al. (2006) employed a cyclical naming task and demonstrated that semantic blocking affected the performance of Broca's aphasics more than non-Broca's controls, and that this effect increased with repetition of the blocked sets. These results are in accord with the findings from other studies that examined the performance of patients with lesions of LIFG and compared it to that of other patients with temporoparietal lesions supporting the conclusion that LIFG plays a key role in semantic selection as well as lexical retrieval (e.g., Jefferies et al., 2007; Noonan et al., 2010; see also Jefferies and Ralph, 2006).

Our hypothesis moves from the assumption that if competition is at the basis of the semantic inhibition effect in a picture naming task where exemplars of the same semantic category are present, a sort of control may be required to resolve competition. The need for control is not effortless, and a cost in both cognitive and neural terms may arise; the former translates in terms of a linear increase in reaction times (Costa et al., 2009; Howard et al., 2006), and the latter may reside in one or some of the brain areas responsible for lexicosemantic control (such as LIFG) or cognitive control in general (such as in a more distributed network comprising not only the LIFG but also the caudate and the Anterior Cingulate Cortex (ACC).

The current study aims at bringing forward novel evidence concerning the cerebral underpinnings of SI and hereby contributing to our understanding concerning the enactment of lexicosemantic control mechanisms to resolve SI through specific brain regions or areas more generally involved in cognitive control. Furthermore, we investigate also potential changes in the pattern of brain connectivity elicited between LIFG and other brain areas underlying both lexicosemantic processing and cognitive control mechanisms as a function of the degree of SI. This could elucidate both the nature and the level at which control acts out to resolve SI.

To this aim we implemented the same material and experimental paradigm used in Howard et al. (2006) in an event-related fMRI (er-fMRI) experiment in order to unravel the neural underpinnings of the SI effect, in terms of lexicosemantic control.

MATERIALS AND METHODS

Subjects

Twenty-four healthy right-handed subjects (14 males and 10 females; mean age 21.61 years, standard deviation [SD] ±2.44, age range 18–26 years) were enrolled among undergraduate students of the San Raffaele University in Milan.

All subjects were native Italian speakers, had no history of neurological or psychiatric disorder, and had normal (or corrected-to-normal) vision and hearing. All participants fulfilled a written consent form to participate in this study, which was approved by the Ethics Committee of the San Raffaele Scientific Institute and performed in accordance with the Declaration of Helsinki II.

Stimuli and Design

The experimental material and design have been adapted from Howard et al. (2006). One hundred sixty-five different pictures, consisting of 120 experimental pictures (five exemplars for each of 24 semantic categories) (Alario and del Prado Martin, 2010; Costa et al., 2009) and 45 fillers, were used (see Appendix) to create each list. Twenty-four experimental lists were created with the constraints that no experimental picture could appear in the first five positions (practice), and experimental pictures from the same category were randomly separated by a lag of at least two and maximum eight items. Intervening items could either be fillers (25%) or experimental pictures from other semantic categories (75%). A latin square was built in order to fully rotate semantic categories on lags combinations, so that across participants, items of each semantic category appeared once in each of the possible 24 (4!) orderings (namely 2-4-6-8, 2-4-8-6, 2-6-4-8, 2-8-6-4, 2-6-8-4, 4-2-6-8, 8-2-4-6, 4-2-8-6, 6-2-4-8, 4-6-2-8, 4-8-2-6, 4-6-8-2, 8-2-6-4, 6-2-8-4, 2-8-4-6, 6-4-8-2, 6-4-2-8, 6-8-2-4, 8-4-2-6, 4-8-6-2, 8-6-2-4, 8-6-4-2, 6-8-4-2, and 8-4-6-2). There were three main differences with respect to Howard et al.'s (2006) design: (1) We used black and white line drawings (instead of colored pictures). (2) Items within a category were semirandomized to control for physical differences between stimuli. (3) Each participant was presented with two different experimental lists to ensure sufficient statistical power to the er-fMRI paradigm. Each experimental trial consisted of a picture displayed at the center of the screen for 1,217 ms and ISI (interstimulus interval) was jittered (from 1,175 to 2,759 ms; mean 1,975 ms) according to Dale (1999). An asterisk was presented for 500 ms before the first trial and after the last trial to signal the beginning and end of each list.

Participants underwent two consecutive experimental er-fMRI sessions, separated by an interval ranging between 3 and 5 minutes. A total of 330 to-be-named pictures ((120 experimental pictures + 45 fillers) × 2 sessions) were presented. The total scan time for each subject was about 40 minutes.

Procedure

Pictures were presented to participants via a PC placed outside the magnet room equipped with Presentation software (http://www.neurobs.com/menu_presentation). A projector delivered stimuli on a translucent screen placed at the foot of the magnet bore. Participants viewed the screen through a mirror system attached to the top of the

head coil. All participants underwent a training session on a different set of pictures in order to familiarize them with the task and the timing of each experimental session. After positioning in the scanner, participants were asked to speak into a plastic tube attached to the head coil and were trained to minimize jaw and tongue movements in order to reduce movement artifacts while naming. A small microphone connected to the PC was used to record naming responses. The implementation of a fairly short ISI in the present experiment was intended to cope with the fMRI artifacts produced by naming, although did not allow for the collection of voice onset times given that each participant was required not to speak aloud enough to tease apart voice onsets for each item from scanner noise in order not to mask BOLD responses modeled at stimulus onset (Birn et al., 2004).

However, in order to relate brain activity and a behavioral correlate of the CSI effect in the absence of latency measures, we have collected a naming agreement measure of accuracy. According to Howard et al. (2006), the more semantically related items the speaker previously uttered, the slower the naming latencies for a subsequent item of the same semantic category. Therefore, if stronger interference slows down the lexical selection process, the CSI effect may plausibly translate into a cost also in terms of accuracy in the sense that cumulative interference can result in more error-prone naming performance, which in turn can request more cognitive control to avoid performance to drop below critical levels and remain in alignment with task goals.

Participants' accuracy scores were successively analyzed to explore the: (1) cumulative SI effects also on the accuracy of the response for successive category-repetition trials and (2) the relationship of the BOLD estimate of the linear increase in CSI with accuracy scores at each category repetition step.

Figure 1.
Patterns of activation for pictures (light blue) and fillers (yellow) and common patterns between these two different experimental conditions (green) superimposed on the mid axial slice of mean anatomical image of all subjects (n = 24 subjects). The red square (top left) highlights the cluster (shown in sagittal view) peaking in LIFG at the borders with insula only for pictures. All activations are thresholded at $P < 0.05$ with FWE correction at the voxel level with a minimum cluster extent of 10 voxels. [Color figure can be viewed at wileyonlinelibrary.com]

Image Acquisition

Image acquisition was performed using a 3 T Intera Philips body scanner (Philips Medical Systems, Best, NL) equipped with an eight channels-sense head coil. Functional scans were acquired using an echo planar imaging (EPI) fMRI event-related scanning sequence (sense reduction factor = 2, Time of Acquisition (TA) = 1,933 ms, Time of Repetition (TR) = 2,000 ms, Echo Time (TE) = 30 ms, FOV = 240 × 120 × 240, matrix size 128 × 128). Thirty contiguous axial slices were acquired for each volume (slice thickness = 4 mm) and 282 volumes for each run. In order to optimize signal, each run was preceded by 10 dummy scans, which were discarded prior to analysis.

For structural imaging, an axial high-resolution structural MRI scan was obtained for all subjects (magnetization prepared rapid gradient echo, 150 slice T1-weighted image, TR = 8.04 ms, TE = 4.1 ms; flip angle 8°, TA = 4.8 minutes, resolution = 1 mm × 1 × 1 mm). An EPI-based field map was also acquired with the same parameters as those set for the functional scans in order to correct for field inhomogeneities during image preprocessing of EPI volumes. A temporal signal-to-noise ratio (tSNR) average map showing EPI image quality over the whole brain is displayed in Figure S1. Subject tSNR maps were obtained by dividing the mean of each voxel time-course by its temporal standard deviation after motion correction, smoothing, and temporal filtering.

Image Preprocessing

Data were preprocessed using SPM8 v4290 (Statistical Parametric Mapping; Wellcome Department of Cognitive Neurology, London, UK), running on Matlab R2008 a (Mathworks, Natick, MA).

Time series diagnostics were ran using tsdiffana (Matthew Brett, MRC CBU, http://imaging.mrc-cbu.cam.ac.uk/imaging/DataDiagnostics) to inspect quality of the functional data. Variance of corresponding voxels from image to image, from slice to slice and mean number of voxels per image were analyzed relatively to their own mean values. No data were discarded due to excessive motion

and/or noise, leaving 24 subjects. Origin was manually set for both structural-T1 and functional-T2 volumes to match the AC-PC line: this was done in order to maximize sharpness of the following coregistration (and further steps) and avoid spatial mismatch due to excessive coordinates' distance.

Since functional volumes were acquired using interleaved acquisition, slice-timing correction was carried out on all EPIs to correct for different sampling times: this was done by resampling the time series to a reference slice (the 15th, i.e., the middle one on a total of 30) using a sinc interpolation procedure.

Due to the intrinsic nature of the task (overt responses) which implies subject's head's movement, we performed a sharp work of noise removal throughout preprocessing: first of all, before coregistration, we used the "art repair: repair bad slices" tool (Mazaika et al., 2009) to inspect the average intensity and scan to scan motion of fMRI data and repaired (by interpolation between the nearest non-repaired scans) any scan whose global intensity was different from the mean, or whose scan-to-scan motion was large, that is, outliers scans (defined as scans showing 1.3% variation in global intensity, 0.5 mm/TR scan-to-scan motion) using an automatically generated mask. Motion correction was carried out using rigid body transformations to realign each subject's EPIs to the first volume in the time series and then to their mean functional image (generated during this process). EPIs were then unwarped by applying a voxel displacement map (VDM) reconstructed from EPI-based field maps scans, in order to control for susceptibility-by-movement's generated variance in the time series. For two subjects signal distortion was estimated by applying "derivative fields" (estimated using an unwarping procedure), given that VDMs were not available due to scanner failure during the reconstruction of the field map scans. Residual interpolation errors after realignment were removed on resliced images using art repair's reduce realignment residuals tool (Grootoonk et al., 2000; Mazaika et al., 2009), which removes variations on edge and nonedge voxels. Each subject's T1-high definition structural image was then coregistered to its corresponding mean functional image and then segmented to generate normalization parameters. These spatial transformations parameters were then applied to all the realigned functional volumes to warp them into the standardized MNI space. Finally, normalized EPI volumes were smoothed using a Gaussian kernel with a 6-mm full-width at half-maximum, in order to account for any between-subject residual variations and thus allowing group statistical inference.

