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Cortical Dynamics of Semantic Priming and Interference During Word Production: An Intracerebral Study

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Abstract

Language production requires that semantic representations are mapped to lexical representations on the basis of the ongoing context in order to select the appropriate words. This mapping is thought to generate two opposing phenomena, *semantic priming*, where multiple word candidates are activated, and *interference*, where these word activities are differentiated in order to make a goal-relevant selection. In previous neuroimaging and neurophysiological research, priming and interference have been associated to activity in regions of a left frontotemporal network. Most of such studies relied on recordings which either have high temporal or high spatial resolution, but not both. Here we employed intracerebral electroencephalography (iEEG) techniques to explore with both high resolutions, the neural activity associated with these phenomena. The data came from 9 epileptic patients who were stereotactically implanted for pre-surgical diagnostics. They performed a cyclic picture naming task contrasting semantically homogeneous and heterogeneous contexts. Out of the 84 brain regions sampled, 39 showed task-evoked activity that was significant and consistent across 2 patients or more. In 9 of these regions, activity was significantly modulated by the semantic manipulation. It was reduced for semantically homogeneous contexts (*i.e.* priming) in 8 of these regions, located in the temporal ventral pathway as well as frontal areas. Conversely, it was increased only in the pre-supplementary motor area (pre-SMA), notably at an early post-stimulus temporal window (200-300 ms) and a pre-response temporal window (700-800 ms). These temporal effects respectively suggest the pre-SMA's role in initial conflict detection (e.g. increased response caution), and in pre-response control. Such roles of the pre-SMA are traditional from a history of neural evidence in simple perceptual tasks, yet are also consistent with recent cognitive lexico-semantic theories that highlight top-down processes in language production. Finally, while no significant semantic modulation was found in the anterior cingulate cortex (ACC), future iEEG work should continue to inspect the ACC with the pre-SMA.

Keywords: language production, cortical dynamics, semantics, lexical selection, pre-SMA

Cortical Dynamics of Semantic Priming and Interference During Word Production: An Intracerebral Study

Introduction

Word selection, or retrieval of a lemma, is a crucial step in the process of language production (Levelt, 1989, Chapter 6), linking semantics with the lexical entries to be articulated. The need for distinguishing and linking such representations is typically motivated by interpretations of tip-of-the-tongue or anomie states (Badecker et al., 1995; Caramazza & Miozzo, 1997; Vigliocco et al., 1997). Word selection has received a lot of attention, both in behavioural research (e.g. Levelt et al., 1999; Oppenheim et al., 2010; Rapp & Goldrick, 2000), as well as in cognitive neuroscience (for reviews, see: Indefrey, 2011; Munding et al., 2016; Strijkers & Costa, 2016; Ganushchak et al., 2011). Processing models have been thoroughly debated along multiple dimensions, such as: the nature of semantic representations driving word selection (features vs. holistic), the structure of lexical entries (e.g. lemmas vs. lexemes), the flow of information between the semantic and the lexical levels (serial vs. interactive), the mechanisms by which individual items are selected (competition vs. threshold), and so forth.

Here we focus on the previously-proposed hypothesis that the links between semantic and lexical representations can generate two opposing phenomena during word production: priming and interference (originally: La Heij, 1988; Roelofs, 1992). Semantic priming is the well-known phenomenon in which processing a given information, or item (e.g. the word “doctor”), facilitates the processing of semantically-related items (e.g. “nurse”). This has been extensively documented in the word and picture recognition literature (e.g. Neely, 1991). Semantic interference is the phenomenon in which processing two semantically-related items leads to impaired performance in selection tasks, compared to unrelated items, and is extensively documented in the word production literature (at least since Glaser & Dünghoff, 1984, see also MacLeod, 1991).

Semantic priming and interference play a central role in our understanding of the cognitive architecture of word selection processes. In the most consensual views, the activation of an information that has to be expressed overtly leads to the activation of multiple lexical candidates, a process known as semantic priming. Priming is typically conceived of in terms of spreading activation among related representations (à la Collins & Loftus, 1975). The difficulty of selecting a single item among a cohort increases when the activation levels of alternative, related candidates are higher, a phenomenon known as semantic interference. The actual mechanisms hypothesized to account for semantic interference are diverse (such as differential levels of activation, lateral inhibition, response buffering, and top-down control: Abdel Rahman & Melinger, 2009; Belke & Stielow, 2013; Berg & Schade, 1992; Howard et al., 2006; Mahon et al., 2007; Nozari & Hepner, 2018; Oppenheim et al., 2010; Roelofs, 2003).

Semantic priming and interference are not easily teased apart in measures of behavioral performance. This is because the two mechanisms drive opposing effects on performance that may cancel each other out or that may compensate to variable extents. For example, in the picture word interference paradigm, priming is observed for certain semantic relationships, interference is observed for others (e.g. Alario et al., 2000; La Heij et al., 1990; Mahon et al., 2007), but both are not observed simultaneously (although see Collina et al., 2013; Finkbeiner & Caramazza, 2006; Hantsch et al., 2009; Zhang et al., 2016, for manipulations that can turn interference into facilitation). In the cyclic picture naming task used in the present research (Damian et al., 2001; see also Kroll & Stewart, 1994), participants are instructed to name pictures presented in blocks that contain a randomly-repeated item set (typically 4-7 items, repeated 4-7 times). The item set in the blocks may be semantically-homogeneous (HOM) or heterogeneous (HET), meaning the items either belong to a single category or different semantic categories. In HOM contexts, interference is most frequently observed, yet priming is consistently thought to be an underlying processing component (Navarrete et al., 2012; Oppenheim et al., 2010).

The general principles of spreading activation and the resulting increase in selection difficulty have been implemented in various theories and models of word selection (Howard et al. 2006; Oppenheim et al. 2010; Roelofs, 2018). For example, Oppenheim et al. (2010) proposed a neural network

model with a selection mechanism. In this model, priming originates from a spreading activation network that incrementally learns over productions (e.g. trials), and increasingly co-activates words that share repeatedly-elicited semantic properties (i.e. exaggerated in the HOM condition). In this model, increased interference is viewed as a symptom of priming, and is present *as a result of selection demands*. Indeed, with a task instruction in which any of the primed alternatives (e.g. relevant picture synonyms) are considered equally-correct in the task, then facilitation is observed instead of interference (Oppenheim, 2017).

In addition, Oppenheim et al.'s (2010) influential cognitive model describes selection interference via an accumulator mechanism (in their terms, a “booster”), where multiple words accumulate activity towards a selection threshold. The threshold is defined as a sufficient activity difference in favor of a target word versus all others. Equivalently, many word activities can be reduced to a single term, referred to as word preference or “inverse conflict” (Nozari & Hepner, 2018), that is, how much higher a word's activity is compared to that of alternative words. When inverse conflict reaches a criterial threshold, that word is selected for production. Empirically, this mechanism where a single word-preference value evolves over time can be modelled by an evidence accumulation approach (Anders et al., 2015; 2017). When fit to behavioral data, empirical modeling successfully separated the two opposing effects of priming and interference. Moreover, in both studies Anders et al. found the selection criterion to increase during conflict (i.e. during HOM). This result is compatible with Nozari and Hepner's proposal that a criterion is adjusted to preserve accuracy at a cost to speed (response caution, a kind of speed-accuracy tradeoff account in language), and is also compliant with the cognitive control account of language interference (Belke & Stielow, 2013), where top-down control mediates HOM interference.

In combination with such current cognitive-behavioral models of semantic priming, interference, and selection dynamics, neurophysiological measures could provide a major source of information on these processes. Word production and selection recruits a broad network of cortical areas, that each merit in-depth analyses; these include the inferior, middle, and superior temporal lobe, as well as the inferior and superior frontal lobe (reviewed in Indefrey, 2011; Price, 2012). Within this network, processes such

as word selection, lexico-semantic mapping, and the top-down mechanisms needed to regulate their dynamics have been targeted by recording neural activity during various paradigms including, prominently, the cyclic naming task described previously. Table 1 provides a summary of the 18 published studies so far that combined this task with measures of brain function, or with stimulation targeting regional brain function. Note that when reviewing this literature, we disregarded various aspects of each study, including variations in signal processing procedures or secondary task differences, in order to focus on the functional interpretations given to semantic contrast effects in cyclic naming. This was done for the sake of simplicity, and because theoretical discussions have been built on such encompassing functional interpretations.

Akin to the tradition of cognitive-behavioral modeling, which aims link behavioral performance to quantitative cognitive models, a major aim in the field is to also link neurophysiological measures to cognitive processes using insightful computational functions (Friederici & Singer, 2015). However, as this latter practice is only beginning to emerge, it is currently much less developed especially in language production study (e.g. see Strijkers & Costa, 2016; note that Llorens et al, 2016, provide an explicit if tentative discussion of the links between cognitive dynamics and neurophysiological modulations). So far in these studies of Table 1, the linking functions postulated to associate the HOM–HET contrast of neural activity to cognitive function have essentially been based on the direction (i.e. “more” activity in HOM or in HET), the location, and the timing of the effect. As in Table 1, semantic priming has been linked to observations of differential HOM < HET activity in the left middle temporal cortex and, more generally, the left frontal and temporal regions, in a broad time window ranging from 200 ms post-stimulus to 400 ms before response. In contrast, semantic interference, especially the resolution of conflict, has been associated with differential HOM > HET activity in the left inferior frontal gyrus and left middle temporal cortex, and with neurophysiological components observed in a broad time-window ranging from 150 to 450 ms post-stimulus (also described as 350 ms before response onset); semantic interference was affected by stimulation of the left inferior frontal gyrus or left temporal gyrus.

Such activity modulations by region in Table 1 can be related to the previously-discussed, dominant cognitive theories for word selection (e.g. Oppenheim et al., 2010). For example, bottom-up visual to temporal lobe modulations (e.g. Zubizaray et al., 2017) are consistent with spreading activation dynamics after viewing a picture, and hippocampus modulations (Llorens et al., 2016) have been argued to be consistent with incremental learning; these two processes are considered generative to *priming*, and in the cited effects, HOM < HET. As for *interference*, recent theories consider that it is introduced by contextual selection demands (Oppenheim 2017, Nozari & Hepner 2018), and is mediated by top-down cognitive control (Belke & Stielow, 2013). For example, Nozari and Hepner propose that individuals modulate their response caution as a result of conflict detection (in a paradigm of conflict monitoring). In this respect, Aristei et al. (2011) found a frontal ERP of HOM > HET (250-350 ms), suggesting an early onset of top-down activity for conflict detection. However due to the constraint of using surface EEG, they are unable to specify the region involved. Furthermore, almost no other other studies in Table 1 are able to provide high enough spatial resolution (specific brain region[s]) and the pertinent temporal window simultaneously, to target the region involved in initial conflict detection for example (i.e. top-down control). Thus in this study, having greater spatial resolution through iEEG techniques while preserving also temporal resolution, we aim to further clarify the regions involved in priming and interference during semantically driven word selection.

