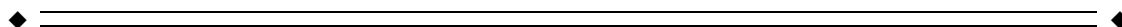


Topographical Gradients of Semantics and Phonology Revealed by Temporal Lobe Stimulation

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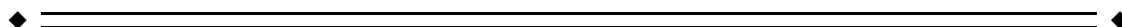
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Abstract: Word retrieval is a fundamental component of oral communication, and it is well established that this function is supported by left temporal cortex. Nevertheless, the specific temporal areas mediating word retrieval and the particular linguistic processes these regions support have not been well delineated. Toward this end, we analyzed over 1000 naming errors induced by left temporal cortical stimulation in epilepsy surgery patients. Errors were primarily semantic (*lemon* → “pear”), phonological (*horn* → “corn”), non-responses, and delayed responses (correct responses after a delay), and each error type appeared predominantly in a specific region: semantic errors in mid-middle temporal gyrus (TG), phonological errors and delayed responses in middle and posterior superior TG, and non-responses in anterior inferior TG. To the extent that semantic errors, phonological errors and delayed responses reflect disruptions in different processes, our results imply topographical specialization of semantic and phonological processing. Specifically, results revealed an inferior-to-superior gradient, with more superior regions associated with phonological processing. Further, errors were increasingly semantically related to targets toward posterior temporal cortex. We speculate that detailed semantic input is needed to support phonological retrieval, and thus, the specificity of semantic input increases progressively toward posterior temporal regions implicated in phonological processing. *Hum Brain Mapp* 00:000–000, 2016. © 2016 Wiley Periodicals, Inc.

Key words: cortical stimulation; epilepsy; language production; lexical access; naming errors



Speaking requires retrieving the words that best communicate the thoughts and concepts one wishes to express. A task of such a complexity must be supported by widely

distributed sensory, motor, and linguistic neural systems. Beginning with the earliest neurological theories [Wernicke, 1874], the left temporal region has been considered a primary contributor to the retrieval of the linguistic information associated with spoken words. Nevertheless, questions remain regarding which specific temporal areas are engaged in this task and which linguistic processes they support.

We addressed these questions using electrical stimulation mapping (ESM) in surgical epilepsy patients, a procedure in which low level current applied to a discrete cortical site induces brief, reversible dysfunction to the area stimulated [Penfield and Roberts, 1959]. Unlike more widely used, noninvasive techniques (e.g., fMRI or MEG) that provide correlative measures of brain activity associated with cognitive functions, cortical stimulation enables more direct

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access to brain structure–function relations, applying the lesion method, yet with greater precision. Using tasks that are performed with reliable accuracy without stimulation, testing during the time window of stimulation enables identification of cortical sites that are critical for the function tested. Furthermore, the speech and language errors produced during stimulation can provide deeper insight into the nature of the function supported by the site stimulated. In this study, we analyzed a large corpus of naming errors elicited during the application of electric current to temporal cortical surfaces during intra- or extra-operative cortical mapping to identify eloquent language cortex.

Spoken errors in word retrieval have received considerable attention because it is assumed that the different types of errors provide information regarding the specific mechanisms that underlie word production [Fromkin, 1980; Garrett, 1992]. Accordingly, word retrieval has traditionally been conceived as involving two broad selection processes: one concerning word meaning (i.e., semantic processing), and the other related to information about word sounds that functions as input to articulation (i.e., phonological processing). Direct cortical stimulation can give rise to specific and differentiated naming errors [Corina, et al., 2005, 2010; Hamberger, 2015; Hamberger et al., 2016; Ojemann et al., 1989; Tate et al., 2014] resembling errors that are produced naturally by neurologically intact speakers or individuals suffering from neuropathologies that impair language (e.g., aphasia). To the extent that cortical stimulation induces language dysfunction at an extremely localized neural level, naming errors elicited by stimulation in temporal cortices provide a unique opportunity to shed a more detailed light on the neurofunctional organization of word production in this region.

Results from various methodologies including behavioral [Gorno-Tempini et al., 2008; Kay and Ellis, 1987; Miozzo and Hamberger, 2015; Hodges and Patterson, 2007], lesional [Cloutman et al., 2009; Mesulam et al., 2013; Schwartz et al., 2009; Tsapkini et al., 2011; Walker et al., 2011], electrophysiological [Costa et al., 2009; Miozzo et al., 2014] and neuroimaging [Graves et al., 2007; Peramunage et al., 2011; Wilson et al., 2009] studies have revealed both functional and anatomical dissociations between semantic and phonological processes. A meta-analysis of neuroimaging and electrophysiological studies by Indefrey and Levelt [2004] implicated posterior temporal-anterior occipital areas in semantic processing. Posterior inferior temporal regions were also found to respond to semantic features of objects named in an MEG study of picture naming [Miozzo et al., 2014]. Furthermore, analyses of tissue dysfunction (infarct and/or hypoperfusion) in acute stroke patients who

produced semantic errors in naming but not in other tasks also implicated the involvement of posterior temporal areas in semantic processing, particularly in posterior middle temporal gyrus/inferior temporal gyrus (MTG/ITG) and fusiform gyrus [Cloutman et al., 2009; Tsapkini et al., 2011]. On the other hand, analysis of tissue dysfunction with more chronic stroke patients found semantic naming errors to be associated with damage to anterior to middle MTG [Schwartz et al., 2009; Walker et al., 2011]. Similarly, failures of mapping meaning-to-word sounds in semantic dementia appeared to be caused by atrophy within the anterior temporal cortex [Mesulam et al., 2013].

Regarding phonological processing, meta-analysis found that studies utilizing methods such as fMRI and MEG implicated posterior regions of the superior temporal gyrus (STG) and MTG [Indefrey and Levelt, 2004]. Neuroimaging studies have also shown that these temporal areas responded to variations in word sound retrieval [Graves et al., 2007; Peramunage et al., 2011; Wilson et al., 2009]. Altogether, findings generally converged to suggest an inferior to superior gradient, with more superior temporal regions becoming increasingly involved in phonological processing. This view is also consistent with the dual stream model [Hickok and Poeppel, 2007], a general account of the brain mechanisms encompassing language production and comprehension, in which posterior STG is a critical component of a left-lateralized dorsal pathway that is responsible for translating phonological input into articulation for speech production. Nevertheless, conflicting results were found using a voxel-based lesion symptom mapping analysis of phonological naming errors (*pear* → “bear”) produced by chronic aphasia patients [Schwartz et al., 2012]. Voxels associated with phonological errors were found in extra-temporal areas, with minimal extension into posterior STG.

