

Recruitment of Control and Representational Components of the Semantic System during Successful and Unsuccessful Access to Complex Factual Knowledge

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Our ability to effectively retrieve complex semantic knowledge meaningfully impacts our daily lives, yet the neural processes that underly successful access and transient failures in access remain only partially understood. In this fMRI study, we contrast activation during successful semantic access, unsuccessful semantic access because of transient access failures (i.e., “tip-of-the-tongue,” “feeling-of-knowing”), and trials where the semantic knowledge was not possessed. Twenty-four human participants (14 female) were presented 240 trivia-based questions relating to person, place, object, or scholastic knowledge domains. Analyses of the recall event indicated a relatively greater role of a dorsomedial section of the prefrontal cortex in unsuccessful semantic access and relatively greater recruitment of the pars orbitalis of the inferior frontal gyrus in successful access. Successful access was also associated with increased activation in knowledge domain-selective areas. Generally, knowledge domain-selective areas showed increased responses for both preferred and nonpreferred stimulus classes. The exception was place-selective regions (parahippocampal gyrus, transverse occipital sulcus, retrosplenial complex), which were recruited during unsuccessful access attempts for all stimulus domains. Collectively, these results suggest that prefrontal semantic control systems and classical spatial knowledge-selective regions work together to locate relevant information and that access to complex knowledge results in a broad activation of semantic representation extending to regions selective for other knowledge domains.

Key words: domain; feeling of knowing; fMRI; semantic; tip of the tongue

Significance Statement

The ability to access the deep factual knowledge we possess has a meaningful influence on our scholastic, professional, and social lives. In this fMRI study, we investigate the neural processes associated with successful access to this knowledge as well as transient failures in semantic access (tip-of-the-tongue/feeling-of-knowing). Participants attempted to answer trivia-style general knowledge questions drawn from four different knowledge domains. Results suggest that prefrontal semantic control systems and classical spatial knowledge-selective regions work to locate relevant information and that access to complex knowledge results in a broad activation of semantic representation extending to regions selective for other knowledge domains.

Introduction

A defining characteristic of the human experience is our ability to learn and retrieve a broad range of complex factual knowledge. Our capacity to access this stored semantic knowledge impacts our ability to perform, scholastically, professionally, and

interpersonally, in our daily lives. Yet, the cortical processes underlying this capacity, and the mechanism underlying transient failures in our ability to access this knowledge, remain partially understood.

While we can find ourselves in a situation where we can successfully access a piece of knowledge, for instance, “what is the capital of Hungary?,” we can also find ourselves certain we know the answer but are unable to retrieve it, only to be able to do so minutes, hours, or days later. Unsuccessful semantic access (also called “blocking”; Schacter, 1999) can be operationally characterized as a temporary failure in access, accompanied by accurate prediction of one’s capacity to recall the knowledge in a future test. Subjectively, this can be represented in the common experience of searching through our memory, navigating from related

Received Dec. 17, 2021; revised Apr. 29, 2022; accepted May 2, 2022.

Author contributions: S.U., G.R., and S.L.F. designed research; S.U. and G.R. performed research; S.L.F. analyzed data; S.L.F. wrote the paper.

This project was funded by the European Research Council Cortical Representation of Abstract Semantic Knowledge (CRASK) Grant 640594, under the European Union Horizon 2020 research and innovation program.

The authors declare no competing financial interests.

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<https://doi.org/10.1523/JNEUROSCI.2485-21.2022>

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fact to related fact, in an attempt to get closer to the elusive piece of knowledge or lexical entry. Such states can be accompanied by an acute sensation that successful semantic access is imminent but just out of grasp, the so-called “tip-of-the-tongue” (ToT) state (Brown and McNeill, 1966; Brown, 1991), or the feeling that the knowledge is possessed without the accompanying sense of imminent retrieval [“feeling-of-knowing” (FoK); Hart, 1965]. Understanding these states can provide insight into both the neural substrates of these transient failures and into retrieval processes themselves.

Previous neuroimaging work has highlighted increased activation of bilateral prefrontal control systems when comparing unsuccessful access to a combination of successful and knowledge-absent trials (Maril et al., 2001, 2005) or when parametrically comparing unsuccessful semantic-access trials and knowledge-absent trials (Kikyo et al., 2002). The identified prefrontal regions include those implicated in guiding the retrieval of semantic control [left inferior frontal gyrus (IFG), dorsomedial prefrontal cortex-supplementary motor area (dmPFC-SMA); Jackson, 2021], as well as those that are not (right IFG, bilateral anterior PFC). One potential consideration is that studies comparing known to blocked states have included in the modeled fMRI response both the recall event and the subsequent metacognitive evaluation of the participants internal cognitive state during the recall event. Consequently, the involvement of frontal regions may reflect extrasemantic processes, such as response selection of cognitive conflict associated with the metacognitive judgment (Maril et al., 2005).

At the same time, the semantic system of the brain includes an extensive left-lateralized set of brain regions that reliably activate more strongly to semantically richer stimuli (Binder et al., 2009), including regions showing univariate and multivariate sensitivity to the semantic content of probe stimuli that may be more closely linked to the representation of semantic knowledge (Fairhall and Caramazza, 2013a; Fernandino et al., 2015; Liuzzi et al., 2017, 2020, 2021). Failures in semantic access may also arise from a failure to ignite such semantic representations.

