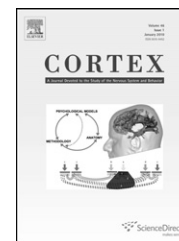


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Research report

On the selection of words and oral motor responses: Evidence of a response-independent fronto-parietal network

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ABSTRACT

Several brain areas including the medial and lateral premotor areas, and the prefrontal cortex, are thought to be involved in response selection. It is unclear, however, what the specific contribution of each of these areas is. It is also unclear whether the response selection process operates independent of response modality or whether a number of specialized processes are recruited depending on the behaviour of interest. In the present study, the neural substrates for different response selection modes (volitional and stimulus-driven) were compared, using sparse-sampling functional magnetic resonance imaging, for two different response modalities: words and comparable oral motor gestures. Results demonstrate that response selection relies on a network of prefrontal, premotor and parietal areas, with the pre-supplementary motor area (pre-SMA) at the core of the process. Overall, this network is sensitive to the manner in which responses are selected, despite the absence of a medio-lateral axis, as was suggested by Goldberg (1985). In contrast, this network shows little sensitivity to the modality of the response, suggesting of a domain-general selection process. Theoretical implications of these results are discussed.

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1. Introduction

Response selection occurs at the interface between cognitive and motor systems; it is a central component in planning actions. Despite the importance of this process, it is unclear whether different modes of response selection are implemented through similar or distinct neural networks. Selection can be implemented in many different ways, ranging from volitional to stimulus-driven. Volitional response selection corresponds to the most internally controlled selection mode,

requiring the awareness of selecting or rejecting possible responses, and a decision of which response to produce from among several equally appropriate response alternatives (Jahanshahi and Frith, 1998). At the opposite end of the spectrum, stimulus-driven selection corresponds to the least internally controlled mode, whereby the context determines the response to be performed, leading to a “forced choice”. While developed mainly to characterize simple motor actions, such as button presses, these concepts also apply to the production of more complex actions, such as spoken language

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(LNG) production. Volitional selection occurs, for instance, in verbal fluency and verb generation, tasks widely used as indexes of frontal lobe function (e.g., Frith et al., 1991; Milner, 1964). Forced selection occurs, for example, in picture naming and word repetition.

Currently, there is little attention focusing on incorporating response selection into contemporary models of LNG and speech. One important question is whether response selection is a domain-general process, or, alternatively, whether there are number of specialized selection processes across different domains and/or tasks. The existence of domain-general processes has important theoretical implications for modelling of spoken LNG behaviour. Contemporary models of LNG (e.g., Indefrey and Levelt, 2004) detail LNG-specific processes, such as lexical selection, morpho-phonological code retrieval and phonetic encoding, to the exclusion of generalized neural processes that might be shared across related behaviours. Similarly, speech production models (e.g., Guenther et al., 2006; Riecker et al., 2005) often either ignore higher-level motor aspects or rely on poorly defined and very general constructs such as motor planning/preparation as representing domain-general processes. Despite the lack of attention that domain-general processes have received in models of spoken LNG production, there is some evidence suggesting a link between LNG and other functional motor behaviours. For instance, behavioural studies have shown a connection between speech and hand gestures (Gentilucci et al., 2001; Gentilucci, 2003), and between LNG and oral motor gestures (Alcock et al., 2000; Alcock, 2006). Moreover, left hemisphere aphasic patients with speech-related impairments often have concomitant non-verbal oral movement impairments (Alcock et al., 2000; Alcock, 2006). The inclusion of non-verbal oral motor exercises in the treatment of acquired and developmental speech disorders is a common practice among speech–LNG pathologists (Skahan et al., 2007) despite the controversy that surrounds it (Ballard et al., 2003; Kimura and Watson, 1989; Ludlow et al., 2008; Weismer, 2006; Ziegler, 2003). One possibility is that the speech/LNG production system relies on processes that are used by other non-speech and LNG behaviours. A global understanding of brain functioning requires a thorough understanding of the extent to which neural systems supporting different behaviours overlap with one another. Examining the extent to which speech production and response selections reflect a domain-general processes was one of the objectives of the current study.

Another aspect of response selection that needs to be clarified concerns its neural implementation. Several brain areas, including the pre-supplementary motor area (pre-SMA), the anterior cingulate area (ACC), the dorso-lateral prefrontal cortex (DLPFC) and the inferior frontal gyrus (IFG), have been implicated in response selection. The pre-SMA has a connectivity pattern that is characterized by important projections from executive centers in the prefrontal cortex, in particular from the DLPFC (Lu et al., 1994; Luppino et al., 1993; Wang et al., 2005), suggesting an involvement in higher-order aspects of action. In line with this hypothesis, it has been shown recently, using functional magnetic resonance imaging (fMRI), that the presence of uncertainty regarding which motor response to prepare (random vs regular stimulus

presentation) is associated with enhanced activity in the pre-SMA as well as the dorsal premotor area (PMAd), suggesting a role for these areas in response selection (Sakai et al., 2000). The pre-SMA, however, appears to be modulated by the manner in which responses are selected, being more strongly active for volitional than forced selection of overt (Alario et al., 2006; Etard et al., 2000; Tremblay and Gracco, 2006) and covert words (Crosson et al., 2001), as well as for the volitional selection of finger movements (e.g., Deiber et al., 1996; Lau et al., 2004, 2006; Oostende et al., 1997; Sakai et al., 2000; Ullsperger and von Cramon, 2001). A role for the pre-SMA in response selection, however, is not without controversy. It has been suggested that the pre-SMA is not involved in response selection but instead in response set reconfiguration or in resolving conflict among competing response alternatives (Garavan et al., 2003; Nachev et al., 2005; Rushworth et al., 2002, 2004;) or in response initiation (Mueller et al., 2007). Proponents of these alternative hypotheses have suggested that the PMA and the anterior cingulate area (ACC), but not the pre-SMA, are involved in response selection. Thus, although it is clear that frontal premotor areas play a role in response selection, the specific contribution of each area to this process remains ambiguous.

