

RESEARCH ARTICLE

Functional connectivity reveals dissociable ventrolateral prefrontal mechanisms for the control of multilingual word retrieval

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Abstract

This functional magnetic resonance imaging study established that different portions of the ventrolateral prefrontal cortex (vIPFC) support reactive and proactive language control processes during multilingual word retrieval. The study also examined whether proactive language control consists in the suppression of the nontarget lexicon. Healthy multilingual volunteers participated in a task that required them to name pictures alternately in their dominant and less-dominant languages. Two crucial variables were manipulated: the *cue-target interval* (CTI) to either engage (long CTI) or prevent (short CTI) proactive control processes, and the *cognate status* of the to-be-named pictures (noncognates vs. cognates) to capture selective pre-activation of the target language. The results of the functional connectivity analysis showed a clear segregation between functional networks related to mid-vIPFC and anterior vIPFC during multilingual language production. Furthermore, the results revealed that multilinguals engage in proactive control to prepare the target language. This proactive modulation, enacted by anterior vIPFC, is achieved by boosting the activation of lexical representations in the target language. Finally, control processes supported by both mid-vIPFC and the left inferior parietal lobe, were similarly engaged by reactive and proactive control, possibly exerted on phonological representations to reduce cross-language interference.

KEYWORDS

fMRI, language control, multilingualism, proactive control, ventrolateral prefrontal cortex, word retrieval

1 | INTRODUCTION

Speech production is a fundamental human activity and a core cognitive operation involved in this skill is word retrieval from the mental

lexicon. Although word retrieval is often error-free and apparently effortless, the cognitive challenges are nontrivial. In fact, even a simple task such as naming a single object requires efficient control of processes involved in retrieving conceptual representations as well as

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post-retrieval selection processes that enhance the activation of target lexical representations relative to irrelevant competing representations (e.g., Costa, Strijkers, Martin, & Thierry, 2009; Indefrey & Levelt, 2004; Levelt, Roelofs, & Meyer, 1999; Roelofs, 1992).

A handful of neuroimaging studies have demonstrated a key role for the left ventrolateral prefrontal cortex (vIPFC) in word retrieval (e.g., Canini et al., 2016; Kan & Thompson-Schill, 2004; Saur et al., 2008; Snyder et al., 2010; Thompson-Schill, D'Esposito, Aguirre, & Farah, 1997), with the anterior portion proving particularly important for controlled retrieval and the middle portion recruited for post-retrieval selection (Badre, Poldrack, Paré-Blagoev, Insler, & Wagner, 2005; Crescentini, Shallice, & Macaluso, 2010; but see Snyder, Banich, & Munakata, 2011) (the two-process account; Badre et al., 2005; Badre & Wagner, 2007).

For multilingual individuals, comprising approximately half of the world's population (Grosjean, 2010), word retrieval involves managing two or more languages. Thus, a distinctive feature of multilingual language production is that post-retrieval selection requires managing competition, not only between target and nontarget lexical representations within a language, but also between translation equivalents across languages (de Bot, 1992; Poulisse & Bongaerts, 1994; Green, 1986, 1998; Hermans, Bongaerts, De Bot, & Schreuder, 1998; Lee & Williams, 2001; see also Baus, Branzi, & Costa, 2015 and Branzi, Calabria, & Costa, 2018 for a review). Not surprisingly, activation in the left mid-vIPFC is a key feature of efficient word retrieval in multilingual language production (e.g., Branzi, Della Rosa, Canini, Costa, & Abutalebi, 2016; Luk, Green, Abutalebi, & Grady, 2012; Wang, Xue, Chen, Xue, & Dong, 2007). Nevertheless, previous functional magnetic resonance imaging (fMRI) studies have not manipulated variables related to lexicalisation processes, hence, the extent to which activity in mid-vIPFC during language switching reflects lexical access is still unclear.

Another unique feature of multilingual language production relates to the possibility that multilinguals prepare the target language. That is, even without knowing which specific words they will utter, multilinguals may make use of visual or auditory cues to prepare the language in which they will have to speak (Martin, Molnar, & Carreiras, 2016; Molnar, Ibáñez-Molina, & Carreiras, 2015; Wu & Thierry, 2017). Some evidence suggests that the anterior vIPFC might play a key role in language preparation. In fact, activity in this area is thought to reflect top-down influences and has been implicated in a variety of semantic tasks in which activation of task-relevant representations in the temporal lobe was observed prior to the arrival of the sensory-evoked activity (referred to as proactive top-down control processing; e.g., Bar et al., 2006; Chaumon, Kveraga, Barrett, & Bar, 2013). Accordingly, in addition to the mid-vIPFC enacting post-retrieval control of lexical competitors (henceforth 'reactive language control') (Green, 1998; Green & Abutalebi, 2013), it is entirely possible that the left anterior vIPFC supports language preparation, biasing activity in the multilingual mental lexicon (henceforth 'proactive language control'). The nature of this controlled activity may consist in down-regulation (i.e., inhibition) of the nontarget language (Green, 1998). Indeed, since preparation to speak in multilinguals involves preparing to use the target language, lexical representations of the

nontarget language could be inhibited even before speakers know the specific words they will utter.

Nevertheless, some results do not fully support this hypothesis linking the anterior vIPFC to language preparation. Reverberi et al. (2015) tested a group of bilinguals and found that preparation to speak in a different language (switch vs. stay trials) elicited activation in the precuneus and posterior cingulate cortex (see also Seo, Stocco, & Prat, 2018 for similar results). Even though these areas may play a role in language preparation, it is not clear from these studies whether their involvement reflected task switching-specific cognitive operations (e.g., retrieving the naming rule associated with the task cue) or language preparation processes per se.

Thus, prior research has not been able to establish whether reactive and proactive language control processes are supported by different vIPFC regions, and whether proactive language control involves suppression of nontarget lexical representations.

The present study addresses these important research questions with the following experimental design. We used fMRI and tested multilingual speakers in a picture-naming task that required them to switch between their dominant and less-dominant languages. As in previous studies (see Ruge, Jamadar, Zimmermann, & Karayanidis, 2013 for a review; Czernochowski, 2015), we manipulated the cue-target interval (CTI) to either engage (long CTI) or prevent (short CTI) proactive language control processes. In order to measure how language preparation affects multilingual lexical access, we also manipulated the cognate status of the to-be-named pictures. The cognate status of a word is determined by the extent to which it shares orthographic and phonological features with its translation equivalent in another language. Thus, cognates are translation words that have similar orthographic-phonological forms in two languages (e.g., tomato-English, tomate-Spanish). By contrast, noncognates are translation equivalents that share only their meaning (e.g., apple-English, manzana-Spanish). Typically, behavioural and neural differences between noncognate and cognate processing indicate that the lexical representations of two languages are simultaneously active (cognate effect; Christoffels, Firk, & Schiller, 2007). Hence, in the present study, differing from previous research (e.g., Reverberi et al., 2015; Wu & Thierry, 2017), we could examine whether activity in middle and anterior vIPFC is modulated by cross-language competition.

We determined two vIPFC regions of interest (ROIs), that is, the middle and anterior vIPFCs, and via functional connectivity (FC) we determined the networks associated with these regions during language switching. First, we hypothesised that left middle and anterior vIPFC would support partially dissociable mechanisms during multilingual language production. Hence, we expected these areas to be strongly coupled with different brain regions. Specifically, we expected activation of left mid-vIPFC to show tighter coupling with activation in the left inferior parietal lobe/supramarginal gyrus (IPL/SMG), reflecting attentional mechanisms for post-retrieval response conflict (Badre & Wagner, 2006; Green & Abutalebi, 2013). By contrast, we expected activation of left anterior vIPFC to show stronger coupling with activation in the left middle temporal gyrus

(MTG), a brain region associated with lexical processing (Badre & Wagner, 2007; Strijkers, Costa, & Pulvermüller, 2017).