Functional Data Analysis

Functional data were analyzed using SPM8, adopting a two-stage random-effects model. At the single-subject level a "parametrical" model was specified including two regressors (i.e., experimental pictures and fillers were modeled separately) and six parametric modulators associated to the regressor coding pictures specified in the following order: (1) a "no category" modulator (nCm) coding only the sequence and repetition order of pictures independently from their category membership; (2) a "category" modulator (Cm) coding the sequence, repetition order and category membership of pictures; (3) four modulators coding respectively repetition intervals occurring with lag 2, lag 4, lag 6, and lag 8, meaning the number of pictures occurring between two pictures belonging to the same category.

The "no category" repetition parametric modulator was created in order to account for the incremental nature of the "category" repetition modulator in a symmetrical fashion, meaning that it codes repetitions of pictures in the same sequence and with the same lags as the "category" repetition regressor with the only difference that the pictures occurring in specific repetition positions belonged to different categories. It was included in the regression model before the category repetition regressor in order to capture any variance due to an incremental or task load effect only and tease it apart from any possible lexicosemantic effect exclusively linked to category repetition.

We computed a total of four contrasts coding (1) the positive linear effect of naming object members of the predefined 24 semantic categories (i.e., experimental pictures), (2) the positive linear effect of naming pictures, which do not belong to any of the predefined categories (i.e., fillers), (3) the positive linear increase effect on BOLD signal of the "no category" modulator, and (4) the positive linear effect on BOLD signal of the category repetition modulator. All effects were modeled by convolving a delta function of each event type with the hemodynamic response function. Contrast images for each of the four individual effects of all subjects were then entered into a second-level random effects group analysis (one sample *t*-test).

Activations pertaining to both the "experimental pictures" and "fillers" effect were deemed significant if they reached a statistical threshold of 0.05 FWE-corrected at the voxel level and a minimum cluster extent of 10 voxels in order to verify activity in areas recruited by picture naming and extensively described in the literature as involved in the naming network (Démonet et al., 2005; Price et al., 2005, 1996).

However, in order to investigate more subtle effects on BOLD signal, either task-related or semantic in nature, as those possibly induced by repetition, sequence order, and category membership of the pictures we used a more lenient threshold ($P < 0.005$ at the voxel level, with a minimum cluster extent of $k = 10$ voxels) given that when investigating semantic effects there is a high probability of incurring in type II (false negative) errors, when using a very conservative threshold (i.e., FWE-corrected) (de Zubicaray et al., 2006).

Functional Connectivity Analysis

In order to address the specific role of the LIFG, that is, in terms of retrieval of semantic information or lexical selection in situations which pose control demands (Badre

et al., 2005; Thompson-Schill et al., 1997; Thompson-Schill and Botvinick, 2006; Whitney et al., 2012), and to reveal which LIFG-related network increases its connectivity as the SI builds up, in terms of areas which linearly increase their connectivity to LIFG over and above what can be accounted for from the first presentation of category-member pictures, we conducted psychophysiological interaction (PPI) analyses.

We used a functional region of interest (ROI) for LIFG based on the region that showed significant activation with specific coordinates based on the group-analysis results of the "parametrical" general linear model.

The generalized PPI (gPPI) toolbox (http://www.nitrc.org/projects/gppi; McLaren et al., 2012) in SPM8 (Statistical Parametric Mapping, Wellcome Department of Cognitive Neurology) was used for connectivity analysis, given that gPPI has the flexibility to accommodate multiple task conditions and specifically the nC and the C parametric modulators in the same connectivity model.

Specifically, the gPPI toolbox was used to (1) extract the deconvolved times series from the LIFG ROI for each participant to create the physiological variables; (2) convolve each trial type and parametric modulators with the canonical HRF, creating the psychological regressor; and (3) multiply the time series from the psychological regressors with the physiological variable to create the PPI term. This interaction term identified regions that covaried in a task-dependent manner with the LIFG. For each participant, one regressor representing the deconvolved BOLD signal was included alongside each psychological and PPI term for each event type to create a gPPI model.

A whole-brain analysis (single-subject level) was then performed using the general linear model in SPM8 and two PPI contrasts were created: (1) nCm-positive linear increase and (2) Cm-positive linear increase identifying functional connectivity increases of the LIFG with other regions in the brain as (1) the task load effect increases and (2) the SI builds up. These individual PPI contrast images were entered into a random effects one-sample *t*-test to test for group effects of the two contrasts. Connectivity analyses were also thresholded at voxelwise $P < 0.005$ (cluster threshold of $k = 10$).

RESULTS

Accuracy Analysis

Naming accuracy and agreement were assessed in the whole sample ($n = 24$ subjects). Overall naming accuracy was 91.63% (i.e., 90.1% for experimental pictures and 93.2% for fillers). Agreement values for all items closely overlapped with those reported by normative data on the same set of pictures in Italian (Nisi et al., 2000) (Pearson's $r = 0.70$, $P < 0.001$ for pictures and $r = 0.820$, $P < 0.001$ for fillers).

In order to assess cumulative SI (CSI) effects in terms of possible accuracy differences between successive category repetitions, a within-subjects ANOVA on accuracy scores for each category repetition has been conducted. The analysis revealed a main effect of repetition ($F = 2.66$; $P = 0.043$), and post hoc paired *t*-tests revealed that the third category repetition (i.e., rep3) (mean = 0.898) showed significant lower accuracy scores for each subject as compared only to the first presentation (i.e., rep0) (mean = 0.934; $t = -3.63$; $P = 0.003$) and the last repetition (i.e., rep4) (mean = 0.929; $t = -2.86$; $P = 0.013$).

The Picture Naming Network

Both "experimental pictures" and "fillers" elicited activity in a network of areas known to be involved in picture naming, including occipital and temporal regions bilaterally and the left prefrontal cortex (see Table I for detailed activations). When superimposing statistical T-maps for pictures and fillers (as shown in Fig. 1), the LIFG was found to be activated exclusively for pictures but not for fillers (see magnified area in Fig. 1).

"No Category" and "Category" Repetition

The one-sample *t*-test of the category modulator revealed a linear semantic-dependent modulation of signal intensity in the LIFG (*pars triangularis*, area 45)—extending to the insula (peak coordinates: $x = -28$, $y = 42$, $z = 10$; $k = 45$ voxels) and in the head of left caudate nucleus (LCN) (peak coordinates: $x = -14$, $y = 6$, $z = 18$; $k = 43$ voxels) (see Fig. 2). Importantly, no significant linear relationship was observed between the nCm and BOLD signal in any brain area.

Contrasts Plots

Given the association observed between the consecutive number of presentations ($n = 5$) of pictures exemplars of the same category (i.e., the first repetition corresponds to the second picture belonging to a same category until the fourth repetition, which corresponds to the fifth picture) and a linear increase in BOLD response for both LIFG and the LCN, we extracted and plotted the intensity values for each presentation (as coded by the Cm parametric modulator) from LIFG (at group level coordinates $x = -28$, $y = 42$, $z = 10$) and the LCN (at group level coordinates $x = -14$, $y = 6$, $z = 18$) for each of the 24 subjects and for both sessions.

Our aim was to verify if the linear semantic modulation isolated at the group level could be traced for BOLD activity in both areas (i.e., LIFG and LCN) for each single subject in order to verify if both the consistency and nature (i.e., linear) of the semantic effect of Cm can be observed in each subject beyond an average effect observed at the group level. Signal intensity values resulting from the

TABLE I. Significant peaks of activation for pictures (left panel) and fillers (right panel)

Pictures						Fillers					
	Coordinates						Coordinates				
Anatomical location	*x*	*y*	*z*	*Z*-value	Area	Anatomical location	*x*	*y*	*z*	*Z*-value	Area
L inf frontal gyrus	−34	30	2	5,201	45	L ant cingulate cortex	−6	20	26	5,519	24
L ant cingulate	−4	22	26	5,360	24	L mid cingulate cortex	−2	10	42	5,674	23
L SMA	−2	10	46	5,483	6	L SMA	−2	0	54	5,164	6
L postcentral gyrus	−52	−6	38	5,432	4	L postcentral gyrus	−50	−8	18	5,640	3
L postcentral gyrus	−62	0	14	5,449	4	L sup temp gyrus	−56	−2	−6	5,228	41
L temp pole	−46	12	−10	5,130	15	L mid temp gyr	−62	−14	−2	5,917	21
L mid temporal gyrus	−62	−16	−2	5,743	21	L mid temp gyr	−52	−18	−2	5,883	21
	−12	−22	−14	5,589		L hipp	−30	−20	−14	5,269	Hipp(CA)
L Cerebellum	−36	−50	−26	6,617		L hipp	−22	−30	−10	5,044	Hipp(Sub)
						L cerebellum	−10	−44	−22	6,217	Lobule I–IV
						L cerebellum	−36	−50	−26	6,485	Lobule VI
R postcentral gyrus	54	−6	34	5,733	4	R postcentral gyrus	52	−6	34	5,661	4
R temp pole	50	14	−10	5,123	15	R sup temp gyrus	58	−12	−2	5,562	41
R sup temp gyrus	56	−2	−6	5,066	41	R temp pole	50	12	−14	5,429	15
R sup temp gyrus	62	−14	−7	5,087	41	R inf occipital gyrus	34	−78	−6	5,032	17
R sup temp gyrus	52	−18	−2	4,939	41	R inf occipital gyrus	30	−88	−6	5,504	17
R cerebellum	28	−62	−26	6,632		R cerebellum	8	−40	28	5,793	Lobule I–IV
						R cerebellar vermis	2	−46	−10	5,769	Lobule I–IV
						R cerebellum	24	−50	−22	6,043	Lobule VI
						R cerebellum	30	−66	−26	6,434	Lobule VI

$P < 0.05$ (FWE-corrected at the voxel level), minimum cluster extent $k = 10$ voxels.

average of both fMRI sessions were then plotted by subject for Cm (see Fig. 3). As shown in the figure below, 15 out of 24 subjects (62.5%) showed an incremental pattern in the LIFG and 19 out of 24 (79.2%) in the LCN.