Aside from the premotor areas, different parts of the prefrontal cortex have also been implicated in response selection: the left IFG and the DLPFC. Several studies have shown that activity in the left IFG is modulated by response selection, being more strongly active for volitional word selection compared with constrained word selection (Abrahams et al., 2003; Crosson et al., 2001; Etard et al., 2000; Phelps et al., 1997; Thompson-Schill et al., 1997; Tremblay and Gracco, 2006). This finding suggests that the left IFG is involved in the selection of words. Alternatively, the IFG might be involved in the selection of all kinds of motor responses, not restricted to the production of words (Thompson-Schill et al., 1997). This latter interpretation, however, is challenged by the fact that selection of motor responses (e.g., button presses), as well as spatial location, both appear to recruit the dorso-lateral prefrontal area (DLPFC) (Frith et al., 1991; Hyder et al., 1997; Jahanshahi et al., 1999a, 1999b; Lau et al., 2004; Rowe et al., 2000; Schumacher and D'Esposito, 2002; Schumacher et al., 2007), but not the IFG, suggesting that the left IFG might be involved only in selecting words, not other types of responses. Recent repetitive transcranial magnetic stimulation (rTMS) experiments have shown that stimulation over the left DLPFC affects the manner in which responses (numbers and letters) are selected (Jahanshahi and Dürnberger, 1998). Word generation typically requires some linguistic processing to take place (e.g., semantic search), processes that are not involved in the selection of oral motor responses, such as finger movements, which might explain the absence of the IFG in many studies of finger movement selection, and its presence in the overwhelming majority of studies involving the production of words. In sum, although several brain areas (pre-SMA, ACC, PMA, DLPFC and IFG) appear to play a role in response selection, their precise contribution remains unclear. The goal of the present study was therefore to examine, using sparse-sampling fMRI (Eden et al., 1999; Edmister et al., 1999; Gracco et al., 2005), the contribution of these areas to volitional and forced response

selection. In order to extract the most general, response-independent aspects of the selection process, two different response modalities, words and oral motor gestures, were used.

2. Methods

2.1. Participants

Eighteen (18) healthy right-handed adults, balanced for gender, participated in this study (mean age 29.31 ± 5 years). All participants were right-handed according to the Edinburgh Handedness Inventory (Oldfield, 1971) and were native speakers of either Canadian English or Canadian French. The mean number of years of education was 18.24 ± 1.9 years. All participants scored normal or above normal on a test of mild cognitive disorder, the Montreal Cognitive Assessment (Nasreddine et al., 2005). All participants had normal or corrected-to-normal vision, and reported no history of speech, LNG or learning difficulties. Participants were screened for any contraindication to MRI. Informed written consent was obtained from each participant. The study was approved by the Magnetic Resonance Research Committee (MRC) and the Montreal Neurological Institute (MNI) Research Ethics Committee.

2.2. Study procedure

The experiment consisted of participants producing words aloud (either in French or in English, depending on participants' native LNG) and non-verbal oral motor gestures. The possible response was one of three different words or three different oral motor gestures. The words and oral gestures were matched such that each response was short, articulated mainly with the lips, and required the production of a sound

or a noise. Table 1 provides the characteristics of these words and gestures. As shown in Fig. 1, all trials began with the presentation of a visual stimulus on an LCD projector, which the participants viewed through a mirror that was attached to the head coil. All stimuli were delivered by a Dell Precision laptop computer running Presentation software (Neuro-behavioural System, Albany, CA, USA).

Each response was elicited under two different selection modes: forced choice and volitional. In the forced choice condition, the visual cues were single digit numbers (1–3), which completely specified the required response. On each trial, a digit was presented within a geometrical shape (a circle or a square). The geometrical shape determined the response modality (words or gestures), while the number indicated which particular response to produce (see Table 1). In the volitional selection condition, the number 0 was presented on the screen, within a circle or a square, indicating to participants that they could select any of the response within the appropriate response modality (words, gestures). The forced choice and volitional selection conditions differed only along one dimension, the selection mode. All other aspects of the tasks were comparable: the working memory load, the required attention level (sustained), the motor planning and motor output and the complexity of the visual stimuli. Anticipatory effects were avoided by presenting the experimental conditions in a completely randomized fashion.

For half the participants, circles were initially paired with gestures while squares were paired with words. For the other half, the assignment was reversed. The meaning of the geometrical shapes was randomly switched during the experiment. Since these response-switching trials were included to address a separate issue (response conflict), they were not included in the current analyses and will not be discussed further. The structure of these trials is illustrated in Fig. 1.

Table 1 – Characteristics of the motor responses (words and gestures) used in the experiment.

LNG	Word	Gestures	Concret. ^a	Fam. ^b	KFFRQ ^c	T-LFRQ ^d	Freq ^e	Written freq ^f	Phon. ^g	Syll. ^h	Artic ⁱ
English	Gray	Growling	471	531	80	891	N/A	N/A	3	1	Back
	Fish	Raspberry	597	583	70	505	N/A	N/A	3	1	Lips
	Pot	Kiss	584	548	35	597	N/A	N/A	3	1	Lips
French	Grand	Growling	N/A	N/A	N/A	N/A	93	144	3	1	Lips
	Fils	Raspberry	N/A	N/A	N/A	N/A	382	247	3	1	Lips
	Point	Kiss	N/A	N/A	N/A	N/A	192	272	3	1	Lips

Note: to accommodate the native LNG of the participants, two comparable sets of three words were created, one in French and one in English. All participants were native speaker of one of these LNGs. Words and gestures on the same row were paired.

a Concreteness rating (100–700) for the English words according to the MRC Psycholinguistic database (http://www.psy.uwa.edu.au/mrcdatabase/uwa_mrc.htm).

b Familiarity rating (100–700) for the English words according to the MRC Psycholinguistic database.

c KFRQ: Kucera–Francis written frequency (>0) for the English words according to the MRC Psycholinguistic database.

d T-LFRQ: Thorndike–Lorge written frequency (0–3,000,000) for the English words according to the MRC Psycholinguistic database.

e Frequency rating for the French words based on a corpus of recent movie sub-titles containing 16.6 millions words taken from 2960 movies (www.lexique.org). The maximal frequency is 33,959.88 and the average is 64.83.

f Written frequency rating for the French words based on a corpus of texts containing 14.7 millions words taken from 218 books published between 1950 and 2000 (FranText; www.lexique.org). The maximal frequency is 38,943.65 and the average is 48.37.

g Number of phonemes.

h Number of syllables.

i Main place of articulation.