To test our second hypothesis, that left mid-vIPFC and left anterior vIPFC would support reactive and proactive language control processes, respectively, we also examined neural responses in the two vIPFC ROIs and other regions determined by the FC analysis. On the one hand, we expected increased activation in mid-vIPFC for short versus long CTIs, reflecting reactive control processes involved in resolving post-retrieval interference. On the other hand, we expected increased activation in anterior vIPFC for the opposite contrast, reflecting mainly proactive modulations of the multilingual lexicon.

To test our third hypothesis, that proactive language control reduces co-activation of the two languages (preparation to speak in the target language), we examined the interaction between cognate status and CTI. Based on the hypotheses set out above, we expected a reduced cognate effect during long versus short CTIs in the left anterior vIPFC (proactive language control), but not in the left mid-vIPFC (reactive language control).

Finally, to test our fourth hypothesis, that proactive language control involves inhibitory processes, we assessed the pattern of CTI and cognate status interaction. The inhibitory control model (ICM) proposes that lexical representations are controlled at multiple levels (Green, 1998). One level of control is exerted locally by 'language task schemas'. These schemas directly regulate outputs from the lexico-semantic system by selecting target lexical representations and inhibiting nontarget lexical representations. A second level of control is implemented by a supervisory attentional system (SAS) that proactively alters the activation level of the selected language task schema. This modulation might indirectly bias activation of target language representations. While SAS modulation of the selected language task schema might not completely erase the consequences of post-retrieval competition, that is, reactive inhibition, it may nevertheless reduce competition by down-regulating the activation level of the nontarget language task schema. Hence, if proactive language control involves inhibition of the nontarget language (via SAS), this should be observed for cognates when comparing long versus short CTIs. In fact, cognates (e.g., *tomato* in English) should benefit from co-activation of their translation equivalents in the nontarget lexicon (e.g., *tomate* in Spanish) when both languages are co-activated (short CTI), but no longer benefit when the nontarget lexicon is proactively inhibited (long CTI). In other words, neural activation in anterior vIPFC should vary for long and short CTIs when naming cognates, but not noncognates.

2 | MATERIALS AND METHODS

2.1 | Participants

A total of 30 Spanish-Basque-English multilingual volunteers took part in the experiment. Four participants were excluded from further analyses due to excessive head motion during scanning (see 'Section 2.5.1'). Furthermore, a criterion for fMRI data inclusion in the analyses was adopted such that task blocks in which participants produced more than one erroneous response were modelled separately

and excluded from the main analyses. Importantly, given that the present experiment conformed to a block fMRI design, this criterion ensured that only those epochs or blocks containing at least 80% correct responses were included. Thus, three additional participants were excluded because they had more than 23% of epochs with more than one error. The final study sample consisted of 23 participants (mean age = 24 years \pm 4; 12 females).

For all participants, Spanish was the first and dominant language (L1), whereas English was a nondominant language, acquired later in life (i.e., L3; mean age of L3 acquisition = 5 years \pm 3). All participants were right-handed and had normal or corrected-to-normal vision. No participant had a history of major medical, neurological disorders, or treatment for a psychiatric disorder. The study protocol was approved by the Ethics Committee of the Basque Center on Cognition, Brain and Language (BCBL) and was carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. Prior to their inclusion in the study, all subjects provided informed written consent. Participants received monetary compensation for their participation.

2.2 | Stimuli

Two-hundred and eight line drawings of common and concrete objects, belonging to a wide range of semantic categories (e.g., animals, body parts, buildings, furniture) were selected for the study (International Picture Naming Project [IPNP] database, see Szekely et al., 2004). Of the selected pictures (160 experimental and 48 filler pictures), 50% were cognates and the remaining 50% were noncognates. Experimental pictures were matched for visual complexity (reported in the IPNP database) [$t(158) = 0.141, p = .888$] and picture names were matched for lexical frequency in Spanish and English [$t(158) = -0.689, p = .492$; and $t(158) = -0.689, p = .73$, respectively].

2.3 | Experimental task and procedure

Participants were presented with a language-switching task divided into eight experimental runs. Our analyses focused on switching blocks that were intermixed with single-language naming blocks (L1 naming and L3 naming) during functional data collection. Within each switching block, the two languages were continuously alternated (e.g., L1, L3, L1, L3, L1 or L3, L1, L3, L1, L3). We manipulated two variables: CTI (long, short) and the cognate status of the pictures (cognates, noncognates). This resulted in a total of 16 switching blocks for each condition of interest (i.e., short cognates, long cognates, short noncognates, and long noncognates). Each naming block included five experimental and two filler to-be-named pictures. Filler pictures had the same properties as experimental pictures. However, similarly to the single-language naming blocks, they were modelled separately in the fMRI analyses.

Because languages were continuously alternated within each switching block, we adopted different strategies to avoid predictability effects. This was particularly important in the present study, since being able to predict the upcoming language could attenuate

differences between proactive and reactive control conditions. Therefore, rather than inserting resting periods between the various types of naming blocks (switching and single-language naming blocks), we inserted filler trials. In this way, no temporal interval could be detected between different types of naming blocks.

Furthermore, by inserting filler trials and single-language naming blocks, we generated sequences in which language switches occurred at variable intervals. More precisely, language switches could occur after either one switch trial, or after one, two, three or four repeat trials. This ensured that the experimental task did not favour the detection of blocks as separated entities, or the extraction of statistical regularities, and therefore did not enable switch-repeat predictions.

Before participants underwent MRI scanning, they received the task instructions, were familiarised with picture names in both languages and performed a practice session. Instructions emphasised both speed and accuracy. During familiarisation, the experimenter suggested the correct response when participants could not retrieve the name of the object depicted in the picture. This was done in order to reduce the likelihood of errors during the actual fMRI experiment. Participants were also instructed to minimise jaw-tongue movements while producing overt vocal responses to pictures and to say 'skip' when they were not able to retrieve the name of the picture.

Once inside the MRI scanner, participants were presented with written instructions again. Then, the first trial started with a 'language cue' (i.e., Spanish or English flag) presented for 100 ms and then followed by the target picture for 700 ms. During the time interval between the cue and the picture (i.e., CTI), a fixation cross was presented either for 50 ms or for 900 ms. Hence, the total time between the cue and the target picture presentation was either 150 ms (i.e., short CTI) or 1,000 ms (i.e., long CTI), respectively. Since every trial had a fixed duration, that is, 3 s, the time between the presentation of the target picture and the beginning of the following trial was variable (either of 2,850 ms or of 2,000 ms).

Four resting fixation baseline intervals were included within each functional run in which a fixation cross was displayed for 18 s at the centre of the screen. The task was presented by means of Presentation software (Neurobehavioural systems: <http://www.neurobs.com/>). We opted for an fMRI block design because using an event-related design would not have allowed us to disentangle proactive control effects (cue evoked responses) from effects arising during target presentation without modifying the CTIs (in the present study, both CTIs were less than 1 s). Since such modifications could unintentionally have altered the deployment of proactive and reactive control (see Ruge et al., 2013 for a discussion), we preferred to avoid them. Instead, as in other studies (see Ruge et al., 2013), we contrasted blocks with and without language preparation. Second, relative to an event-related design, the block design allowed us to maximise statistical power (Friston, Zarahn, Josephs, Henson, & Dale, 1999).

Vocal responses to each picture were classified as correct responses, incorrect responses or omissions (nonresponses) for the assessment of accuracy. The background noise in the scanner did not allow us to obtain accurate measures for naming latencies. Hence, we only report the behavioural analysis for accuracy (see 'Section 2.4').