The current study

The purpose of the current study is to contribute to the knowledge in Table 1 by assessing whether variations of neural activity computed with high anatomical and temporal precision are consistent with the joint manifestation of semantic priming and interference during naming. To our knowledge, only one other iEEG study has previously explored the HOM-HET cyclic naming paradigm (Llorens et al., 2016; see Ries et al., 2017, for an ECoG exploration), and herein we include a larger sampling area of brain regions. Based on Table 1 and the previously-discussed cognitive models, it was predicted that regions involved in the generative processes of priming will be facilitated (requiring less activity, HOM < HET)

due to the effect of pre-activation or increased network calibration via incremental learning (the same semantics are more frequently repeated; see Van Turennout et al., 2000) in areas within the temporal cortex (a ventral visual-temporal stream) including hippocampus. Secondly, increased activity (HOM > HET) should occur in any regions associated with interference control, conflict detection and response inhibition/management (e.g. Ridderinkhof et al., 2004), such as the pre-SMA, ACC, and more generally prefrontal cortex. As a result of these hypotheses, it should be more likely that regions in a ventral occipito-temporal stream will exhibit HOM < HET activity, while regions involved in top-down streams or response control would be more likely to exhibit HOM > HET.

Methods

Patients

All procedures were performed in accordance with the INSERM Institutional Review Board (N 0000388), and the patients (or their legal representatives in the case of minors) provided written informed consent. A total of 9 epileptic patients volunteered to participate in the experimental protocol. All patients were undergoing pre-surgical evaluation for pharmacologically intractable epilepsy at the Hôpital de La Timone (in Marseille, France). Their clinical details are provided in Table 2. None of the patients had previously undergone brain surgery. The experiment was conducted only when a patient had been seizure-free for at least the 12 previous hours. Anatomical and functional data were available for all 9 patients. Language lateralization was determined by multiple criteria per patient including: (1) the recording of auditory evoked potentials in auditory cortex in response to French voiced and voiceless stop consonants (/ba/, /pa/; detailed methods in Trébuchon-Da Fonseca et al. (2005); (2) functional mapping of language using direct electrical stimulation, whereby left hemisphere stimulation induced language deficits in all patients; (3) fMRI or WADA tests; and (4) patterns of ictal aphasia when seizures involved the left hemisphere.

Materials and design

Each patient had between 5 to 11 depth-electrodes implanted, which provided for functional stereotactic data acquisition. The locations of the electrode implantations had been strictly guided by clinical indications. Each *electrode* (0.8 mm in diameter; Alcis, Besançon, France) contained 10 to 15 recording sites (also referred to as *contacts*) along the length of the electrode. Contacts were 2 mm in length and separated by a 1.5 mm distance. Bipolar *channels*, referred to later on, are calculated by subtracting activity recorded at one contact from activity recorded at a neighboring contact on the same electrode. Such computation of (bipolar) channels improves the acquisition of local activity.

The experimental materials consisted of 36 pictures of common objects depicted in black and white, with highly consensual names (Alario & Ferrand, 1999; Bonin et al., 2003). The pictures were drawn from six different semantic categories, with six items per category. The pictures were named in blocks involving six different items, either from the same semantic category (semantically homogeneous blocks, HOM) or from six different semantic categories (semantically heterogeneous blocks, HET). The items were repeated five times within a block, yielding 30 trials per block. There were 6 homogeneous and 6 heterogeneous blocks, yielding 360 trials in total. The order of the blocks and of the items within each block were pseudo-randomized (Van Casteren & Davis, 2006). We created 4 different block lists by pseudo-randomly arranging the order of the blocks to vary the alternation between homogeneous and heterogeneous contexts. Within each block, adjacent trials did not involve the same single item nor items beginning with the same phoneme.

Procedure

The experiment was performed in an electrically-shielded room routinely used for experimental tasks.¹ Participants were comfortably seated, facing a display monitor. They were first familiarised with the materials by naming them once in a random order, and were then tested according to the design described above. The pictures were presented at the center of the screen, subtending an angle of 6° by 6°.

¹ Experimental tasks involving implanted patients are generally performed at the bedside in many institutions. The epilepsy unit at La Timone Hospital, where these patients were followed, includes a specialized research laboratory in which the patients can be tested collaterally to their medical monitoring.

Each trial began with a fixation cross, followed by the target item for 1000 ms. Between trials, a fixation cross was presented for $1,750 \text{ ms} \pm 350 \text{ ms}$ (random jitter). The patients were instructed to name each object (picture) as fast as possible while avoiding errors. They were asked to remain silent if they did not recognize the object or could not come up with an answer. Responses were recorded with a microphone placed in front of the patients, and the experimenter was present in the room in order to monitor the patients' performance and mark any erroneous responses. The software used to execute the experiment was E-Prime 1 (Psychology Software Tools, Pittsburgh, PA). Note that as this software did not allow by-trial voice recordings, its automatic voice key was utilized to compute naming latencies relative to picture onset. While the absence of recordings is sub-optimal for detecting millisecond-exact response times on every single trial, our design compared the very same items across conditions, thus we could reasonably expect no systematic bias on the response times averaged by condition.

Anatomical data

For all patients, both a structural pre-operative MRI scan and an intra-operative computed tomography (CT) scan were acquired as part of the clinical routine. We used the co-registration between the MRI and CT information, obtained within the Leksell SurgiPlan software (Elekta, Stockholm, Sweden). Visual inspection of the fused images allowed the precise localization of every contact within each patient's anatomy. These locations were then visually classified by the neurologist on the basis of a human brain atlas (Mai et al., 2008), with only minor modifications to its parcellation. The lateral basal and temporal regions, as well as the medial cingular areas, were divided into anterior, middle and posterior subregions. These subdivisions were intended to capture relevant functional distinctions made in Price's (2012) review of functional-imaging studies of language. Finally for visualization purposes, all patients' contacts were mapped onto a common parcellated brain template (ICBM152), as implemented in Brainstorm (Tadel et al., 2011). The parcels were either adapted from the predefined Destrieux and Desikan-Killiany atlases in Brainstorm, or created from Brainstorm's user interface.

Functional data acquisition

Intracerebral EEG signals were recorded continuously at a sampling rate of 1000 Hz using a 256-channel BrainAmp amplifier system (Brain Products GmbH, Munich, Germany). An acquisition band-pass filter was used to limit the bandwidth of the output signal to between 0.16 and 200 Hz. A scalp electrode placed in Fz was used as the recording reference. Off-line preprocessing was performed with BrainVision Analyzer software (Brain Products GmbH, Munich, Germany).

Signal processing

Off-line pre-processing was conducted using BrainVision Analyzer software (Brain Products GmbH, Munich, Germany). Time-frequency and statistical analyses were performed using MIA (Multi-patient Intracerebral data Analysis toolbox, freely available at <http://www.neurotrack.fr/neurophysiology/seeg/mia/>) and used with MATLAB 2017a (The MathWorks, Natick, MA); see also Dubarry et al. (2017) for similar methods. The cortex representations were created in Brainstorm (Tadel et al., 2011), which is also freely available for download, under the GNU general public license (<http://neuroimage.usc.edu/brainstorm>).

All analyses performed were based on activity in bipolar channels. When two different regions were involved in a bipolar channel (i.e., the two member contacts belonged to different regions each), we adopted a conservative approach that classified the channel as belonging to both regions. All bipolar channels that were classified as being outside the brain (by at least one of their contacts), or when both contacts were located in white matter, were rejected from the analysis. Note that a precise localization of each contact (region, grey/white matter, or outside) was achieved as described in the subsection Anatomical data. Furthermore any faulty contacts, such as those with flat or highly noisy activity were removed.

Epochs were extracted from 1 s before to 2 s after the onset of each picture. Epochs with an incorrect or missing behavioral response (4.5% of trials), with epileptic spikes (identified by visual inspection), were removed from the analysis. The mean number of trials left for analysis was 325 (range: 290-353) out of 360 total possible. Our analyses focused on activity in the high-gamma range (80-150 Hz range), which has been repeatedly linked to cognitive processing, notably in research on language (Fries,

2015; Lachaux et al., 2012). The signal was bandpass filtered via the `filtfilt()` function in Matlab (using the default setting and the “iir” digital filter option, providing a zero-phase forward and reverse digital Infinite Impulse Response [IIR] filtering), on consecutive non-overlapping 10 Hz bands between 80 Hz and 150 Hz. We then extracted the amplitude envelope using the standard Hilbert transform. A z-score normalization was applied separately for each 10-Hz band against baseline (-600ms to -50ms locked on picture onset, so as to exclude edge effects). This provided 8 time series per channel and per trial. Then in order to create a single high-gamma power band per channel and trial, these 8 time series of z-scores were summed. This procedure was used to compensate for the characteristic that low frequencies have much larger power than high frequencies (Buzsáki et al., 2012).

Statistical analysis of behavioral data

Behavioral differences between the HOM and HET conditions were tested with an analysis of variance (ANOVA) on the conditions' response time means by participant, with participants as a random factor.

Statistical analysis of functional data

To identify task-related activations within each patient's channels, the statistical significance of high gamma activity was assessed by computing one-sample Student's t tests against zero ($\alpha = .001$) across trials at each data sample (each channel and each millisecond). These tests were performed in the time window of -400 ms to 1,600 ms after picture onset. The multiple-comparison problem in the time domain was avoided by estimating a minimum duration threshold T for consecutive, significant t -values. This bootstrap procedure consisted of randomly selecting the same number of trials as in the original data set with repetitions allowed (see also Guthrie & Buchwald, 1991), and identifying periods with significant activity within the baseline window from -600 ms to -50 ms. The procedure was repeated 1,000 times, where in each iteration, the maximum number of contiguous points passing the significance threshold (corresponding to uncorrected $p < .001$) was the duration value pooled into a bootstrap distribution. The significance threshold (minimum duration of consecutive significant t -values, $p < .001$) for a region r , as T_r , was defined at the right-tail 95% quantile of that bootstrap distribution.