For this same purpose, a complementary analysis was carried out on first eigenvariate values extracted across voxels of each of the two areas in each subject (i.e., the weighted mean of the data where maximal signal is captured in each area as defined by a ROI), in order to test for differences between Cm and nCm parameter estimates by accounting for response heterogeneity in each of the two regions across modulators and subjects. First, two 6mm spherical ROIs were centered on LIFG ($x = -28$, $y = 42$, $z = 10$) and LCN ($x = -14$, $y = 6$, $z = 18$) peak group coordinates and the EasyROI utility (Pernet; http://www.sbirc.ed.ac.uk/cyril/Downloads.html) was used to extract first eigenvariate values from each of the two functional ROIs localized on contrast maps coding for Cm or

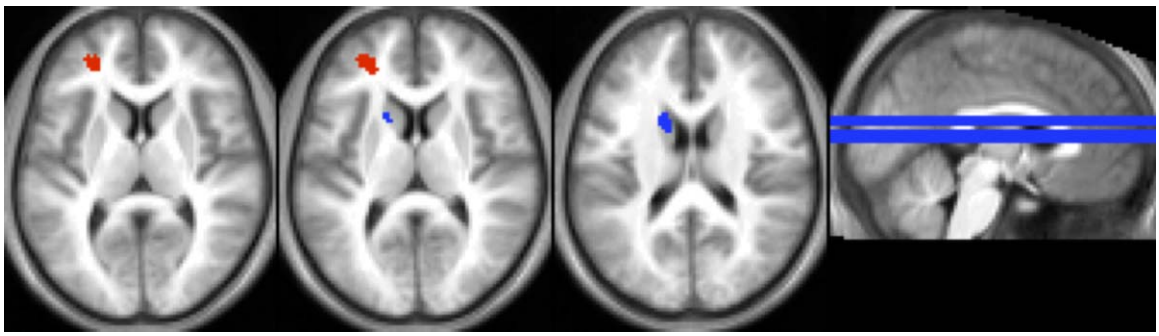

Figure 2.
BOLD semantic-dependent linear increase for the category repletion modulator in the LIFG (peak coordinates: $x = -28$, $y = 42$, $z = 10$) (red) and in the head of LCN (peak coordinates: $x = -14$, $y = 6$, $z = 18$) (blue). [Color figure can be viewed at wileyonlinelibrary.com]

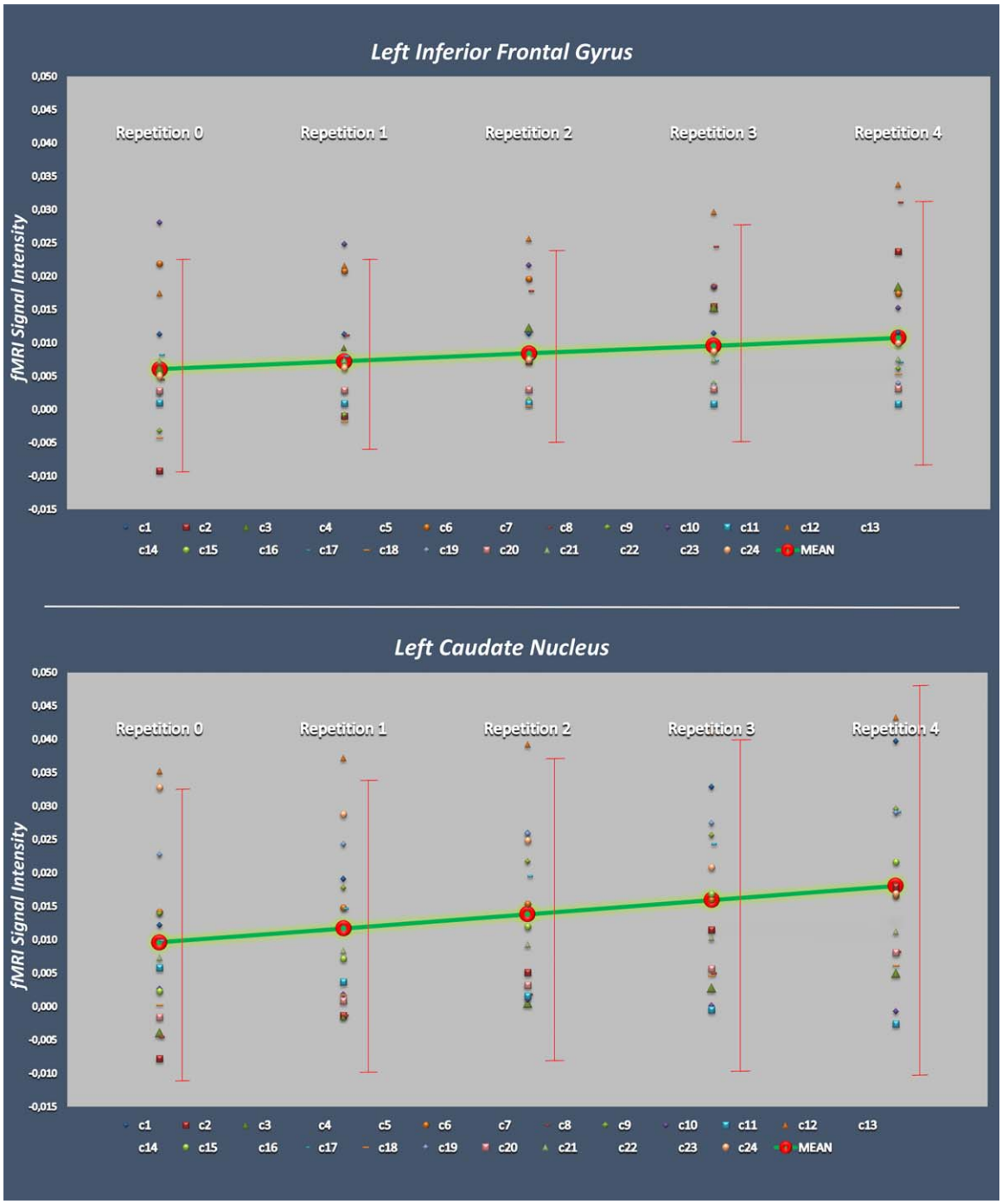

Figure 3.

Signal intensity values for each subject ($n = 24$) (y-axis, expressed as eigenvariate values) in LIFG (upper panel) and LCN (lower panel) peaks resulting from the average of both fMRI sessions plotted by the consecutive number of presentations of pictures belonging to the same semantic category, ranging from 1 to 5 (x-axis). For both areas, single subject's mean values are displayed (colored markers), along with the distribution's confidence interval (solid red lines). Mean group value ($n = 24$) (red void circles) is also displayed for each time point in the series, showing the activity trend (solid green line) across repetitions. [Color figure can be viewed at wileyonlinelibrary.com]

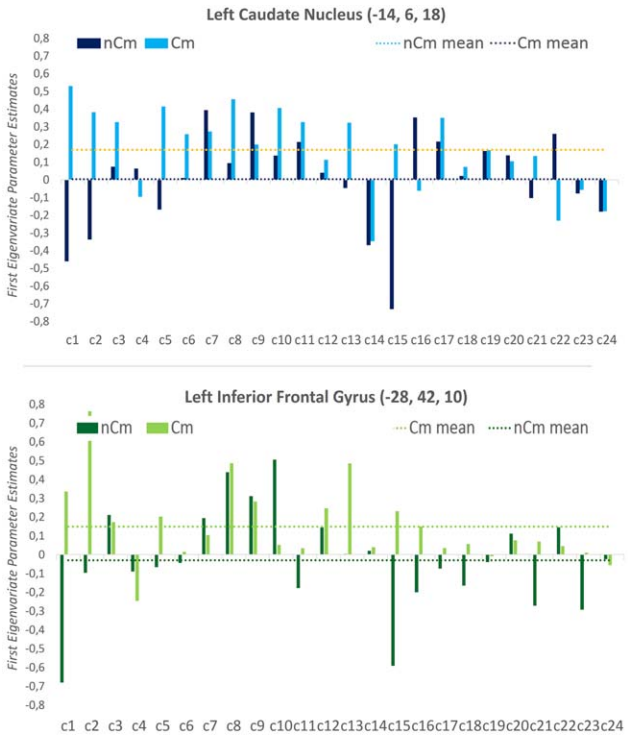

Figure 4.

Eigenvariate parameter estimates (*Y*-axis) for each subject (*X*-axis) extracted from LIFG (upper panel) and L caudate nucleus (lower panel). Light green and light blue lines indicate values extracted from the category parametric modulator (Cm) t-contrast map while dark green and dark blue lines indicate values extracted from the no category parametric modulator (nCm) t-map. [Color figure can be viewed at wileyonlinelibrary.com]

nCm BOLD increases. Extracted first eigenvariate values, which represent "typical" subject response over voxels in each region, were plotted for visual, subject-wise comparison of signal estimates and showed overall higher values for the Cm modulator (see Fig. 4). In addition, we performed a paired *t*-test between Cm and nCm values which revealed a significant difference between the BOLD signal increase induced by the two modulators in each of the two ROIs, marked by higher mean values in both LIFG ($P < 0.009$; mean eigenvariate value nCm: −0.030, mean eigenvariate value Cm: 0.149) and LCN ($P < 0.018$; mean eigenvariate value nCm: 0.004, mean eigenvariate value Cm: 0.170) ROIs.

Regression analysis on the average signal values (i.e., for both sessions) for all subjects confirmed a role of the ordinal position in linearly predicting both LIFG ($\beta = 0.202$, $P < 0.05$) and LCN ($\beta = 0.237$, $P < 0.01$) activity for Cm. Neither the squared nor the cubic component significantly reduced variance in the regression model.

In order to disentangle the relationship between the BOLD estimate of the linear increase in CSI with accuracy scores and to highlight the possible neural correlates of the performance difference observed between accuracy measures on the third category-repetition (i.e., a significant lower performance) with respect to the first presentation and the last repetition of a category exemplar, correlations were also performed between values for Cm BOLD estimates in LIFG and LCN in each subject and accuracy scores at each category repetition and for fillers. A significant association was found only between accuracy performance in the last repetition (i.e., rep4) and Cm values in the LCN (Pearson's $r = 0.61$, $P = 0.020$).

Functional Connectivity—gPPI

A PPI analysis with the LIFG functional ROI (i.e., group-level significant activation for the Cm modulator resulting from the parametrical model) as seed region revealed a significantly increased task-load connectivity with the anterior division of the cingulate cortex (peak coordinates: $x = -4$, $y = 32$, $z = -2$; $k = 34$ voxels; $x = 10$, $y = 38$, $z = 2$; $k = 13$ voxels), with the anterior division of the left supramarginal gyrus (peak coordinates: $x = -56$, $y = -34$, $z = 30$; $k = 15$ voxels) and the left angular gyrus (peak coordinates: $x = -38$, $y = -52$, $z = 38$; $k = 23$ voxels) and with the right precuneus (peak coordinates: $x = 10$, $y = -56$, $z = 54$; $k = 11$ voxels; $x = 14$, $y = -66$, $z = 34$; $k = 14$ voxels) for the nCm (see Fig. 5, yellow clusters).