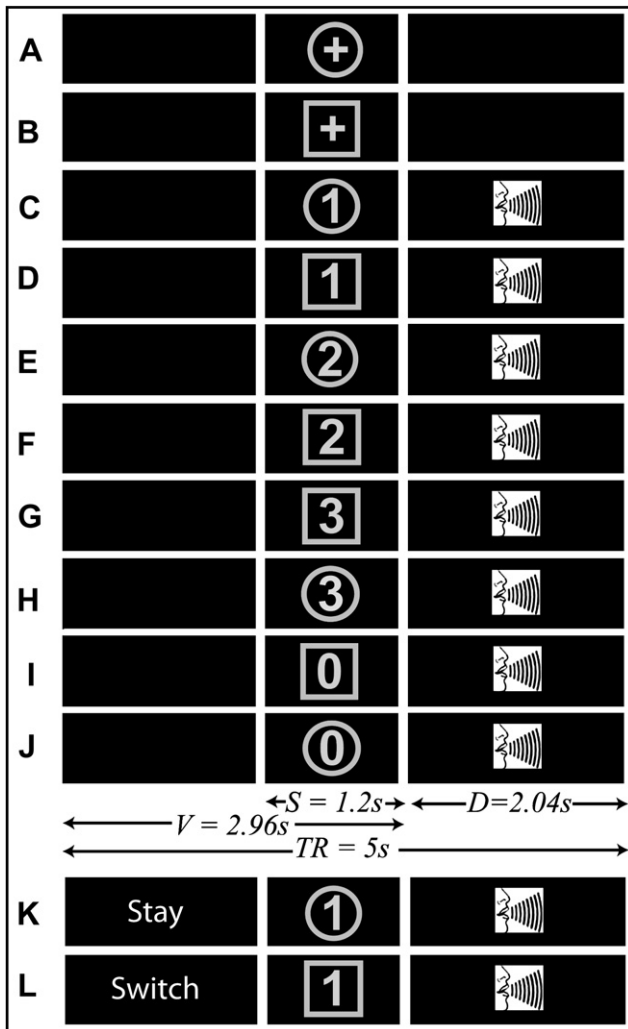


Fig. 1 – Schematic representation of the stimuli presented to the participants. Each experimental trial had the same general organization, starting with a blank screen followed by a visual cue for 1.2 sec. Participants were instructed not to respond until the cue had disappeared from the screen. The disappearance of the cue was time-locked to the end of the volume acquisition during the delay in TR. During the baseline trials (panels A and B) participants produced no response. Panels C through H illustrate the six forced choice trials and panels I and J illustrate the two types of volitional selection trials. V = volume acquisition.

D = delay in TR. S = stimulus presentation. Panels K and L illustrate the organization of the response-switching trials (not included in the analysis). Instead of a blank screen, the trials started with an instruction to either switch between rules (switch) or to continue with the same rule (stay).

The experiment contained a total of 656 trials (328 exp; 328 baseline), of which 120 were forced choice and 120 were volitional selection. On each trial, a visual stimulus was presented for 1.2 sec. Participants were instructed to produce a response as quickly as possible following the offset of the stimulus, which was time-locked to the end of volume acquisition. Each experimental trial was followed by

a baseline trial (rest), during which a fixation point was presented in the middle of the screen.

On the day of scanning, participants were introduced to the stimulus/responses (SR) associations through a short computer-training program and then practiced the tasks until they were able to perform the task without error.

2.3. Behavioural data: acquisition and analysis

Participants' responses were recorded through an MR compatible microphone (Resonance technology, Northridge, CA, USA) and digitized directly to disk. The recordings were evaluated by a research assistant naïve to the purpose of the study and the number and types of errors were calculated. Four types of errors were documented: misses (no response), within-class errors (*number errors*), across-class errors (*type errors*) and a combined (*number and type*) error. A *number error* was defined as a failure to retrieve/produce the appropriate word or gesture corresponding to the digit stimuli (1, 2 or 3) with the correct response modality (word, gesture). For example, producing the word *fish* instead of the word *gray* in response to stimulus 1. A *type error* was defined as the failure to retrieve/produce the appropriate response modality. For example, producing the word *pot* instead of producing a kissing gesture, both responses being associated with the same stimulus number, but belonging to different response modalities. For the forced choice condition, all three types of errors could and did occur. For the volitional selection condition, only misses and type errors could occur, since no number decoding was required. For each participant, the percentage of errors within and across response modality (compared to total the number of experimental trials) was derived. Fisher non-parametric sign test was used to determine whether accuracy was influenced by response modality.

To accommodate the native LNG of the participants, two comparable sets of words were created, one in French and one in English. A LNG variable (English, French) was included in the analysis as a between-subject factor only to ensure that the performance of all participants was similar regardless of the LNG in which they performed the experiment. Paired-sample t -tests were used for post hoc comparisons.

The RTs were not analyzed because a delayed response paradigm was used, in which participants were given over 1 sec to prepare their response.

2.4. Image acquisition

The data were acquired on a 3T Siemens Sonata MR scanner at the MNI. Thirty-four axial slices (whole brain coverage) oriented parallel to an imaginary line passing connecting the anterior and posterior commissure (AC-PC line) line [thickness = 4 mm, no gap, field-of-view (FOV) = $256 \times 256 \text{ mm}^2$, matrix = 64×64] were acquired in 2.06 sec using a multislice gradient-echo EPI sequence [echo time (TE) = 50 msec, repetition time (TR) = 5 sec, delay in TR = 2.94 sec]. The delay in TR occurred following each volume acquisition. The slices had a spatial resolution of $4 \times 4 \times 4 \text{ mm}$. Four experimental runs (13 min each) resulted in the acquisition of 656 T2*-weighted BOLD images

acquired in an interleaved order. High-resolution T1-weighted volumes were acquired for anatomical localization (matrix 256×256 mm, 160 slices, $1 \times 1 \times 1$ mm, no gap, TE = 9.2 msec, TR = 22 msec). Participant's head was immobilized by means of a vacuum-bag filled with polystyrene balls and a forehead-restraining device (Hybex Innovations, St-Leonard, QC, Canada).

2.5. Image analysis

The functional images were realigned across runs by performing a rigid-body transform with the 4th frame of the 1st functional run as the target image (AFNI, Cox and Jesmanowicz, 1999). The six movement parameters (x, y, z and roll, pitch and yaw) were inspected for each volume. Data were low pass filtered using an 8-mm full width at half maximum (FWHM) Gaussian kernel. Statistical analysis of fMRI data was performed using a linear model with correlated errors (NeuroLans, Montreal). The design matrix of the linear model was convolved with a hemodynamic response function modeled as a difference of two gamma functions timed to coincide with the acquisition of each slice. The motion parameters were included in the model as a covariate of no interest (Friston et al., 1996). Temporal drift was removed by adding a cubic spline in the frame times to the design matrix (one covariate per 2 min of scan time), and spatial drift was then removed by adding a covariate in the whole volume average. The correlation structure was modeled as an autoregressive process of degree 1. At each voxel, the autocorrelation parameter was estimated from the least squares residuals using the Yule-Walker equations, after a bias correction for correlations induced by the linear model. In order to compute group data, participants' data were transformed into stereotaxic space using the MNI305 template and re-sampled to $1 \times 1 \times 1$ mm (Collins et al., 1994), and combined using a mixed effects linear model for the effects (as data) with fixed effects standard deviations taken from the previous analysis. This was fitted using restricted maximum likelihood (REML) implemented by the Expectation/Maximization (EM) algorithm. A random effects analysis was performed by first estimating the ratio of the random effects variance to the fixed effects variance, then regularizing this ratio by spatial smoothing with a Gaussian filter. The variance of the effect was then estimated as the smoothed ratio multiplied by the fixed effect variance. The amount of smoothing was chosen to achieve 100 effective degrees of freedom (Worsley et al., 2002).