Significant activities of individual patients were then combined in a group analysis. The goal was to compensate for the inevitable variability of implantation sites across patients and for any potential patient idiosyncrasies in their functional activity, by identifying functional consistency within each region across patients (see Lachaux et al., 2012, pp. 291-292, for pros and cons). Only regions that were sampled in at least 2 patients and that showed significant signal (as defined above) were considered. By region and for each patient, we averaged the previously-computed t -values per millisecond (see paragraph above) of the patient's channels belonging to that region. Thus each patient contributed one averaged t -value time series to that region's analysis.

These averaged t -value time series per patient in each region, were then used to assess the degree of functional consistency across patients. To do so, for each region we calculated a Pearson correlation r per each pair of patient's time series. The average of these pairwise correlations \bar{r} , for a region was then used to determine functional consistency. In calculating this functional consistency statistic, or \bar{r} value, for every region, an approximately normal distribution of \bar{r} values resulted, in which outliers or a large drop in \bar{r} magnitudes occurred, for example, between $\bar{r} = 0.35$ and the next values (i.e. 0.27, 0.23, see Table A1 and Figure A1). We hence used $\bar{r} \geq 0.35$ as a criterion for functional consistency. Thus in total, only regions which passed both tests, having sustained significant activity according to the duration bootstrap test, and functional consistency according to the $\bar{r} \geq 0.35$ criterion, were candidates for interpretation in the Results.

We then tested for significant differences related to the HET-HOM contrast. No attempt was made to analyze separately the different repetitions within each block (e.g. Python et al., 2017). A permutation approach for EEG data was used (Maris, 2012; Maris & Oostenveld, 2007), adapted here for intracerebral EEG with trials as a random variable. The method was applied independently to each of the regions that satisfied the criteria described in the previous paragraph (no clustering across regions was sought).

First, for each region, we extracted a matrix including all trials for all channels and patients that were sampled within the region, separated for the two semantic conditions (HOM, HET). This was used

to compute the average time-courses on Figures 3-5, and 7. Then differences between the two conditions were identified on each millisecond by calculating a two-tailed unpaired t-test, with trials as a random factor and disregarding patient and channel structure. The t -test values were grouped in temporal clusters of adjacent/consecutive time-samples with significant ($p < 0.05$) differences. The durations T_r of these clusters were extracted and, to control for multiple comparisons, within each region, they were tested against a duration threshold obtained from permuted data.

The permutation exchanged randomly the semantic condition assignments (HOM, HET) while preserving channel and patient structure, i.e. a trial could only be re-assigned to the channel and patient where it was recorded to control for variability across channels and patients. For each of the 1000 permutations, the same t -test calculations followed by duration clusters were computed to generate a surrogate distribution of cluster durations, that would reflect durations arising from noise. Then p -values for the observed duration clusters, T_r , were obtained based on their location (the T_r 's) in respect to the surrogate distribution of cluster durations arising from the random HOM-HET permutations. Over all regions, the resulting p -values of the observed T_r durations were subjected to a False Discovery Rate (FDR, Genovese et al., 2002) test correction for multiple comparisons *via* the `ft_fdr` function from Fieldtrip with $q = 0.05$ (Oostenveld, et al. 2011). Out of 144 uncorrected p -values of T_r duration clusters obtained from the permutation test, 11 T_r duration clusters survived the FDR correction.

Results

The intracerebral data stemmed from 9 patients having a total of 83 electrodes (mean per patient = 9.0, minimum = 8, maximum = 11) that recorded activity in 1,397 cortical sites, 676 located in the left hemisphere and 721 located in the right hemisphere. This led to 84 regions explored, based on the anatomical classification of recording sites described in Methods.

Response times

The average response time for word production was 809 ms, with a mean standard error (s.e.) across patients of 13.4 ms. Responses were significantly faster ($F(1,9) = 11.35, p = .008, \eta_p^2 = 0.56$) in the

HET context condition (mean 786 ms; s.e.18.7 ms) than in the HOM context condition (mean 833 ms; s.e. 19.0 ms), as depicted in the left plot of Figure 1. Furthermore, there was a main effect of faster responses with repetition ($F(1,9) = 7.70, p = .021, \eta_p^2 = 0.46$) but the interaction between context and repetition, as in the right plot of Figure 1, was not statistically significant ($F(1,9) = 1.45, p = .26, \eta_p^2 = 0.14$).

Activations generated by the task

The criteria for activation and consistency across patients revealed 39 regions with significant power in the high-gamma range. The dynamics of their neural activities are provided in Figure 2, in which the regions are organized anatomically as in Table 3.

Beginning with the basal part of the occipital lobe, significant activity was found in the lingual gyri of both the left and right hemispheres. Notable activity occurred in the left lingual gyrus (L.LgG) between 100-400 ms, while in the right lingual gyrus (R.LgG) between 100-200 ms, but at a fraction of the power compared to the left lingual gyrus.

In the basal temporal lobe, the significant regions consisted of the fusiform gyri in both the left (L.pFuG, L.mFuG, L.aFuG) and right hemispheres (R.aFuG). The strongest activation peaks occurred earliest in the left posterior fusiform gyrus (near 100 ms). As one moves to the middle (left) and anterior (left and right) fusiform parts, these activations reduce in magnitude and their activation peaks occur later in time (e.g. near 200 ms).

In the temporal medial section, the significant regions consisted of the hippocampus, amygdala, entorhinal cortices, and the parahippocampal gyri. In the left hemisphere, activity is graduated in power as one moves from the posterior to the anterior regions, for example moving from the entorhinal cortex, which is afferent to the hippocampus (e.g. Steward & Scoville, 1976), to the parahippocampal gyrus. In the right hemisphere, strong early activity is observed in the hippocampus and caudal hippocampus, and parahippocampal gyrus between 100-300 ms.

In the lateral part of the temporal lobe, significant activity is mainly observed at the inferior and middle temporal gyri, ranging from the anterior to posterior parts. For example, strong early activity is observed in the left and right posterior inferior temporal (L.pITG, R.pITG), and after in the left middle

temporal gyri (L.aMTG, L.mMTG), and only marginally in the right (R.mMTG, R.pMTG). In contrast, later significant activity (after 700 ms) is notably observed in the transverse temporal gyri bilaterally (TTG1), and in the right superior temporal gyrus (r.pSTG).

Regarding the frontal lobe, significant average evoked activity was observed in the left orbital gyri (L.mOrG, L.MOrG) shortly after (200 ms) stimulus onset. The anterior cingulate gyrus (L.aCG) demonstrated significant activity near stimulus onset, but subsequent gains in power did not occur until much later (> 1000 ms). With respect to the right medial superior frontal gyrus (R.MSFG) two distinct peaks of gamma power emerged near 100 ms and 200 ms, to which activity then dropped to a low at 400 ms and steady increases then followed.

Finally, in the lateral part of the frontal lobe near 200 ms, steep activity increases occurred in the left pars orbitalis (L.IFGOr), pars triangularis (L.IFGTr), and left middle frontal gyrus (L.MFG) from standardized gamma power values of near 1.5 to at least 4. In contrast in the right lateral frontal lobe, more steady increases in power were observed in the right middle frontal gyrus (R.MFG), the right lateral superior frontal gyrus (R.LSFG), and the right pars orbitalis (R.IFGOr).

For these 39 regions discussed, note that Figure 2 provides the number of channels for every region (and patient) that were each found to have significant activity. For the other regions (45) excluded due to lack of sufficient patient numbers, significance, or functional consistency between patients (i.e. an activity correlation $\bar{r} < 0.35$), see Table A1 in the Appendix.

Activations sensitive to the semantic context contrast

As reported in Table 4, the contrast analysis revealed 9 regions (of the previous 39) that had significant differences between the HET-HOM conditions in high gamma band power. Activity in these regions was fairly consistent, as the mean correlation of the power time series between patients sharing channels in a given region was $\bar{r} = .64$ (s.d. = 0.15; range $r = .42$ to $r = 0.78$).

Nearly all of these regions (8 out of 9) were sensitive to the contrast by showing significantly reduced activity in the HOM condition compared to the HET condition. The time courses of activity in these regions broken down into experimental conditions are presented in Figures 3-5. Figures 3 and 4

correspond to the four left and four right hemisphere regions in which HOM activity was less than HET, and Figure 5 corresponds to the single region in which HOM activity was greater than HET (the R.MSFG). In addition, Table 4 tentatively presents cognitive processes associated with each region in the context of this and similar tasks, to be discussed in more detail after the results.

In the left hemisphere, two significant effects were observed before the mean RT, in the L.aITG this effect was between 240 and 450 ms after picture presentation and in the La.FuG near 500 ms until 620 ms. The two others effects were in the same time window as the response times, from 600 to 1000 ms for the L.IFGOr and near 700 ms to 1150 ms for the L.MFG. In the right hemisphere, R.mPHG elicited a significant sustained difference from 180 ms to 650 ms. Later, the R.mITG revealed significant difference from 400 to 1100 ms. The effect in the R.pSTG surrounded the mean RT from 600 to 850 ms. Finally the R.A reported a late activity starting at 1400 ms after picture presentation and lasting for 200 ms.

The sole region in which the opposite effect was observed, significantly higher activity in the HOM condition compared to the HET condition, was labeled as the right medial superior frontal gyrus (R.MSFG), with contacts more specifically located in the the pre-SMA. This localization was based on careful assessment of the magnetic resonance imaging (MRI) scans of the two patients with R.MSFG electrodes (Figure 6). These scans demonstrate that their electrodes were located precisely in the pre-SMA (pre-supplementary motor area, e.g. see Nachev et al., 2008, Figure 1a). The time windows of the two significant differences observed there in were early, from 190 ms to 350 ms, and late, right before the mean RT, from 700 to 790 ms.

General Discussion

We investigated the neurophysiological correlates of two principal cognitive processes underlying word selection: i.e. semantic priming and interference. The evidence presented is an intracerebral EEG (iEEG) study that analyzed 84 brain regions sampled from 9 epileptic patients while they performed a picture naming task. The task was setup as a cycling naming protocol, which involved blocks of semantically homogeneous items (HOM), known to induce increased priming and as a consequence, increased interference during lexical selection, as compared to blocks of semantically heterogeneous items (HET). The main effects observed on the RTs (Figure 1) are typical of the cyclic naming paradigm (e.g. Belke & Stielow, 2013; Oppenheim et al., 2010). Here, the slowing of RTs in the HOM context has been traditionally associated with increased selection interference, perhaps hiding in the overall performance an underlying semantic priming effect.