As SI builds up instead, we observed greater connectivity exclusively between the LIFG seed and the fusiform gyri bilaterally, in a specular fashion (left peak coordinates: $x = -32$, $y = -54$, $z = -10$; $k = 18$ voxels; right peak coordinates: $x = 32$, $y = -52$, $z = -6$; $k = 11$ voxels) for the Cm (see Fig. 5, red clusters).

Category "Differential" Repetition Effect

In order to translate the semantic incremental effect in terms of a positive difference in signal intensity between the last and the first occurrence of an exemplar from the same category (i.e., whether BOLD signal intensity for the last repetition is significantly higher than for the first presentation) and to assess a possible functional relationship in "semantic" terms between activity in the LIFG and the LCN we performed a second GLM analysis at the first level on all subjects ($n = 24$).

In this model, category repetition was explicitly modeled in the sense that we included a total of five "category repetition" regressors in the GLM model, namely one regressor coding the first presentation of a category exemplar and four regressors coding the first, second, third, and fourth repetition, added with a sixth regressor coding fillers separately. Lags between category repetitions were also included in the model.

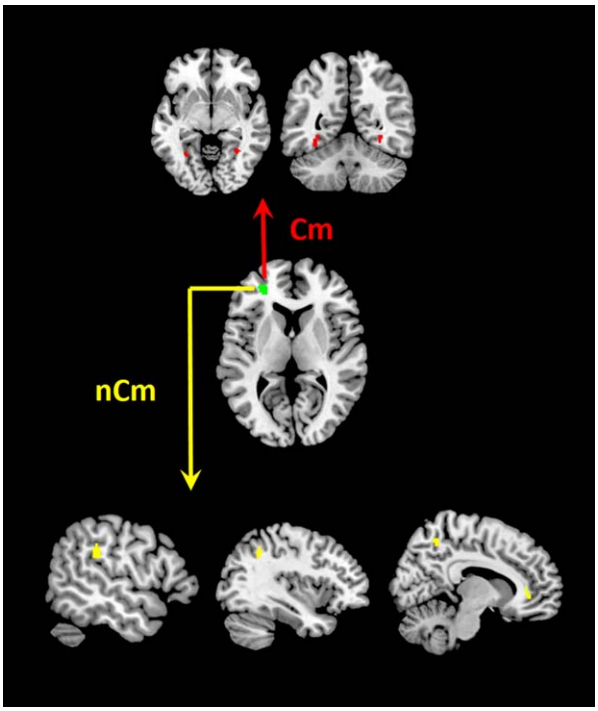

Figure 5.
gPPI connectivity using LIFG Cm functional ROI as seed. Patterns of significantly increased connectivity between the LIFG Cm functional ROI seed (central axial slice, green cluster) and areas related to (i) semantic interference increase (i.e., category modulator, Cm) (top sagittal slices, red clusters) and (ii) task-load increase (i.e., no category modulator, nCm) (bottom sagittal slices, yellow clusters). Results are shown at a voxelwise $P < 0.005$ threshold ($k = 10$). [Color figure can be viewed at wileyonlinelibrary.com]

First level contrasts coding the main effect were then computed independently for each of the five "category repetition" regressors for all subjects and MarsBar was then used (Brett et al., 2002) to define two binarized spherical ROIs (with an 8 mm diameter) centered on the group peak coordinates for both the LIFG ($x = -28$, $y = 42$, $z = 10$) and the LCN ($x = -14$, $y = 6$, $z = 18$) highlighted in the parametrical analysis assessing the semantic modulation effect. For each ROI, we extracted mean activation values from single subject contrast images for the first presentation of a category exemplar and for the last repetition of a picture belonging to the same category.

It must be stated that mean activation values extracted from the LIFG and LCN ROIs from contrast images specified through a second categorical GLM model avoids potential issues regarding circularity and double dipping (Kriegeskorte et al., 2009), as we used data from a different and independent analysis (i.e., parametrical) to define category repetition-sensitive ROIs in the LIFG and LCN and then applied these ROI masks to extract mean activation values from independent contrast images (i.e., coding category repetition in a different categorical statistical model) to investigate whether the difference in activity in both areas between the first and last presentation (i.e., last repetition) is significant. Furthermore we assessed if this difference, assumed to capture the highest variation of this linear semantic effect, calculated for both LIFG and the LCN is somehow functionally associated.

We then performed a paired sample *t*-test to test for differences between activity values at the two extremes of the category repetition dimension: the activation values for LIFG significantly differed ($P < 0.004$, $t = 3.23$) between the first category presentation (mean = −0.177; SD = 1.003) and the last category repetition (mean = 0.568; SD = 1.016), being significantly higher for the latter condition. Comparison between LCN activity values for the same two conditions revealed a significant difference as well ($P < 0.007$; $t = 2.98$) with a significant increase in activity from the first presentation (mean = 0.320; SD = 1.35) to the last repetition (mean = 0.965; SD = 1.089) condition. A correlation analysis was also performed to assess the association between differential scores for LIFG and LCN showing a significant correlation between the variation in activity between first-last semantic category presentation for these two areas (two-tailed Pearson correlation, $r = 0.528$; $P = 0.008$).

Seed-to-Voxel Connectivity Analysis on the Category "Differential" Repetition Effect

A seed-to-voxel analysis task-based functional connectivity analysis was implemented in MATLAB using the CONN toolbox (http://www.nitrc.org/projects/conn; Whitfield-Gabrieli and Nieto-Castanon, 2012) to explore "category-repetition" connectivity differences for the first (rep1), second (rep2), third (rep3), and fourth (rep4) repetition with respect to the first presentation of a category exemplar (rep0) between LIFG and other brain regions.

For each participant, the CompCor method (Behzadi et al., 2007) in CONN was implemented to identify principal components associated with segmented white matter (WM) and cerebrospinal fluid. Individual participants' motion parameters and main effects of task condition (i.e., rep0, rep1, rep2, rep3, rep4, and fillers, as specified in the second GLM analysis in which repetition order was explicitly modeled as separate regressors) (see above), were also entered as confounds in a first-level analysis (Behzadi et al., 2007) to avoid affecting intrinsic functional connectivity or measuring simple task-related coactivation. er-fMRI normalized and smoothed data were not band-pass filtered and default "hrf" temporal weights were set.

The *a priori* selected seed was the pars triangularis region of left inferior frontal gyrus (i.e., LIFG area 45) from the Tzourio-Mazoyer template (Tzourio-Mazoyer et al., 2002). Temporal correlations were computed between the mean time course across voxels within the seed and all other

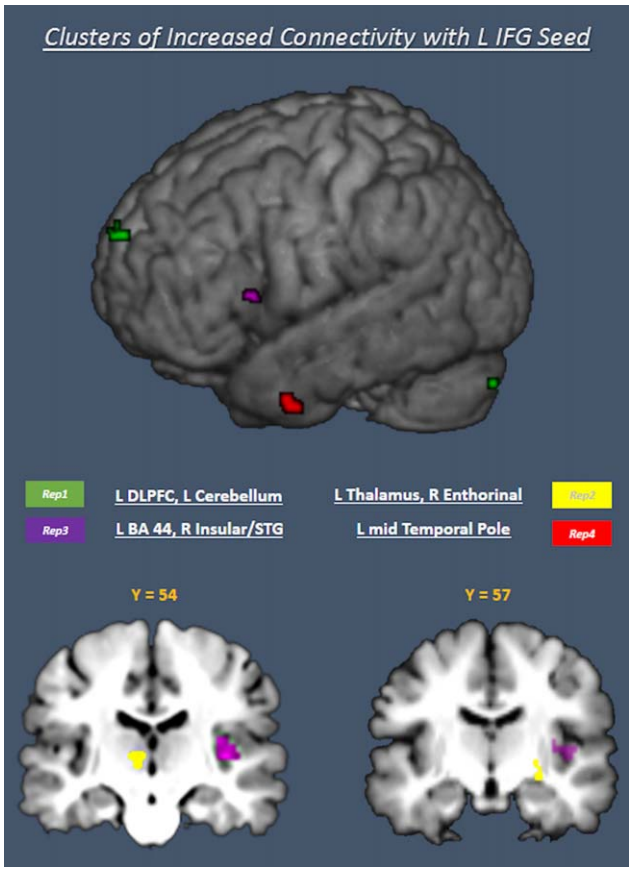

Figure 6.
Functional connectivity using LIFG—*pars triangularis*—as seed. Different colors represent regions observed to have significantly greater connectivity with LIFG during the first (rep1–rep0, green), second (rep2–rep0, yellow), third (rep3–rep0, violet), and fourth (rep4–rep0, red) category repetitions compared to the first presentation of an image of the same semantic category (rep0). Rep1–rep0 (green) shows a significantly increased connectivity between the LIFG seed and the left dorsolateral prefrontal cortex and the left cerebellum. Rep2–rep0 (yellow) shows an increased connectivity of LIFG with the left thalamus and the right posterior enthorinal cortex. Rep3–rep0 (violet) shows an increased lef-lateralized connectivity with Broca's area 44 and with a large, right-lateralized cluster in the insular cortex extending to the superior temporal gyrus (BA 22) and to the primary auditory cortex (BA41). Rep4–rep0 (red) shows an increased connectivity with the middle anterior portion of the left temporal pole. Maps are shown at a voxel-wise threshold of $P < 0.001$uncorrected and a cluster extent threshold of $P < 0.05$ uncorrected (minimum cluster extent: $k = 27$). [Color figure can be viewed at wileyonlinelibrary.com]

voxels in the brain. Seeded voxel correlations between the signal from LIFG and that at every brain voxel provided seed-to-voxel connectivity estimations using the signal from the five conditions (rep0, rep1, rep2, rep3, and rep4) as the temporal variable.

Temporal connectivity maps were generated for each subject by estimating the correlation coefficient between all brain voxels and the seed signal across the conditions. These images were included in a second-level group (between-subjects), random-effects analysis. *t*-Tests were used to compute differences in functional connectivity between the first (rep1), second (rep2), third (rep3), and fourth (rep4) repetition with respect to the first presentation of a category exemplar (rep0) (i.e., rep1–rep0, rep2–rep0, rep3–rep0, and rep4–rep0). Seed-to-voxel results are reported when significant at a voxel-wise threshold of level of $P < 0.001$ uncorrected and a cluster-level threshold of $P < 0.05$ uncorrected (minimum cluster extent: $k = 27$). All coordinates reported below refer to peak activations in anatomical MNI space.