The statistical analysis was based on a set of subtractions and focused on the main effect of selection mode (volitional-forced; forced-volitional), the main effect of response modality (words-gestures; gestures-words), and the interaction between selection mode and response modality [(volitional words-forced words) – (volitional gestures-forced gestures)]. A t-statistical image for each of these contrasts was computed. The resulting t-statistic images were searched automatically for significant clusters of voxels activated at $p \leq .05$, corrected for multiple comparisons using the minimum given by a Bonferroni correction and random field theory, taking into account the non-isotropic spatial correlation of the errors and the number of voxels (1,000,000)

(Worsley et al., 2002). Only peaks within clusters of 50 voxels (.05 ml) or more were considered significant.

In addition to the subtraction analyses, we also performed two complementary conjunction analyses (Price and Friston, 1997). These analyses were performed in order to reveal the commonalities between the volitional and the forced selection modes, and the two response modalities. For each subject, we first computed four pairs of contrasts, two for the selection mode (volitional-baseline; forced-baseline), and two for the response modality (words-baseline; gestures-baseline). Using NeuroLens, we then performed two conjunction analyses based on the subjects' contrasts (selection, modality). To test the conjunction null hypothesis (Nichols et al., 2005), only voxels that were significantly active at $p \leq .05$ (corrected) in all the subjects for each contrast were included in the final image.

3. Results

3.1. Spontaneous production of words and gestures

The percentage of use of each word and each gesture for the VOL condition was tabulated and is presented in Table 2, for each participant.

3.2. Errors

In general, the percentage of errors was low (mean = $5.03 \pm 2.89\%$; median 4.27%). The most common type of error, for both volitional and forced selection, was type errors, i.e., the production of the correct response within the incorrect response modality (saying *gray* instead of *growling*, for instance). This error occurred in 2.83% of all experimental trials. The analysis of the errors in the volitional condition revealed no significant overall difference between the words and gestures, with average errors at 1% ($p = .77$), and no significant difference ($p \geq .05$) between words and gestures within any of the errors (misses and type errors). The analysis of errors in the forced condition also revealed no significant overall difference between words and gestures, with average errors at 1.47 and 1.53% respectively ($p = 1.00$), and no significant difference ($p \geq .05$) between words and gestures within any of the errors (misses, type, and number errors). Given the very small number of errors, all trials were included in the analysis of the fMRI data.

3.3. Neuroimaging results

3.3.1. Selection mode

As shown in Fig. 2A, the conjunction analysis revealed that the volitional and the forced selection conditions were associated with activations in a large network of cortical and subcortical areas that were bilaterally distributed. This network included the pre-SMA (extending into the anterior cingulate sulcus – ACS), large segments of the parietal lobe, the premotor area (dorsal and ventral), the thalamus and the globus pallidus (see Table 3(A) for the list of all activations). Of these regions, five showed a significant main effect of selection (volitional > forced), as revealed by the direct contrast of volitional and

Table 2 – Percentage of use of each word and each gesture, in the VOL trials.

SID	LNG	G	Words				Gestures			
			Gray/grand (%)	Fish/fils (%)	Pot/point (%)	Total (%)	Growl (%)	Kiss (%)	Raspberry (%)	Total (%)
1	E	F	31.7	27.0	41.3	100.0	46.7	28.3	25.0	100.0
2	E	F	45.6	29.1	25.3	100.0	48.8	29.8	21.4	100.0
3	E	F	25.4	40.7	33.9	100.0	30.8	26.2	43.1	100.0
4	E	F	15.3	40.3	44.4	100.0	37.6	25.9	36.5	100.0
5	E	M	30.0	47.5	22.5	100.0	15.5	36.9	47.6	100.0
6	E	M	20.7	49.4	29.9	100.0	26.9	17.9	55.1	100.0
7	E	M	27.5	41.3	31.3	100.0	26.5	55.4	18.1	100.0
8	E	M	38.9	14.8	46.3	100.0	41.9	43.5	14.5	100.0
9	E	M	33.3	34.5	32.2	100.0	35.1	42.9	22.1	100.0
10	F	F	52.5	30.0	17.5	100.0	13.6	55.6	30.9	100.0
11	F	F	28.4	56.8	14.8	100.0	34.2	15.8	50.0	100.0
12	F	F	45.7	29.6	24.7	100.0	54.1	27.0	18.9	100.0
13	F	F	33.7	29.1	37.2	100.0	43.0	44.3	12.7	100.0
14	F	F	27.2	33.3	39.5	100.0	28.0	45.1	26.8	100.0
15	F	M	26.8	51.2	22.0	100.0	22.0	34.1	43.9	100.0
16	F	M	38.3	30.9	30.9	100.0	40.0	42.5	17.5	100.0
17	F	M	37.5	28.8	33.8	100.0	28.2	28.2	43.5	100.0
18	F	M	32.1	28.6	39.3	100.0	44.4	27.2	28.4	100.0
GA			32.8	35.7	31.5	100.0	34.3	34.8	30.9	100.0

Note: SID = subject identification number. LNG = language (F = French; E = English). G = gender: (M = male; F = female). GA = grand average.