Semantically Driven Word Production Network

A general network for semantically-driven word production (semantics derived from visual input, i.e. picture naming) was revealed in our analyses as a set of 39 brain regions that exhibited task-related activity which was significant and consistent across at least two patients (Table 3 and Figure 2). These average data can be roughly associated with the relevant task events: i.e. activity evoked by the stimulus; activity sustained throughout the stimulus-response interval; and activity tied to response, including auditory processes, such as for self-monitoring. The regions comprising this network are compatible with much previous work outlining the task-relevant regions, both in their spatial and temporal properties reported (e.g. Indefrey, 2011; Munding et al., 2016; Strijkers & Costa, 2011). Here, we observed these spatial and temporal signatures simultaneously within the same signal.

For example, our 39 regions included the left fusiform gyrus, which is classically associated with semantic activation and word retrieval (anterior part, Price, 2012), as well as its right anterior part, specialized more to semantic activation and less to word retrieval (Mion et al., 2010). Next, the frontotemporal regions in the middle temporal gyrus (MTG) and inferior frontal gyrus (IFG) observed

herein, have been regularly associated to standard sub-processes in language production (e.g. Indefrey, 2011). We also observed involvement of the left and right transverse temporal gyri (TTG), known to be sensitive to simple sounds (Mirz et al., 1999), and of the superior temporal gyrus (STG), sensitive to heard words (Zatorre & Belin, 2001). Significant activity in these regions is consistent with accounts that they are implicated in self-monitoring during word articulation (Christoffels et al., 2007, 2011; Schuhmann et al., 2011).

As this recovered network of 39 task-relevant regions (Table 3) closely corresponds to those found from a review of previous studies, an appropriate stage is set for a detailed interpretation of the 9 out of 39 regions (Table 4), which had activity significantly modulated by the HOM-HET contrast. In the following subsections, we elaborate on these 9 regions beyond previous literature listed in Table 4 through interpreting their modulation by the HOM-HET contrast. First, we will discuss the 8 out of 9 regions that exhibited HOM < HET activity, which we associate with processes related to priming. Then, we discuss the one region (pre-SMA) exhibiting HOM > HET activity, which we associate with conflict detection and response control.

Disperse Semantic Effects that can be Related to Semantic Priming

The earliest temporal activities among the HOM < HET regions occurred in the right parahippocampal and the left inferior temporal gyrus, which can be strongly associated with a bottom-up stream of spreading activation dynamics (i.e. vision to semantics to lexical entries). Specifically, the parahippocampal gyri are known to be involved in object recognition (Malach et al., 2002) and the left inferior temporal gyrus is known to be involved in semantico-lexical activation (Price, 2012): to link the semantics of the recognized objects to lexical entries. These findings are consistent with the hypotheses (see Introduction) gleaned from the theoretical frameworks previously discussed. Particularly that ventral, bottom-up streams would be facilitated through priming. In this framework, the dynamic is explained by an increased network calibration through stronger incremental learning in HOM (the same semantics are

more-frequently repeated in the HOM condition); in turn, words are retrieved with less activity by those same semantics (pictures).

The next-earliest HOM < HET effect may reflect facilitation in the right middle inferior temporal gyrus, which has been previously described as preferentially active in noun production (see Khader et al., 2010). The longer temporal window (observed up to response) and stronger magnitude may also invite an interpretation for facilitation in category-specific processing (Hauk et al., 2008). As a result, this may be an interesting region for future work in HOM-HET paradigms (which also involve object words), or that contrast categories of object and action words (such as in Zubicaray et al., 2017, an imaging study that reported contrast effects in the left middle temporal cortex but not the left inferior temporal cortex, though see their Figure 5, lower).

Note that the facilitation hypothesis discussed here is essentially equivalent to that of Aristei et al. (2011), although in their EEG study they discuss it conversely: HET > HOM occurs as an increased effort due to lack of priming. The neural mechanism proposed to account for the facilitation hypothesis (via network calibration), is known as repetition suppression, where top-down processes suppress incremental learning effects in HOM, leading to reduced activity, hence diminishing the repetition effects of semantic features across the items within these blocks (Gotts et al., 2012). Repetition suppression is discussed by Llorens et al. (2016), Python et al. (2017), and Riès et al. (2017) in various respects.

Other Processes that can Be Tied to Reduced Activity in HOM

Some regions elicited a significant HOM < HET window later than the expected time frame, which would make it difficult to directly link them to priming processes. The most pertinent to discuss first are the left anterior fusiform gyrus and the left middle frontal gyrus, which, in similar tasks, have been previously known to be involved in processes like semantic activation and (word) retrieval from semantics, respectively (Price, 2012). The lack of early window findings herein may be due to the statistical parameters used. For example, each of these regions exhibited an early sustained HOM < HET activity near 200 ms (+- 100 ms), but neither time clusters were found to be a significant. Maris (2012)

clarifies that upon finding a significant time cluster with this method, it does not exclude the possibility of other time clusters (i.e. these early sustained activities) from also having significant differences. We hence recommend that these regions remain candidates for assessment in future iEEG studies of priming phenomena.

Next, the left pars orbitalis exhibited a significant $HOM < HET$ effect in a temporal window around the response, which is consistent with a facilitation account in its role for articulatory processes in language production (Price, 2012). However, this (interpretation) would be in contrast to previous findings (Janssen et al. 2015, surface EEG in Table 1), where a $HOM > HET$ effect was observed around the same timing (around response), and as a result was linked to semantic decision and conflict resolution between words, and to the ventrolateral prefrontal cortex. We propose that these contrasting accounts are likely due to a difference in spatial resolution between surface EEG and intracerebral EEG herein (surface EEG is measuring larger synchronous streams, while iEEG is measuring local activity); and which algorithms a surface EEG experiment may use to attribute such activity to specific brain regions.

In the right hemisphere, the right posterior superior temporal gyrus exhibited a significant $HOM < HET$ effect, also in a temporal window around the response, and this region is known to be involved during auditory self-monitoring and association (Christoffels et al., 2007, 2011). Notably, an fMRI activation effect of opposite sign ($HOM > HET$) was revealed in the middle to posterior superior temporal cortex of the left hemisphere (Hocking et al., 2009). While it would definitely be premature to interpret the opposition of effect signs across hemispheres, these two observations combined suggest modulations of monitoring processes that are typically not considered in barebone lexical networks that account for semantic priming and inhibition (but see Nozari & Hepner, 2018). The timing of the effects, that was absent in fMRI but was revealed here with iEEG, is compatible with a functional interpretation in terms of monitoring.

Lastly, the right amygdala exhibited a significant $HOM < HET$ time window long after the response. This effect is the most obscure to interpret, due to the timing of the effect and the region involved. In previous research, the amygdala has been mostly associated with emotion. In this respect,

disregarding HOM-HET differences, a peak activity in the amygdala occurred for both conditions shortly after stimulus onset (150-200 ms), which suggests an expected role in linking picture semantics to emotional qualities. The amygdala has been linked to lexical processing in an experiment involving written words of low vs. high frequency (Scott et al., 2009). To our knowledge, since this is the first time that the amygdala was found to be modulated by semantic HOM-HET contrasts, replications would be needed before its functional role in this task can be addressed.

Localized Semantic Effect in the right pre-SMA Tied to Semantic Interference

The second principal finding was indeed the converse of the priming results: a single brain region revealed significant HOM > HET activity, and at two time points: first shortly after picture presentation, and, later, close to the overt naming response. This region was the right medial superior frontal gyrus (R.MSFG). The R.MSFG consists of, from rostral to caudal, the pre-SMA (medial BA6) and the supplementary motor area (SMA), each with diverse functional roles (Chauvel et al., 1996). As per the anatomical localizations of the electrodes in Figure 6, these R.MSFG contacts (blue circles) were all located in the pre-SMA. We note that our sampling and signal processing criteria revealed that there were no electrodes recording activity in the L.MSFG in any patient; hence, we cannot develop a detailed discussion of the lateralization of this effect with the current data.

We will relate the early and late interference effects to, respectively, conflict detection and response control. The HOM > HET activity of the right pre-SMA, a region extensively associated with response and cognitive control (reviewed by Ridderinkhof et al., 2004), suggests that its over-activation during semantic interference (HOM) would contribute to resolve the conflict that arises from multiple words being strongly activated due to shared semantic category features (de Zubicaray et al., 2001; Piai et al., 2014). The timing of the first significant time window suggests an early involvement of the pre-SMA in conflict detection. With regard to the cognitive mechanisms discussed in the Introduction, this would be compatible with raising response caution, or raising the activity threshold needed to trigger production of the word (see Nozari & Hepner 2018, see also Anders et al., 2015 and Oppenheim et al., 2010 models).

The second significant time window, which is just prior to response, is compatible with conflict monitoring accounts (Ridderinkhof et al., 2004), and inhibiting incorrect responses (Forstmann et al. 2008 and 2010). For example, Forstmann et al. found increased activity in the pre-SMA when subjects prepared to stop an ongoing action.

With these interpretations, our study supports previous reports that the pre-SMA may play an important role in conflict management during selection, but makes the critical addition that it is involved in language production, particularly in handling interference between highly-activated competitors (e.g. HOM). Conflict may also be increased by poorer, rather than more intense, lexico-semantic mapping (see Nozari & Hepner, 2018) such as induced by temporal lobe lesions (Harvey & Schnur, 2015), in which we would predict increased pre-SMA activity. We can also speculate that increased conflict management may be introduced in other situations, e.g. when it is highly important for a speaker to choose the best word among alternatives to express a concept. In this view, just before articulatory programming or execution, the pre-SMA would be significantly implicated in the resolution processes between competing lexical items. There are previous findings showing worse performance in prefrontal patients during conflict (Riès et al., 2015), which may be explained by reduced top-down connectivity of the pre-SMA to ventral processing streams, through damage to the frontal aslant tract (FAT, Chernoff et al., 2018).

Our study, in combination with those previously discussed, is hence compatible with the idea that the pre-SMA may be involved in the final decision mechanism before a word is produced (2nd time window), in a ventral pathway that is temporal to frontal to the SMA; and that the pre-SMA also communicates in an early top-down fashion (1st time window) for conflict detection and improved response control. These findings imply that the pre-SMA should be considered more carefully during word production paradigms (in line with the discussion by Riès et al., 2016).