In part, the variability in previous findings might be due to the use of brain localization procedures that are indirect, thereby introducing certain margins of error in brain localization. In contrast, cortical stimulation mapping permits discrete localization, at a level of resolution that is generally not attainable with other methods, representing the “gold standard” for assessing cortical function” (Tate et al., 2014; p. 2775). Corina et al. [2010] and Tate et al. [2014] analyzed naming errors elicited by cortical stimulations over the entire left hemisphere, but only a limited number of errors [e.g., 91 in Corina et al., 2010] were induced in temporal cortices. We analyzed a larger corpus of naming errors elicited in temporal cortices (>1000) and, replicating Corina et al. [2010] and Tate et al. [2014], we expected the corpus to include semantic and phonological errors as well as non-responses. As in previous studies, we assumed that semantic errors reflect dysfunction in semantic processing and/or in the mapping of semantics onto phonology, whereas phonological errors arise due to perturbations in phonological processing. Therefore, we inferred that the temporal sites at which semantic or phonological errors were elicited are likely engaged in

Abbreviations

ESM	Electrical stimulation mapping
MTS	Medial temporal sclerosis
STG	Superior temporal gyrus
TG	Temporal gyrus

semantic vs. phonological processing. In line with previous findings, we expected phonological errors and delayed responses to show a different distribution than semantic errors. Although the results of Corina et al. [2010] and Tate et al. [2014] brought to light the varied nature and general distribution of semantic and phonological errors, the descriptive statistics used by Corina et al. [2010] and the cluster analysis used by Tate et al. [2014] did not allow direct comparison of the frequencies with which errors were elicited in temporal cortical areas along the vertical and horizontal axes. This comparison was carried out in the current study. Our analyses of semantic and phonological errors could potentially clarify unresolved questions concerning the organization of lexical processing in left temporal regions, specifically, whether anterior and posterior temporal cortices contribute differently to semantic processing, and whether phonological processing exhibits increasingly greater representation toward more superior regions, reflecting an inferior to superior gradient. It is worth noting that our results would not clarify questions that are under debate in cognitive theories on semantics and lexical organization and concerns the nature of semantic representations (conceptual vs. lexical-semantic) and levels of lexical processing (e.g., if lemmas mediate access to phonology). Nevertheless, these theories assume a general distinction between the processing of word meaning and word sounds. Our results aim to clarify the organization of these processes in the left temporal cortex.

In our corpus, we found a number of responses in which cortical stimulation delayed naming, with the correct name produced after an initial delay, yet during the period of cortical stimulation. These delayed naming responses resemble the momentary word finding difficulties occasionally experienced by unimpaired speakers, commonly known as tip-of-the-tongues. As speakers experiencing tip-of-the-tongue typically retrieve the meaning of the recalcitrant word, their transitory word-production failures would seem to result from problems in accessing, not so much semantics, but other features of the words, including their sounds [Miozzo and Caramazza, 1997; Schwartz, 2002]. We reasoned that if the source of the delayed naming responses induced by cortical stimulations were the same as those in tip-of-the-tongue, semantic access would be intact during cortical stimulations inducing delayed naming responses. We should therefore find little overlap between sites of delayed naming responses and sites characterized by semantic errors, as cortical stimulation possibly impaired semantic access only with semantic errors. This prediction was tested to further characterize the topography of semantic processing in the left temporal cortex.

Further analyses concentrated on the nature of semantic errors. These errors can vary in kind, with coordinate errors involving confusion between items from the same category (e.g., *lemon* → “pear”) and associated errors reflecting more functional relations (e.g., *clock* → “time”).

In aphasia, coordinate errors were found in patients with left temporal lesions, whereas associated errors occurred primarily in patients with lesions in left inferior prefrontal cortex [Jefferies and Lambon Ralph, 2006]. Our large error corpus from cortical stimulation of temporal cortices provides an opportunity to further explore whether coordinate and associated errors have different neural underpinnings. Specifically, the hypothesis that associated errors are related to processes in left inferior prefrontal cortex anticipates a lack of these errors with cortical stimulations in left temporal cortices. Semantic errors can also vary by the degree of semantic relatedness between target and errors, a relatedness that is quantifiable in different ways, for example through statistical computations applied to large corpora of text [Landauer and Duamis, 1997]. We reasoned that error relatedness could reflect the level of detail of the semantic information mediated by temporal sites where cortical stimulation was applied. For example, the semantic error “goose” would be more closely related to *duck* than the semantic error “eagle,” a difference reflecting the availability of more detailed semantic features of *duck* with the first than the latter error.

METHODS

Participants

We queried a database of 102 surgical patients who underwent cortical language mapping intraoperatively or extraoperatively at Columbia University Medical Center as part of epilepsy surgery that involved the left temporal region. We only analyzed data from patients who met the following inclusion criteria: (a) age >18 years at mapping; (b) left hemisphere language dominance, as determined by Wada testing [Loring et al., 1992]; (c) acquisition of English before 7-years of age, if English was used for language mapping; and (d) one or more stimulated naming errors in temporal sites. A total of 34 patients were excluded because of age <18 at mapping (6), late acquisition of English (5), naming errors limited to extra-temporal sites (15); and data missing (8). A total of 68 patients (30 female; 58 right handed) qualified for the study. Of these patients, 11 had medial temporal sclerosis (MTS), defined as MRI evidence of abnormal signal and hippocampal atrophy, five had left posterior temporal lobe tumor, one had a vascular malformation (Sylvian fissure), and 23 showed no abnormality on MRI. All patients had focal seizure onset in the left hemisphere (temporal: 64 patients; parietal: three patients; occipital: one patient) based on subdural EEG monitoring or a combination of MRI evidence, MTS or other lesions, and scalp EEG/video recording. Language mapping was conducted extraoperatively via subdural electrodes (42 patients), or intraoperatively prior to resection (24 patients), or using both of these procedures (two patients). Additional demographic and clinical information is reported for these patients in Table I.

TABLE I. Demographics and number of elicited errors for the 68 patients included in the study

	Range	Mean	SD	Quartile		
				1st	2nd	3rd
Education (years) ^a	8–20	13.9	2.5	13	14	16
IQ ^a	70–126	94.0	13.3	84	94	102
Age at seizure onset (years) ^c	1.5–65	19.6	12.7	12	18	27
Age at mapping (years)	18–66	34.0	11.2	25	32	41
Number of elicited errors	1–66	15.3	13.3	5	13	21

^aFull Scale IQ. Information available from 64 patients for education, from 54 patients for IQ, and from 67 patients for age at seizure onset.

Cortical Mapping

Electrodes

The number of stimulated sites differed across patients due to variations in clinical objectives and priorities. For the patients who underwent intraoperative mapping, 4–31 sites along the superior, middle and inferior temporal gyri, and the posterior perisylvian cortex were stimulated and tested for language using a carbon tipped bipolar stimulating electrode with 2 mm diameter ball contacts separated by 5 mm (Ojemann Cortical Stimulator, Radionics Inc.). The sites were chosen based on gyral/vascular anatomy and spaced <10 mm apart.

Patients who underwent extraoperative mapping had an eight by eight (i.e., 64 contact) grid array, with 5 mm diameter electrodes embedded in Silastic with center-to-center interelectrode distances of 1 cm (Ad-Tech, Racine, Wisconsin). Language was tested at 10–60 sites per patient. Grids were positioned over the frontal-parietal-temporal region (trimmed as needed to conform to the covered area).

Location of electrode sites

For extraoperative mapping, the exposed cortical surface and grid position were documented by digital photography and schematic diagrams. Initial schematics were drawn by the surgeon intra-operatively, while looking directly at the brain surface. Digital photos were then used post-operatively to refine the diagrams and subdural electrode positions were verified by skull X-rays, post-operatively. In addition to skull X-rays, electrode location was confirmed with post-operative MRI and/or CT neuroimaging. Post-operative volumetric studies were loaded into a frameless stereotactic workstation and a 3D model was rendered. Electrode location was verified in comparison to the intra-operative digital photographs. For intraoperative mapping, electrode positions were documented using digital photography and schematic diagrams.

Mapping procedures

For all patients, mapping took place while antiepileptic drug levels were in the therapeutic range, to minimize afterdischarges and seizure activity. Extraoperative language mapping was conducted following video/EEG monitoring to identify the seizure onset zone. Testing was carried out during electrical stimulation applied to adjacent electrodes. When results were positive, each electrode was studied individually and referenced to a remote electrode in “silent cortex.” All available sites along the lateral temporal cortex as well as parietal sites in the perisylvian area were stimulated. Patients who underwent intraoperative mapping were initially anaesthetized with propofol. Language mapping began following craniotomy/dural opening, electrocorticography and stimulation to determine the threshold for afterdischarges. Several practice trials were conducted to ensure an adequate level of patient responsiveness. Stimulation sites were primarily in the vicinity of the anticipated resection, as determined by the presence of a lesion or intracranial EEG evidence of seizure onset. If naming cortex was not identified, additional perisylvian sites were tested with the goal of positively identifying language cortex (rather than relying on negative responses alone). Sites were tested with a bipolar stimulator (see above).