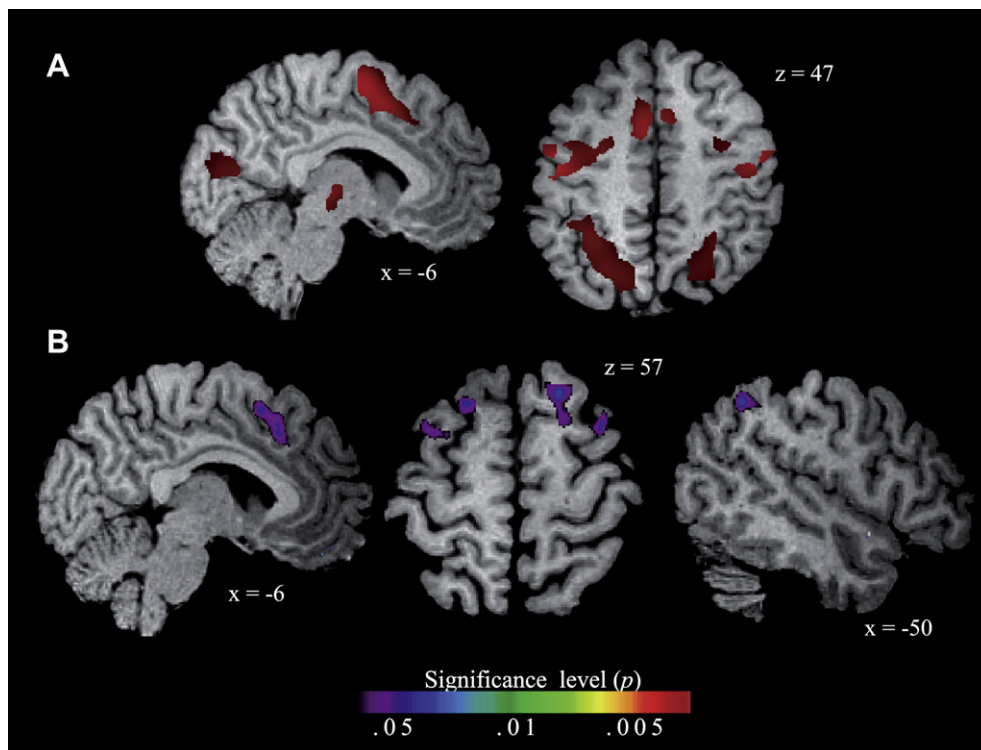


Fig. 2 – Top panel (A): conjunction of the subject-level volitional and forced selection contrasts (volitional selection–baseline and forced selection–baseline). In red are activations that survived a set significance threshold ($p \geq .05$, corrected). The data are overlaid on sagittal and axial views of a participant’s T1-weighted MRI transformed into stereotaxic space using the MNI305 template. **Bottom panel (B):** group-level activation ($N = 18$) for the contrast of volitional–forced selection, collapsed across response modality. Only significant activations are displayed ($p \leq .05$), corrected for multiple testing, taking into account the size of the search region (1,000,000 voxels) and the smoothness of the data (Worsley et al., 1996). All coordinates are in MNI space.

Table 3 – Commonalities and differences between Volitional and Forced selection (collapsed across response modality). Coordinates are in MNI space.

Location	Hemi	p	X	Y	Z	N voxels
<i>A. Conjunction of the forced and volitional selection conditions</i>						
SMA-proper	L + R	≥.00001	-4	-2	58	6882
Pre-SMA/ACS		≥.00001	-7	6	50	
Primary sensorimotor area	L	≥.00001	-47	-16	39	8790
Ventral premotor cortex		≥.00001	-49	-2	34	
Dorsal premotor cortex		≥.00001	-26	-7	52	
IFG, pars opercularis		≥.00001	-52	6	24	
Primary sensorimotor area	R	≥.00001	47	-13	36	7034
Ventral premotor cortex/IFG, pars opercularis		≥.00001	44	6	27	
Dorsal premotor cortex		.000072	34	-5	49	
Posterior cingulate gyrus	L	.001	-10	-73	11	26,020
	R		15	-66	11	
IPC	L	≥.00001	-32	-48	44	
	R	.00003	32	-48	46	
Central sulcus/postcentral gyrus	R	.003	21	-29	62	1075
	L	.002	-19	-31	61	1074
Thalamus	L	.002	-8	-21	2	1652
	R	.003	10	-18	1	547
Globus pallidus	R	.029	22	3	3	314
	L	.004	-21	0	3	904
Planum temporale	L	≥.0001	-36	-33	14	1116
	R	≥.0001	40	-30	14	1102
<i>B. Volitional > forced</i>						
Pre-SMA/ACS	L	.019	-6	13	50	449
Middle frontal gyrus (dorsal premotor area)	L	.019	-35	6	55	140
	R	.014	36	11	53	532
Angular gyrus	L	.007	-48	-57	48	486
Superior frontal gyrus	L	.019	-21	19	57	115
	R	.007	19	26	56	403
Middle frontal gyrus	L	.050	-34	53	-12	84
<i>C. Forced > volitional</i>						
Inferior occipital gyrus	L	.019	-38	-88	-5	71
	R	.009	35	-88	-5	221

forced selection (collapsed across response modality) (see Fig. 2B). These regions were the left pre-SMA, the bilateral middle frontal gyrus (corresponding to the dorsal premotor area), the bilateral superior frontal gyrus, and the ventral part of the middle frontal gyrus (see Table 3 for the coordinates). The opposite contrast, forced minus volitional selection (collapsed across response modalities) revealed only two significant clusters, which were located on the left and right inferior occipital gyrus (see Table 3 for the coordinates).

3.3.2. Response modality

Fig. 3A illustrates the results of the conjunction analysis. As can be seen in the figure, a number of areas were bilaterally

activated for the words and the gestures, including the primary sensorimotor cortex, the SMA, ACS, premotor cortex (ventral) and many others (see Table 4 for the coordinates). The contrast of the words minus the gestures yielded no significant activation. The opposite contrast, the gestures minus the words, yielded significant activation in two frontal lobes regions: in the most anterior portion of the superior frontal gyrus, on the left hemisphere, and on a more ventral portion of the superior frontal gyrus, corresponding to the frontopolar area (see Fig. 3B).

3.3.3. Response selection within modality

The contrast of volitional–forced selection, for the words, yielded significant activation in four cortical regions: the pre-SMA, the superior frontal gyrus, the middle frontal gyrus, corresponding to the rostral aspect of the dorsal premotor area (PMAd), and the ventral part of the IFG, corresponding to area orbitalis (see Fig. 4). The coordinates of the local maxima are presented in Table 5(A and B). For the gestures, activation was found in the pre-SMA and in the ventral part of the left middle frontal gyrus, anterior to area orbitalis.

3.3.4. Selection by modality interaction

This analysis revealed an interaction in the left angular gyrus, in the ventral part of the left middle frontal gyrus and in the rostral PMAd, bilaterally. The coordinates of the local maxima are presented in Table 5(C).

In order to better understand the pattern of activation in the PMAd, we conducted a region of interest analysis (ROI) on this region with mean coordinates $-22, 17, 57$ and $36, 17, 57$. Each ROI was defined as a 10 mm^3 region. For each participant, the mean percent change for the left and right PMAd was computed for each condition compared to the visual fixation baseline (forced words, forced gestures, volitional words, volitional gestures) and inspected to ensure that all values were within the known normal range for signal originating from the brain. Mean percent change ranged from $-.7$ to 1% with an overall mean of $.46\%$ ($\pm .39$ SD), well within normal range (e.g., Hoge et al., 1999; Kemeny et al., 2005). A set of Bonferroni corrected paired-sample t-tests (two-tailed) was conducted on the mean percent change data. Results showed that the contrast of volitional and forced selection was only significant for the words, in both the left (words: $p < .001$; gestures: $p = .37$) and the right PMAd (words: $p = .008$; gestures: $p = .21$), consistent with the whole brain analyses. The contrast of the two volitional conditions revealed no statistically significant difference for the left ($p = .31$) and for the right PMAd ($p = .54$). The contrast of the two forced conditions, however, revealed lower activation intensity for the forced words than for the forced gestures, in both the left ($p = .02$) and in the right PMAd ($p = .09$), although in the latter the effect was only marginally significant after correction.