Previous works have found a role of the pre-SMA in general selection, without conflict manipulations (Alario et al., 2006; Tremblay & Gracco, 2009), while herein we find evidence that the region is increasingly modulated during conflict manipulations. In respect to current theories largely based on behavioral data, these findings are consistent with the proposal that top-down cognitive control

processes act to mitigate interference in lexical selection for appropriate response execution (Belke 2013; Belke & Stielow, 2013; Schnur et al., 2009).

While word production has indeed been proposed to engage cognitive control (Nozari & Novick, 2017), the pre-SMA/R.MSFG have not been previously highlighted as critical in this process. However, in other interference or cognitive control tasks such as Stroop, go/no-go and stopping tasks, the medial superior frontal gyrus (BA 6, notably the pre-SMA), *especially in the right hemisphere*, has been linked to cognitive control processes such as response selection, inhibition, response switching, and detection or monitoring of conflict (George et al., 1994; Ridderinkhof et al., 2004; Simmonds et al., 2008; Verbruggen & Logan, 2008). Our results are hence consistent with these across-domain studies, and provides neurophysiological support to a standing hypothesis that cognitive control in language production may utilize domain-general mechanisms (e.g., Riès et al., 2011).

Another strong candidate for handling interference was the anterior cingulate cortex (ACC), herein sampled in the left anterior cingulate gyrus (L.aCG). However, although the L.aCG was found significant in the general task (Table 3, Figure 2), no significant difference was found in the HOM-HET contrasts (see Figure 7). Hence these results do not provide support for other cognitive control theories that could link a role of the ACC for resolving semantic interference (Botvinick et al., 2001, 2004; Janssen et al., 2015; Piai et al., 2013). Though these studies involve different recording techniques (EEG and fMRI), which could obtain different results when for instance, clustering surface electrodes to make inferences about specific brain regions (EEG), or averaging activities over time (fMRI). Further reproduction of these functional distinctions in the case of word production is needed to assure the interpretation we propose.

In respect to the selection mechanism discussed in the Introduction, there are different ways in which one could view the actual dynamic in which the pre-SMA may handle response conflict. For example in a more serial perspective, competitors may race with accumulating activity until a selection deadline (threshold) is activated which triggers motor preparation and execution (e.g., see Anders et al., 2015; Oppenheim et al., 2010; Roelofs, 1992). Alternatively, the top-2 or -3 closest candidates may be

selected and prepared for possible execution, and the response triggering process may continuously switch between these already-prepared responses (which is plausible here due to the small response set, 6 items per block) until an absolute threshold is crossed. The former paradigm has been one of the most popular approaches in quantitative cognitive modelling of choice behavior (Ratcliff et al., 2004; Busemeyer & Townsend, 1992; Townsend & Ashby, 1983; Ratcliff & Smith, 2004), and has been successfully applied to the word production paradigm with semantic contrasts (Anders et al., 2015, 2017). Support for the latter hypothesis has also been found by Isoda and Hikosaka (2007) who found neurons in the rostral portion of the superior medial wall (or, pre-SMA; BA6) active in Rhesus monkeys during response switching. While both mechanisms may be able to account for observed performance, further neurophysiological work, which combines also computational modeling, would be interesting to clarify the mechanism that best represents the underlying cognitive operations. In regard to either modeling approach, our hypothesis is that the pre-SMA would be principally implicated in the threshold modulation for final word selection or triggering for production.

Lateralization in the picture naming network

While not specifically designed to assess lateralization patterns (Riès et al., 2016), the sampling available in our study revealed several noteworthy observations in this respect (Figure 2). In the occipital lobe (Row 1) between 50-400 ms, the t -values of activity in the left lingual gyrus (L.LgG) were multiple times higher than those in the right lingual gyrus (R.LgG; see however Tanji et al., 2005). This is an interesting result that inspires future work to clarify the mechanism, such as to whether top-down language processes may also interact with the left visual gyri for improved lexico-semantic processing.

Secondly in the medial temporal lobe (Row 3), activity is graduated in power as one moves from the posterior to the anterior regions, for example as one moves from the entorhinal cortex which is afferent to the hippocampus (e.g. Steward & Scoville, 1976) to the parahippocampal gyrus. In the right hemisphere however, early activity is also observed in these regions, but without a marked peak in the entorhinal cortex to prime such activity. This result may lead to a speculation that a different mechanism in the right hemisphere may trigger such activity.

In the lateral temporal lobe (Row 4), larger *t*-values of activity were also observed in the left transverse temporal gyrus (L.TTG1) than the right transverse temporal gyrus (R.TTG1), also known as Heschl's gyri. This result is consistent with studies of this region (Morillon et al., 2012) that have found stronger activity in the left hemisphere for higher frequencies (25-45 Hz), versus stronger activity in the right hemisphere for lower frequencies (5-6 Hz). This occurrence, known as asymmetric sampling time (AST, Poeppel et al., 2003) between hemispheres, has been established as a function of language specialization (Dorsaint-Pierre et al., 2006; Liegeois-Chauvel et al., 1999). The contribution of the current study shows that the AST preference for higher frequencies in the left transverse temporal gyrus extends even to the high gamma range (80-150 Hz).

With regard to a lateralized specialization of the pre-SMA for handling word-selection conflict in language production, as we did not have electrodes implanted in the left pre-SMA in any patient, it is too soon to conclude that these operations are handled more often in the right than the left. Support for the right pre-SMA is provided in a previous imaging experiment of picture naming with HET/HOM distractor-word conditions (de Zubicaray et al., 2001), as well as in non-linguistic experiments of cognitive control (e.g. Ridderinkhof et al., 2004). In contrast during an active lexical selection experiment in which there was no interference condition, the left pre-SMA was much more active than the right (Alario et al., 2006). It is also important to note however, that there is evidence for bilateral plasticity of the pre-SMA. That is for example, resection studies of the pre-/SMA have found language deficits after removal of a unilateral portion of the pre-/SMA, in which language performance recovery was associated with increased activity in the contralateral side of the pre-/SMA (e.g. Krainik et al., 2003, see also Chainay et al. 2009). Overall, these works and ours provide interesting arguments to further probe the pre-SMA bilaterally in future language experiments, especially those that involve conflict management or cognitive control.

This research has hence led to several lateralization observations, and suggests their further investigation through a follow-up study formally designed to assess lateralization.

Limitations

Our study has the regular limitations which are inherent to studies of intracerebral activity in epileptic patients (Lachaux et al., 2012). These populations may show strong inter-individual variability. However, our group analyses was anatomically and functionally grounded, compensating to some extent for this aspect. Indeed, fair levels of spatial sampling were achieved, certainly at the expense of the highly-specific anatomical details that come with each patient's stereotactic implantation coordinates, and with the risk that the cross-patient consistency constraint excludes potentially-relevant signal diversity and signal information. Our focus on high-gamma activity was strongly motivated by the current view that it efficiently reflects cognitive processing. Having done this, we did not explore the other potentially meaningful frequency bands (as, e.g., Canolty et al., 2007; Gaona et al., 2011), and subsequent research is needed to broaden the search space to these levels as well, which may reveal further information.

Relatedly, our study assessed significant task activities and semantic effects on trial based statistics, yet what we report and interpret are the averages within and across patients. Such averaging, together with the signal processing procedures, smoothes the signal in time and puts limits on the temporal resolution available. Single trial measures may be better located in time and might be usable in some contexts (Dubarry et al., 2017), but they were not easily adaptable to assess effects across conditions involving different trials, as in the design we used.

Finally, we used an anatomical approach to associate cognitive processes with the brain regions sampled. Such approaches are currently a form of common practice, and have been identified as a case of reverse inference (Poldrack, 2006). While such approaches can be particularly detrimental when inferences are made across cognitively different tasks, the cognitive associations we have made with brain regions were quite specific, came from previously published meta-analyses (e.g. Price, 2012, See Table 2), and involved the same task we used (picture naming) or very similar tasks (e.g., word reading).

Conclusion

We detected a network of 39 brain regions with significant task-related activity recruited during semantically-driven word production. These regions are compatible with much previous work on the picture naming network, both in their spatial and temporal properties, yet observed here *simultaneously* within the same signal. Several lateralization contrasts within this network were also identified, offering insights for future work.

The lexico-semantic dynamics of semantic priming and interference resulted in 9 of the previous 39 regions being modulated by the semantic context manipulation. Within our sampling, priming appeared to modulate brain activity dispersedly (in 8 out of 9 regions), while interference appears to be resolved more locally (1 out of 9 regions), notably in the pre-supplementary motor area (pre-SMA). These observations are consistent with the hypothesis that both priming and interference underlie semantically-driven word retrieval. They further suggest a significant role of the pre-SMA in resolving interference, perhaps as the final mechanism for response selection before articulation. Such interpretation is consistent with previous hypotheses regarding the role of top-down cognitive control in language production, although they did not explicitly consider the pre-SMA. It remains to be determined to what extent the left vs. right pre-SMA might be involved in handling interference in language, as the current study did not involve implanted electrodes in the left pre-SMA.

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Table 1: Summary of Previous Neuro-Scientific Results in the Cyclic Picture Naming Task, Organized by Process of Interest.