The objective of the current study is to gain insight into both the processes underlying temporary blocks in semantic and lexical access and those that allow successful access to stored knowledge. We contrast the fMRI response associated with successful and unsuccessful semantic access, and trials where semantic knowledge is absent. This study extends the existing literature in two ways. First, we use an fMRI design that permits the deconvolution of the cortical responses to the cognitive recall event from subsequent metacognitive decisions about the degree of confidence that the knowledge is possessed. Second, we further examine the role of representational components of the semantic system in successful and unsuccessful semantic access. To accomplish this, we use general knowledge questions drawn from four different knowledge domains. This manipulation of the semantic content of the probe stimuli allowed us to better isolate regions involved in representational processes as well as to understand the relationship between knowledge domain selectivity in the cortex and successful and unsuccessful semantic access.

Materials and Methods

Participants

Twenty-nine right-handed native-Italian speakers with no history of neurologic disorders were recruited for the study. As previous estimates of relevant effects sizes were not available, this sample size was based on a recent study that considered the role of domain in sentence processing and conceptual combination (Rabini et al., 2021) and is larger than

previous studies that have investigated successful/unsuccessful access regardless of knowledge domain ($N = 14\text{--}16$; Maril et al., 2001, 2005; Kikyo et al., 2002). Three participants were excluded because of within-run head motion >2 mm or excessive ocular artifacts during scanning (excessive condition-specific signal emanating from the eyes). One subject was excluded as they did not report any of the place or scholastic facts to be unknown, and a further participant did not complete the entire experiment. Thus, the final sample included 24 participants (14 female; mean age, 26.4 years). Participants gave informed consent and were compensated for participation (15 €/h). The study was conducted in line with the Declaration of Helsinki (1964; amended in 2013) and was approved by the Ethics Committee at the University of Trento.

Experimental design

Stimuli. Stimuli were composed of 240 general knowledge questions written in Italian. The questions were equally divided into the following four knowledge domains: person in which there were questions about famous historic or fantasy characters or famous contemporary people (e.g., “Which philosopher uttered the phrase ‘I know I don’t know?’”); places, where they were asked about famous geographic places or monuments (e.g., “In which Spanish city is the Alhambra complex located?”); and objects, in which the questions were about specific objects or materials (e.g., “What is the name of the element that supports the weight of an arch?”). The final domain of knowledge, “scholastic,” was designed to capture general category factual knowledge that was unrelated to direct experience with the environment, more likely to be learned verbally, and did not involve person-, place-, or object-related information (e.g., “What is the name of the transition of matter from the solid to the gaseous state?”).

Stimuli were matched across knowledge domain by number of words ($F_{(3,236)} = 1.13$, $p = 0.337$, $\eta^2 = 0.01$) and number of letters ($F_{(3,236)} = 1.12$, $p = 0.343$, $\eta^2 = 0.01$). The full list of stimuli is available at the following site: <https://figshare.com/s/194aa97ca67800f4c658>.

Word frequencies (WFs) were estimated via the PAISA Corpus (Piattaforma per l’Apprendimento dell’Italiano Su corpora Annotati; Lyding et al., 2014). Specifically, questions were lemmatized, and average \log_{10} word frequencies were calculated for each sentence. One-way ANOVA indicated no significant differences in the average WF of questions across domains ($F_{(3,236)} = 1.35$, $p = 0.26$, $\eta^2 = 0.02$). Analysis of the average WF of the target answer indicated a difference across domains ($F_{(3,236)} = 9.15$, $p < 0.001$, $\eta^2 = 0.10$) that was driven by lower question-target WFs in the object knowledge domain compared with the other three categories (p -values < 0.005), which did not differ from one another (p -values > 0.2).

fMRI experimental task. The fMRI session was divided into four experimental runs. In each run, 15 questions from each knowledge domain were presented in a pseudorandomized order using MATLAB (www.mathworks.com) and Psychtoolbox version 3 (www.psychtoolbox.org). Each trial was divided into two parts. First, the recall event included the 3 s written presentation of the question followed by a 3 s fixation cross. Participants were instructed to read the question once and indicate, via two-option button press with their right hand, whether the knowledge was accessible or inaccessible, within the 6 s from question onset [non-responses ($<1\%$) were coded as inaccessible]. If participants indicated they could access the answer, the experiment continued to the next trial. Inaccessible response prompted a 0–8 s jitter followed by a metacognitive judgment. Here, participants were cued to indicate, via three-option button press with the same hand, whether they experienced a ToT or an FoK, or their answer was unknown (4 s duration). Participants were instructed to respond “known” if they could access the answer in that moment; to indicate a ToT if they were convinced they knew the answer and were on the verge of producing it but could not quite do so; to respond FoK when, while the answer was not presently accessible, they felt they knew it and were certain they would be able to recognize the correct answer; and to respond “unknown” if they did not think they knew the answer. This paradigm was designed to focus on the neural response associated with the cognitive state during the initial response (and associated MR scans). It is possible that ToT or FoK responses could have been resolved if more (or unlimited) time was allowed.