2.4 | Behavioural data analysis

Behavioural analysis was performed on accuracy measures in order to explore the consequences of proactive (long vs. short CTI) and reactive control (short vs. long CTI) on multilingual lexical access (cognate effect). To this end, we conducted a 2 (CTI: long, short) \times 2 (cognate status: cognate, noncognate) repeated measures analysis of variance (ANOVA).

Importantly, we first excluded from this analysis those blocks that were not included in the fMRI analysis, that is, all the blocks in which more than one erroneous response was found (10.1%, $SD = 6.3$ of the blocks in total). Productions of incorrect names and verbal disfluencies (stuttering, utterance repairs, and production of nonverbal sounds) were also considered erroneous responses. Conversely, responses were considered correct whenever the expected name was given, but also when participants consistently used the appropriate label for the item (e.g., 'letterbox' instead of 'mailbox') when this did not affect its cognate status.

2.5 | MRI data acquisition and analysis

Whole-brain MRI data acquisition was conducted on a 3 T Siemens TRIO whole-body MRI scanner (Siemens Medical Solutions) using a 32-channel whole-head coil. Snugly fitting headphones (MR Confon) were used to dampen background scanner noise and to enable communication with experimenters while in the scanner. Participants viewed stimuli back-projected onto a screen with a mirror mounted on the head coil. To limit head movement, the area between participants' heads and the coil was padded with foam and participants were asked to remain as still as possible to minimise jaw-tongue movements while producing vocal responses. Participants' responses were recorded with a 40 dB noise-reducing microphone system (FOMRI-III, Optoacoustics Ltd.). A dual adaptive filter system subtracted the reference input (MRI noise) from the source input (naming) and filtered the production instantly while recording the output. This optic fibre microphone was also mounted on the head coil and wired to the sound filter box, whose output port was directly wired to the audio in-line plug of the computer sound card. The audio files were saved and analysed to obtain participants' in-scanner naming accuracy.

Functional images were acquired in eight separate runs using a gradient-echo (GE) echo-planar pulse sequence with the following acquisition parameters: time to repetition (TR) = 2,500 ms, time to echo (TE) = 25 ms, 43 contiguous 3 mm³ axial slices, 0-mm inter-slice gap, flip angle = 90°, field of view (FoV) = 192 mm, 64 \times 64 matrix, 235 volumes per run. Each functional run was preceded by four functional dummy scans to allow for T1-equilibration effects that were discarded. High-resolution MPRAGE T₁-weighted structural images were also collected for each participant with the following parameters: TR = 2,300 ms, TE = 2.97 ms; flip angle = 9°, FoV = 256 mm, voxel size = 1 mm³, 150 slices.

2.5.1 | Preprocessing

Standard SPM8 (Wellcome Department of Cognitive Neurology, London) preprocessing routines and analysis methods were employed. Images were corrected for differences in timing of slice acquisition and were realigned to the first volume by means of rigid-body motion transformation. Motion parameters extracted from the realignment were used, after a partial spatial smoothing of 4-mm full width at half-maximum (FWHM) isotropic Gaussian kernel, to inform additional motion correction algorithms implemented by the Artefact Repair toolbox (ArtRepair; Stanford Psychiatric Neuroimaging Laboratory), so as to repair outlier volumes with sudden scan-to-scan motion exceeding 0.5 mm and/or 1.3% variation in global intensity, and correct these outlier volumes via linear interpolation between the nearest non-outliers time points (Mazaika, Hoefft, Glover, & Reiss, 2009). To further limit the influence of motion on our fMRI results, participants with more than 10% of to-be-corrected outlier volumes across functional runs were excluded. Before applying this additional motion correction procedure, we also checked for participants who showed a drift over 3 mm° in any of the translation (x, y, z) and rotation (yaw, pitch, roll) directions within each functional run. As a result of applying these motion correction criteria, we excluded a total of four participants from further data analyses.

After volume repair, structural and functional volumes were spatially normalised to T1 and echo-planar imaging templates, respectively. The normalisation algorithm used a 12-parameter affine transformation together with a nonlinear transformation involving cosine basis functions. During normalisation, the volumes were sampled to 3 mm^3 voxels. Templates were based on the MNI305 stereotaxic space (Cocosco, Kollokian, Kwan, Pike, & Evans, 1997), an approximation of Talairach space (Talairach & Tournoux, 1988). Functional volumes were then spatially smoothed with a 7-mm FWHM isotropic Gaussian kernel. Finally, time series were temporally filtered to eliminate contamination from the slow drift of signals (high-pass filter: 128 s).

2.5.2 | Whole-brain analysis

Statistical analyses were performed on individual participant data using the general linear model (GLM). The fMRI time series data were modelled by a series of impulses convolved with a canonical haemodynamic response function (HRF). The experimental conditions were modelled as 15 s epochs from the onset of the presentation of the first stimulus within each block until the end of the presentation of the last experimental stimulus within the block. The resulting functions were used as covariates in a GLM, along with the motion parameters for translation (i.e., x, y, z) and rotation (i.e., yaw, pitch, roll) as covariates of noninterest. The least-squares parameter estimates of the height of the best-fitting canonical HRF for each condition were used in pairwise contrasts. Contrast images, computed on a participant-by-participant basis, were submitted to group analyses. At the group level, the whole-brain contrast for all switching conditions (Switch > Rest) was computed by performing a one sample t test on these images, treating participants as a random effect. The standard

statistical threshold for whole-brain maps corresponded to a voxel-level significance threshold of $p < .001$, and a family wise error (FWE)-corrected critical cluster level of $p < .05$. Brain coordinates throughout the manuscript are reported in MNI atlas space (Cocosco et al., 1997).

2.5.3 | Seed-based whole-brain FC analysis

To identify the functional networks coupled with anterior vIPFC and mid-vIPFC activation during language switching, two separate seed-based whole-brain FC analyses were performed. The seeds used in these whole-brain FC analyses were identified from the Switch > Rest whole-brain functional T-contrast across all participants (see above) combined with target ROIs (anterior vIPFC and mid-vIPFC) determined according to the Automated Anatomical Labeling available in SPM. FC analysis was conducted via the beta-series correlation method (Rissman, Gazzaley, & D'Esposito, 2004), implemented in SPM with custom MATLAB scripts. The beta series correlation is a well-established FC method, which is particularly appropriate for the present fMRI design (e.g., Mumford, Turner, Ashby, & Poldrack, 2012).

The canonical HRF in SPM was fit to each trial in each of the experimental conditions and the resulting parameter estimates (i.e., beta values) were sorted according to the study conditions to produce a condition-specific beta series for each voxel. The beta series associated with these seeds were correlated with voxels across the entire brain to produce beta correlation images for each subject for the contrast Switch > Rest. These contrasts were subjected to an arc-hyperbolic tangent transform (Fisher, 1921) to allow for statistical inference based on the correlation magnitudes. Group-level one sample t test FC maps were performed on the resulting subject Switch > Rest contrast images for each of the selected seeds (i.e., left anterior vIPFC and left mid-vIPFC) using a voxel-wise FWE-corrected significance threshold of $p < .05$. The use of a more stringent corrected threshold in this whole-brain FC connectivity analysis is due to the different nature of this analysis, which derives from a GLM that includes all the betas for each single epoch (Rissman et al., 2004).

Given our hypothesis regarding the involvement of anterior vIPFC in proactive control and mid-vIPFC in reactive control during language switching, we expected to observe two distinct functional networks associated with each of these seed-based whole-brain FC analyses. Hence, to determine differential coupling strength between the anterior vIPFC and mid-vIPFC networks, these maps were submitted to a paired t test, using a voxel-level significance threshold of $p < .001$, and an FWE-corrected critical cluster level of $p < .05$.