Stimulation mapping parameters followed well-established methods [Ojemann, 1983, 1991]. For both intra- and extraoperative mapping a constant current stimulator (Ojemann Cortical Stimulator, Radionics Inc.) delivered a biphasic square waveform at a frequency of 20 or 50 Hz, with a 1 ms pulse duration and amperage ranging from 3–15 mA during extraoperative mapping and 2–12 mA during intraoperative mapping. Afterdischarge levels were determined by increasing amperage until an afterdischarge was elicited, with an upper limit of 15 mA. Amperage for stimulation was set at 1 mA below the level that elicited an afterdischarge (or 15 mA), which was determined for each site individually. Errors reported here are from trials during which no afterdischarges were elicited. Furthermore, patients were constantly monitored for level of alertness via direct observation and ongoing EEG, and errors included in our analyses did not occur while patients were in a drowsy or sleep state.

The naming tasks tested during language mapping involved the presentation of either pictures (visual naming) or orally presented descriptions (auditory naming). Pictures were line drawings or colored photographs of common items (e.g., *glove*, *broom*). Descriptions contained less than 10 words (e.g. “The yellow part of an egg”) and could be presented clearly within 4 seconds. Only the pictures and descriptions the patient successfully named during preoperative baseline testing were utilized for language mapping. Electrical stimulation began immediately before the presentation of pictures or auditory descriptions and lasted for a maximum of 8 seconds, but terminated immediately upon the patient’s production of a correct response. Patients were instructed to respond as rapidly as possible and, in picture naming, to begin with the phrase

“This is a.” Sites were considered critical for task performance if (a) the patient could not name target items during stimulation, but provided correct responses upon cessation of stimulation and (b) at least 75% of responses were inaccurate. Visual and auditory naming was tested for language mapping with 50 patients, whereas only visual or auditory naming was tested with 15 and 3 patients, respectively. Patients named the stimuli using their dominant language (English: 65; Spanish: 2; Macedonian: 1).

Error Scoring and Localization

Naming errors elicited during cortical mapping were classified in one of the following categories.

- a. *Semantic errors*: incorrect responses in which target words were substituted by words similar in meaning. In some of the analyses, semantic errors were further divided into coordinate, superordinate, and associated errors. For coordinate errors, incorrect words corresponded to items from the same semantic category of the target words, as in *lemon* → “pear” or *brush* → “comb.” For superordinate errors, the name of the item category was provided as a response (*apple* → “fruit”). Associative errors corresponded to objects or actions related to the target concept (*clock* → “time;” *cake* → “eating”) though from different semantic categories.
- b. *Phonological errors*: incorrect responses that sounded like the target words. Utilizing a criterion widely used in neuropsychology research, phonological errors were defined as responses sharing at least 50% of the target phonemes, as in the examples *brush* → “brish” or *horn* → “corn.” Errors in which only the first syllable of multisyllabic words was produced (*camera* → “ca”) were scored as phonological errors even if the response comprised less than 50% of target phonemes. We reasoned that these errors were likely to arise from a weak activation of phonological information, like those in which more target phonemes were preserved. Phonological responses could correspond to real words or neologisms.
- c. *Other errors*: incorrect responses not classifiable as semantic or phonological errors.
- d. *Non-responses*: failures to produce spoken responses within the 8 seconds during which electrical stimulation was applied. However, the classification of non-responses further required correct naming soon after the cessation of the electrical stimulation. This procedure ensured that naming failures were not due to inability to recognize the pictures or understand the descriptions.
- e. *Delayed responses*: correct responses produced after 3 seconds from stimulus presentation, but still within the 8 seconds stimulation interval.

The scoring of semantic errors and delayed responses was problematic in auditory naming. Considering that the presentation of oral descriptions could require 4 seconds, and that delayed responses required a minimum interval of 4–6 seconds, there was frequently insufficient time for a delayed response within the 8 seconds stimulation interval. Furthermore, responses could be semantically related to one of the words included in the description instead of the word the description was supposed to prompt. For example, the response “diner” to the description “The list of food served at a restaurant” could have been induced by the word *restaurant* rather than the target word *menu*. Given these issues, semantic errors and delayed responses were not scored in auditory naming; only phonological errors and non responses were scored in this task. Phonological errors and non-responses were combined from picture and auditory naming in order to analyze the largest response pool available. Semantic errors, other errors, and delayed responses were analyzed only in picture naming.

By using the precise localization of the cortical stimulation that induced an error, we identified (a) in which temporal gyrus (ITG, MTG, or STG) the error occurred, and (b) its distance from the temporal pole obtained using 0.5 cm intervals. Errors were grouped within three temporal regions: anterior (1–3 cm), middle (4–6 cm), and posterior (7–9 cm).

Error Analyses

Analyses aimed to determine whether a specific type of error (e.g., semantic) was elicited with similar or different frequencies across temporal cortices along either the vertical or the horizontal axis. Analyses were of three kinds.

(a) Whole corpus analyses

A first type of aggregated analyses was based on the whole error corpus and compared error distributions across the three temporal gyri (ITG, MTG, and STG) or the three temporal regions (anterior, middle, posterior). For example, we compared the total number of semantic errors elicited during cortical stimulation in ITG, MTG, and STG, respectively. Because the same error set was used for comparing multiple types of errors ($N=4$), a Bonferroni correction was applied ($\alpha=0.012$). Follow-up analyses were carried out to explore significant differences obtained in whole corpus analyses and aimed to identify the specific temporal gyri (or temporal regions) in which error frequencies varied. For example, in one of the follow-up analyses we compared the number of semantic errors induced in MTG and STG.

(b) Same-items analyses

Because different stimuli were probed across sites, we were concerned that errors might, in part, have been related to the particular stimuli tested at each site. To address

this, in *same-items* analyses we only included those responses elicited by items that were tested in multiple temporal gyri or temporal regions. We reasoned that if same-items analyses confirmed the results of the whole corpus analyses, this would suggest that errors reflected the nature of the brain region being tested (unrelated to the specific items) and thus, could conclude more firmly that variation in error distribution was related to cortical organization. Because not all items elicited errors in multiple temporal gyri or temporal regions, same-items analyses were based on only a set of errors from the whole corpus. Furthermore, same-items analyses could be conducted on a substantial number of errors (>100) only if pairwise comparisons were used. Therefore, the total occurrences of a type of error (e.g., semantic) were compared between temporal gyri (ITG vs. MTG; ITG vs. STG; MTG vs. STG), or between temporal regions (anterior vs. middle; anterior vs. posterior; middle vs. posterior). It should be noted that due to differences in the particular stimuli tested over sites, the set of errors varied across same-items analyses. Whenever a set of errors was used for comparing multiple types of errors, a Bonferroni correction was applied.

(c) Same-patients analyses

The analyses described above were carried out on errors aggregated from all patients. In contrast, same-patients analyses examined errors produced by individual patients in order to assess whether data from individual patients replicated results that emerged with aggregated data. Errors were available from all of the temporal gyri or all of the temporal regions with only a few patients, since, in some locations, mapping was not a clinical priority or naming failures could not be elicited. Only semantic errors and non-responses were produced in sufficient numbers by these patients to permit adequately reliable analyses. Demographics and clinical information regarding these patients are presented in Table II. These patients are generally comparable to the rest of patients in our study for demographic as well as clinical features. Error proportions for each error and from each location were entered in same-patients analysis. For example, for the semantic errors in MTG, we used the proportion of semantic errors in MTG out of the total errors in MTG. Because of multiple testing, Bonferroni correction was used.