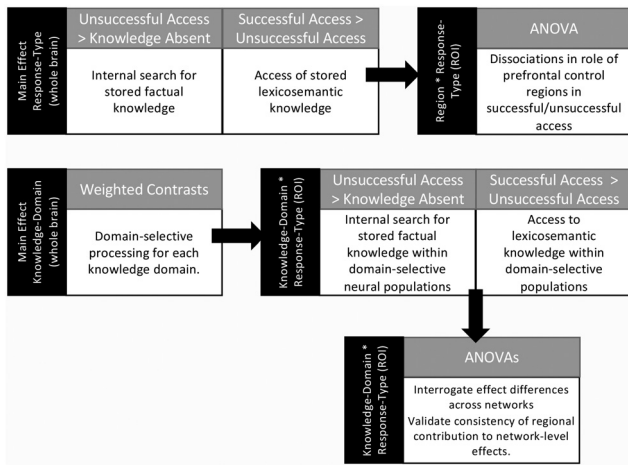


Figure 1. Schematic of group-level analyses for the access event, showing the contrast/statistical test, form (whole brain, ROI), and related cognitive process.

Postscanner knowledge verification test. To validate the self-reported responses in the scanner, after the fMRI session participants were again presented with the questions classified as ToT, FoK, or unknown, as well as 20% of the “known” questions. Participants were allowed 5 s to type the answer to each question without any cue. If the participant did not respond or the participant opted to proceed to the cue (via button press), the first letter of the answer appeared, and they had an additional 5 s to start typing the response.

MRI scanning parameters

Functional and structural data were collected at the Center for Mind/Brain Sciences (CIMEC), University of Trento, with a Prisma 3 T scanner (Siemens), using a 64-channel head coil. Participants lay in the scanner and viewed the visual stimuli through a mirror system connected to a 42 inch, MR-compatible LCD monitor (NordicNeuroLab) positioned at the back of the magnet bore. Functional images were acquired using echo-planar T2*-weighted scans. Acquisition parameters were as follows: repetition time (TR), 2 s; echo time (TE), 28 ms; a flip angle, 75°; field of view (FoV), 100 mm; matrix size, 100 × 100. Each volume consisted of 78 axial slices (which covered the whole brain) with a thickness of 2 mm, anterior commissure/posterior commissure aligned. High-resolution (1 × 1 × 1 mm) T1-weighted MPRAGE sequences were also collected (sagittal slice orientation; centric phase encoding; image matrix, 288 × 288; FoV, 288 mm; 208 slices with 1 mm thickness; TR, 2290 s; TE, 2.74 ms; inversion time, 950 ms; flip angle, 12°).

fMRI data analysis

Data were analyzed and preprocessed with SPM12 (<http://www.fil.ion.ucl.ac.uk/spm/>). The first four volumes of each run were dummy scans. All images were slice time corrected, realigned to correct for head movement, normalized to MNI space, and smoothed using a 6 mm FWHM isotropic kernel. Before computing the general linear model (GLM), the four runs were concatenated, to avoid empty parameters in one or more conditions. The following 16 trial types were modeled for the recall event: the 4 different recall types (successful access, ToT, FoK, and knowledge-absent trials) for each of the four knowledge domains. The type of these different recall events, for ToT, FoK, and knowledge-absent trials, was determined by recoding based on the subsequent metacognitive judgment. Twelve additional regressors were included to capture the metacognitive part of the trials, with ToT, FoK, and knowledge-absent responses modeled for each of the four categories. Subject-specific parameter estimates (β -weights) for each of these 28 conditions were derived through the GLM. The six head motion parameters were included as additional regressors of no interest. Group-level analysis was performed in two separate random-effects GLMs, one for the recall event and one for the metacognitive judgment.

A schematic of the group-level analysis strategy is presented in Figure 1. Group-level whole-brain analyses of recall type were performed using weighted contrasts for unsuccessful access [(ToT + FoK) > knowledge absent], to isolate the internal search for stored knowledge in the absence of activation of that representation, and successful access [known > (ToT + FoK)], to isolate access to the targeted lexicosemantic knowledge. An initial region of interest (ROI) analysis was performed to assess the effect of recall type across semantic control systems. Here, 5 mm spherical ROIs were constructed in the pars orbitalis and pars triangularis sections of the IFG and in the dmPFC-SMA based on coordinates previously published in a recent meta-analysis of semantic control processes (Jackson, 2021).

To identify cortical regions sensitive to semantic content, domain-selective responses were identified by contrasting each domain with the average of the other three domains [e.g., place > mean (person, object, scholastic)] across the whole brain. Following this, a second ROI analysis was performed to assess the influence of the internal search for stored knowledge and in successful lexicosemantic access in these knowledge domain-selective brain regions. Knowledge domain-selective ROIs were constructed by taking the union between a sphere with a radius of 5 mm centered at the selectivity peak for the knowledge domain (see Table 2) and statistically significant voxels for the relevant domain-selective contrast (see Fig. 5). As the ROI-defining contrasts contain no information about recall type, subsequent analyses of recall type or recall type × domain interactions are orthogonal and statistically unbiased (Friston et al., 2006). Within knowledge domain-selective ROIs, data were analyzed for all domains, preferred domain, or the average of the nonpreferred domains in a series of weighted contrasts that isolated the effects of interest, as detailed in the relevant section of the results. To reduce multiple comparisons over the large number of identified domain-selective regions, analyses were performed by averaging the responses of the most selective ROIs within each network. Effects of interest were compared across networks via ANOVA, and supplementary ANOVAs were used to assess the consistency of effects within the regions composing the knowledge domain-selective networks.

Whole-brain analysis of the metacognitive judgment was performed by contrasting ToT, FoK, and unknown responses with one another.

All whole-brain analyses were performed within an inclusive mask designed to isolate regions previously implicated in semantic processing (see Results). Unless otherwise specified, results are reported at an initial voxel-wise threshold of $p < 0.001$, with familywise error (FWE) correction for multiple comparisons at the cluster level ($p < 0.05$) as implemented in SPM12.