Additionally, based on previous evidence (Badre & Wagner, 2007), we employed a lower threshold (i.e., a voxel-level significance threshold of $p < .001$, uncorrected) to examine differential coupling strength between anterior vIPFC and mid-vIPFC and ventral temporal areas. Based on prior evidence, we were aware that it might be difficult to detect these effects since the fMRI acquisition protocol employed in this study (i.e., GE) is typically susceptible to signal dropout in ventral parts of the lateral temporal cortex, including our target area (see for a discussion Halai, Welbourne, Embleton, & Parkes, 2014). Therefore, as in previous studies (Barredo, Öztekin, & Badre, 2013; Binney,

Embleton, Jefferies, Parker, & Lambon Ralph, 2010; Brambati, Benoit, Monetta, Belleville, & Joubert, 2010; Zahn et al., 2007), we employed a more liberal threshold to increase statistical power and the chances of observing effects only for the lateral temporal ventral region reported in the following section.

2.5.4 | ROI analysis

ROI analysis was conducted on a set of key regions determined from the literature (e.g., Badre & Wagner, 2006; Badre & Wagner, 2007) in order to examine interactions between CTI and cognate status. The specific coordinate for each region was derived from the highest local maximas within the seed-based FC networks associated with proactive (i.e., anterior vIPFC) and reactive control (i.e., mid-vIPFC) (see Table 1). Note that identifying these ROIs from the networks derived from seed-based whole-brain FC during language switching (i.e., Switch > Rest) allowed us to avoid biases associated with the effects tested in the ROI analyses (i.e., CTI and cognate status main effects and interaction). In fact, we constrained the ROIs to voxels that were coupled with left anterior and mid-vIPFC across all the experimental task conditions. Importantly, in this analysis, as well as in the pairwise FC analysis (see below), we employed 5-mm radius spheres centred on the highest local maximas within each ROI, also for left anterior vIPFC and left mid-vIPFC regions. This was done to ensure that differences in coupling strength in the pairwise FC analysis (see below) were not determined by differences in the size of the functionally defined ROIs. Note that the choice of 5-mm spheres was made to restrict all the ROIs, including those defined around small clusters (e.g., MTG), to voxels within the functional networks.

Parameter estimates (i.e., beta values) for each ROI were extracted with the MARSBAR toolbox (Brett, Anton, Valabregue, & Poline, 2002). Then, to specifically examine to what extent multilingual lexical access was affected by proactive and reactive control, we submitted percent signal change values from each ROI to a 2 (CTI: long, short) \times 2 (cognate status: cognate, noncognate) repeated measures ANOVA. Bonferroni corrections for multiple comparisons were applied to the post hoc analyses.

2.5.5 | Pairwise FC analysis

Finally, to examine whether coupling strength between pairs of ROIs within these two networks was modulated by CTI variables and/or

cognate status, pairwise FC analysis was conducted using the beta-series correlation method (Rissman et al., 2004). The canonical HRF in SPM was fitted to each occurrence of each single condition and the resulting parameter estimates (i.e., beta values) were sorted according to the study conditions to produce a condition-specific beta series for each voxel. To examine pairwise FC between the ROIs, beta correlation values for each pair of ROIs per subject and condition were calculated. Then, an arc-hyperbolic tangent transform (Fisher, 1921) was applied at the subject level to the beta-series correlation values (r values) of each pair of ROIs and each study condition. Since the correlation coefficient is inherently restricted to range from -1 to 1 , this transformation served to make its null hypothesis sampling distribution approach that of the normal distribution. Then, in order to test for significant differences in coupling strength between conditions of interest, we submitted these Fisher's z normally distributed values for each pair of ROIs, participant and condition, to paired t tests using a false discovery rate correction for multiple comparisons set at $q < 0.05$.

3 | RESULTS

3.1 | Behavioural results

We performed behavioural analysis on accuracy measures to explore the behavioural consequences of proactive and reactive control on multilingual lexical access. Results revealed a significant main effect of CTI [$F(1, 22) = 11.438, p = .003, \eta^2 = 0.342$], indicating that responses for short CTI (93.9%, $SD = 1$) were more accurate than those for long CTI (92.2%, $SD = 3$) (see Figure 1). Results also revealed more accurate responses for cognates (94.5%, $SD = 2$) as compared to noncognates (91.6%, $SD = 3$) [main effect of cognate status: $F(1, 22) = 33.152, p < .001, \eta^2 = 0.601$]. The interaction between CTI and cognate status was not significant [$F(1, 22) = 1.035, p = .32, \eta^2 = 0.045$], suggesting that cognates and noncognates were similarly modulated by long and short CTIs.

3.2 | fMRI results

3.2.1 | Whole-brain contrast results

To identify brain regions associated with language switching across all participants, we computed a whole-brain T-contrast for Switch > Rest.

TABLE 1 Coordinates of ROIs (spheres) for each FC network

Network	x	y	z	Location
Left mid-vIPFC network	-51	29	19	Left mid-vIPFC (BA45)
	-45	29	25	Left MFG (BA46)
	-42	-46	49	Left IPL/SMG (BA40)
Left anterior vIPFC network	-27	29	-8	Left anterior vIPFC (BA47)
	39	32	-11	Right anterior vIPFC (BA47)
	-57	-13	-23	Left MTG

Abbreviations: FC, functional connectivity; IPL, inferior parietal lobe; Mid, Middle; MFG, middle frontal gyrus; MTG, middle temporal gyrus; ROI, region of interest; SMG, supramarginal gyrus; vIPFC, ventrolateral prefrontal cortex.

The contrast revealed the involvement of a bilateral network of regions, including both language control and representational areas. Importantly, both left mid- and anterior vIPFCs were significantly activated by this contrast (see Figure 2).

3.3 | Seed-based whole-brain FC results

This analysis aimed to identify which areas were strongly coupled with left mid-vIPFC and left anterior vIPFC during multilingual word retrieval. Whole-brain FC from left mid-vIPFC (left: $-43, 28, 15; 10,840 \text{ mm}^3$) and left anterior vIPFC (left: $-35, 28, -10; 4,392 \text{ mm}^3$) (see green and blue regions in Figure 2) revealed partially overlapping

brain networks, including both cortical and subcortical cognitive control regions, as well as temporal brain areas (see Figure 3a).

Paired *t*-test results indicated significant differential coupling strength between whole-brain FC originating from these two seeds (see Figure 3b). On the one hand, whole-brain FC from left mid-vIPFC versus left anterior vIPFC was significantly tighter in lateral dorsal PFC regions, left IPL/SMG, and posterior temporal regions. On the other hand, whole-brain FC from left anterior vIPFC versus left mid-vIPFC was significantly stronger in left MTG and right anterior vIPFC.

3.4 | ROI results

We conducted ROI analyses to examine interactions between CTI and cognate status variables. The results (see Table 2 and Figure 4) can be summarised as follows: The left IPL/SMG and the two frontal ROIs within the mid-vIPFC network were not sensitive to the CTI manipulation, suggesting that they were similarly recruited for reactive and proactive control. Moreover, these regions were sensitive to the cognate manipulation and showed increased neural responses for cognates as compared to noncognates (i.e., cognate status main effect). This effect was also qualified by a significant interaction between cognate status and CTI. Follow-up *t* tests revealed that the significant interaction was determined by a larger cognate effect (cognate vs. noncognate difference) during short as compared to long CTIs [left mid-vIPFC (BA45): $t(22) = 2.133, p = .044$; left middle frontal gyrus (MFG, BA46): $t(22) = 3.056, p = .006$; left IPL/SMG (BA40): $t(22) = 4.493, p < .001$]. The left MTG showed sensitivity to the