RESULTS

There were 594 errors in picture naming and 449 in auditory naming.

The frequencies of the various types of errors in picture naming is shown in Table III. Non-responses represented the most common type of error (57%) in picture naming followed by semantic errors (23%). By contrast, phonological errors (2%) and other errors (1%) occurred rather

infrequently. Non-responses and phonological errors were also scored in auditory naming and their rates (non-responses: 73%; phonological errors: 6%) were similar to those in visual naming. The whole error corpus examined in our study comprised 136 semantic errors, 35 phonological errors, 670 non-responses, and 93 delayed responses. As described in the Methods section, semantic errors and delayed responses were from picture naming, whereas phonological errors and non-responses were from picture naming and auditory naming. The number of errors that individual patients contributed to the whole error corpus ranged from 1 to 66, with a median of 13 (further information on the error distribution is presented in Table I). Although 51% of the errors were from patients in the 4th quartile, a substantial proportion of errors were from the other patients. Figure 1 shows how the errors from the whole corpus distribute over the left temporal cortices. Table IV shows, for each type of error, the number of occurrences across temporal gyri or temporal regions. Individual patients contributed an average of 1–2 semantic errors, phonological errors, and delayed responses, which indicates that a rather diversified group of patients produced these errors and responses. Non-responses occurred more frequently (~5–8 per patient), which reflects the large number of non-responses in our corpus; nevertheless, even non-responses were elicited in many patients.

Within the whole error corpus, error frequencies varied across gyri (ITG = 20%; MTG = 40%; STG = 40%) but comparably in picture and auditory naming. Furthermore, more errors were induced in posterior than middle and anterior temporal cortices (49% vs. 38% vs.13%), and such differences were found in both picture naming and auditory naming.

Error Localization: Whole Corpus Analyses

As shown by Figure 2, each type of error appears to distribute differently across temporal gyri. Comparisons conducted for each type of error confirmed that error occurrences varied across temporal gyri (semantic errors: $\chi^2(2) = 33.57$, $P(\text{corrected}) < 0.0001$; phonological errors: $\chi^2(2) = 9.66$, $P(\text{corrected}) < 0.01$; non-responses: $\chi^2(2) = 20.00$, $P(\text{corrected}) < 0.001$; delayed responses: $\chi^2(2) = 20.65$, $P(\text{corrected}) < 0.001$). The results of follow-up tests that were carried out to explore the nature of the differences observed with each type of error are shown in Table V. These results indicate that differences were attributable to each error type having a significantly higher frequency in one of the gyri: non-responses in ITG, semantic errors in MTG, and phonological errors and delayed responses in STG.

As illustrated in Figure 3, the various types of errors appear to distribute differently also across horizontal temporal regions (anterior, middle, and posterior). Significant differences were found with semantic errors ($\chi^2(2) = 17.33$, $P(\text{corrected}) < 0.0001$), non-responses [$\chi^2(2) = 10.39$, $P(\text{corrected}) < 0.01$], and delayed responses [$\chi^2(2) = 7.70$,

TABLE II. Demographics of patients included in same-patients analyses

Patient	Sex ^a	Handedness ^b	Education (Years) ^b	IQ ^c	Epilepsy Onset Age (Years)	Age (Years)	MTS ^d	Lesion
1	M	R	13	85	6	36		Yes
2	M	R	12	74	4	42		Yes
3	F	R	14	77	3	27		Yes
4	M	R	13	114	26	29	Yes	
5	F	R	12	103	18	22		Yes
6	F	R	16	90	4	28		Yes
7	F	R	13	75	13	32		
8	M	L	14	93	26	29		
9	F	R	14	83	5	47		
10	M	R	8	71	17	64	Yes	
11	F	R	16	n.a.	10	33		
12	M	R	13	93	22	24		Yes
13	M	R	11	101	13	18		Yes
14	F	R	13	85	15	19		
15	F	R	16	116	11	48		Yes
16	F	R	11	78	40	45		Yes
17	F	R	13	78	19	23		
18	F	R	14	93	12	41		
19	F	R	10	84	16	40	Yes	
20	M	L	16	126	20	33		Yes
21	M	L	14	102	8	20		
22	M	R	16	104	31	51		
23	F	R	10	75	10	32		
24	M	R	12	87	6	37	Yes	
25	M	R	17	101	12	41	Yes	
26	F	L	13	88	15	33		Yes
27	F	R	18	98	17	45		
28	F	R	16	82	34	39		

^aM = male, F = female.

^bR = right, L = left.

^cFull scale IQ.

^dMTS = medial temporal sclerosis. Patients 1–8 contributed errors for analyses in temporal gyri, patients 9–17 in temporal regions, and patients 17–28 in both temporal gyri and temporal regions.

$P = 0.02$]. However, each type of error showed a different gradient, as revealed by further follow-up tests presented in Table III. Non-responses accounted for more errors in anterior cortical regions (76%) as compared to middle (61%) and posterior (63%) cortical regions. By contrast, semantic errors were more frequent among errors induced in middle

temporal regions (33%) than anterior (15%) or posterior (18%) temporal regions. Furthermore, delayed responses occurred more so among the errors in posterior temporal regions (17%) than anterior and middle temporal regions (both 4%).

Error Localization: Same-Items Analyses

The results of analyses restricted to items that elicited errors in two temporal gyri or temporal regions largely replicated results obtained with the whole error corpus. Concerning gyri distributions, results of same-item analyses (Table V) revealed that each type of error occurred most frequently in one gyrus: in ITG for non-responses, in MTG for semantic errors, and in STG for phonological errors and delayed responses. The results concerning the errors in temporal regions (Table VI) showed that non-responses were especially frequent in the anterior

TABLE III. Error distribution in picture naming

Type of errors	N	%
Semantic errors	136	23%
Phonological errors	9	1%
Other errors	15	2%
Non-responses	341	57%
Delayed responses	93	16%
Total responses	594	