Results

Behavioral

During the main experiment, participants reported that the fact was known on 45.6% of trials, ToT states on 12.7% of trials, and FoK states on 16.3% of trials, and that the fact was unknown on 25.5% of trials, which is in keeping with previous results using similar paradigms (Maril et al., 2001, 2005). Postscanner testing indicated that known responses were genuine, with 79.5% of correct responses being correctly provided either through free recall (48.8%) or when cued by the first letter of the word (30.8%). Accuracy for ToTs (60.0%; unprompted, 32.3%; cued, 27.2%) was significantly lower ($t_{(23)} = 5.33, p < 0.0001$, Cohen’s $d = 2.2$), and accuracy for ToT responses (38.0%; unprompted, 16.9%; cued, 21.1%) was progressively lower ($t_{(23)} = 7.41, p < 0.0001$, Cohen’s $d = 3.1$). Finally, subjects could accurately report 20.4% of unknown responses (unprompted, 8%; cued, 11.9%), which was significantly lower than those for FoKs ($t_{(23)} = 6.56, p < 0.0001$, Cohen’s $d = 2.7$).

Repeated-measures ANOVA revealed that response type differed across knowledge domain ($F_{(9,207)} = 6.20, p < 0.001, \eta^2 = 0.21$). While the number of known responses did not differ significantly across domains, ToTs were less frequent for person

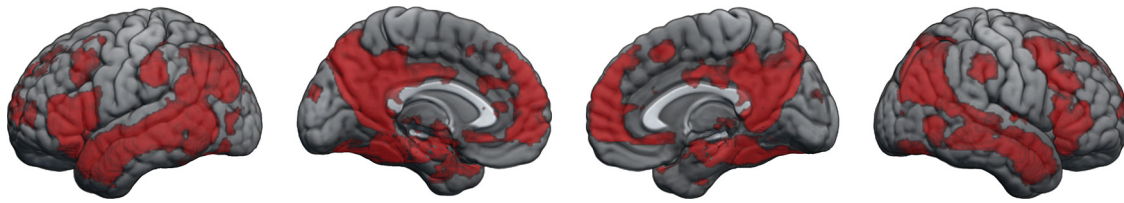


Figure 2. Inclusive functional mask applied to all contrasts in this study. The mask was defined as regions showing sensitivity to knowledge domain at a lenient statistical threshold ($p < 0.05$, uncorrected).

(10.9%) and place (11.0%) domains compared with both object (14.9%) and scholastic (14.1%, p -values < 0.02) domains. FoKs were less likely in the person domain (12.2%) compared with place (18.2%, $p = 0.003$), object (16.4%, $p = 0.019$), and scholastic (18.4%, $p = 0.002$) domains. These effects were balanced by an increase in confirmed unknown responses for person (33.5%) and place (27.9%) domains compared with object (22.0%, p -values < 0.05) and scholastic (18.4%, p -values < 0.005) domains.

To assess reaction times (RTs) for the initial recall event (measured from the onset of the probe sentence), the responses were decomposed based on the subsequent metacognitive judgment. The effects of recall type (known, ToT, FoK, and knowledge absent) and knowledge domain (person places, objects, and scholastic) were then assessed via repeated-measures ANOVA. RTs differed as a function of recall type ($F_{(3,69)} = 41.6$, $p < 0.001$, $\eta^2 = 0.64$). Paired t tests revealed that ToT (3797 ms) and FoK (3730 ms) responses did not significantly differ ($t_{(23)} = 1.57$, $p = 0.13$, Cohen's $d = 0.65$) and were slower than responses subsequently confirmed to be unknown (3464 ms; vs ToT: $t_{(23)} = 5.43$, $p < 0.001$, Cohen's $d = 2.3$; vs FoK: $t_{(23)} = 5.08$, $p < 0.001$, Cohen's $d = 2.1$). Unknown responses were in turn slower than known responses (3238 ms; $t_{(23)} = 4.97$, $p < 0.001$, Cohen's $d = 2.1$). RTs also differed as a function of knowledge domain ($F_{(3,69)} = 28.3$, $p < 0.001$, $\eta^2 = 0.55$). Judgments for person trials (3361 ms) were faster than those for places (3548 ms; $t_{(23)} = 4.31$, $p < 0.001$, Cohen's $d = 1.8$), which were in turn faster than those for objects (3670 ms; $t_{(23)} = 3.49$, $p = 0.002$, Cohen's $d = 1.5$) and scholastic items (3651 ms, $t_{(23)} = 2.84$, $p = 0.009$, Cohen's $d = 1.2$), which did not differ significantly from one another ($t_{(23)} = 0.64$, $p = 0.53$, Cohen's $d = 0.2$). There was no interaction between recall type and knowledge domain ($F_{(9,207)} = 0.99$, $p = 0.45$, $\eta^2 = 0.04$).

RTs for the metacognitive judgment differed modestly as a function of category ($F_{(3,69)} = 2.88$, $p = 0.042$, $\eta^2 = 0.11$), with faster responses for person (559 ms) than for object (618 ms, $t_{(23)} = 2.42$, $p = 0.024$, Cohen's $d = 1.0$) and scholastic (604 ms, $t_{(23)} = 2.46$, $p = 0.022$, Cohen's $d = 1.0$) domains. Recall type had a more pronounced influence on RTs ($F_{(2,46)} = 10.63$, $p < 0.001$, $\eta^2 = 0.32$), with slower responses for FoK (673 ms) compared with both ToT (569 ms, $t_{(23)} = 3.59$, $p = 0.002$, Cohen's $d = 1.5$) and unknown (560 ms, $t_{(23)} = 5.90$, $p = 0.001$, Cohen's $d = 2.5$) responses.