For the first repetition (rep1) relative to the first presentation (rep0) (i.e., rep1–rep0), group analysis showed significant stronger connectivity between the LIFG seed and the left dorsolateral prefrontal cortex (BA 9) ($x = -12$; $y = +66$; $z = +28$; $k = 35$) and the left cerebellum (lobule 7a, crus I) ($x = -36$; $y = -84$; $z = -36$; $k = 32$) (see Fig. 6, green clusters).

The second repetition (rep2) minus the first presentation (rep0) contrast (i.e., rep2–rep0) revealed significant increased connectivity between the LIFG seed and the left thalamus ($x = -6$; $y = +22$; $z = -4$; $k = 32$) and right posterior entorhinal cortex (BA 28) ($x = +26$; $y = -12$; $z = -12$; $k = 28$) (see Fig. 6, yellow clusters).

The contrast testing the third repetition (rep3) against the first presentation (rep0) showed significantly stronger connectivity between LIFG area 45 seed and area 44 ($x = -62$; $y = +18$; $z = +12$; $k = 27$) on the left and a large cluster of voxels in the right insular cortex (BA 13) ($x = +42$; $y = -24$; $z = +4$; $k = 246$) extending to the superior temporal gyrus (BA 22) and primary auditory cortex (BA 41) (see Fig. 6, violet clusters).

LIFG functional connectivity contrasted instead between the fourth repetition (rep4) and the first presentation (rep0) was significantly stronger with the middle anterior portion of the left temporal pole (BA 21) ($x = -60$; $y = +4$; $z = -32$; $k = 43$) (see Fig. 6, red cluster).

DISCUSSION

In this study, we investigated the neural correlates of the CSI effect during an overt picture naming task by implementing the experimental design of Howard et al. (2006) in an er-fMRI experiment.

The first "parametrical" analysis showed an involvement of a large network of areas encompassing occipitotemporal and prefrontal regions during picture naming task, in line with previous studies (Démonet et al., 2005). Interestingly, a specific focus of brain activity in the LIFG was identified

solely for experimental pictures and not for filler pictures (see Fig. 1).

A linear increase in BOLD response for both LIFG (with adjacent parts of the insular cortex) and the LCN was found to positively be associated with the consecutive number of presentations of pictures exemplars of the same category, at both group and individual levels (see Figs. 2 and 3). Interestingly, the signal change in both regions was not correlated with increasing levels of task load due to the mere repetition of items across the whole experiment.

In order to test for a "functional covariance" between the increase in activity observed in LIFG and LCN and to assess the semantic nature of their relationship, we correlated the difference between BOLD changes measured at the first presentation of an item belonging to a specific semantic category and changes observed during the last presentation of a category resulting from a second analysis, which explicitly modelled "category repetition." We observed a strong functional coupling between these two areas suggesting that lexicosemantic control at this level is exerted in a monotonic fashion through similar control mechanisms found to be involved in other cognitive domains (Casey et al., 2001) and entailed for bilingual language control as well (Abutalebi and Green, 2007; Abutalebi et al., 2013; Luk et al., 2012).

Results from the first analysis and second analysis are consistent with the view of lexical origin in terms of lexical competition as suggested by several other observations (Costa et al., 2009; Howard et al., 2006). Furthermore, the LIFG and LCN may collaborate at the same level, that is, the lexical level.

We propose that the LIFG responds to the increased demands during retrieval and selection of the target word in conflicting situations, while the LCN, because of its well-known role in monitoring and controlling (Abutalebi and Green, 2007), may be more involved in guiding and supporting the LIFG during the selection process with inhibitory and excitatory resources.

Given the cumulative nature of the SI effect, which increases in magnitude with the increasing number of presentations of semantically related pictures, we could hypothesize that the neural activity in both LIFG and LCN during the last presentation should be greater than that of the first presentation. Hence, estimates of SI brain activity in both areas should show a cumulative increase as that observed for the correlation between SI and ERP peaks in Costa et al. (2009). Indeed, the comparison between estimates of BOLD activity for the first and last presentations of category exemplars revealed significantly greater activity in both areas for the last presentation. Indeed, values increased with a linear pattern across successive repetitions at the individual level for more than 60% of the subjects in LIFG and ~80% in the LCN (see plots displayed in Fig. 3). Both the linear increase and strong association between the amount of activity change (differential repetition effect) from the first to the last presentation for these two areas points to the "control" nature of the mechanism at the basis of the SI effect given the interplay between LIFG and LCN.

Similar to our findings, de Zubicaray et al. (2015) report a cumulative increase across ordinal positions in the LIFG, employing the same CSI protocol. However, contrary to what we observed, there was no cumulative modulation of the LCN, while they did observe perfusion signal changes associated with the CSI in the left MTG. Although we do not have a clear explanation for the differences in brain imaging results, some protocol differences between both studies need to be taken into account. For one, unlike in the study of de Zubicaray et al. (2015), we have semi-randomized item presentation within a semantic category to avoid for consistent physical variance between the stimuli. Hence, such potential physical variance may be particularly sensitive to "object-related" brain regions in the temporal cortex (although admittedly that would not necessarily predict cumulative effects). Another noteworthy difference is that in our study participants were presented with two experimental lists in order to increase statistical power. Given that repetition is known to decrease the haemodynamic response to repeated items (adaptation), in particular for stimulus-specific brain regions (e.g., Grill-Spector et al., 2006), this may have attenuated a potential cumulative signal increase in the left MTG in our data (while the control regions observed in our data—nonstimulus specific—potentially suffered less from the signal attenuation). Finally, an important difference between the studies also concerns the acquisition of fMRI data. While we applied a "parametric" BOLD fMRI imaging method, de Zubicaray et al. (2015) relied on arterial spin labelling perfusion method. The latter method has less sensitivity and temporal resolution compared to BOLD acquisitions, but may have increased sensitivity to group-level effects. Taken together, the differences in protocol and acquisition methods, may have caused that the data of de Zubicaray et al. (2015) is better tailored to pick up the sources of lexical competition such as the left MTG (and arguably LIFG), while our data displayed higher sensitivity to the sources responsible to control and overcome the lexical competition such as the LCN coupled to the LIFG. Put differently and tentatively for now, the differences in results between our study and that of de Zubicaray et al. (2015) are not necessarily contradictory, but may in fact be complementary to one and another.

However, an important advancement on the role of the LIFG, with respect to the previous studies, derives from our results of the connectivity analysis. The gPPI analysis showed that LIFG demonstrated a different neural connectivity pattern for increases of task-load or SI. Specifically, changes in functional connectivity between the LIFG and the left supramarginal and angular gyri are likely reflecting a more general "extrinsic" semantic activity for ongoing semantically-driven task demands (Noonan et al., 2013). That is, despite these areas are generally involved in

semantic control tasks, they are also part of the default mode network (Buckner et al., 2008). Recent results have suggested a domain-general role for this area in the control of semantic information (Hoffman et al., 2015; Humphreys et al., 2015). Importantly, when the repetitions of exemplars from the same semantic category increase, interference seems to cumulate in a more semantically specific fashion and strengthen the positive coupling between the LIFG and more "intrinsically" and semantically driven area, such as the fusiform gyri (see Humphreys et al., 2015; Martin and Chao, 2001). The recruitment of the fusiform gyrus has been related to the computation of visual/semantic representations of the items, with right fusiform gyrus generally selectively associated with nonverbal conceptual and structural object processing (Marconi et al., 2013; Thierry and Price, 2006; Vandenberghe et al., 1996 as in Butler et al., 2009; Hocking and Price, 2009; Mion et al., 2010; Thierry and Price, 2006). The fusiform gyrus is activated by tasks requiring the discrimination of an object from many similar visual or semantic competitors (Joseph and Gathers, 2003; Price et al., 2003). An activation of the fusiform gyrus has been reported when subjects had to classify at a more specific level (e.g., Labrador or BMW) with respect of an intermediate (or basic, e.g., dog or car) level of categorization, suggesting a role in a finer-grained discrimination required to differentiate between visually or semantically similar objects (Rogers et al., 2005). According to Tyler et al. (2013), the activity of the fusiform gyrus may be in particular driven by the similarity of conceptual structure reflecting category structure, namely the relative amount of shared features within a concept. Similar evidences derive also from fMRI studies in neurodegenerative disease. For example, greater recruitment of the left fusiform gyrus has been also observed in a blocked paradigm, in the homogeneous condition in which pictures were closely related to each other, in individuals with amnestic mild cognitive impairment when compared to controls, notwithstanding a similar behavioral performance for the two groups (Catricalà et al., 2015).

One possibility is that when SI increases, feedback responses from LIFG cortex to more posterior object-sensitive regions (i.e., fusiform) facilitate stimuli processing by constraining lexicosemantic processing only to the most relevant candidates (see Bar et al., 2006; Miller and D'Esposito, 2005). In accord with the idea that the coupling between the LIFG and the fusiform gyri may reflect increased demands on controlled processing directed to the selection of relevant lexicosemantic representations, recent findings have demonstrated that successful object recognition is enacted by recurrent interactions between prefrontal and ventral temporal cortices, and in particular the fusiform gyrus (see Bar et al., 2006). Moreover, a recent study has shown that within different areas of the semantic network, the left fusiform gyrus and the LIFG were active for different types of semantic task but deactivated for the nonsemantic tasks, supporting the hypothesis that the coupling related activity in the present study is semantic specific (see Humphreys et al., 2015).

The seed-to-voxel connectivity analysis instead revealed the functional coupling underlying the category "differential" repetition effect enacted through LIFG, confirming the role of LIFG for lexicosemantic control, however seemingly exerted through increased connectivity with different brain areas across different degrees of interference. For instance, we found that for the first repetition of a category member, the left IFG seed was more strongly connected to the left DLPFC, a region underlying controlled attention and working memory capacity (Dobbins et al., 2004; Curtis and D'Esposito, 2003; MacDonald et al., 2000). Hence, the coupling of the activity between these two areas might reflect the cognitive control demands directed for the formation of new stimulus-response bindings, when a category member is repeated for the first time.

The second and third repetition triggered greater connectivity between the LIFG (BA 45) seed and the left thalamus and the right insula, which are areas more linked with general executive control functions, the pars opercularis (BA 44) presumably for a deeper evaluation of the appropriateness of the recovered semantic information (Gabrieli et al., 1998), and the right hippocampus. In a series of experiments exploring SI in the blocked cyclic naming paradigm de Zubicaray and collaborators (e.g., de Zubicaray et al., 2014; Vieth et al., 2015) consistently report that the interference elicited in semantically homogenous naming blocks (compared to heterogeneous ones) was associated with perfusion signal increases in the hippocampus. The hippocampal involvement may indeed highlight an important role for working memory (e.g., Vieth et al., 2015).