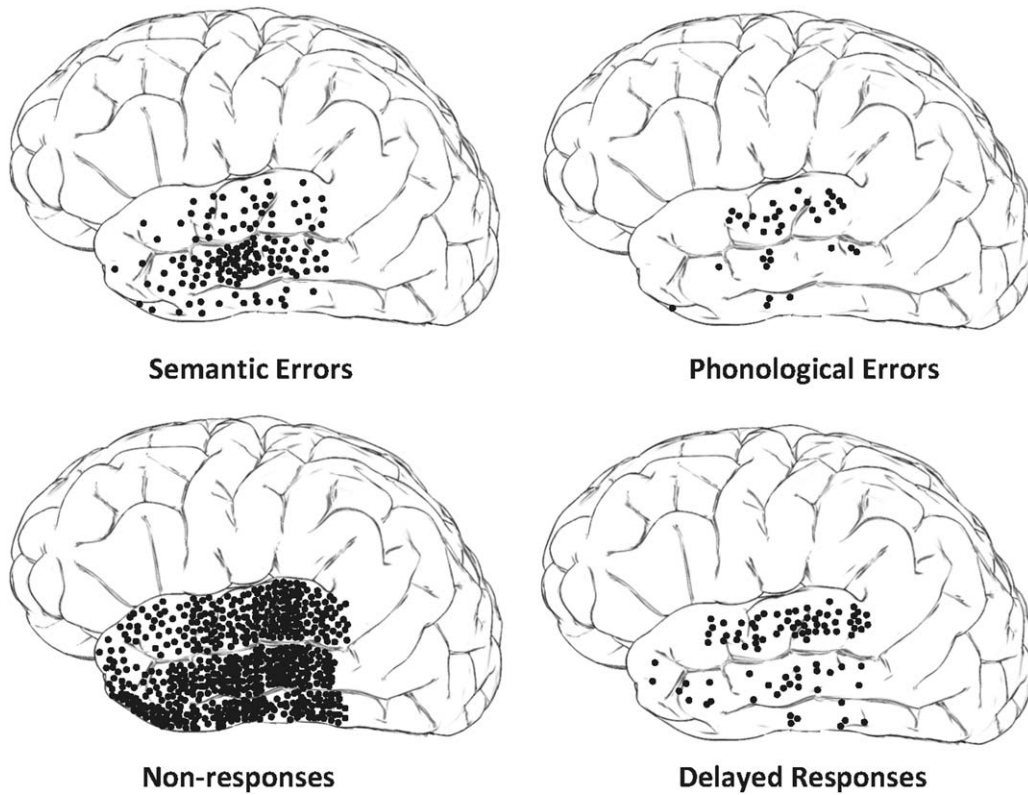


Figure 1.

Localization of naming errors elicited in left hemisphere cortices. Semantic errors = 136; phonological errors = 35; non-responses = 670; delayed responses = 93. Semantic errors and delayed responses were elicited in picture naming; phonological errors and non-responses in picture and auditory naming.

temporal region, semantic errors in the middle temporal region, and delayed responses were produced significantly more often in posterior than anterior regions (there was insufficient data to carry out the same-item analysis with phonological errors).

Error Localization: Same-Patients Analyses

With a few patients, cortical stimulation affected naming in all temporal gyri and temporal regions and induced a sufficiently large number of semantic errors and non-responses.

TABLE IV. Number of errors (N), number of patients who produced the errors (Pts), and number of errors per patient (N/Pt) across temporal areas

	Semantic errors			Phonological errors			Non-responses			Delayed responses		
	N	Pts	N/Pt	N	Pts	N/Pt	N	Pts	N/Pt	N	Pts	N/Pt
ITG	16	12	1.3	4	3	1.3	160	22	7.3	7	2	3.5
MTG	82	32	2.6	8	6	1.3	257	41	6.3	25	14	1.8
STG	38	23	1.7	23	14	1.6	253	46	5.5	61	22	2.8
<i>Total</i>	<i>136</i>			<i>35</i>			<i>670</i>			<i>93</i>		
Ant.	17	13	1.3	2	2	1.0	133	31	4.3	12	11	1.1
Mid.	78	40	2.0	20	11	1.8	282	44	6.4	40	16	2.5
Post.	41	18	2.3	13	8	1.6	255	32	8.0	41	13	3.2
<i>Total</i>	<i>136</i>			<i>35</i>			<i>670</i>			<i>93</i>		

ITG = inferior temporal gyrus; MTG = middle temporal gyrus; STG = superior temporal gyrus; Ant. = anterior temporal region; Mid. = middle temporal region; Post. = posterior temporal region.

◆ Temporal Lobe Topography of Semantics and Phonology ◆

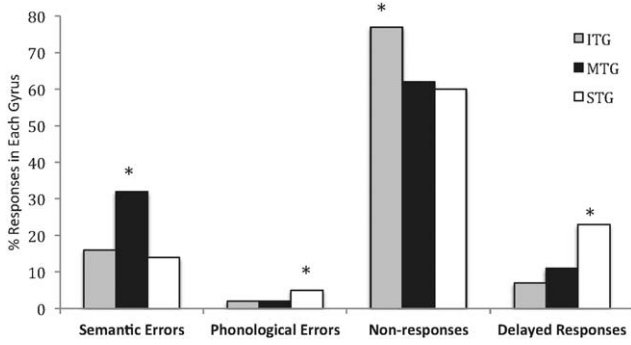


Figure 2.

Percentages of errors elicited in each gyrus. ITG = inferior temporal gyrus; MTG = middle temporal gyrus; STG = superior temporal gyrus. * indicates the gyrus where a type of errors occurred significantly more frequently.

Semantic errors occurred unevenly, both across temporal gyri [$F(2, 36) = 4.71, P(\text{corrected}) < 0.05$] and temporal regions [$F(2, 38) = 4.14, P(\text{corrected}) < 0.05$]. These differences reflect the greater incidence of semantic errors in MTG than STG [25% vs. 6%; $t(18) = 4.12, P < 0.001$; ITG = 18%], and in middle than anterior temporal regions [25% vs. 7%; $t(19) = 2.4, P < 0.05$; posterior = 17%]. Although semantic errors were numerically more frequent in MTG than ITG (25% vs. 18%) and in middle than posterior temporal regions (25% vs. 17%), these differences did not reach significance ($P > 0.05$). No significant differences were found with non-responses across temporal gyri (ITG = 74%, MTG = 63%, STG = 65%) or temporal regions (anterior = 82%, middle = 64%, posterior = 73%).

Semantic errors

The corpus of semantic errors included 96 coordinate errors (*lemon* → “pear;” 71%), 33 associated errors (*clock* →

TABLE V. Errors (%) and results of whole corpus analyses and same-items analyses – Temporal gyri

	Whole-corpus analyses	Same-items analyses	
			N Analyzed Errors
<i>Semantic errors^a</i>			
ITG vs. MTG	16% vs. 35% *** $\chi^2(1) = 14.56, P = 0.0001$	17% vs. 38% * $\chi^2(1) = 7.48, P(\text{corr}) < .05$	132
ITG vs. STG	16% vs. 14% $\chi^2(1) < 1$	18% vs. 16% $\chi^2(1) < 1$	134
MTG vs. STG	35% vs. 14% *** $\chi^2(1) = 19.32, P < 0.0001$	32% vs. 15% ** $\chi^2(1) = 10.22, P(\text{corr}) = .01$	262
<i>Phonological errors^b</i>			
ITG vs. MTG	2% vs. 2% $\chi^2(1) < 1$	2% vs. 2% $\chi^2(1) < 1$	302
ITG vs. STG	2% vs. 5% * $\chi^2(1) = 4.12, P < 0.05$	2% vs. 9% * $\chi^2(1) = 5.92, P(\text{corr}) = 0.05$	278
MTG vs. STG	2% vs. 5% ** $\chi^2(1) = 7.38, P < 0.01$	2% vs. 7% * $\chi^2(1) = 9.01, P(\text{corr}) < 0.05$	462
<i>Non-responses^b</i>			
ITG vs. MTG	77% vs. 62% *** $\chi^2(1) = 15.13, P < 0.0001$	77% vs. 64% * $\chi^2(1) = 7.02, P < (\text{corr}) 0.05$	302
ITG vs. STG	77% vs. 60% *** $\chi^2(1) = 18.69, P < 0.0001$	81% vs. 60% *** $\chi^2(1) = 14.44, P(\text{corr}) = 0.001$	278
MTG vs. STG	62% vs. 60% $\chi^2(1) < 1$	65% vs. 58% $\chi^2(1) = 2.62, P = 0.11$	462
<i>Delayed responses^a</i>			
ITG vs. MTG	7% vs. 11% $\chi^2(1) = 1.87, P = 0.17$	9% vs. 18% $\chi^2(1) = 2.31, P = 0.13$	132
ITG vs. STG	7% vs. 23% *** $\chi^2(1) = 17.46, P < 0.0001$	4% vs. 19% * $\chi^2(1) = 6.89, P(\text{corr}) < 0.05$	134
MTG vs. STG	11% vs. 23% *** $\chi^2(1) = 16.41, P < 0.0001$	10% vs. 24% ** $\chi^2(1) = 8.85, P(\text{corr}) < 0.01$	262

ITG = inferior temporal gyrus; MTG = middle temporal gyrus; STG = superior temporal gyrus.