Inclusive masking

Unexpectedly, when the answer to a question was thought to be known [(successful or unsuccessful access) $>$ knowledge absent], strong activation was seen in regions associated with reward, bilateral caudate, anterior insula, and the substantia nigra of the midbrain (but see, Kikyo et al., 2002). As the contribution of these regions is uncertain, and to focus analyses on regions previously implicated in semantic processing, subsequent analyses have been restricted to regions showing sensitivity to

semantic category at an uncorrected ($p < 0.05$) threshold (omnibus ANOVA, main effect of category; Fig. 2). At this lenient threshold, the mask can be seen to encompass both control and representational aspects of the semantic system. Examination of excluded regions showing a stronger response on trials where the response was thought to be known with Neurosynth image decoder (<https://neurosynth.org/decode/>; Yarkoni et al., 2011; Rubin et al., 2017) indicated correspondence with reward-related terms (gain, 0.359; incentive, 0.263; reward, 0.252; three highest nonanatomic reverse-inference term). Full details of the excluded regions are available at the following: <https://figshare.com/s/2f4be0ba0278ea79a7d5>.

Neural correlated of blocked and successful semantic access

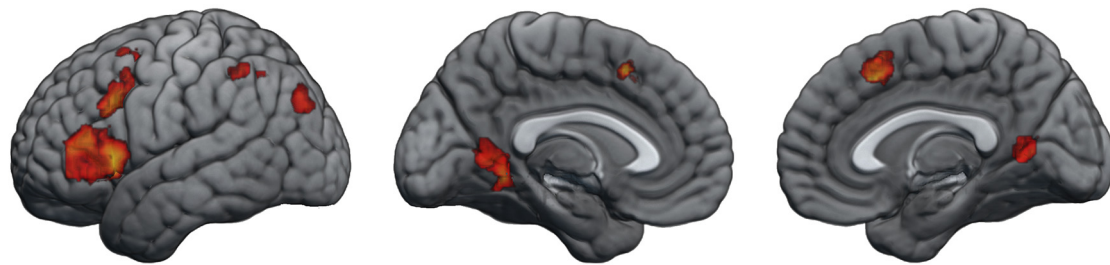
Within the inclusive mask, we first compared unsuccessful retrieval (ToT/FoK) to trials where the knowledge was absent to identify neural activation associated with the internal search for stored knowledge (Fig. 3, Table 1). Relative to knowledge-absent trials, unsuccessful access recruited semantic control circuitry in the left lateral prefrontal cortex and medial supplementary motor cortex. Additionally, the bilateral retrosplenial complex (RSC), left parahippocampal gyrus (PPA), transverse occipital sulcus (TOS), and a region of the supramarginal gyrus were more active during FoK/ToT trials than during knowledge-absent trials.

To delineate the neural processes associated with successful access to stored lexicosemantic knowledge, we contrasted successful to unsuccessful (ToT/FoK) access. Results show increased cortical activity in a network of regions associated with the representation of semantic knowledge: the precuneus, medial PFC (mPFC), bilateral sections of the middle temporal gyrus (MTG), and the left angular gyrus and hippocampus. Additionally, lateral orbitofrontal cortices in both hemispheres were seen to be more active when stored information was successfully accessed. Notably, activation in the left orbitofrontal cortex (OFC) was seen to extend laterally into the pars triangularis of the IFG.

No regions showed a significant difference between ToT and FoK trials during the recall event. Trial counts were relatively low for ToT and FoK trials, which may reduce statistical power, and it is possible that true differences between these response types exist during the recall event that were below the ability of the present paradigm to resolve (but see the section Metacognitive judgments of knowledge confidence).

Reaction times were shorter in successful-access trials than in unsuccessful-access trials, and increased cortical responses for successful access are unlikely to be attributable to increased RT or effort. However, increased responses for unsuccessful compared with knowledge-absent trials may be attributable to the longer RTs associated with the former. In a supplementary analysis, we considered this issue by including the RT of each trial as a covariate at the first-level GLM. At the a priori statistical threshold ($p < 0.001$ voxel, $p < 0.05$, cluster corrected), differences between unsuccessful and knowledge-absent trials were not

A Unsuccessful Access > Knowledge-Absent



B Successful > Unsuccessful Access

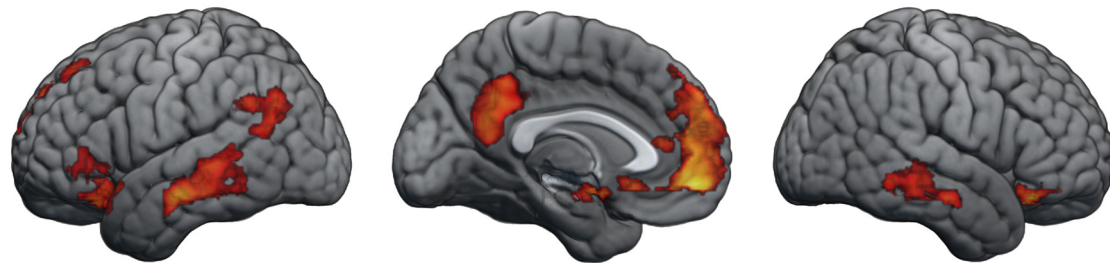


Figure 3. Successful and unsuccessful access during the recall event. **A, B**, The response to unsuccessful semantic access compared with trials where the knowledge was absent (ToT and FoK trials > knowledge-absent trials; **A**) and successful > unsuccessful access (**B**). Brain maps show the response during the recall event, when participants indicated whether the knowledge was accessible or inaccessible (with inaccessible responses coded into ToT, FoK, or knowledge-absent trials based on the subsequent metacognitive judgment). Brain maps were thresholded with an initial voxel-wise threshold of $p < 0.001$ and cluster corrected at $p < 0.05$ (Table 1, significance, extent, and location of clusters).