Reference	Method	Discuss Effect Directions	Direction of Effect	Locus	Timing	Process
Aristei et al. (2011)	EEG	Yes	HOM < HET	L&R Temporal electrodes	200-300 ms	Semantic priming
de Zubicaray et al. (2017)	fMRI	Yes	HOM < HET	L MTC	N/A	Semantic priming
Janssen et al. (2015)	EEG	Yes	HOM < HET	Frontal & Temporal electrodes	250-400 ms	Semantic priming
Riès et al. (2017)	ECoG	Yes	HOM < HET	L Frontal & Temporal Regions	0-350 ms bef. response	Semantic priming
de Zubicaray et al. (2014)	fMRI	No	HOM < HET	L Hippocampus	N/A	Increm. learning
Vieth et al. (2015)	fMRI	Yes	HOM > HET	L Hippocampus	N/A	Increm. learning
Llorens et al. (2016)	iEEG	Yes	HOM < HET	L&R Hippocampus	600 ms	Increm. learning
de Zubicaray et al. (2017)	fMRI	Yes	HOM > HET	L Hippocampus	N/A	Increm. learning
Maess et al. (2002)	MEG	No	HOM > HET	L Temporal Region	150-225 ms	Semantic interf.
Aristei et al. (2011)	EEG	Yes	HOM > HET	L&R Temporal electrodes	200-300 ms	Semantic interf.
Janssen et al. (2011)	EEG	Yes	HOM > HET	Anterior electrodes	220-450 ms	Semantic interf.
Ewald et al. (2012)	EEG	No	HOM > HET	R Frontal - L Occipitotemporal Connectivity	X	Memory load
Python et al. (2017)	EEG	Yes	HOM < HET	ERP Anterior/Posterior electrodes	270-315 ms	Semantic interf.
Riès et al. (2017)	ECoG	Yes	HOM > HET	L Frontal & Temporal Regions	0-350 ms bef. response	Semantic interf.
Schnur et al. (2009)	fMRI	No	HOM > HET	L IFG	N/A	Conflict resolution
Schnur et al. (2009)	fMRI	No	HOM > HET	L TC / L MTG	N/A	Conflict resolution
Aristei et al. (2011)	EEG	Yes	HOM > HET	Frontal ERP	250-350 ms	Conflict resolution
Pisoni et al. (2012)	tDCS	Yes	HOM faster	L IFG	N/A	Conflict resolution
Janssen et al. (2015)	EEG	Yes	HOM > HET	Frontal electrodes	500-750 ms	Conflict resolution
de Zubicaray et al. (2017)	fMRI	Yes	HOM > HET	L IFG	N/A	Conflict resolution
Hocking et al. (2009)	fMRI	Yes	HOM > HET	L STC	N/A	Self-monitoring
Maess et al. (2002)	MEG	No	HOM > HET	L Temporal Region	450-475 ms	Self-monitoring
Python et al. (2017)	EEG	Yes	HOM > HET	ERP Central Electrodes	365-410 ms	Self-monitoring
Krieger-Redwood & Jeffries (2014)	TMS	No	HOM slower	L IFG	N/A	Top-down control
Krieger-Redwood & Jeffries (2014)	TMS	No	HOM slower	pMTG	N/A	Top-down control
Meinzer et al. (2016)	A-tDCS	Yes	HOM slower	L IFG	N/A	Top-down control
Hocking et al. (2009)	fMRI	Yes	HOM > HET	L&R Hippocampus	N/A	Episodic memory
Vieth et al. (2015)	fMRI	Yes	HOM < HET	L Dorsolateral PFC	N/A	Working memory
Pisoni et al. (2012)	tDCS	Yes	HOM slower Overall slower	L STF	N/A	Lexical activation
de Zubicaray et al. (2014)	fMRI	No	HOM < HET	L M&P Lateral TC	N/A	Lexical interf.
de Zubicaray et al. (2017)	fMRI	Yes	HOM > HET	L mMTC	N/A	Action processing
de Zubicaray et al. (2017)	fMRI	Yes	HOM < HET	IPS	N/A	Action processing
de Zubicaray et al. (2017)	fMRI	Yes	HOM < HET	L&R Visual extrastriate cortices	N/A	Percep. processing
Wirth et al. (2011)	A-tDCS	No	HOM faster	L DPFC	N/A	Not proposed
Meinzer et al. (2016)	A-tDCS	Yes	HOM faster	L pMTG/STG, Connectivity	N/A	Not proposed
Ewald et al. (2012)	EEG	No	HOM < HET	Global Field Power ERP	> 280 ms	N/A
Llorens et al. (2014)	EEG	No	HOM = HET	ERP Anterior/Posterior electrodes	X	N/A

Wirth et al. (2011) EEG No HOM < HET Left Scalp ERP (ROI) 200-400 ms N/A

Note: EEG: ElectroEncephalography; iEEG: intracerebral stereotactic EEG; MEG: MagnetoEncephalography; ECoG: ElectroCorticoGraphy; fMRI: functional Magnetic Resonance; ERP: event-related potential; ROI: region of interest; HOM: Semantically homogeneous naming context; A-/tDCS: (anodal) trans-cranial direct current stimulation; HET: Semantically heterogeneous naming context; LIFG: left inferior frontal gyrus; MTC: middle temporal cortex; STC: superior temporal cortex.

Table 2: Participant clinical data

Patient	Age	Gender	Handedness	Language Lateralization	Epileptic Zone
1	33	Male	Left	Left	Left Temporal
2	19	Female	Right	Left	Right Temporal
3	36	Female	Right	Left	Bilateral Temporal
4	40	Male	Right	Left	Right Fronto-temporal
5	14	Male	Right	Bilateral	Left Temporo-occipital
6	27	Female	Right	Left	Left Prefrontal
7	21	Male	Right	Left	Bilateral Temporal
8	21	Female	Right	Left	Right Temporal Lateral
9	31	Male	Right	Left	Right Temporo-occipital

Table 3: Summary of the 39 Regions With Significant and Consistent Activity During Word Production in Picture Naming

Lobe	Subdivision	Abbreviation	Full Name
Occipital	Basal	L.LgG, R.LgG	Left and right lingual gyri
	Basal	L.aFuG, L.mFuG, L.pFuG	Left anterior, middle, and posterior fusiform gyri
		R.aFuG	Right anterior fusiform gyrus
	Medial	L.Ent, R.Ent	Left and right entorhinal area
		R.A	Right amygdala
		L.Hi, R.Hi	Left and right hippocampus
		R.cHi	Right caudal hippocampus
		L.aPHG, R.aPHG	Left and right anterior parahippocampus
		R.mPHG	Right middle parahippocampus
	Temporal	Lateral	L.TTG1, R.TTG1
R.TTG2			Right posterior transverse temporal gyrus
R.pSTG			Right posterior superior temporal gyri
L.aMTG, L.mMTG, L.pMTG			Left anterior, middle, and posterior middle temporal gyri
R.mMTG, R.pMTG			Right middle and posterior middle temporal gyri
Medial		L.aITG, L.pITG	Left anterior and posterior inferior temporal gyri
		R.aITG, R.mITG, R.pITG	Right anterior, middle, and posterior inferior temporal gyri
		L.aCG	Left anterior cingulate gyrus
		R.MSFG	Right medial superior frontal gyrus
		L.MOrG, L.mOrG	Left medial and middle orbital gyri
Frontal	Lateral	L.IFGOr, R.IFGOr	Left and right pars orbitalis
		L.IFGTr	Left pars triangularis
		R.LSFG	Right lateral superior frontal gyrus
		L.MFG, R.MFG	Left and right middle frontal gyri

Table 4: The 9 Regions Showing Functional Consistency and Significant Differences in the HET/HOM Contrast

Abbreviation	Region	Previously Associated Cognitive Process
L.aFuG ●	Left anterior fusiform gyrus	Semantic activation, retrieval (Price, 2012)
L.aITG ●	Left anterior inferior temporal gyrus	Semantic activation, comprehension (Price, 2012)
L.IFGo ●	Left pars orbitalis	Semantic decision and articulation (Price, 2012)
L.MFG ●	Left middle frontal gyrus	Word retrieval from semantics (Price, 2012)
R.MPHG ●	Right middle parahippocampal gyrus	Object recognition (Malach et al., 2002)
R.MSFG ●	Right superior medial frontal gyrus	Semantic interference (de Zubicaray et al., 2001)
R.pSTG ●	Right posterior superior temporal gyrus	Self-monitoring and auditory association (Christoffels et al., 2011)
R.mITG ●	Right middle inferior temporal gyrus	Specificity for object word production (Khader et al., 2010)
R.A ●	Right amygdala	Word processing: emotion and frequency (Scott et al., 2009)

Note: Green: HOM < HET; Magenta: HOM > HET.

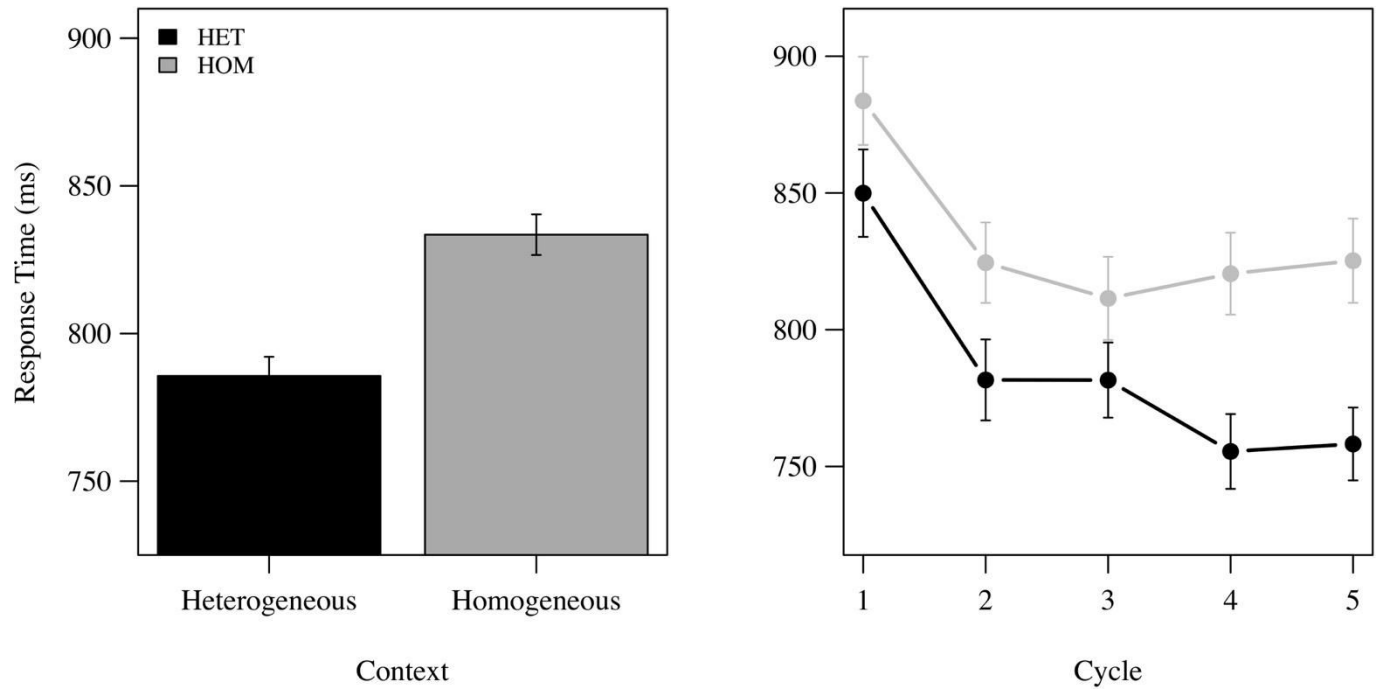


Figure 1: Behavioral results.