For the fourth repetition, a significant increased functional coupling of LIFG and the middle portion of the anterior temporal pole was instead observed, suggesting that this region may be called upon more strongly in order to resolve competition driven by similarity relations among exemplars of the same category (e.g., Jackson et al., 2015). Probably, when SI is cumulated to a maximum degree, the involvement of regions enrolled in the previous contrasts is not sufficient to disentangle ambiguity between semantically similar concepts, and a further (or a detailed) semantic discrimination is needed.

Both neuroimaging and neuropsychological research focusing on semantic control have highlighted the importance of the left inferior frontal gyrus (LIFG). Many studies have reported that increases of LIFG activity are linked to semantic retrieval, while other studies employing picture naming have led to some inconsistencies (Bookheimer et al., 1995; Etard et al., 2000; Murtha et al., 1999; Salmelin et al., 1994; Sergent et al., 1992). For instance, Wagner et al. (2001b) suggested the LIFG is recruited only when the retrieval process is controlled, not automatic. On the other hand, Thompson-Schill et al. (1997, 1998, 1999) and Kan and Thompson-Schill (2004) after a series of fMRI experiments and patients studies concluded that activity in the

LIFG is triggered by demands concerning the selection of information among competing alternatives. Noteworthy, Thompson-Schill and Botvinick (2006) have argued that the distinction between retrieval processes on the one hand and selection demands on the other hand is a "false dichotomy." This is because bottom-up or top-down influences, respectively, driven at the lexicosemantic representation or at the task level, conjointly result in the final strength of the item competing for output in the speech production system. Interestingly, Duffau et al. (2005) demonstrated that electrical stimulation of the *pars orbitalis* of the LIFG during picture naming leads to semantic paraphasia. As to lesion studies, LIFG lesions in patients with aphasia due to stroke produce impairments on similar tasks, establishing a causal relationship between LIFG and multimodal semantic control deficits (Corbett et al., 2009a,b; Jefferies et al., 2008; Noonan et al., 2010; Novick et al., 2009; Soni et al., 2009). Schnur et al. (2009) found a significant greater involvement of the LIFG during semantic blocked naming when manipulating the semantic or phonological relatedness of the items presented in different blocks during a naming task. A whole brain analysis at the group level confirmed that the *pars triangularis* in the posterior portion of the LIFG adjacently to the insular cortex was more involved in the semantic blocking effect when compared to the phonological blocking effect. In the same study, with the intent to clarify whether the LIFG is necessary to resolve competition during word production, lesion analysis in a group of patients with post-stroke aphasia (Schnur et al., 2006) highlighted that greater extent of damage in the LIFG is paralleled with higher levels of interference over cycles of semantically blocked naming.

The CSI effect that we have observed in the LIFG (*pars triangularis*) includes the anterior insula, which has been found to respond to increases in cognitive processing demands, regardless of task or stimulus material (Duncan and Owen, 2000). There is robust evidence for a more general role of anterior insula in subserving attentional demands in terms of monitoring and control of performance as a function of goal-directed behavior (Dosenbach et al., 2006; Nelson et al., 2010). WM projections have also been traced between the insula and striatum including the LCN (Chikama et al., 1997). Based on the cognitive processes for which it is entailed and its crucial anatomical location halfway between LIFG and LCN, the anterior insula fits perfectly in a semantic control network responsible for retrieval and selection of one targeted item among many possible competitors for output in the speech production system.

As aforementioned, the LCN is also part of a cognitive control network and is generally recruited in tasks necessitating for resolution of conflict between competing responses. For instance, the LCN is involved in the inhibition of previously learned movement (Parsons et al., 2005; Shadmehr and Holcomb, 1999) or to prevent prepotent responses (Li et al., 2008) and in controlling interference in the Stroop task (Ali et al., 2010). Taken together, this evidence supports an inhibitory role of the caudate in both action planning and control of both verbal and nonverbal types of interference. It is relevant to note here that some studies reveal a more specific role for LCN in language control (Abutalebi et al., 2008; Abutalebi and Green, 2016; Branzi et al., 2016). Intraoperative direct electrical stimulation of the head of caudate, but not of other basal ganglia systems, leads to perseverations in picture naming (Robles et al., 2005), suggesting a role in inhibiting a previously active representation. Lesions to LCN can lead to naming difficulties following a defective selection of words (Cappa and Abutalebi, 1999) and in bilinguals may result in impaired language control and thus leading to pathological switching between languages (Abutalebi et al., 2000; Abutalebi and Green, 2007; Calabria et al., 2014), caused by the erroneous selection of words in one language rather than another.

Anatomically, the LCN is the major afferent of corticostriatal projections from frontal, temporal, and parietal regions in the language-dominant hemisphere, which represent the neural underpinnings of semantic cognition and in turn sends reciprocal connections via the thalamus. Given these anatomical characteristics the LCN may represent the privileged candidate for conveying the bottom-up and top-down biases on lexical access to the control network in order to resolve competition for output in the speech production system.

An important matter of debate is why cognitive control should be necessary for the resolution of SI. Oppenheim et al. (2010) suggested that lexical selection may be accomplished through an incremental learning mechanism (i.e., booster) that amplifies activity of each targeted lexical-semantic representation to constantly override its competitors. This mechanism has been linked to some evidence reporting a greater LIFG activity as a function of increased lexical competition (Schnur et al., 2009).

However, to the extent to which cognitive control mechanisms influence lexical selection, the additional linear recruitment of the LCN evokes the presence of an inhibitory mechanism tailored to SI. For instance, our results point to a mechanism entailed to adjust performance, once it drops below a critical level due to high levels of SI. At the fourth repetition, in order to bring task performance up to the same levels of naming accuracy observed for the first presentation of an item, increased cognitive control (i.e., LCN activity) seems to be exerted in order to hamper cumulated interference at the third repetition and accurately name the category exemplar occurring on the fourth repetition. Consistently, our results show a significant difference between accuracy scores for the third repetition in terms of a worse performance only with respect to the first presentation and the fourth repetition paralleled to a significant correlation only between accuracy scores on the fourth repetition and LCN activity. LIFG could mediate task-dependent biases on lexical access (Thompson-Schill

and Botvinick, 2006), while LCN seems to calibrate semantic demands with task performance. Thus, it appears extremely important that any neurocognitive model of speech production incorporate both LIFG and LCN as neural control components involved in the resolution of bottom-up or top-down interference during lexical selection. Such interference during lexical access may occur because the target representation and any other viable candidate for output compete at any level and the irrelevant item is activated enough to interfere with processing on hand. In that, cognitive control may be a critical factor in facilitating interference resolution and guaranteeing successful task completion.

Very surprisingly, we also showed that LIFG exhibits a different pattern of whole-brain functional connectivity as a function of the degree of SI. In fact, on one hand, at lower levels of interference, we found increased connectivity between the LIFG and the DLPFC, a domain-general area for cognitive control (see Ridderinkhof et al., 2004). This area is thought to have a crucial role whenever some behavioral adjustment is required for correct response selection. Its involvement has been observed across a wide range of tasks, involving different levels of mental representations (Dobbins et al., 2004; Rowe et al., 2000; Rowe and Passingham, 2001), from the higher-order representations, including semantic representations (e.g., Dobbins et al., 2004) to the lower-order ones, such as motor representations in the primary motor cortex (e.g., Hadland et al., 2001). Based on these findings, we suggest that the increased connectivity between the LIFG and DLPFC might reflect domain-general control processes likely directed to the selection of new stimulus-response bindings. On the other hand, at higher levels of interference, we found significant increased functional coupling between the LIFG and the middle portion of the anterior temporal pole, a brain area functionally bound to semantic cognition (e.g., Pobric et al., 2007, 2010; Whitney et al., 2012). This finding might suggest that when SI increases, the activity of frontal and anterior temporal areas becomes functionally coupled in order to boost the activation of target lexical-semantic representations.

All in all, these results might suggest a qualitative difference in terms of control mechanisms. We observed a shifting from a more general executive control process (i.e., DLPFC and cerebellum) at lower levels of interference, towards a more semantically driven control mechanism (i.e., anterior temporal region) at higher levels of interference.

On the basis of all this evidence, we can presumably hypothesize that SI is resolved at the lexical level; however, the cumulative effect is mirrored not only by a quantitative difference in activity levels between the same set of cognitive-control brain regions (i.e., LIFG-LCN) but also by a qualitatively different control process, exploiting more general executive control or tapping into deeper semantic neural resources in order to efficaciously cope with different levels of SI.

APPENDIX

Items Per Category Used in the Experiment

Fruits: apple, banana, lemon, grapes, and pear
Musical instruments: drum, guitar, piano, trumpet, and violin
Tools: axe, drill, hammer, saw, and screwdriver
Transport: bus, car, helicopter, airplane, and truck
Fish: eel, wale, shark, ray, and swordfish
Body parts: ear, eye, finger, hand, and nose
Clothes: bra, jacket, shirt, skirt, and sock
Tableware: cup, fork, glass, knife, and spoon
Furniture: bed, chair, desk, stool, and table
Bugs: beetle, butterfly, ladybug, spider, and wasp
House parts: chimney, door, stairs, roof, and window
Computer equipment: computer, joystick, keyboard, mouse, and printer
Farm animals: cow, donkey, horse, pig, and sheep
Shellfish: crab, lobster, snail, clam, and prawn
White goods: iron plate, fridge, toaster, stove, and washing machine
Reptiles and amphibians: crocodile, frog, lizard, snake, and turtle
Vegetables: pepper, carrot, cauliflower, onion, and pumpkin
Buildings: castle, church, house, lighthouse, and windmill
Celestial phenomena: clouds, sun, lightning, moon, and rainbow
Headgear: beret, cap, crown, hat, and helmet
Audiovisual: headphones, microphone, radio, record player, and television
Landscape features: island, volcano, mountain, ocean, and desert

Filler Items Used in the Experiment

Anchor, tree, astronaut, flag, barrel, sandwich, lightbulb, button, peanut, calendar, bell, lock, cannon, carousel, ashtray, brush, basket, heart, thimble, plug, arrow, glasses, balloon, stapler, leaf, pencil, book, key, suitcase, puppet, cake, clown, ball, spinning top, hanger, clothespin, pipe, well, racquet, watering can, watch, wheel, trafficlight, envelop, and candle.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

REFERENCES

Abutalebi J, Miozzo A, Cappa SF (2000): Do subcortical structures control 'language selection'in polyglots? Evidence from pathological language mixing. Neurocase 6:51–56.