^aErrors from picture naming.

^bErrors from picture and auditory naming.

^cDifferences significant at $P = 0.05$ (*), $P = 0.01$ (**) and $P = 0.001$ (***); $P(\text{corr}) = p$ corrected (by .05) for same-items analyses repeated with the same error sets.

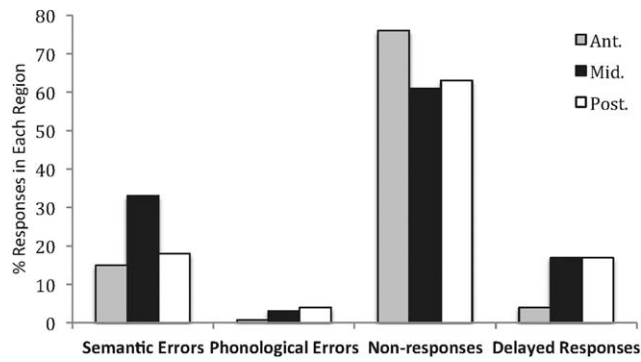


Figure 3.

Percentages of errors elicited in each temporal region. Ant. = anterior temporal region; Mid. = middle temporal region; Post. = posterior temporal region.

“time;” 24%), and 7 superordinate errors (*grape* → “fruit;” 5%). The distribution of coordinate errors varied across gyri [$\chi^2(2) = 26.96, P < 0.0001$] as well as across posterior,

middle and anterior cortical regions [$\chi^2(2) = 20.99, P < 0.0001$]. As shown in Figure 4, this reflected a greater proportion of coordinate errors in MTG than ITG

TABLE VI. Errors (%) and results of whole corpus analyses and same-items analyses – Temporal regions

	Whole corpus analyses	Same-items analyses	
			N Analyzed Errors
<i>Semantic errors^a</i>			
Ant. vs. Mid.	15% vs. 33% ** $\chi^2(1) = 7.62, P < 0.01$	19% vs. 31% * $\chi^2(1) = 5.05, P (\text{corr}) < 0.05$	266
Ant. vs. Post.	15% vs. 18% $\chi^2(1) < 1$	14% vs. 22% $\chi^2(1) = 1.07, P = 0.29$	102
Mid. vs. Post.	18% vs. 33% *** $\chi^2(1) = 14.34, P = 0.0001$	17% vs. 30% * $\chi^2(1) = 6.84, P (\text{corr}) < 0.05$	262
<i>Phonological errors^b</i>			
Ant. vs. Mid.	1% vs. 3% $\chi^2(1) = 2.51, P = 0.12$		
Ant. vs. Post.	1% vs. 4% * $\chi^2(1) = 3.71, P = 0.05$		
Mid. vs. Post.	3% vs. 4% $\chi^2(1) < 1$		
<i>Non-responses^b</i>			
Ant. vs. Mid.	76% vs. 61% *** $\chi^2(1) = 10.28, P = 0.001$	62% vs. 47% ** $\chi^2(1) = 6.68, P (\text{corr}) < 0.01$	266
Ant. vs. Post.	76% vs. 63% ** $\chi^2(1) = 7.71, P < 0.01$	80% vs. 53% ** $\chi^2(1) = 10.78, P (\text{corr}) < 0.01$	102
Mid. vs. Post.	61% vs. 63% $\chi^2(1) < 1$	49% vs. 62% $\chi^2(1) = 4.46, P (\text{corr}) = 0.07$	262
<i>Delayed responses^a</i>			
Ant. vs. Mid.	4% vs. 17% ** $\chi^2(1) = 7.28, P < 0.01$	15% vs. 19% $\chi^2(1) < 1$	266
Ant. vs. Post.	4% vs. 17% ** $\chi^2(1) = 7.40, P < 0.01$	2% vs. 24% ** $\chi^2(1) = 10.66, P (\text{corr}) < 0.01$	102
Mid. vs. Post.	17% vs. 17% $\chi^2(1) < 1$	19% vs. 17% $\chi^2(1) < 1$	262

Ant. = anterior temporal region; Mid. = middle temporal region; Post. = posterior temporal region.

^aErrors from picture naming.

^bErrors from picture and auditory naming. Differences significant at $P = 0.05$ (*), $P = 0.01$ (**) and $P = 0.001$ (***); $P (\text{corr}) = P$ corrected (by .05) for same-items analyses repeated with the same error sets. The number of phonological errors was too small to conduct the same-item analyses..

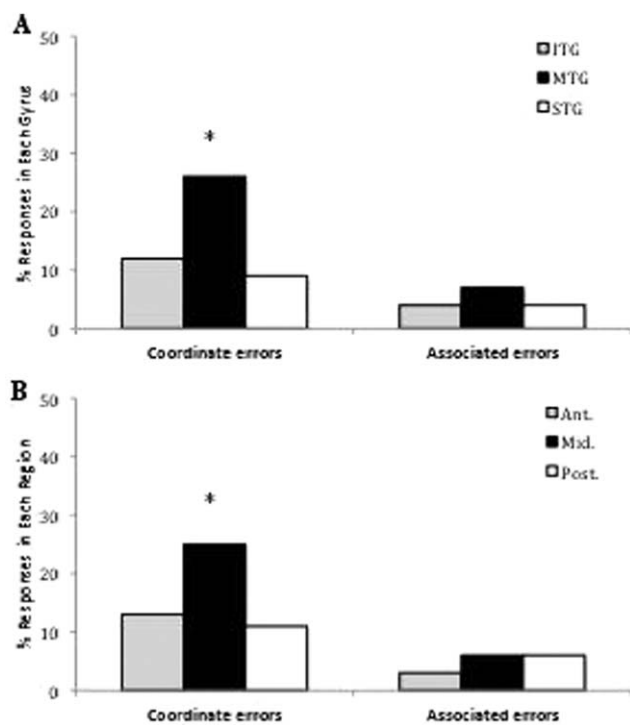


Figure 4.

Percentages of coordinate or associated errors elicited in each gyrus (A) or temporal region (B). ITG = inferior temporal gyrus; MTG = middle temporal gyrus; STG = superior temporal gyrus; Ant. = anterior temporal region; Mid. = middle temporal region; Post. = posterior temporal region. * indicates the gyrus/region in which coordinate errors occurred significantly more frequently. No significant differences were found in the distribution of associated errors.

$[\chi^2(1) = 7.48, P < 0.01]$ or STG $[\chi^2(1) = 24.69, P < 0.0001]$ and, horizontally, in middle temporal regions than anterior temporal regions $[\chi^2(1) = 5.03, P < 0.05]$ or posterior temporal regions $[\chi^2(1) = 19.77, P < 0.0001]$. Associated errors differed from coordinate errors, demonstrating no significant differences in their distribution, either on the vertical or the horizontal plane.

We also examined the strength of the semantic relatedness between the target word and the word erroneously produced as a semantic error. Latent Semantic Analysis [LSA; Landauer and Duamis, 1997], which provides semantic relatedness scores based on co-occurrence frequencies in large text corpora, was used to quantify the degree of semantic relatedness between correct and incorrect words. LSA scores range from 0 (maximum semantic dissimilarity) to 1 (maximum semantic similarity). LSA scores were positively correlated with distance from the temporal pole of the stimulated site eliciting semantic errors $[r = 0.21, t(134) = 2.49, P = 0.01]$. Further analyses showed that this correlation is carried entirely by the

coordinate errors $[r = 0.25, t(94) = 2.56, P = 0.01]$ with negligible contribution from associated errors ($r = 0.04$)—see also Figure 5. In short, targets and errors tend to be more similar toward posterior temporal cortices.