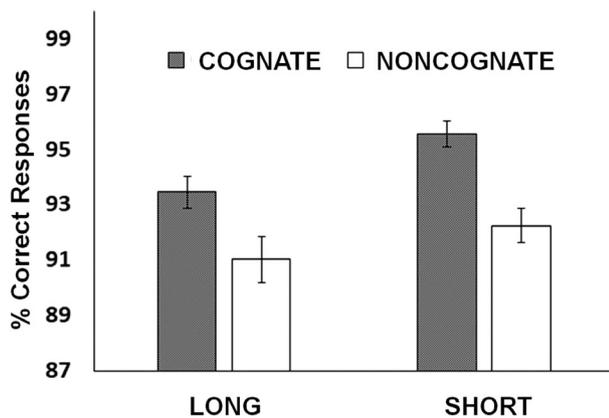


FIGURE 1 Behavioural results for accuracy. Error bars denote standard errors (SEs)

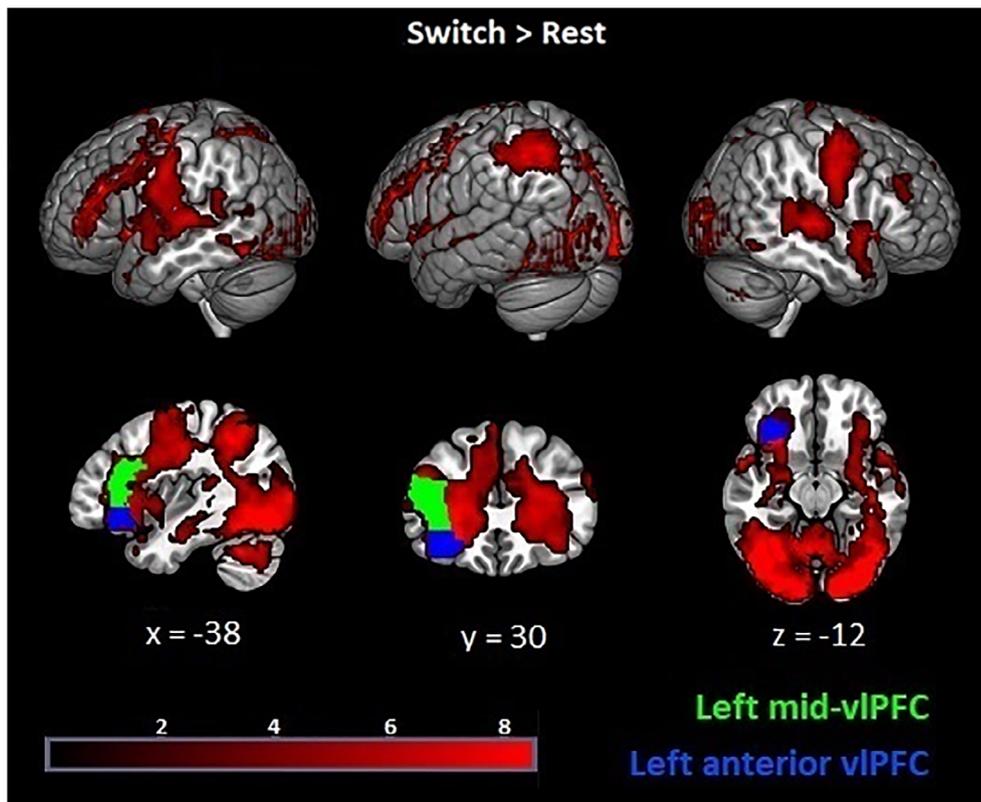
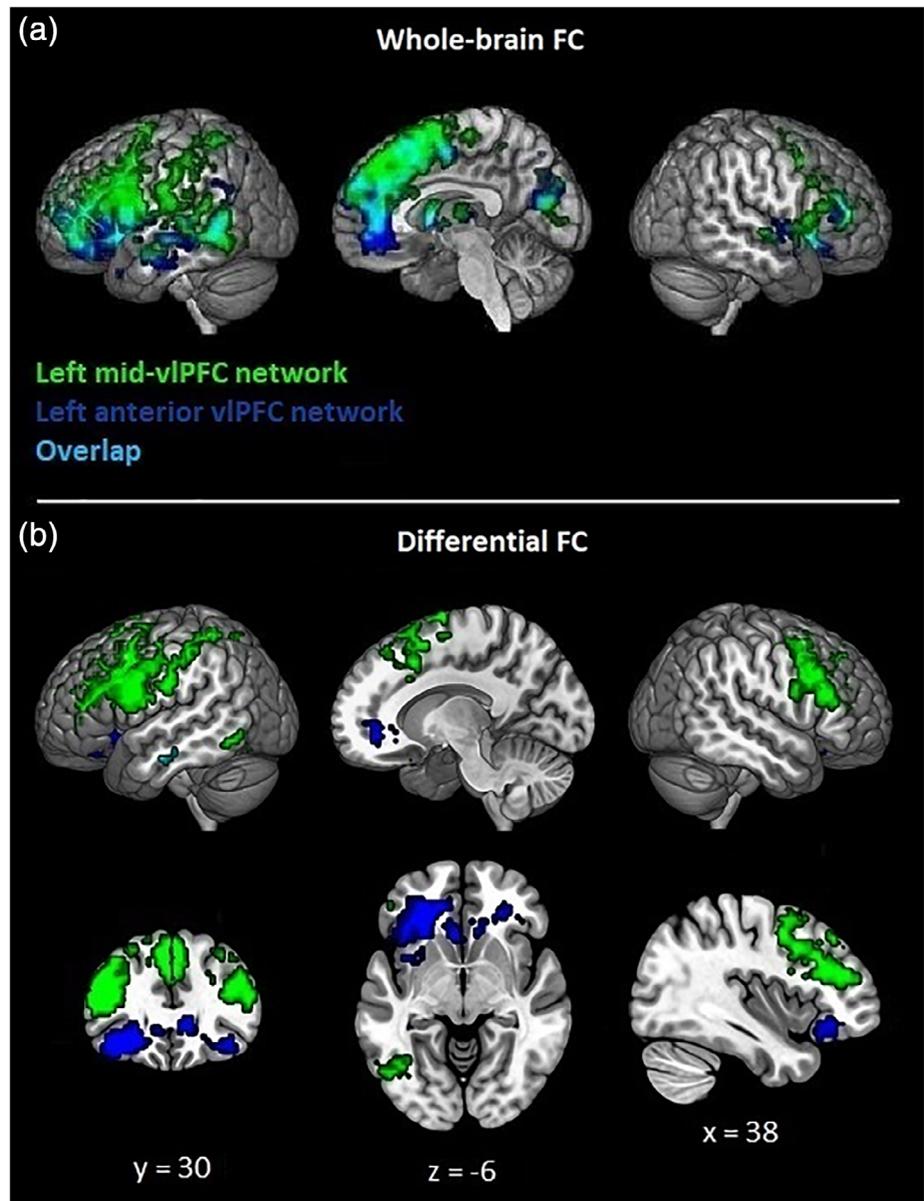


FIGURE 2 Whole-brain Switch > Rest contrast (voxel-level significance threshold of $p < .001$, and a family wise error (FWE)-corrected critical cluster level of $p < .05$). Seed regions used in the subsequent whole-brain functional connectivity (FC) analyses are highlighted in green and blue colours, respectively, for left mid-ventrolateral prefrontal cortex (vIPFC) and left anterior vIPFC

FIGURE 3 (a) Whole-brain functional connectivity (FC) for left mid-ventrolateral prefrontal cortex (vIPFC) (green) and left anterior vIPFC (blue) networks (voxel-wise significance threshold was set at $p < .05$, family wise error [FWE] corrected); (b) differential FC for left mid-vIPFC network > left anterior vIPFC network (green) and for left anterior vIPFC network > left mid-vIPFC network (blue) (voxel-level significance threshold of $p < .001$, and an FWE-corrected critical cluster level of $p < .05$). Differential FC for left anterior vIPFC network > left mid-vIPFC network is also reported in the left ventral lateral temporal cortex at a voxel-level significance threshold set at $p < .001$, uncorrected (cyan blob in left lateral sagittal rendering)



cognate status manipulation with increased activation for cognates and reduced activation for noncognates.