4. Discussion

The present study examined the brain areas contributing to the selection of words and oral motor gestures. Most studies of word selection have employed tasks involving both a search through the mental lexicon and some form of linguistic

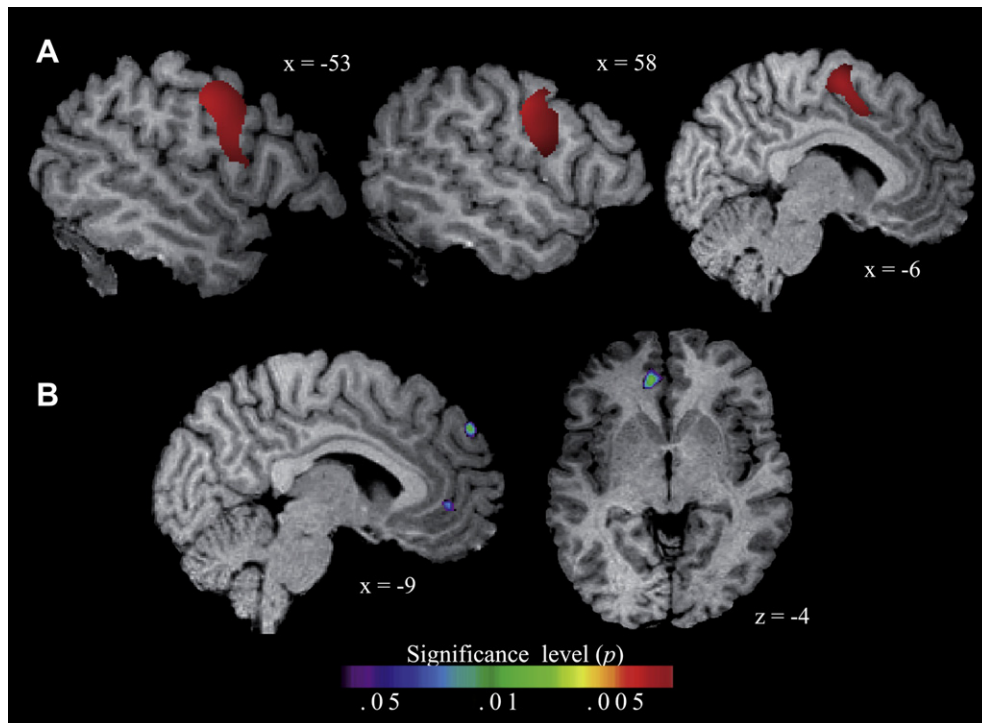


Fig. 3 – Top panel (A): conjunction of the subject-level words and gestures contrasts (words–baseline and gestures–baseline). In red are activations that survived a set significance threshold ($p \geq .05$, corrected). Bottom panel (B): group-level activation ($N = 18$) for the contrast of gestures–words, collapsed across selection mode. See Fig. 2 for more details.

processing, such as semantic-based word generation (e.g., Crosson et al., 2001; Thompson-Schill et al., 1997; Tremblay and Gracco, 2006). In such studies, the focus is usually on the specific linguistic processes, rendering the comparison of word selection with the selection of other types of motor responses difficult. In the present study, we used a selection paradigm in which no search in the mental lexicon and no

linguistic analysis were required. All responses (words and oral gestures) were held in working memory throughout the study, and retrieved based on arbitrary SR associations. Response selection was either stimulus-driven (forced) or volitional. In general, our results demonstrate that the selection of both words and oral motor responses using the same set of effectors activates a similar network of brain areas,

Table 4 – Commonalities and differences between WORDS and GESTURES (collapsed across selection mode). Coordinates are in MNI space.

Location	Hemi	p	X	Y	Z	N voxels
A. Conjunction of the WORDS and GESTURES						
Primary sensorimotor area	L	$\geq .00001$	-47	-16	39	8028
Ventral premotor cortex/IFG pars opercularis		$\geq .00001$	-56	-1	24	
Primary sensorimotor area	R	$\geq .00001$	47	-13	36	7236
Ventral premotor cortex/IFG pars opercularis		$\geq .00001$	61	1	21	
SMA/pre-SMA/ACS	L	$\geq .00001$	-4	-2	58	5974
Central sulcus/postcentral gyrus	L	.003	-19	-31	61	1416
	R	.007	22	-29	60	224
Posterior cingulate gyrus	L	.020	-15	-72	10	718
	R	.002	16	-66	11	819
Planum temporale	R	.001	41	-28	12	329
B. Gestures > words						
Superior frontal gyrus, frontopolar area	L	.010	-9	42	-4	192
Superior frontal gyrus	L	.016	-5	53	37	103

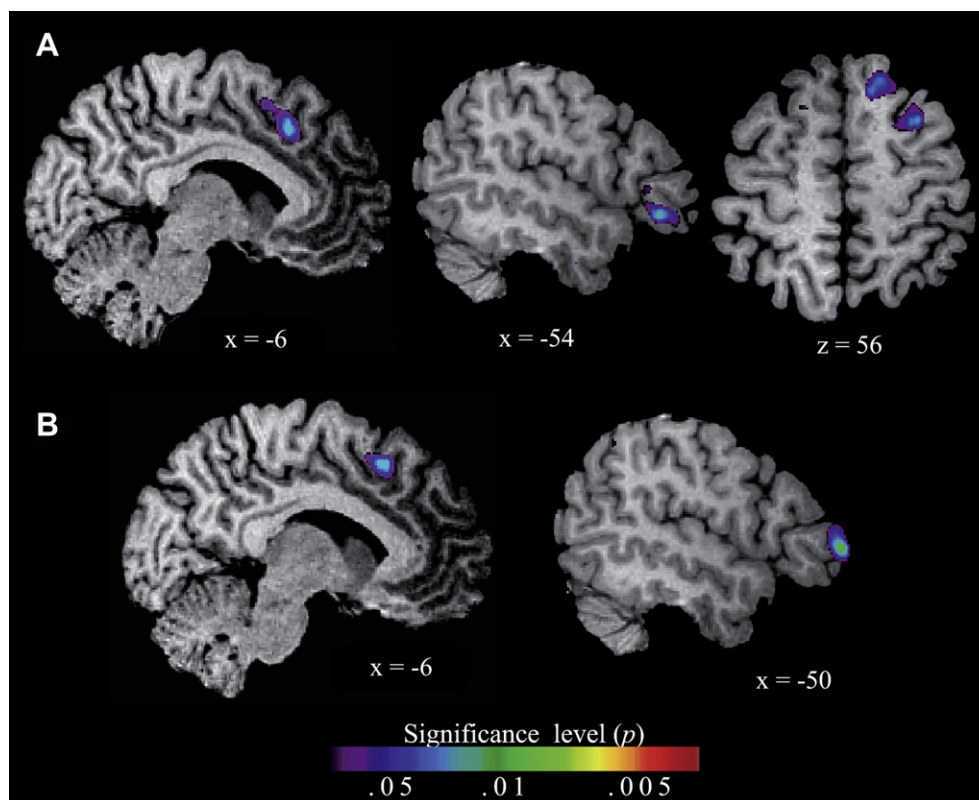


Fig. 4 – Top panel (A): group-level activation ($N = 18$) for the contrast of volitional–forced selection, for the words. Bottom panel (B): group-level activation ($N = 18$) for the contrast of volitional–forced selection, for the gestures. See Fig. 2 for more details.

including the medial frontal (pre-SMA and ACS bilaterally) and the prefrontal cortex. These areas have previously been identified as contributing to the response selection process (Alario et al., 2006; Buckner et al., 1995; Crosson et al., 2001; Friston et al., 1991; Frith et al., 1991; Goldberg, 1985; Hyder et al., 1997; Lau et al., 2004, 2006; Rowe et al., 2000; Rushworth et al., 2002; Tremblay and Gracco, 2006; Thut et al., 2000; Tremblay et al., 2008). The present results and those of previous studies suggest that these distributed neural regions reflect a number of potential functional contributions to the response selection process.