GENERAL DISCUSSION

Our results confirm the differences in error frequencies reported by Corina et al. [2010]: non-responses represented the most frequent errors, phonological errors were relatively infrequent, and, among semantic errors, coordinate errors were more common than associated errors. With over a thousand responses acquired from a large group of patients tested over two decades, using the same mapping protocol in the same brain region (i.e., left temporal cortex), this unique data set provided the opportunity to investigate topographical patterns of stimulation evoked naming errors. Analysis of these errors revealed distinct distributions across the left temporal cortex, with each error type appearing predominantly in a specific left temporal region: semantic errors in middle MTG, phonological errors and delayed responses in middle and posterior STG, and non-responses in anterior ITG. Furthermore, these error distributions were unrelated to particular stimuli, as no effect of stimuli differences appeared in analyses that controlled specifically for such effects. Moreover, the predominance of semantic errors in middle MTG was confirmed with same-patients analyses that examined errors produced by individual patients. Cluster analyses were used by Tate et al. [2014] to determine the distribution of semantic and phonological errors induced in spoken naming by cortical stimulation. Results of these cluster

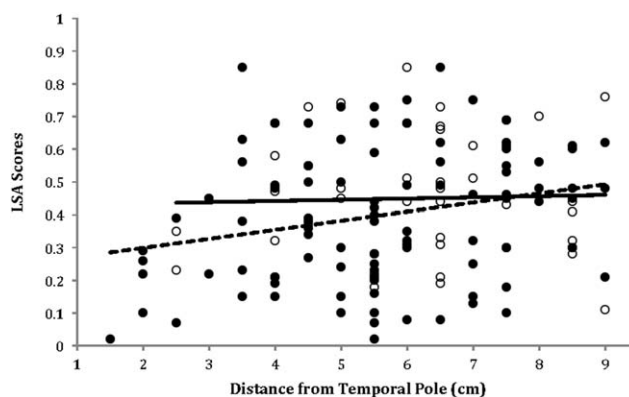


Figure 5.

Target error similarity (LSA scores). Errors were elicited at various distances from the temporal pole and were of two kinds: coordinate (filled circles) and associated (open circles). The broken line indicates the best fit for the coordinate errors ($r = 0.25, P = 0.01$), the solid line for the associated errors ($r = 0.04$). Only coordinate errors were increasingly related to target words toward posterior temporal regions.

analyses converge with our findings in showing partially distinct distributions between semantic and phonological errors induced in left temporal cortex. Further convergences appeared with phonological errors, which Tate et al. [2014] also found to occur especially in middle STG. However, while their analyses revealed clustering of semantic errors at the junction of posterior STG and supramarginal gyrus, in our corpus semantic errors tended to occur more inferiorly, a discrepancy possibly reflecting the smaller error sample analyzed by Tate et al. [2014]. Interestingly, these results converged with those from Hamberger et al. [2016] who probed the information available to patients during left temporal stimulation despite naming failure. Patients were queried about semantic features (*Is it found indoors?*) or phonological features (*Does it begin with the sound "t" as in toy?*). At sites below STG stimulation especially disrupted access to semantic information, whereas above STG, phonological processing was disrupted—the same topography we found with naming errors.

The distinct frequencies and distributions demonstrated by the various types of errors carries implications for the interpretation of the naming errors during speaking and the neurofunctional organization of word retrieval within temporal cortices, two issues discussed in turn below.

The Functional Causes of Naming Errors

In considering the component processes that underlie word production, semantic errors have been functionally localized to both the semantic level and a subsequent level at which semantics and phonology interface. The hypothesis of a later source has been supported by results from computer simulations as well as by observations of semantic errors in patients with intact semantic processing [Caramazza and Hillis, 1990; Cloutman et al., 2009; Rapp and Goldrick, 2000], and has been explained as stemming from cascading of activation. Because activation of phonology is not restricted to the target word (*chair*), but also extends to other words similar in meaning (*stool, bench, table*), a semantically related word can be selected incorrectly in conditions of disturbed phonological processing. Under this explanation, the same phonological processes responsible for semantic errors could also give rise to phonological errors. This type of explanation would account for the semantic errors we found in middle and posterior STG, the region where phonological errors exhibited their peak of occurrence. However, the distinct cortical distribution we found for semantic and phonological errors makes it a plausible explanation for only a small set of semantic errors. A semantic source is more likely to account for most of the semantic errors in our corpus, which were elicited in MTG. Importantly, our results converge with results from neuroimaging [Binder et al., 2009; Fairhall and Caramazza, 2013; Wei et al., 2012] and transcranial magnetic stimulations using words [Whitney et al., 2010]

and picture stimuli [Hoffman et al., 2012] in identifying MTG as a region associated with semantic processing.

In theory, the delayed responses observed in our corpus could result from momentary problems in processing either semantic or phonological information. However, the cortical distribution of delayed responses constrains the interpretation of these errors. The different distribution demonstrated by delayed responses and semantic errors appears to rule out the possibility that delayed responses reflected problems in processing semantic information. This interpretation is in line with our working hypothesis that delayed responses were functionally equivalent to tip-of-the-tongues, temporary word-production failures in which access to semantics is generally intact [Schwartz, 2002]. Our working hypothesis predicted—as we found—little overlap in the distributions of delayed responses and semantic errors. On the other hand, the overlap consistently demonstrated by delayed responses with phonological errors suggests that delay responses results from momentary problems in accessing phonology. This interpretation strengthens our working hypothesis of a similarity between delayed responses and tip-of-the-tongues, as tip-of-the-tongues frequently arise from temporary failures in accessing phonological information [Schwartz, 2002]. Uncertainties similar to those discussed for delayed responses concern non-responses, which can also relate to semantic and/or phonological processing. The non-responses found in temporal regions where we also observed the highest concentrations of semantic errors, phonological errors, and delayed responses, were probably related to both semantic and phonological processes. However, the unique distribution of non-responses, which concentrated especially in anterior ITG, implies that these errors had other, more specific sources. Nevertheless, conclusions about non-responses should be drawn very cautiously – not only because the ‘opacity’ of non-responses makes their interpretation particularly difficult, but also because results with non-responses were replicated in whole corpus analyses and same-items analyses, but not in same-patients analyses.

The Temporal Processing of Semantics and Phonology

Prior investigations of temporal lobe regions underlying semantic processing have focused primarily on mid-posterior regions and anterior temporal regions. The clustering of semantic errors we found in middle MTG appears to be most consistent with models that postulate significant contribution to semantic processing in picture naming mediated by the mid-posterior temporal region. An alternative view—the hypothesis of anterior temporal cortex as the primary site of semantic processing—was originally proposed based on results from semantic dementia [Hodges et al., 1992], a neuropathology caused by extensive bilateral damage in this region [Acosta-

Cabronero et al., 2011]. Semantic naming errors in semantic dementia are similar to those elicited during language mapping [Lambon et al., 2001; Mesulam et al., 2013; Rogers et al., 2004], frequently involving words from the same conceptual category as the target (coordinate errors). However, in semantic dementia, difficulties in processing semantic information are not confined to naming, but appear in a wide range of tasks critically depending on meaning [Hodges and Patterson, 2007]. The extensive semantic deficit observed in semantic dementia could be linked to damage in the anterior temporal region, which in turn, could interfere with other semantic operations than those supported by MTG. Indeed, anterior temporal regions have been proposed to function as a supramodal ‘hub’ in which semantic information is integrated and coordinated, and computed for various processes including categorization and inferences [Patterson et al., 2007]. It might be important to note that whereas our results likely reflect cortical organization, semantic dementia might also affect subcortical structures (Noppeney et al., 2007; Rohrer et al., 2009) that are components of the semantic system that encompasses temporal and posterior frontal regions as well [Brambati et al., 2009; Geranmayeh et al., 2015]. Differences with respect to semantic dementia might (at least in part) arise subcortically.