evident. Because of the systematic variations in RT between conditions, the covariate is expected to dilute statistical differences, and this is expected even if RT is not driving cortical effects. At an exploratory voxel-level threshold of $p < 0.005$, with the same inferential threshold ($p < 0.05$, cluster corrected) effects were present in all reported clusters (p -values < 0.008 , cluster-corrected), with the exception of the dmPFC-SMA ($p = 0.148$). In this way, we can be reasonably confident that the reported difference between unsuccessful and knowledge-absent trials in those regions are not solely attributable to RT differences.

To more fully characterize the differences between recall types in prefrontal semantic control regions, unbiased ROI analysis was performed based on published coordinates. Specifically, 5-mm-radius spheres were constructed around peak coordinates for the left IFG pars triangularis (MNI coordinates $(xyz_{MNI}) = -48, 22, 20$, IFG_{tri}), the pars orbitalis $(xyz_{MNI} = -46, 24, -2$, IFG_{orb}), and the dmPFC-SMA $(xyz_{MNI} = -2, 20, 52)$, as reported in a recent meta-analysis of semantic control studies (Jackson, 2021). As expected from the whole-brain analysis, the response was greater for successful access and unsuccessful access than for knowledge-absent trials in all regions (Fig. 4). However, different profiles were evident across the three regions (region \times recall type interaction: $F_{(4,92)} = 12.16$, $p < 0.0001$, $\eta^2 = 0.35$) and when each region was compared with each other (IFG_{orb} \leftrightarrow IFG_{tri}: $F_{(2,46)} = 6.53$, $p = 0.003$, $\eta^2 = 0.22$; IFG_{tri} \leftrightarrow dmPFC-SMA: $F_{(2,46)} = 7.49$, $p = 0.002$, $\eta^2 = 0.25$; IFG_{orb} \leftrightarrow dmPFC-SMA: $F_{(2,46)} = 21.32$, $p < 0.0001$, $\eta^2 = 0.48$). While responses were equivalent for successful and unsuccessful access in the left IFG pars triangularis ($t < 1$), responses in the dmPFC-SMA were stronger during unsuccessful compared with successful access ($t_{(23)} = 3.36$, $p = 0.003$, Cohen's $d = 1.4$) and stronger for successful than unsuccessful access in the pars orbitalis ($t_{(23)} = 2.94$, $p = 0.007$, Cohen's $d = 1.2$). The dissociation between regions persisted when comparing only successful and unsuccessful trials (IFG_{orb} \leftrightarrow IFG_{tri}: $F_{(1,23)} = 9.46$, $p = 0.005$, $\eta^2 = 0.29$; IFG_{tri} \leftrightarrow

Table 1. Significance, extent, and location of regions showing differential responses for successful and unsuccessful semantic access as shown in Figure 3 for large clusters spanning multiple regions (local maxima are listed separately)

| | Cluster | | Peak | |
|---|---------------------|--------|------|----------------|
| | p (FWE corrected) | Extent | t | x, y, z (mm) |
| Unsuccessful access > knowledge-absent | | | | |
| Left IFG (opercular) | <0.001 | 1071 | 6.98 | -34, 20, -4 |
| Left IFG (triangular) | | | 5.29 | -44, 30, 12 |
| dmPFC-SMA | 0.001 | 227 | 6.22 | 4, 20, 44 |
| Left posterior PHG | <0.001 | 627 | 5.74 | -20, -50, -6 |
| Right RSC | | | 4.79 | 18, -56, 10 |
| Left RSC | | | 4.01 | -8, -56, 2 |
| Left premotor | <0.001 | 342 | 5.38 | -44, 16, 34 |
| Left MFG | 0.010 | 140 | 4.53 | -28, 10, 50 |
| Left inferior parietal | 0.003 | 172 | 4.32 | -32, -58, 38 |
| Left TOS | 0.008 | 144 | 4.07 | -34, -82, 30 |
| Successful access > unsuccessful access | | | | |
| vmPFC | <0.001 | 2732 | 6.48 | -4, 48, -10 |
| Medial OFC | | | 6.05 | 6, 18, -12 |
| Right OFC | <0.001 | 354 | 6.38 | 30, 38, -18 |
| Left hippocampus | <0.001 | 645 | 6.16 | -12, 6, -14 |
| Left OFC | | | 5.10 | -34, 26, -22 |
| Left MTG | <0.001 | 942 | 5.21 | -58, -18, -18 |
| Precuneus | <0.001 | 1042 | 5.03 | -2, -56, 22 |
| Left AG | <0.001 | 419 | 4.53 | -48, -66, 28 |
| Right mid-MTG | <0.001 | 409 | 4.43 | 64, -16, -18 |