Left: mean response times (786 ms, 833 ms) and mean standard error across participants (18.7 ms, 19.0 ms) respectively for the heterogeneous (HET) and homogeneous (HOM) conditions in the picture naming paradigm. Right: mean response times for HET and HOM respectively by repetition cycle in the picture naming paradigm.



Figure 2: Average Neural Activity During Picture Naming. Stimulus-locked time-frequency activity (t -value gamma power, 80-150 Hz) of the regions listed in Table 3, with the same abbreviations, and region sampling statistics: the number of significant bipolar channels c and patients p . Picture onset occurred at 0 ms. For improved visualization to compare these time courses, the y-axis limit is specified according to lobe (frontal 7 units, temporal 14 units, occipital 16 units). Due to only one frontal basal region being significant (left middle orbital gyrus, L.mOrG), in the interest of parsimony this region was grouped

into the left frontal medial section. Note only visible regions on the surface projection are depicted on the brain anatomies: e.g. in the temporal medial section, the cortical brain atlas can only represent the parahippocampal gyri.

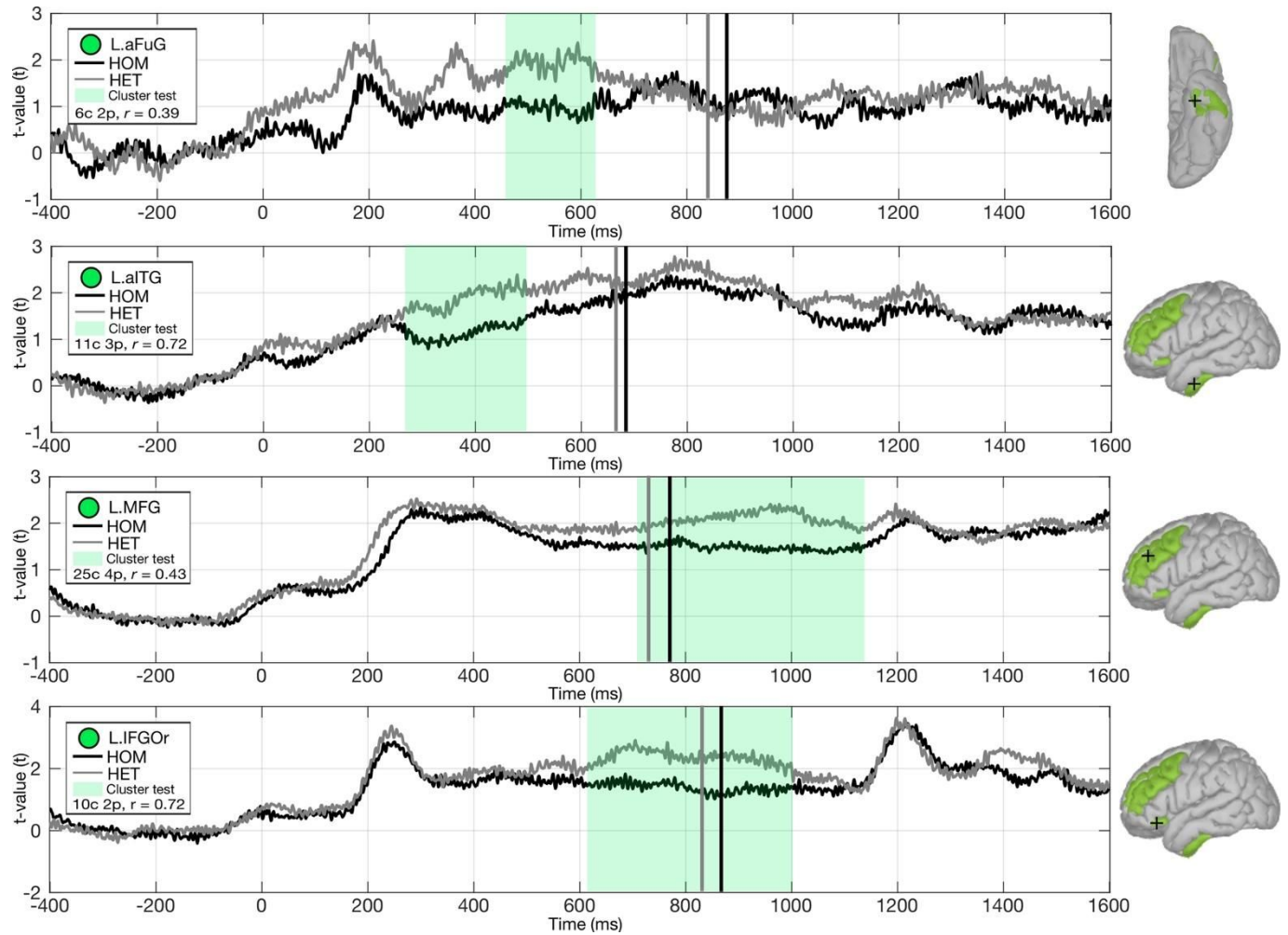


Figure 3: Effect of semantic context across left hemisphere regions, Stimulus-locked time-series of the high-gamma activity (80-150 Hz) in the four regions of the left hemisphere that exhibited significant differences due to HET-HOM conditions (HET grey, HOM black), as determined by a cluster-based permutation analysis (Maris & Oostenveld, 2007). Maris (2012) has clarified that this approach does not exclude the possibility of other potential significant differences existing outside the resulting temporal cluster(s). The number of channels in the region is given by c, number of patients p, and the correlation r between the time series of the patients (the average of their channels). The vertical grey and black lines are the median RTs respectively of the HET and HOM conditions for the patients with significant channels in this region. See Table 4 for full region names and details about the processes associated to each region in previous literature.

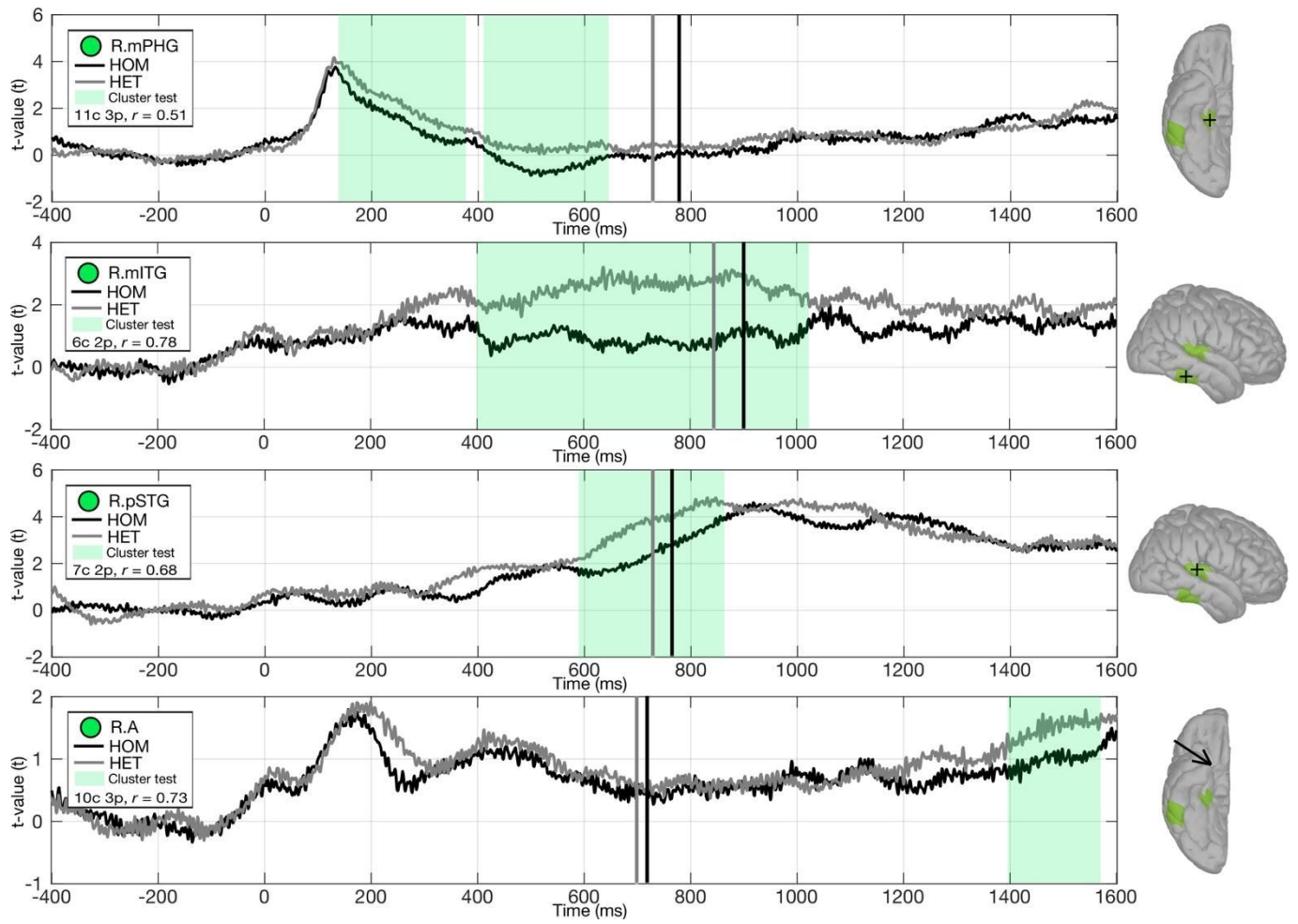


Figure 4: Effect of semantic context across right hemisphere regions. See Figure 3 for details.