The left and right anterior vIPFCs were both sensitive to the cognate status manipulation. Moreover, in these areas, a significant interaction between CTI and cognate status revealed that activation for noncognates was increased during long as compared to short CTIs (proactive modulation). Consequently, the difference between cognates and noncognates was reduced in left anterior vIPFC [$t(21) = 2.45, p = .023$] during long versus short CTIs and eliminated in right anterior vIPFC.

To establish a functional dissociation between left anterior vIPFC and mid-vIPFC for language preparation (reduction of the cognate effect), we sought evidence for a significant ROI (left mid-vIPFC, left anterior vIPFC) \times cognate status (cognate, noncognate) \times CTI (short, long) interaction. Interestingly, a significant triple interaction indicated that in anterior vIPFC neural responses for noncognates were

modulated by preparation time [$F(1, 21) = 6.749, p = .017, \eta^2 = 0.243$]. In other words, a significant increase in activity for long versus short intervals was observed in the left anterior vIPFC ($p = .008$), but not in the mid-vIPFC (i.e., the MFG) ($p = .139$).

3.5 | Pairwise FC results

We further investigated whether coupling strength between our ROIs could be modulated by CTI and cognate status. Hence, we conducted a pairwise FC analysis between the selected ROIs.

FC between pairs of ROIs was modulated by proactive control (long vs. short CTIs) only for noncognates. More precisely, increased FC was observed for long versus short CTIs between left anterior vIPFC (BA47) and left mid-vIPFC (BA45) ($t = 2.34, q < 0.05$), and between right anterior vIPFC (BA47) and left mid-vIPFC (BA45) ($t = 2.58, q < 0.05$) (see Figure 5a). Accordingly, when proactive

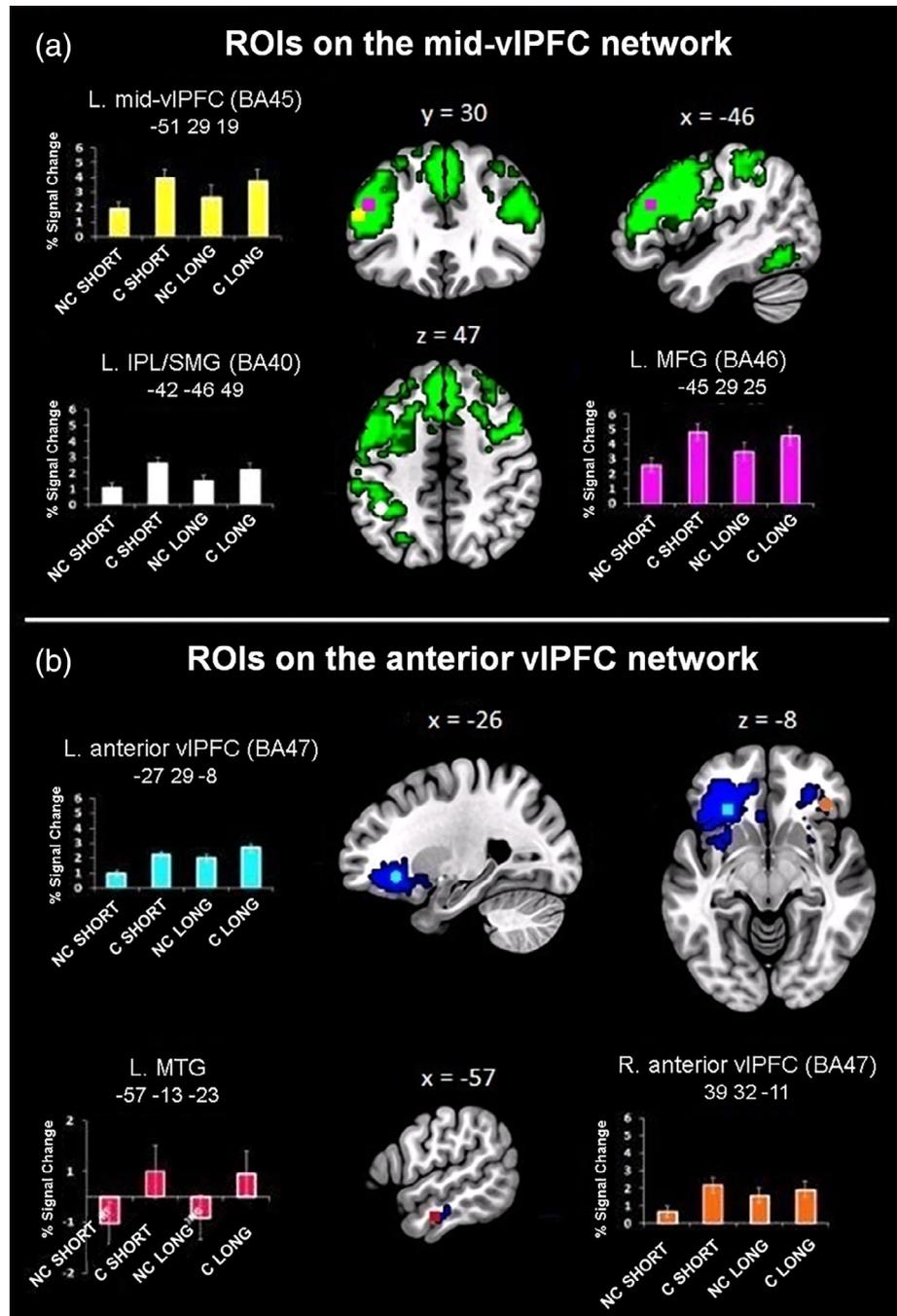
TABLE 2 Summary of results of ROI analyses

ROIs	CTI (long > short)	Cognate status (C > NC)	Interaction	Post hoc test (Bonferroni corrected)	Follow up t tests
1. Left mid-vIPFC (BA45)	F (1, 22) = 1.46 p = .706 $\eta^2 = 0.007$	F (1, 22) = 16.584 p = .001 $\eta^2 = 0.430$	F (1, 22) = 4.546 p = .044 $\eta^2 = 0.171$	a) Short CTI: C > NC (p < .001) b) Long CTI: C > NC (p = .009)	a > b [t (22) = 2.133, p = .044]
2. Left MFG (BA46)	F (1, 22) = 0.202 p = .658 $\eta^2 = 0.009$	F (1, 22) = 16.46 p = .001 $\eta^2 = 0.428$	F (1, 22) = 11.6 p = .003 $\eta^2 = 0.345$	a) Short CTI: C > NC (p < .001) b) Long CTI: C > NC (p = .028)	a > b [t (22) = 3.056, p = .006]
3. Left IPL/SMG (BA40)	F (1, 22) = 0.014 p = .908 $\eta^2 = 0.001$	F (1, 22) = 24.899 p < .001 $\eta^2 = 0.531$	F (1, 22) = 23.214 p < .001 $\eta^2 = 0.513$	a) Short CTI: C > NC (p < .001) b) Long CTI: C > NC (p = .002)	a > b [t (22) = 4.493, p < .001]
4. Left anterior vIPFC (BA47) ^a	F (1, 21) = 5.922 p = .024 $\eta^2 = 0.220$	F (1, 21) = 46.459 p < .001 $\eta^2 = 0.689$	F (1, 21) = 6.003 p = .023 $\eta^2 = 0.222$	NC: Long CTI > short CTI (p = .008) a) Short CTI: C > NC (p < .001) b) Long CTI: C > NC (p < .001)	a > b [t (21) = 2.45, p = .023]
5. Right anterior vIPFC (BA47)	F (1, 22) = 0.775 p = .388 $\eta^2 = 0.034$	F (1, 22) = 9.109 p = .006 $\eta^2 = 0.293$	F (1, 22) = 16.883 p < .001 $\eta^2 = 0.434$	NC: Long CTI > short CTI (p = .029) Short CTI: C > NC (p = .001)	
6. Left MTG	F (1, 22) = 0.008 p = .927 $\eta^2 < 0.001$	F (1, 22) = 9.875 p = .005 $\eta^2 = 0.31$	F (1, 22) = 0.257 p = .617 $\eta^2 = 0.012$		

^aBeta values above the threshold were found only for 22 participants.