Abutalebi J, Green D (2007): Bilingual language production: The neurocognition of language representation and control. J Neurolinguistics 20:242–275.

Abutalebi J, Annoni JM, Zimine I, Pegna AJ, Seghier ML, Lee-Jahnke H, Lazeyras F, Cappa SF, Khateb A (2008): Language control and lexical competition in bilinguals: an event-related fMRI study. Cereb Cortex 18:1496–1505.

Abutalebi J, Della Rosa PA, Ding G, Weekes B, Costa A, Green DW (2013): Language proficiency modulates the engagement of cognitive control areas in multilinguals. Cortex 49:905–911.

Abutalebi J, Green DW (2016): Neuroimaging of language control in bilinguals: neural adaptation and reserve. Biling Lang Cogn. 19:689–698. http://dx.doi.org/10.1017/S1366728916000225.

Alario FX, del Prado Martín FM (2010): On the origin of the "cumulative semantic inhibition" effect. Mem Cognit 38:57–66.

Ali N, Green DW, Kherif F, Devlin JT, Price CJ (2010): The role of the left head of caudate in suppressing irrelevant words. J Cog Neurosci 22:2369–2386.

Badre D, Wagner AD (2004): Selection, integration, and conflict monitoring: assessing the nature and generality of prefrontal cognitive control mechanisms. Neuron 41:473–487.

Badre D, Poldrack RA, Paré-Blagoev EJ, Insler RZ, Wagner AD (2005): Dissociable controlled retrieval and generalized selection mechanisms in ventrolateral prefrontal cortex. Neuron 47:907–918.

Bar M, Kassam KS, Ghuman AS, Boshyan J, Schmid AM, Dale AM, Halgren E (2006): Top-down facilitation of visual recognition. Proc Natl Acad Sci USA 103:449–454.

Behzadi Y, Restom K, Liau J, Liu TT (2007): A component based noise correction method (CompCor) for BOLD and perfusion based fMRI. Neuroimage 37:90–101.

Birn RM, Cox RW, Bandettini PA (2004): Experimental designs and processing strategies for fMRI studies involving overt verbal responses. Neuroimage 23:1046–1058.

Bookheimer SY, Zeffiro TA, Blaxton T, Gaillard W, Theodore W (1995): Regional cerebral blood flow during object naming and word reading. Hum Brain Mapp 3:93–106.

Branzi FM, Della Rosa PA, Canini M, Costa A, Abutalebi J (2016): Language control in bilinguals: monitoring and response selection. Cereb Cortex. 26:2367–2380.

Brett M, Anton JL, Valabregue R, Poline JB (2002): Region of interest analysis using the MarsBar toolbox for SPM 99. Neuroimage 16:S497.

Brown AS (1981): Inhibition in cued retrieval. J Exp Psychol Hum Learn 7:204–215.

Buckner RL, Andrews-Hanna JR, Schacter DL (2008): The brain's default network. Ann N Y Acad Sci 1124:1–38.

Butler CR, Brambati SM, Miller BL, Gorno-Tempini ML (2009): The neural correlates of verbal and non-verbal semantic processing deficits in neurodegenerative disease. Cogn Behav Neurol 22: 73–80.

Calabria M, Marne P, Romero-Pinel L, Juncadella M, Costa A (2014): Losing control of your languages: a case study. Cogn Neuropsychol 31:266–286.

Cappa S, Abutalebi J (1999): Subcortical aphasia. In: The Concise Encyclopedia of Language Pathology. (Ed. F. Fabbro; Pub: Pergamon). pp. 319–327.

Caramazza A, Miozzo M (1997): The relation between syntactic and phonological knowledge in lexical access: evidence from thetip-of-the-tongue'phenomenon. Cognition 64:309–343.

Carter CS, Braver TS, Barch DM, Botvinick MM, Noll D, Cohen JD (1998): Anterior cingulate cortex, error detection, and the online monitoring of performance. Science 280:747–749.

Casey B, Durston S, Fossella JA (2001): Evidence for a mechanistic model of cognitive control. Clin Neurosci Res 1:267–282.

Catricalà E, Della Rosa PA, Parisi L, Zippo AG, Borsa VM, Iadanza A, Cappa SF (2015): Functional correlates of preserved naming performance in amnestic Mild Cognitive Impairment. Neuropsychologia 76:136–152.

Chikama M, McFarland NR, Amaral DG, Haber SN (1997): Insular cortical projections to functional regions of the striatum correlate with cortical cytoarchitectonic organization in the primate. J Neurosci 17:9686–9705.

Corbett F, Jefferies E, Ehsan S, Ralph MAL (2009a): Different impairments of semantic cognition in semantic dementia and semantic aphasia: Evidence from the non-verbal domain. Brain 132:2593–2608.

Corbett F, Jefferies E, Ralph MAL (2009b): Exploring multimodal semantic control impairments in semantic aphasia: Evidence from naturalistic object use. Neuropsychologia 47:2721–2731.

Costa A, Alario FX, Caramazza A (2005): On the categorical nature of the semantic interference effect in the picture-word interference paradigm. Psychon Bull Rev 12:125–131.

Costa A, Strijkers K, Martin C, Thierry G (2009): The time course of word retrieval revealed by event-related brain potentials during overt speech. Proc Natl Acad Sci USA 106:21442–21446.

Curtis CE, D'Esposito M (2003): Persistent activity in the prefrontal cortex during working memory. Trends Cog Sci 7:415–423.

Dale AM (1999): Optimal experimental design for event-related fMRI. Hum Brain Mapp 8:109–114.

Damian MF, Vigliocco G, Levelt WJ (2001): Effects of semantic context in the naming of pictures and words. Cognition 81:B77–B86.

Damian MF, Bowers JS (2003): Locus of semantic interference in picture-word interference tasks. Psychon Bull Rev 10:111–117.

de Zubicaray G, McMahon K, Eastburn M, Pringle A (2006): Top-down influences on lexical selection during spoken word production: A 4T fMRI investigation of refractory effects in picture naming. Hum Brain Mapp 27:864–873.

de Zubicaray G, Johnson K, Howard D, McMahon K (2014): A perfusion fMRI investigation of thematic and categorical context effects in the spoken production of object names. Cortex 54:135–149.

de Zubicaray G, McMahon K, Howard D (2015): Perfusion fMRI evidence for priming of shared feature-to-lexical connections during cumulative semantic interference in spoken word production. Lang Cogn Neurosci 30:261–272.

Dell GS (1986): A spreading-activation theory of retrieval in sentence production. Psychol Rev 93:283–321.

Démonet JF, Thierry G, Cardebat D (2005): Renewal of the neurophysiology of language: functional neuroimaging. Physiol Rev 85:49–95.

Dobbins IG, Schnyer DM, Verfaellie M, Schacter DL (2004): Cortical activity reductions during repetition priming can result from rapid response learning. Nature 428:316–319.

Dosenbach NU, Visscher KM, Palmer ED, Miezin FM, Wenger KK, Kang HC, Burgund ED, Grimes AL, Schlaggar BL,