PHG, Parahippocampal gyrus.

dmPFC-SMA: $F_{(1,23)} = 13.81$, $p = 0.001$, $\eta^2 = 0.38$; IFG_{orb} \leftrightarrow dmPFC-SMA: $F_{(1,23)} = 35.33$, $p < 0.0001$, $\eta^2 = 0.61$). Collectively, these results indicate robust differences between semantic control regions in their involvement in successful and unsuccessful semantic access. Follow-up analysis of differences between ToT and FoK trials revealed no significant differences in the left IFG pars

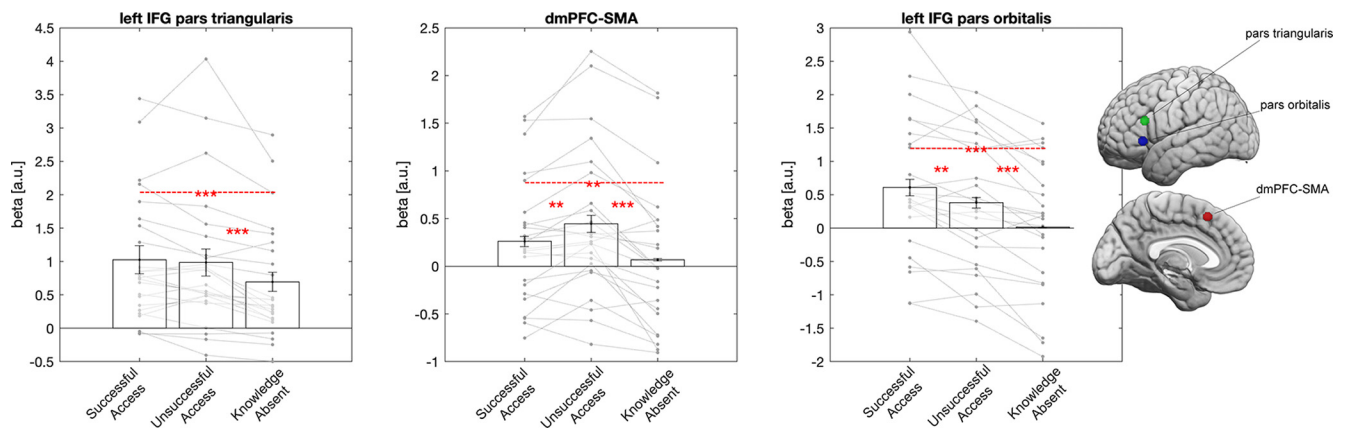


Figure 4. Region of interest analysis of independently localized semantic control regions. Shown are the fMRI response magnitudes as a function of recall type for the left IFG pars triangularis (green), pars orbitalis (blue), and the dmPFC-SMA (red). Error bars indicate ± 1 between-subject SEM. Lines indicate the regional fMRI response of individual participants in each condition. Asterisks indicate within-subject statistical significance, as follows: *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$.

triangularis ($t < 1$), left IFG orbitalis ($t_{(23)} = 1.17$, $p = 0.25$, Cohen's $d = 0.5$), or dmPFC-SMA ($t_{(23)} = 1.72$, $p = 0.10$, Cohen's $d = 0.7$).

Comparing unsuccessful to successful semantic access

Whole-brain analysis of the contrast of unsuccessful > successful access identified two small clusters. One in the left premotor area in a region overlapping with the frontal eye-fields (extent: 174 voxels; p corrected (p_{corr}) = 0.003; xyz_{MNI} : $-22, -2, 52$) and another in the left superior parietal lobe (extent: 163 voxels; p_{corr} = 0.004; xyz_{MNI} : $-8, -72, 52$). Follow-up investigation showed that these regions were not more responsive for unsuccessful access compared with knowledge-absent trials, and the nature of this effect remains ambiguous.

Knowledge domain-selective responses

To identify brain regions sensitive to semantic content, each knowledge domain was contrasted with the average of the other three knowledge domains. Knowledge domain selectivity was evident in an extensive set of temporal, parietal, and prefrontal regions (Fig. 5, Table 2). Person-knowledge trials selectively activated: bilaterally, the mid and anterior middle temporal gyrus, angular gyrus, premotor cortex and hippocampi; medially, the precuneus and mPFC; and the lateral fusiform gyrus in the right hemisphere. In addition to the classic place-selective network (PPA, RSC, TOS), place stimuli more strongly recruited superior aspects of the prefrontal cortex bilaterally, left posterior MTG (pMTG), and the midcingulate cortex. Notably, three regions outside of the semantic control network, which show an increased response during blocked semantic access (Fig. 3A), correspond to left PPA and TOS and bilateral RSC. Object-related retrieval events selectively activated bilateral IFG, pMTG, and lateral fusiform gyri as well as the left supramarginal gyrus and perirhinal cortex. It should be noted that target answers in the object knowledge domain were less frequent than in other knowledge domains, which can influence cortical activity, particularly in the left IFG (Fiebach et al., 2002; Carreiras et al., 2006; Schuster et al., 2016). While the bilateral nature of object knowledge-selective IFG is inconsistent with the classic left-lateralization associated with word-frequency effects, the influence of word frequency on this object-selective pattern cannot be fully discounted. Scholastic retrieval events selectively activated left IFG and the posterior superior temporal sulcus bilaterally. The degree of overlap in voxels showing a preference for more than one domain (Fig. 5, blended color maps) was minimal. Notably,

the reaction times of the conditions comprising the domain-selective contrasts associated with the longest RTs, object and scholastic, did not significantly differ ($t < 1$). Consequently, increased RTs alone are unlikely to account for the domain-selective contrasts seen between these domains.