4.1. A core region for response selection: the pre-SMA

The present results suggest that the pre-SMA contributes substantially to response selection. While a number of regions were activated for the response selection process in general, only the pre-SMA was significantly activated in both volitional and forced selection, and showed differential activation for volitional compared with forced responses regardless of the response modality. Previous fMRI studies have reported increased activation in the pre-SMA for linguistic tasks involving volitional selection of words compared to tasks requiring the production of stimulus-driven words (e.g., Alario et al., 2006; Crosson et al., 2001; Etard et al., 2000; Tremblay and Gracco, 2006). More ecological LNG production tasks, such as the production of narratives, requiring the volitional

selection of multiple words and/or phrases, as well as different forms of linguistic planning (e.g., syntactic encoding, semantic processing, etc.), also engage the pre-SMA (Blank et al., 2002; Braun et al., 2001). However, the implementation of the selection process and associated cognitive/linguistic processes are convolved making observations about either separately difficult. In the present study, the selection of words and oral gestures was based on arbitrary SR associations and involved no linguistic processing. Interestingly, our results are consistent with the imaging literature on word generation, showing an increase in activation level in the pre-SMA. Our results are also consistent with the imaging literature on non-speech movements implicating the pre-SMA in response selection (Deiber et al., 1996; Hyder et al., 1997; Lau et al., 2004, 2006; Nachev et al., 2005; Sakai et al., 2000; Tremblay et al., 2008; Ullsperger and von Cramon, 2001) as well as with a recent rTMS study demonstrating that stimulation of the pre-SMA interferes with the volitional selection of finger movements (Hadland et al., 2001).

Results of a recent fMRI study comparing blocks of self-initiated volitional and forced button presses, however, stand at odds with the present results and those previous ones. In that study, no activation in the pre-SMA was found for the direct comparison of volitional and forced selection and the authors suggested that the pre-SMA is not involved in response selection (Mueller et al., 2007). However, because of the experimental setup used in that study, in which volitional

Table 5 – Local maxima within significant clusters for the contrast of volitional and forced, within response modality, and for the interaction between selection and modality. Coordinates are in MNI space.

Location	Hemi	p	X	Y	Z	N voxels
A. Volitional > forced WORDS						
Pre-SMA/ACS	L	.030	–5	22	44	245
Superior frontal gyrus	L	.06 (n.s.)	–21	18	57	127
	R	.004	15	27	56	1231
Middle frontal gyrus (dorsal premotor area)	L	.1 (n.s.)	–37	7	51	–
	R	.017	34	13	52	670
IFG, pars orbitalis	L	.009	–54	28	–12	519
B. Volitional > forced GESTURES						
Pre-SMA/ACS	L	.04	–7	22	47	154
Middle frontal gyrus	L	.01	–50	49	–2	301
C. Selection by modality interaction						
Angular gyrus	L	.000001	–47	–58	44	1156
Middle frontal gyrus	L	.02	–50	50	–2	145
Middle frontal gyrus (dorsal premotor area)	L	.05	–22	17	57	125
	R	.07 (n.s.)	36	17	57	64

movements were performed in blocks, it is possible that participants prepared sequences of movements ahead of time, instead of selecting one movement at a time, thereby minimizing selection-related activation in the pre-SMA on a trial-by-trial basis, and resulting in similar activation level in for volitional and forced selection trials. Thus, in essence, the comparison of the two conditions used in that study did not equate the comparison of a volitional and a forced selection conditions, which explains the absence of a selection mode effect in the pre-SMA. In sum, by examining the pre-SMA activation pattern in a set of selection conditions matched for the number of response alternative and attention level, we were able to demonstrate that the pre-SMA is not only involved in response selection, but that it plays a central role in this process.

4.2. Contribution of the premotor area to response selection

Results revealed a significant main effect of response selection in the PMAd, which is consistent with a number of previous response selection studies (Goldberg, 1985; Schluter et al., 1998; Rushworth et al., 2002). There was, however, an interaction between response selection and response modality reflecting an increased level of activation for the forced gesture condition compared to the forced word condition; the two volitional conditions did not however differ from one another. One possibility is that the oral gestures were associated with greater (motor) difficulty than the words. However, if this were the case, there should be a greater involvement of the PMAd for volitional gesture selection compared to volitional word selection, but this was not the case. Given that the forced selection tasks require learning SR

associations, it appears that the increased level of activation for forced gestures indicates that selecting novel actions based on SR associations requires greater neural resources than selecting well-learned actions (words). As such it appears that the PMAd is involved in response selection with the strength of SR associations a major contributing factor to the degree to which this area is activated. Although our behavioural (accuracy) data couldn't be used to address this possibility due to the high level of performance introducing a ceiling effect as a result of the delayed response paradigm, an analysis of RT or an analysis of the brain electrophysiological or electromagnetic signal might substantiate a processing advantage for familiar compared to unfamiliar tasks. Reports of familiarity effects on RTs are abundant in the literature; familiarity affects word recognition times (e.g., Forster and Chambers, 1973; Gibson et al., 1970; Howes and Solomon, 1951; Scarborough et al., 1977), lexical decision times (Bradshaw and Nettleton, 1994; Gerhand and Barry, 1999; Morrison and Ellis, 1995), word naming times (Gerhand and Barry, 1998; Morrison and Ellis, 2000), and object/picture naming times (Barry et al., 1997; Ellis and Morrison, 1998).