Abbreviations: C, Cognate; CTI, cue-target interval; IPL, inferior parietal lobe; Mid, Middle; MFG, middle frontal gyrus; MTG, middle temporal gyrus; NC, Noncognate; ROI, region of interest; SMG, supramarginal gyrus; vIPFC, ventrolateral prefrontal cortex.

FIGURE 4 Region of interest (ROI) analyses for regions (a) within left mid-ventrolateral prefrontal cortex (vIPFC) network, including left mid-vIPFC, left middle frontal gyrus (MFG), and left inferior parietal lobe/supramarginal gyrus (IPL/SMG); and (b) within left anterior vIPFC network, including left and right anterior vIPFC and left middle temporal gyrus (MTG). Brain coordinates correspond to the MNI coordinates for the centre of mass of each ROI. Error bars denote *SEs*. Abbreviations: C, Cognate; L, Left; Mid, Middle; NC, Noncognate; R, Right



control was involved (long CTIs), stronger coupling for noncognates versus cognates was observed between left anterior vIPFC (BA47) and left mid-vIPFC (BA45) ($t = 2.47, q < 0.05$), and between right anterior vIPFC (BA47) and left IPL/SMG ($t = 2.21, q < 0.05$) (see Figure 5b).

In summary, we observed that the strength of coupling between different areas was specifically modulated by proactive control (long > short CTI). Importantly, in accordance with our ROI results (see above) the observed proactive modulation seemed to particularly affect noncognates (long: noncognates > cognates) that showed increased coupling between right anterior vIPFC and left IPL/SMG; and between left anterior vIPFC and left mid-vIPFC.

4 | DISCUSSION

This fMRI study addressed whether word retrieval in multilingual speakers is supported by dissociable vIPFC mechanisms reflecting proactive and reactive language control processes, and whether multilinguals use proactive control to suppress lexical representations of the nontarget language (Green, 1998).

By employing FC, we were able to reveal a clear segregation between functional networks related to mid-vIPFC and anterior vIPFC, supporting our first hypothesis that these two regions enact dissociable mechanisms for reactive and proactive control, respectively (see Badre & Wagner, 2007). Activation in left mid-vIPFC was

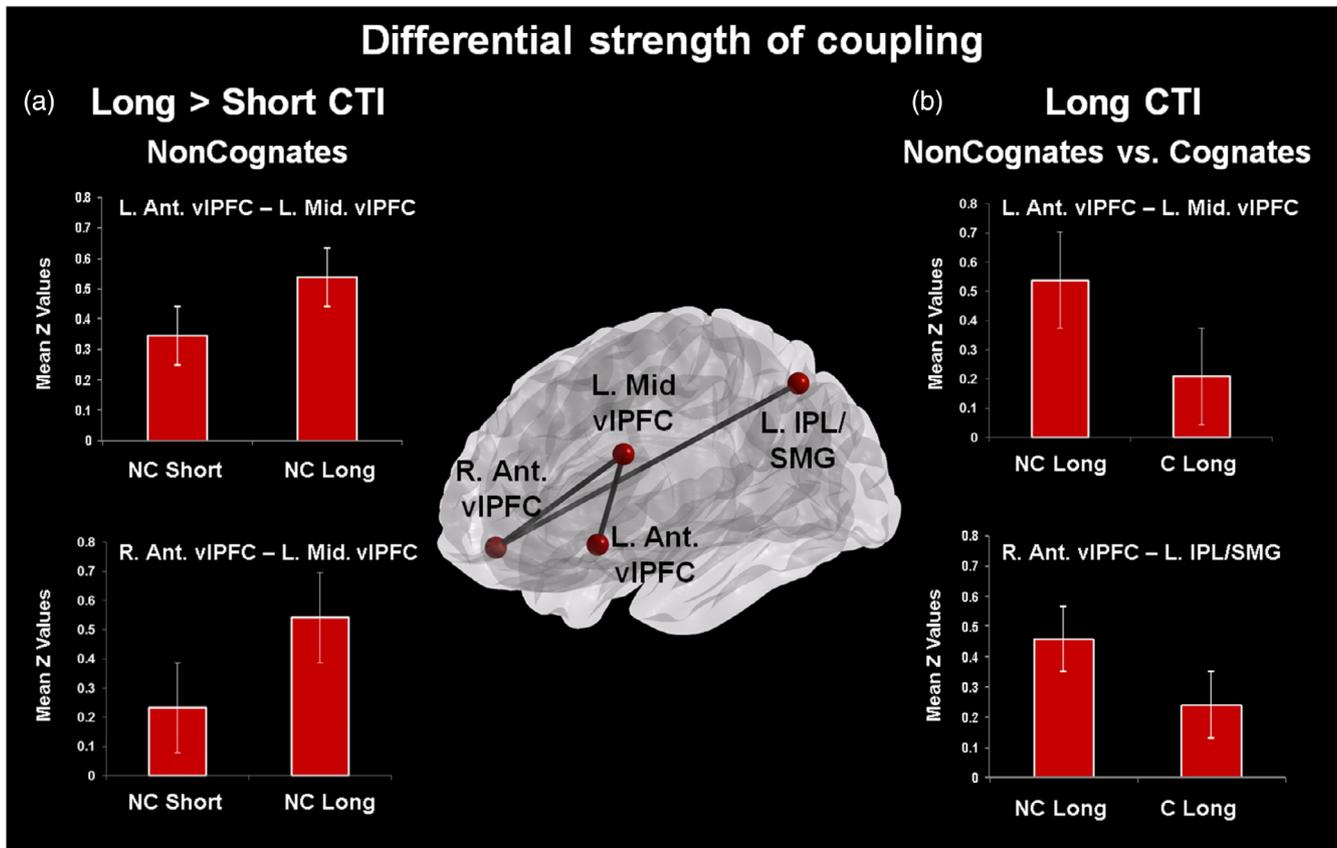


FIGURE 5 Pairwise functional connectivity (FC) results among region of interest (ROIs) showing differential strength of coupling for (a) long > short cue-target interval (CTI) and (b) long CTI. Error bars denote standard errors (SEs). Ant, Anterior; C, Cognate; IPL, inferior parietal lobe; L, Left; Mid, Middle; NC, Noncognate; R, Right; SMG, supramarginal gyrus; vIPFC, ventrolateral prefrontal cortex

coupled with activation in IPL/SMG. Instead, activation in left anterior vIPFC was coupled with activation in left MTG. Increased FC between left mid-vIPFC and left IPL/SMG is consistent with evidence showing that these areas are both engaged during reactive control processes in switching tasks (Badre & Wagner, 2006; Green & Abutalebi, 2013; Vallesi, Arbula, Capizzi, Causin, & D'Avella, 2015). The left IPL/SMG, a key region for phonological control (Hartwigsen et al., 2010), may support language selection enacted by left mid-vIPFC by biasing selection away from nontarget phonological representations (Abutalebi & Green, 2016; Branzi et al., 2016). Instead, increased FC between left anterior vIPFC and left MTG might reflect controlled retrieval of target lexical representations in the temporal lobe (Badre & Wagner, 2007).