Petersen SE (2006): A core system for the implementation of task sets. Neuron 50:799–812.
Duffau H, Gatignol P, Mandonnet E, Peruzzi P, Tzourio-Mazoyer N, Capelle L (2005): New insights into the anatomo-functional connectivity of the semantic system: A study using cortico-subcortical electrostimulations. Brain 128:797–810.
Duncan J, Owen AM (2000): Common regions of the human frontal lobe recruited by diverse cognitive demands. Trends Neurosci 23:475–483.
Etard O, Mellet E, Papathanassiou D, Benali K, Houdé O, Mazoyer B, Tzourio-Mazoyer N (2000): Picture naming without Broca's and Wernicke's area. Neuroreport 11:617–622.
Gabrieli JD, Poldrack RA, Desmond JE (1998): The role of left prefrontal cortex in language and memory. Proc Natl Acad Sci USA 95:906–913.
Glaser WR, Glaser MO (1989): Context effects in stroop-like word and picture processing. J Exp Psychol Gen 118:13.
Goldrick M, Blumstein SE (2006): Cascading activation from phonological planning to articulatory processes: Evidence from tongue twisters. Lang Cogn Process 21:649–683.
Grill-Spector K, Henson R, Martin A (2006): Repetition and the brain: Neural models of stimulus-specific effects. Trends Cogn Sci 10:14–23.
Grootoonk S, Hutton C, Ashburner J, Howseman A, Josephs O, Rees G, Friston KJ, Turner R (2000): Characterization and correction of interpolation effects in the realignment of fMRI time series. Neuroimage 11:49–57.
Hadland KA, Rushworth MFS, Passingham R, Jahanshahi M, Rothwell J (2001): Interference with performance of a response selection task that has no working memory component: An rTMS comparison of the dorsolateral prefrontal and medial frontal cortex. J Cogn Neurosci 13:1097–1108.
Hocking J, Price CJ (2009): Dissociating verbal and nonverbal audiovisual object processing. Brain Lang 108:89–96.
Howard D, Nickels L, Coltheart M, Cole-Virtue J (2006): Cumulative semantic inhibition in picture naming: Experimental and computational studies. Cognition 100:464–482.
Hoffman P, Binney RJ, Ralph MAL (2015): Differing contributions of inferior prefrontal and anterior temporal cortex to concrete and abstract conceptual knowledge. Cortex 63:250–266.
Humphreys GF, Hoffman P, Visser M, Binney RJ, Ralph MAL (2015): Establishing task-and modality-dependent dissociations between the semantic and default mode networks. Proc Natl Acad Sci USA 112:7857–7862.
Jackson RL, Hoffman P, Pobric G, Ralph MAL (2015): The nature and neural correlates of semantic association versus conceptual similarity. Cer Cor 25:4319–4333.
Jefferies E, Baker SS, Doran M, Ralph MAL (2007): Refractory effects in stroke aphasia: A consequence of poor semantic control. Neuropsychologia 45:1065–1079.
Jefferies E, Patterson K, Ralph MAL (2008): Deficits of knowledge versus executive control in semantic cognition: Insights from cued naming. Neuropsychologia 46:649–658.
Jefferies E, Ralph MAL (2006): Semantic impairment in stroke aphasia versus semantic dementia: A case-series comparison. Brain 129:2132–2147.
Joseph JE, Gathers AD (2003): Effects of structural similarity on neural substrates for object recognition. Cogn Affect Behav Neurosci 3:1–16.
Kan IP, Thompson-Schill SL (2004): Effect of name agreement on prefrontal activity during overt and covert picture naming. Cog Affect Behav Neurosci 4:43–57.
Kriegeskorte N, Simmons WK, Bellgowan PS, Baker CI (2009): Circular analysis in systems neuroscience: the dangers of double dipping. Nat Neurosci 12:535–540.
Levelt WJ, Schriefers H, Vorberg D, Meyer AS, Pechmann T, Havinga J (1991): The time course of lexical access in speech production: A study of picture naming. Psychol Rev 98:122.
Levelt WJ (1999): Models of word production. Trends Cogn Sci 3: 223–232.
Li CSR, Yan P, Sinha R, Lee TW (2008): Subcortical processes of motor response inhibition during a stop signal task. Neuroimage 41:1352–1363.
Luk G, Green DW, Abutalebi J, Grady C (2012): Cognitive control for language switching in bilinguals: A quantitative meta-analysis of functional neuroimaging studies. Lang Cogn Process 27:1479–1488.
MacDonald AW, Cohen JD, Stenger VA, Carter CS (2000): Dissociating the role of the dorsolateral prefrontal and anterior cingulate cortex in cognitive control. Science 288:1835–1838.
Marconi D, Manenti R, Catricala E, Della Rosa PA, Siri S, Cappa SF (2013): The neural substrates of inferential and referential semantic processing. Cortex 49:2055–2066.
Martin A, Chao LL (2001): Semantic memory and the brain: Structure and processes. Curr Opin Neurobiol 11:194–201.
Mazaika P, Hoeft F, Glover G, Reiss A (2009): Methods and software for fMRI analysis for clinical subjects. The Organization of Human Brain Mapping. In: 15th Annual Meeting. pp 18–23.
McLaren DG, Ries ML, Xu G, Johnson SC (2012): A generalized form of context-dependent psychophysiological interactions (gPPI): a comparison to standard approaches. Neuroimage 61: 1277–1286.
Miller BT, D'Esposito M (2005): Searching for "the top" in top-down control. Neuron 48:535–538.
Mion M, Patterson K, Acosta-Cabronero J, Pengas G, Izquierdo-Garcia D, Hong YT, Nestor PJ (2010): What the left and right anterior fusiform gyri tell us about semantic memory. Brain 133:3256–3268.
Moss H, Abdallah S, Fletcher P, Bright P, Pilgrim L, Acres K, Tyler L (2005): Selecting among competing alternatives: Selection and retrieval in the left inferior frontal gyrus. Cereb Cortex 15:1723–1735.
Murtha S, Chertkow H, Beauregard M, Evans A (1999): The neural substrate of picture naming. J Cogn Neurosci 11:399–423.
Navarrete E, Mahon BZ, Caramazza A (2010): The cumulative semantic cost does not reflect lexical selection by competition. Acta Psychol 134:279–289.
Nelson SM, Dosenbach NU, Cohen AL, Wheeler ME, Schlaggar BL, Petersen SE (2010): Role of the anterior insula in task-level control and focal attention. Brain Struct Funct 214:669–680.
Nisi M, Longoni AM, Snodgrass JG (2000): Misure italiane per l'accordo sul nome, familiarità ed età di acquisizione, per le 260 figure di Snodgrass e Vanderwart (1980. G Ital Psicol 27: 205–220.
Noonan KA, Jefferies E, Corbett F, Ralph MAL (2010): Elucidating the nature of deregulated semantic cognition in semantic aphasia: Evidence for the roles of prefrontal and temporo-parietal cortices. J Cogn Neurosci 22:1597–1613.
Noonan KA, Jefferies E, Visser M, Ralph MAL (2013): Going beyond inferior prefrontal involvement in semantic control: Evidence for the additional contribution of dorsal angular gyrus and posterior middle temporal cortex. J Cogn Neurosci 25:1824–1850.
Novick JM, Kan IP, Trueswell JC, Thompson-Schill SL (2009): A case for conflict across multiple domains: Memory and

language impairments following damage to ventrolateral prefrontal cortex. Cogn Neuropsychol 26:527–567.
Oppenheim GM, Dell GS, Schwartz MF (2010): The dark side of incremental learning: A model of cumulative semantic interference during lexical access in speech production. Cognition 114: 227–252.
Parsons MW, Harrington DL, Rao SM (2005): Distinct neural systems underlie learning visuomotor and spatial representations of motor skills. Hum Brain Mapp 24:229–247.
Pobric G, Jefferies E, Ralph MAL (2007): Anterior temporal lobes mediate semantic representation: mimicking semantic dementia by using rTMS in normal participants. Proc Natl Acad Sci USA 104:20137–20141.
Pobric G, Jefferies E, Ralph MAL (2010): Category-specific versus category-general semantic impairment induced by transcranial magnetic stimulation. Curr Biol 20:964–968.
Price CJ, Moore C, Humphreys G, Frackowiak R, Friston K (1996): The neural regions sustaining object recognition and naming. Proc R Soc Lond B: Biol Sci 263:1501–1507.
Price CJ, Noppeney U, Phillips J, Devlin JT (2003): How is the fusiform gyrus related to category-specificity? Cogn Neuropsychol 20:561–574.
Price CJ, Devlin JT, Moore CJ, Morton C, Laird AR (2005): Meta-analyses of object naming: Effect of baseline. Hum Brain Mapp 25:70–82.
Robles SG, Gatignol P, Capelle L, Mitchell M, Duffau H (2005): The role of dominant striatum in language: A study using intraoperative electrical stimulations. J Neurol Neurosurg Psychiatry 76:940–946.
Rogers T, Hocking J, Mechelli A, Patterson K, Price CJ (2005): Fusiform activation to animals is driven by the process, not the stimulus. J Cogn Neurosci 17:434–445.
Rowe JB, Toni I, Josephs O, Frackowiak RS, Passingham RE (2000): The prefrontal cortex: Response selection or maintenance within working memory? Science 288:1656–1660.
Rowe JB, Passingham RE (2001): Working memory for location and time: Activity in prefrontal area 46 relates to selection rather than maintenance in memory. Neuroimage 14:77–86.
Ridderinkhof KR, van den Wildenberg WP, Segalowitz SJ, Carter CS (2004): Neurocognitive mechanisms of cognitive control: The role of prefrontal cortex in action selection, response inhibition, performance monitoring, and reward-based learning. Brain Cogn 56:129–140.
Runnqvist E, Costa A (2012): Is retrieval-induced forgetting behind the bilingual disadvantage in word production? Biling Lang Cogn 15:365–377.
Salmelin R, Hari R, Lounasmaa O, Sams M (1994): Dynamics of brain activation during picture naming. Nature 368:463–465.
Schnur TT, Schwartz MF, Brecher A, Hodgson C (2006): Semantic interference during blocked-cyclic naming: Evidence from aphasia. J Mem Lang 54:199–227.
Schnur TT, Schwartz MF, Kimberg DY, Hirshorn E, Coslett HB, Thompson-Schill SL (2009): Localizing interference during naming: Convergent neuroimaging and neuropsychological evidence for the function of Broca's area. Proc Natl Acad Sci USA 106:322–327.
Schriefers H, Meyer AS, Levelt WJ (1990): Exploring the time course of lexical access in language production: Picture-word interference studies. J Mem Lang 29:86–102.
Sergent J, Ohta S, Macdonald B (1992): Functional neuroanatomy of face and object processing. A positron emission tomography study. Brain 115:15–36.
Shadmehr R, Holcomb HH (1999): Inhibitory control of competing motor memories. Exp Brain Res 126:235–251.
Soni M, Ralph MAL, Noonan K, Ehsan S, Hodgson C, Woollams AM (2009): "L" is for tiger: Effects of phonological (mis) cueing on picture naming in semantic aphasia. J Neurolinguistics 22:538–547.
Strijkers K, Costa A, Thierry G (2009): Tracking lexical access in speech production: electrophysiological correlates of word frequency and cognate effects. Cereb Cortex.20:912–928.
Strijkers K, Yum YN, Grainger J, Holcomb PJ (2011): Early goal-directed top-down influences in the production of speech. Front Psychol 2:371.
Thierry G, Price CJ (2006): Dissociating verbal and nonverbal conceptual processing in the human brain. J Cogn Neurosci 18: 1018–1028.
Thompson-Schill SL, D'Esposito M, Aguirre GK, Farah MJ (1997): Role of left inferior prefrontal cortex in retrieval of semantic knowledge: A reevaluation. Proc Natl Acad Sci USA 94: 14792–14797.
Thompson-Schill SL, Kurtz KJ, Gabrieli JD (1998): Effects of semantic and associative relatedness on automatic priming. J Mem Lang 38:440–458.
Thompson-Schill SL, D'Esposito M, Kan IP (1999): Effects of repetition and competition on activity in left prefrontal cortex during word generation. Neuron 23:513–522.
Thompson-Schill SL, Botvinick MM (2006): Resolving conflict: A response to Martin and Cheng (2006). Psychon Bull Rev 13: 402–408.
Tyler LK, Chiu S, Zhuang J, Randall B, Devereux BJ, Wright P, Taylor KI (2013): Objects and categories: Feature statistics and object processing in the ventral stream. J Cogn Neurosci 25: 1723–1735.
Tzourio-Mazoyer N, Landeau B, Papathanassiou D, Crivello F, Etard O, Delcroix N, Mazoyer B, Joliot M (2002): Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. Neuroimage 15:273–289.
Vandenberghe R, Price C, Wise R, Josephs O, Frackowiak RS (1996): Functional anatomy of a common semantic system for words and pictures. Nature 383:254–256.
Vieth HE, McMahon KL, Cunnington R, de Zubicaray GI (2015): Interference from object part relations in spoken word production: Behavioural and fMRI evidence. J Neurolinguist 36:56–71.
Vitkovitch M, Rutter C, Read A (2001): Inhibitory effects during object name retrieval: The effect of interval between prime and target on picture naming responses. Br J Psychol 92:483–506.
Wagner AD, Maril A, Bjork RA, Schacter DL (2001a): Prefrontal contributions to executive control: fMRI evidence for functional distinctions within lateral prefrontal cortex. Neuroimage 14: 1337–1347.
Wagner AD, Paré-Blagoev EJ, Clark J, Poldrack RA (2001b): Recovering meaning: Left prefrontal cortex guides controlled semantic retrieval. Neuron 31:329–338.
Whitfield-Gabrieli S, Nieto-Castanon A (2012): Conn: a functional connectivity toolbox for correlated and anticorrelated brain networks. Brain Connect 2:125–141.
Whitney C, Kirk M, O'Sullivan J, Ralph MAL, Jefferies E (2012): Executive semantic processing is underpinned by a large-scale neural network: Revealing the contribution of left prefrontal, posterior temporal, and parietal cortex to controlled retrieval and selection using TMS. J Cogn Neurosci 24:133–147.