4.3. Contribution of the DLPFC to response selection

Consistent with a number of previous studies, the DLPFC was involved in the volitional and forced selection conditions (e.g., Abrahams et al., 2003; Buckner et al., 1995; Cunnington et al., 2006; Frith et al., 1991; Jahanshahi et al., 1999a, 1999b; Jahanshahi and Dirnberger, 1998; Rowe et al., 2000). There was no effect of selection on the DLPFC, however, a result that is in contrast with the above-mentioned studies, in which the comparison of volitional and forced selection yielded strong DLPFC activation. In these studies, however, selection was confounded with attention; the volitional selection condition required a higher attention level than the forced selection condition, a simple reaction-time task. In our study, attention was comparable across conditions. Similarly, in a study by Lau et al. (2004) attention was carefully controlled in order not to be confounded with selection, and the level of activity in the DLPFC did not vary with selection mode. The hypothesis that the DLPFC is involved in attention to selection is consistent with Petrides (2005), who suggested that the DLPFC is involved in self-monitoring of choices and decisions.

4.4. Contribution of the IFG (pars triangularis) to response selection

As discussed in the Introduction, the pars triangularis of the left IFG has been implicated in response selection. Activation of the pars triangularis (and sometimes of the opercularis) has been observed in semantic-based word generation (e.g., Basho et al., 2007; Alario et al., 2006; Amunts et al., 2004; Buckner et al., 1995; Fu et al., 2002; Petersen et al., 1988; Thompson-Schill et al., 1997; Tremblay and Gracco, 2006), letter-based word generation (Abrahams et al., 2003; Phelps et al., 1997) and word stem completion paradigms (e.g., Buckner et al., 1995; Palmer et al., 2001). In the present study, in which words were selected but not generated, no activation in the pars triangularis of the IFG was found. This finding, which stands at odds with the above results, is consistent with studies of motor

response selection (e.g., finger, hand, and eye movements), which typically do not report activation in pars triangularis (e.g., Cunnington et al., 2006; Deiber et al., 1996; Frith et al., 1991; Hester et al., 2007; Lau et al., 2006). Taken together, these results suggest that pars triangularis plays a role in linguistic processing (accessing or searching the mental lexicon, semantic and phonological search) but not in response selection per se (see also Amunts et al., 2004; Costafreda et al., 2006; Grindrod et al., 2008; Petersen et al., 1988).

4.5. Parietal lobe contribution to response selection

In the present study, large portions of the bilateral parietal lobe were strongly activated, including the intraparietal cortex (IPC) and the superior parietal lobule (SPL). There is extensive literature relating the parietal cortex, especially the IPC, to action planning mechanisms, including the selection of motor responses (Bunge et al., 2002; Deiber et al., 1996; Lau et al., 2004) and the selection of spatial locations (e.g., Rowe et al., 2000; Schumacher et al., 2007). It has been suggested that the IPC is involved in activating or generating a set of competing response alternatives on the basis of SR associations (e.g., Bunge et al., 2002; Huettel, 2006). In the present study, the same number of response alternatives had to be activated/generated for the forced and the volitional conditions, which might explain why there was no difference in the involvement of the IPC across selection conditions. This finding is consistent with the hypothesis that the IPC is involved in activating or generating a set of competing response alternatives.

The anterior part of the left angular gyrus was the only parietal region significantly modulated by selection mode; it also exhibited a selection by modality interaction. It is worth mentioning that this area was not significantly activated in any of the experimental conditions; rather it showed a (non-significant) negative activation (“deactivation”) in the forced selection condition (particularly for the words, hence the interaction). The activation in the volitional conditions, words and gestures, was near zero. Given the overall low activation level, it is difficult to interpret the contribution of this area in response selection. One possibility is that the angular gyrus was relatively more engaged in the volitional selection task compared to the forced selection task due to a shift in attention from forced to volitional selection. While the selection conditions were matched for visual stimuli complexity and attention level, the volitional selection condition required a contribution of motivational centers that was not required for forced selection. This was necessary to bias the choice of a response. In the forced selection task, responses were specified by visual stimuli, thus no motivational input was needed. Previous imaging studies of finger and eye movements have shown the angular gyrus to be sensitive to changes in visual stimulus saliency and cue validity (Vossel et al., 2009) and changes in visual target velocity (Nagel et al., 2008). More related to the current results is that activation in the angular gyrus increases when switching between two movement patterns (De Jong et al., 1999; Nagel et al., 2008). Together, these findings suggest that the angular gyrus in the present study may be contributing to the re-orienting of attention, which may be needed when switching from a stimulus-driven mode of response selection to a more internally driven mode.

4.6. Response selection and word production

The present results reveal a largely overlapping network for the production of words and oral gestures, a finding that is consistent with previous imaging studies of tongue movements and other non-verbal oral gestures (e.g., Bonilha et al., 2006; Bookheimer et al., 2000; Braun et al., 2001; Corfield et al., 1999), which have shown foci of activation distributed across a number of higher-order sensorimotor regions, including the SMA, the thalamus, the basal ganglia, the insula and the cerebellum. This network is similar to the one that is observed during the production of speech (e.g., Gracco et al., 2005; Riecker et al., 2005). A main effect of response modality (gestures > words) was found only in two rostral prefrontal areas, including the frontopolar area, possibly reflecting the necessity to monitor the selection/execution of the less familiar oral motor responses more carefully than the words.

Importantly, the present results provide evidence that a general selection process, independent of response modality, is involved in the selection of words, a finding that is consistent with the result of a recent study using electroencephalography, in which word selection was compared to finger movement selection (Tremblay et al., 2008). Despite the pivotal role of word selection in verbal communication, very few studies have focused on the manner in which motor responses are selected during spoken LNG production. As mentioned in the Introduction, contemporary models of speech and LNG production (e.g., Guenther et al., 2006; Indefrey and Levelt, 2004; Riecker et al., 2005) do not include a general response selection process, and in fact, most models do not include any domain-general processes. In order to integrate the apparent domain-general response selection process into models of word production, it is critical to examine the representational level (conceptual, lexical, phonologic, phonetic, etc.) at which this process operates during the production of LNG. One possibility is that the selection process is a non-specific mechanism capable of comparing activation weights of different types of units (motor, non-motor). This suggestion is supported by the participation of the pre-SMA not only in a wide range of motor tasks but also in non-motor tasks such as lexical decisions (Carreiras et al., 2006, 2007), memory-based decisions (Donohue et al., 2008), verbal trail-making tests (Moll et al., 2002), verbal n-back tasks (Derrfuss et al., 2004) among others.

5. Conclusion

In summary, the present study identified some functional differentiations within the fronto-parietal network supporting response selection. The results show that volitional selection, in general, recruits the same set of brain areas compared to forced (stimulus-driven) selection. What differs across selection modes is mainly the participation of the pre-SMA. The modulation of components within a network independent of response modality is in contrast to suggestions of volitional and stimulus-driven behaviours relying on distinct cortical networks – the medial and lateral premotor areas – previously suggested (Goldberg, 1985; Mushiake et al., 1991; Passingham, 1985). Importantly, the present results also demonstrate that this pre-SMA based process is a domain-general process,

being involved in the selection of words as well as non-communicative oral motor gestures.

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