In line with our second hypothesis that left anterior vIPFC would specifically be recruited for proactive language control, ROI analyses revealed increased neural activation in this area for long versus short CTIs. Contrary to our predictions, however, left mid-vIPFC did not show the expected increased neural responses for short versus long CTIs. Indeed, this region was not sensitive to the CTI manipulation, suggesting a similar involvement for reactive and proactive language control. It is possible that, when conditions allow, language control relies more on proactive control processes (Martin et al., 2016; Molnar et al., 2015). In language switching, this strategy may be crucial to adjust performance according to continuously changing goals. Hence,

this might result in a more extensive use of control areas during proactive control in general, ruling out 'specific' effects for reactive control (i.e., differential neural activation for short vs. long CTI conditions). It is worth mentioning that even if we cannot verify whether the expected increased neural responses in mid-vIPFC for short versus long CTIs were not observed because of fMRIs intrinsic limitations on capturing short-lived neural signals, the literature suggests this is an unlikely explanation. In fact, language switch effects measured via event-related potentials locked either to the language-cue (proactive control) or the target presentation (reactive control) do not substantially differ in their temporal duration (e.g., Christoffels et al., 2007; Jackson, Swainson, Cunnington, & Jackson, 2001; Lavric, Clapp, East, Elchlepp, & Monsell, 2019; Wu & Thierry, 2017).

Taken together, these results suggest that word retrieval in multilingual speakers is enacted by two distinct vIPFC areas, showing a different profile of regional engagement and network connectivity. The left mid-vIPFC supports language selection during proactive and reactive control and its coupling with left IPL/SMG might reflect phonological control. The left anterior vIPFC supports proactive language control specifically, and its connectivity with left MTG might reflect controlled access to lexical representations. Importantly, the ROIs associated with each network showed the same profile of engagement, with the exception of MTG, an area whose profile of activation

is consistent with a representational rather than a control role (see Badre & Wagner, 2007).

In line with our third hypothesis that proactive modulation in left anterior vIPFC, but not in mid-vIPFC, would affect language co-activation (i.e., cognate effect) during long versus short CTIs, we observed both a reduction and elimination of the cognate effect in left and right anterior vIPFC, respectively. Nevertheless, and contrary to our prediction, follow-up *t* tests revealed a reduced cognate effect also in left mid-vIPFC for long versus short CTIs. Even though this result may suggest that some proactive modulation is involved, it is not clear where this modulation was exerted, since neural responses in mid-vIPFC for both cognates and noncognates were not statistically different for long and short CTIs. Furthermore, the fact that activation in left mid-vIPFC was not sensitive to the CTI manipulation suggests that this area may not play a key role in proactive control. Taken together, these results provide evidence that proactive control is enacted by recruiting bilateral anterior vIPFC for selection of target lexical representations.

Supporting this conclusion, some studies have recently shown that preparatory processes affect bilingual language selection (e.g., Reverberi et al., 2015; Wu & Thierry, 2017). However, given that variables related to lexicalisation processes were not manipulated in those studies, it is unclear whether these preparatory processes were exerted on lexical representations. Indeed, the processing of a language-cue is preverbal (speakers do not yet know what they will say, but only which language they should use). Hence, preparation might involve only a general task-schema ('to name in a given language'), without necessarily inducing any modulation of language-specific representations. Our study allows us to make this inference. In fact, by manipulating the cognate status of the to-be-named pictures, we were able to assess how language control proactively modulates neural responses for cognates and noncognates, and therefore to elucidate the mechanisms underlying multilingual lexical access.

Our fourth main goal was to test whether proactive language control consists in an inhibitory modulation of the nontarget language. If so, we expected this effect to be observed for cognates when comparing long versus short CTIs. More precisely, we expected to observe neural activation in anterior vIPFC to vary between long and short CTIs when naming cognates. Contrary to our prediction, ROI results revealed that proactive modulation of the anterior vIPFC was exerted only for noncognates. This modulation consisted of increased neural responses during long versus short CTI conditions. Instead, proactive language control did not modulate neural activation for cognates. In line with the ROI results, pairwise FC results revealed that proactive control modulated the coupling strength between different areas, particularly for noncognate representations. Stronger coupling for noncognates as compared to cognates was observed between regions in the two networks, such as between left anterior vIPFC and left mid-vIPFC, and between right anterior vIPFC and left IPL/SMG. The tighter coupling observed between areas from these two networks during multilingual language production is an interesting and not previously reported finding. One possibility is that during long CTIs proactive control enacted by the anterior vIPFC is applied to lexical representations that are less activated (i.e., noncognates) via

interactions with brain areas involved in phonological control (IPL/SMG) and response selection (left mid-vIPFC). The involvement of the right anterior vIPFC during language switching is in accordance with previous findings that revealed that this region is sometimes co-activated with the left vIPFC during tasks that require overcoming mnemonic conflict (e.g., Shi, Wolfensteller, Schubert, & Ruge, 2018). Particularly, the right anterior vIPFC has been related to processes for feedback-driven reconfiguration and/or reversal of well-learned stimulus-response contingencies (e.g., Ruge & Wolfensteller, 2016; Shi et al., 2018). Hence, it is likely that right anterior vIPFC is engaged during continuous language switching in order to update stimulus-response rules according to the target language.

The present findings provide important insights regarding the neural mechanisms supporting multilingual language control. First, the dissociation found between cognates and noncognates suggests that proactive language control may be differently applied to lexical representations with different phonological overlaps. This observation contradicts models that propose that language control is applied globally to the nontarget language (Green, 1998; Green & Abutalebi, 2013). In fact, according to these models, neural responses for cognates should have been modulated by proactive language control to some extent. However, we did not observe such a result in any of the different functional neuroimaging analyses we performed.

Second, contrary to what we hypothesised, our findings suggest that cognate representations are maintained active during the entire task, and those of noncognates are selectively activated, rather than inhibited, via proactive control. Note that even if this modulation could be interpreted as an effect of task difficulty (i.e., increased demands for retrieving noncognate rather than cognate representations) rather than as a modulation of lexical representations, there are various observations that do not support this hypothesis. In fact, the neural responses that were most enhanced during language switching were those in the less demanding task conditions (i.e., cognates). Given the behavioural results, it is hard to argue that an increase in neural activity for noncognates (long vs. short CTI) reflects increased retrieval demands. Furthermore, it is unclear why retrieving noncognates would become particularly difficult when participants have time to prepare the target language (long CTI) as compared to when they cannot do so (short CTI). If anything, according to the current evidence, we would have expected the opposite result (e.g., Christoffels et al., 2007). For all these reasons, we suggest that the CTI modulation seen for noncognates may reflect a modulation of proactive control over the multilingual lexical system, rather than an effect of task difficulty.

The hypothesis that proactive control reflects activation of the target language predicts that the nontarget language should be activated in spite of proactive control. Ultimately, this activation would remain 'traceable' in the behavioural cognate effect for the long CTI condition. This interpretation and the results that we provide here are in accord with other non-inhibitory models of multilingual language control (Costa & Caramazza, 1999; Costa, Miozzo, & Caramazza, 1999; Runnqvist, Strijkers, Alario, & Costa, 2012). Finally, even though these results are not necessarily inconsistent with the ICM (Green & Abutalebi, 2013), since reactive inhibition may still occur (language task schema level), the fact we have not found

any neural differences between short versus long intervals suggests that when proactive control can be applied, it may reduce the deployment of reactive (inhibitory) control processes.

5 | CONCLUSION

This fMRI study demonstrates that word retrieval in multilinguals is enacted by different portions of the vIPFC associated with reactive and proactive language control processes and that during language switching multilingual speakers engage proactive control to activate the target language. These findings may have an impact on research into a multilingual advantage in domain-general executive control (Antón et al., 2014; Branzi, Calabria, Gade, Fuentes, & Costa, 2018), as they suggest that the extent to which an advantage in proactive control is observed might depend on the ratio of cognates to noncognates in the languages of a multilingual.

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CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available at <https://www.bcbl.eu/Datasharing/HBM2019Branzi/>.

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