The semantically related responses induced by temporal cortical stimulation in naming were a combination of coordinate words (“pear” for *lemon*) and associated words (“time” for *clock*). These two types of semantic errors were also found with aphasic patients who had semantic deficits caused by strokes affecting frontal and temporoparietal areas. Jefferies and Lambon Ralph [2006] explained the associated errors of aphasic patients as arising from left inferior prefrontal cortex, which they viewed as functioning as a semantic control system regulating semantic activation that results in task-appropriate responses. However, this causal link between left inferior prefrontal cortex and associated semantic errors would not anticipate the elicitation of associated errors in temporal cortex. Instead, our data show that both coordinate and associated errors can arise from conditions affecting neural activity within temporal cortex. Interestingly, our data further showed that coordinate and associated errors distributed differently, implying that the two types of errors are neurofunctionally distinct. Comparisons of the semantic errors produced by patient populations support this distinction: associated errors have been found in aphasia but are virtually absent in semantic dementia [Jefferies and Lambon Ralph, 2006]. This distinction is also supported behaviorally, as demonstrated by different effects induced by coordinate and associated relationships in healthy individuals [Alario et al., 2000; Rahman and Melinger, 2007].

Further error analysis revealed that incorrect words produced in semantic errors were more closely related to the meaning of target words in posterior than in anterior temporal sites. The degree of target-error semantic relatedness

can be taken as an index of the specificity of the semantic features that were retrieved, so that as relatedness increases so would the availability of specific semantic features. It is interesting to note that semantic relatedness was especially high in posterior temporal regions that have been associated with the retrieval of the phonological features of spoken words [Graves et al., 2007; Indefrey and Levelt, 2004; Miozzo et al., 2015; Peramunage et al., 2011] and were also the site of the highest concentration of errors caused by perturbations of phonological processing. The anterior-posterior distribution of semantic relatedness could reflect a more general gradient, in which semantic input becomes progressively more detailed toward posterior regions that process phonology. This type of organization would ensure that semantics provides proper input to phonology, and consequently, would result in semantic errors that were increasingly semantically similar to the targets in temporal posterior regions. Interestingly, the notion of an anterior-posterior gradient further anticipates that non-responses would appear more frequently in temporal areas providing little support to semantic processing. This is because the semantic input processed at these sites is too weak to induce the selection of a phonological form. Our results provide some support to this prediction. In fact, as demonstrated at least from results from the whole error corpus, non-responses were more frequent in anterior ITG, where we also found the lowest concentration of semantic errors.

Compared to the other types of errors, phonological errors were relatively infrequent. Corina et al. [2010] reported similarly low rates of phonological errors, not only in temporal regions but brain-wide. The low rates of phonological errors should raise the question as to whether other types of errors are associated with phonological processing. We argued that delayed responses represent such kind of errors, based on evidence that delayed responses overlapped in distribution with phonological errors, and that they concentrated in middle-posterior STG, a region where prior results have also implicated phonological processing [Graves et al., 2007; Indefrey and Levelt, 2004; Miozzo et al., 2015; Peramunage et al., 2011; Scott et al., 2000]. Phonological errors and delayed responses provide further support to the hypothesis of an inferior to superior gradient, with more superior temporal regions becoming increasingly involved in phonological processing. The temporal region is part of a broader left-lateralized system—the dorsal stream—that also includes inferior-parietal and inferior-frontal gyrus regions, and pre-motor cortex [Duffau et al., 2005; Hickok and Poeppel, 2007; Price, 2012; Tate et al., 2015], and would support the complex computations associated with transcoding a phonological input into motor, articulatory patterns. The concentration of phonological errors and delayed responses we found in mid and posterior STG contrasts with the voxel-based lesion-symptom mapping analysis conducted by Schwartz et al. [2012] on the phonological errors

produced by aphasic patients, which revealed weak associations between phonological errors and STG, but stronger associations with other aspects of the dorsal stream, localized more superiorly (supramarginal gyrus) or anteriorly (premotor cortex, pre- and postcentral gyri). These discrepancies could reflect differences in the methodologies used in the two studies; alternatively, they could stem from differences in the word-production errors resulting from cortical stimulations and aphasia. Cortical stimulations in mid-posterior STG might disrupt access to phonological information that provided the input to 'downstream' articulatory processes involving the supramarginal gyrus, the premotor cortex, and the pre- and postcentral gyri. By contrast, aphasia might primarily affect the more superior and anterior aspects of the dorsal stream, giving rise to errors likely to reflect the disruption of articulatory processing.

Implications for Epilepsy and Cortical Mapping

In the clinical context of cortical language mapping, naming errors are typically coded to reflect the identification of a positive language site, without concern regarding the type of error elicited. For patients who undergo cortical mapping prior to surgical resection, the primary goal of the surgery is elimination or reduction of seizures, and results from stimulation mapping either provide clearance to remove epileptogenic cortex, or, unfortunately, limit the resection due to concern that resection of naming sites will result in postoperative language decline. As limiting the resection reduces the likelihood of seizure freedom, it would be extremely useful to know whether, or the extent to which removing a particular naming site would result in postoperative language decline. The current results suggest that naming sites are not all functionally equivalent. Although the consequences of removing a particular type of naming site is unknown and would be difficult to test, the current results raise this as a possibility, and represent a required first step in this direction.

Potential Limitations

As it is fairly well established that reorganization of language function occurs in epilepsy, particularly among individuals with epileptogenic cortex in the left (language dominant) hemisphere, it must be acknowledged that topographical findings from cortical mapping might not represent the distribution of function within a healthy, non-neurological population [Schwartz et al., 1998]. Nevertheless, it is also important to note that language reorganization is more likely to occur in patients with early onset temporal lobe epilepsy (TLE), and that early onset TLE patients typically undergo standard antero-medial temporal lobe resection without cortical language mapping [Hamberger, 2015]. As reported in Table I, the median age of epilepsy onset in the current patient group was 18 years, which is well beyond the age at which language

lateralization and location has stabilized. Furthermore, patients with early epilepsy onset (before age 10) only contributed a very small proportion of errors (16%) in our study. Thus, although some degree of reorganization may be present, we believe that, overall, the current findings provide a reasonably accurate representation of the cortical distribution of function in the general population. We also note that our data were acquired based on clinical procedures, which do not allow for an ideally equivalent sampling of all temporal regions among all patients. The clinical nature of our data particularly constrained same-patients analyses that focus on errors produced by individual patients and are especially relevant for assessing the cross-subject validity of aggregated results. Findings from same-patients analyses should therefore be interpreted extremely carefully.

CONCLUSIONS

Due to the nature of epilepsy—in particular, the brain regions affected and the invasive methods often required for patients who are refractory to pharmacological treatment—epilepsy has a long history of contributing to cognitive neuropsychology and cognitive neuroscience [Loring, 2010]. The current analysis of stimulation induced naming errors provides detailed information regarding temporal lobe mediation of the phonological and semantic processes that give rise to naming. These data not only inform normal cortical language representation, but may also contribute to the understanding and, potentially, treatment of neurologically based language disorders. That stimulation identified naming sites are not functionally equivalent, and that the precise nature of most naming sites can be determined via the monitoring of error type, might be clinically useful, and warrants further study.

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