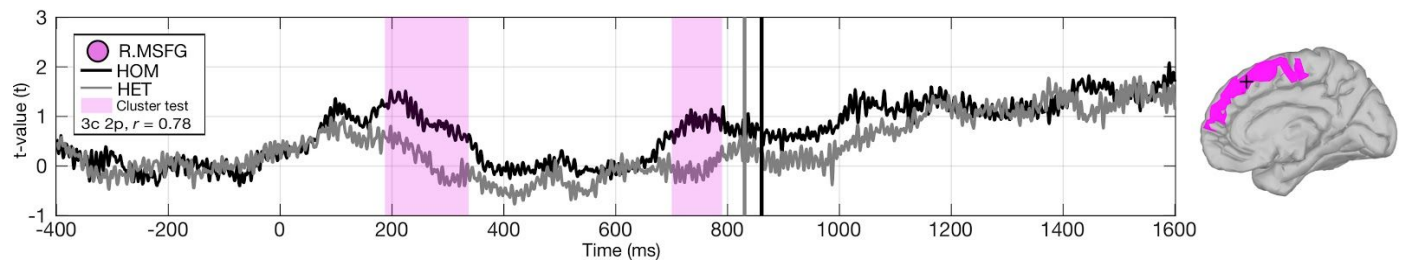


Figure 5: Effect of semantic manipulation resulting in increased activity for HOM compared to HET conditions. The contacts were located in the right medial superior frontal gyrus, more specifically the pre-SMA (see Figure 6). Data organized as in Figure 3.

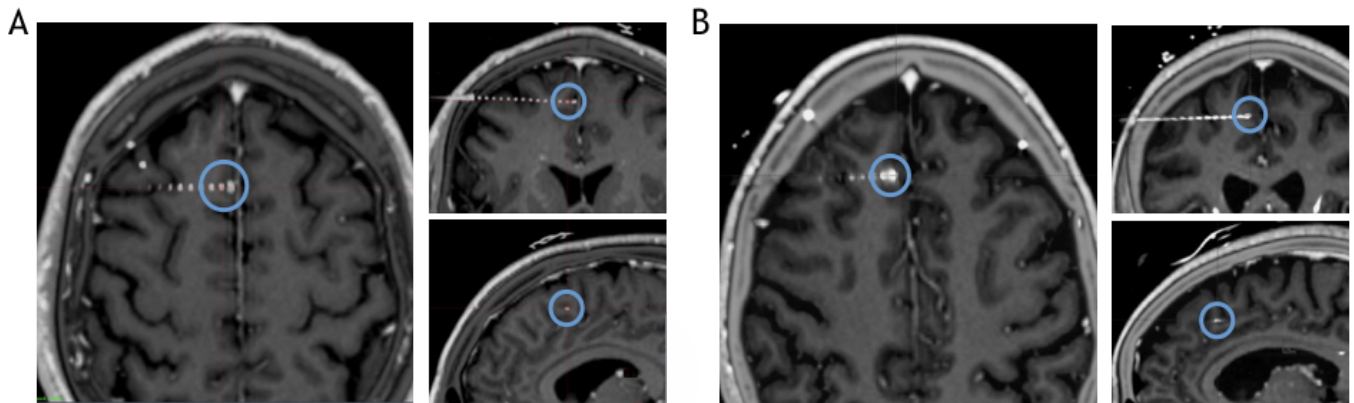


Figure 6: Location of the contacts classified in the R.MSFG.

MRI scans show that the electrodes of the two patients classified in the R.MSFG are indeed located at the pre-SMA: transverse, coronal, and sagittal views of the R.MSFG electrode implantation in patient 4 (A), and in patient 8 (B). The blue circles indicate the specific contacts involved (by patient) in the pre-SMA, the three contacts from patient 4 (A) led to two bipolar channels, and the two contacts from patient 8 (B) led to one bipolar channel.

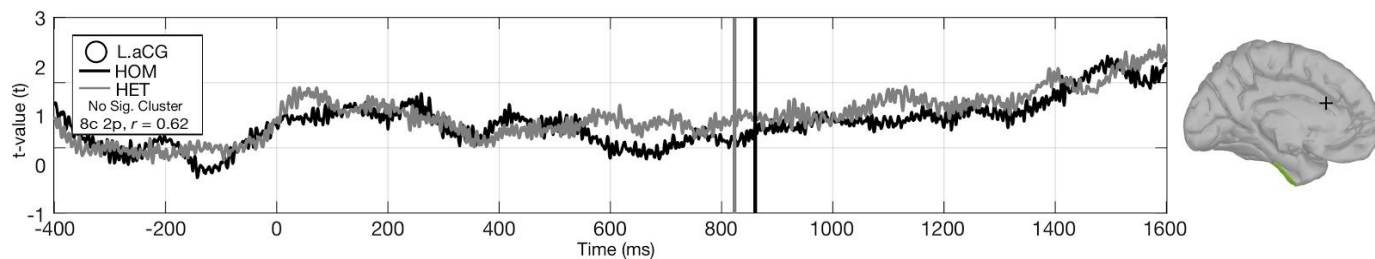


Figure 7: No significant effect of HOM-HET context found in the left anterior cingulate gyrus (L.aCG), namely the left anterior cingulate cortex (ACC). Data organized as in Figure 3.

Appendix

The following Table A1 provides the regions excluded from interpretation due to either failing the functional consistency criterion (an $\bar{r} < 0.35$), or sampling in only 1 patient. The Table includes 45 regions, 6 regions were excluded based the functional consistency criteria (depicted in Figure A1, they are to the left of the vertical line), and 39 due to sampling in only 1 patient. Conversely, the patient and bipolar channel numbers for the regions satisfying the criteria both for significance and functional consistency are provided in Figure 1.

Table A1: Summary of bipolar channel and patient numbers for brain regions not present in Figure 1.

Abbreviation	Name	Channels		Patients		CorrP
		Sig	<i>N</i>	Sig	<i>N</i>	<i>r</i>
L.pCG	Right post cingulate gyrus	2	2	2	2	0.27
R.mFuG	Right mid fusiform gyrus	20	20	5	5	0.23
R.mSTG	Right mid superior temporal gyrus	5	6	2	2	0.08
R.pFuG	Right post fusiform gyrus	4	4	2	2	0.02
L.SMG	Left supramarginal gyrus	6	6	2	2	0.01
L.Pte	Left planum temporale	2	2	1	2	NA
L.A	Left amygdala	3	3	1	1	NA
L.cHi	Left caudal hippocampus	2	2	1	1	NA
L.aSTG	Left ant superior temporal gyrus	2	2	1	1	NA
R.aSTG	Right ant superior temporal gyrus	4	4	1	1	NA
L.mSTG	Left mid superior temporal gyrus	2	3	1	1	NA
R.aMTG	Right ant mid temporal gyrus	9	9	1	1	NA
R.aCG	Right ant cingulate gyrus	3	3	1	1	NA
R.pCG	Right post cingulate gyrus	2	2	1	1	NA
L.IFGOp	Left pars opercularis	3	3	1	1	NA
R.IFGOp	Right pars opercularis	5	5	1	1	NA
L.Pcun	Left post cuneus	1	1	1	1	NA
L.17	Left Brodmann's area	3	3	1	1	NA
R.17	Right Brodmann's area	2	2	1	1	NA
L.aCOL	Left ant collateral sulcus	2	2	1	1	NA
L.pCOL	Left post collateral sulcus	1	1	1	1	NA
L.aCol	Left ant colliculus	2	2	1	1	NA
L.aINS	Left ant insula	3	3	1	1	NA
L.AnG	Left angular gyrus	2	2	1	1	NA
L.Cd	Left caudate nucleus	4	4	1	1	NA
L.Fop	Left frontal operculum	3	3	1	1	NA
L.OcG	Left occipital gyrus	3	3	1	1	NA
L.pOP	Left post pars opercularis	2	2	1	1	NA
L.POTZ	Left parietooccipital transition area	2	3	1	1	NA
L.Ppo	Left planum polare	5	5	1	1	NA
L.PrG	Left precentral gyrus	4	4	1	1	NA
L.SPL	Left superior parietal lobule	3	3	1	1	NA
L.SRoG	Left superior rostral gyrus	0	1	0	1	NA
R.aINS	Right ant insula	3	3	1	1	NA
R.Fop	Right frontal operculum	1	1	1	1	NA
R.mINS	Right mid insula	2	2	1	1	NA
R.MOrG	Right medial orbital gyrus	1	1	1	1	NA
R.mORG	Right mid orbital gyrus	3	3	1	1	NA
R.OcG	Right occipital gyrus	4	4	1	1	NA

R.PRC	Right perirhinal cortex	5	5	1	1	NA
R.PT	Right paratenial thalamic nucleus	4	4	1	1	NA
R.Pte	Right planum temporale	2	2	1	1	NA
R.Pu	Right putamen	5	5	1	1	NA
R.PuL	Right pulvinar	1	1	1	1	NA
R.SMG	Right supramarginal gyrus	7	7	1	1	NA

Note: Number of significant channels and patients (Sig) versus total number (N). CorrP = correlation statistic (r) calculated between patients with significant channels to determine if activity is functionally consistent; regions with $r < 0.35$ were excluded.

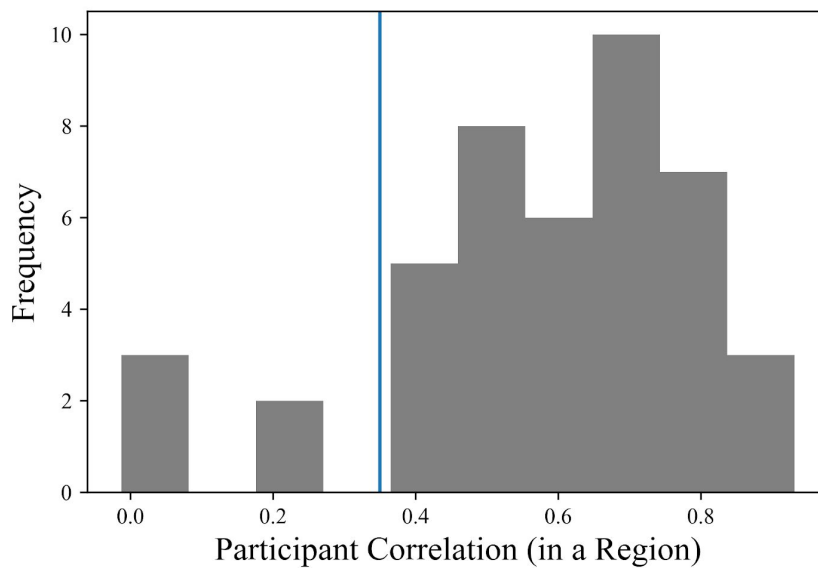


Figure A1: Distribution of functional consistency, or correlations between participants who share significant channels in a region (specific values provided in Table A1). Based on this distribution, a threshold of $r \geq 0.35$ was used (depicted by the blue vertical line) as the inclusion criterion. This resulted in 6 regions excluded and 39 regions retained.