Effect of recall type within domain-selective brain regions

To investigate the influence of recall type within brain regions exhibiting a sensitivity to semantic content, ROIs were defined via the orthogonal domain-selective contrasts presented in Figure 5 and Table 2. To reduce multiple comparisons over the large number of identified domain-selective regions, analyses were performed by averaging the responses of ROIs within each network. Specifically, the six most strongly selective regions (Table 2, regions indicated by italics) were selected for person, place, and object domains, and all three regions were selected for the scholastic domain. This approach was adopted to maximize the signal and balance the number of voxels contributing to each network.

Within person, object, and scholastic domain-selective networks, an overall increase in activity regardless of sentence domain was seen from knowledge-absent to successful-access trials (all p -values < 0.0001) and from unsuccessful access to successful access trials (all p -values < 0.005; Fig. 6A). This increase from successful to unsuccessful trials indicates that access to stored lexicosemantic knowledge is associated with increased recruitment in these networks. On the other hand, increased activation during unsuccessful access compared with knowledge-absent trials was largely absent, with modest effects limited to the object domain-selective network ($p = 0.031$), indicating a minimal role of these networks in the internal search for stored knowledge. Notably, within these domain-selective networks, the modulation by recall type was not sensitive to stimulus domain. For comparison, Figure 6B shows the effect of recall-type for the preferred stimulus type of each network and the response for the average of the three nonpreferred stimulus classes. Descriptively, the response profiles in Figure 6B across different recall types in person, object, and scholastic domain-selective networks can be seen to be largely similar for preferred and nonpreferred stimulus classes. Inferentially, this was assessed through weighted contrasts that demonstrated that increased responses during successful access compared with unsuccessful access were in fact larger for nonpreferred compared with preferred domains in person ($t_{(23)} = 6.38$, $p < 0.001$, Cohen's $d = 2.6$), object ($t_{(23)} = 3.63$, $p = 0.001$, Cohen's $d = 1.5$), and

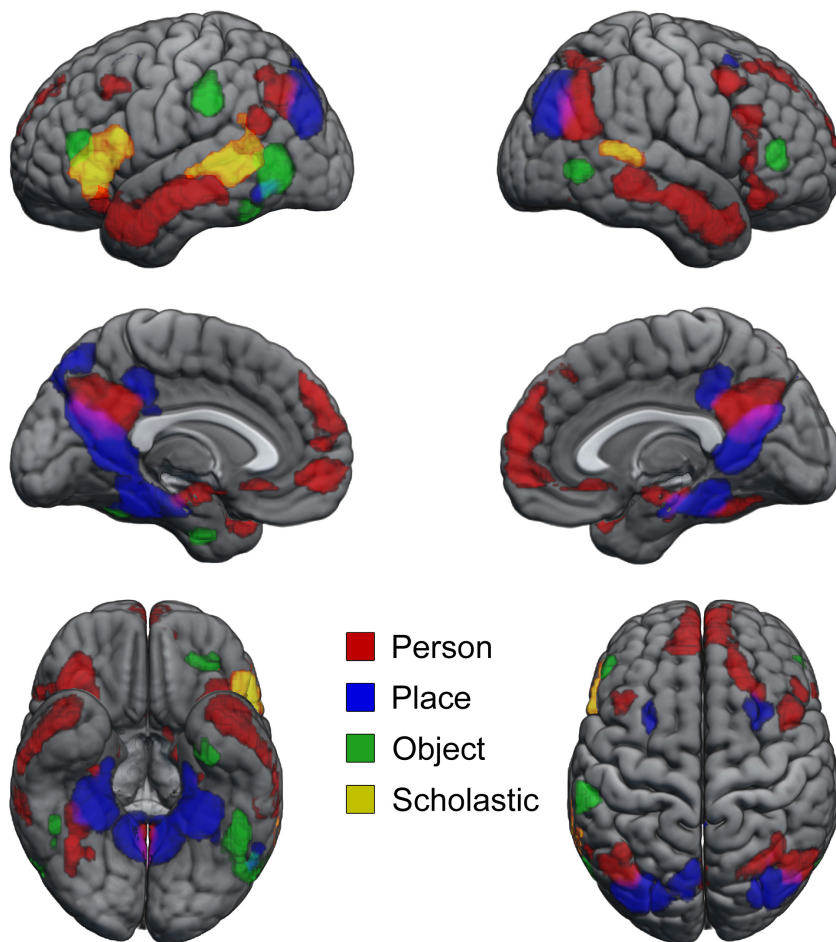


Figure 5. Cortical regions demonstrating a preference for one category versus the average of the others during the recall attempt, regardless of recall outcome. Brain maps are initially thresholded at a voxel-wise threshold of $p < 0.001$ and are cluster-level corrected to $p_{FWE} < 0.05$ (Table 2, significance, extent, and location of clusters).

scholastic ($t_{(23)} = 2.21, p = 0.045$, Cohen’s $d = 0.9$) networks. This indicates that, in person object and scholastic domain knowledge-selective regions, the enhanced response associated with successful access was not domain selective.

A different profile was evident within the place-selective network. Like the other domain-selective networks, a domain-general increase was present from unknown to known trials ($p < 0.0001$). Unlike the other networks, the increased response from knowledge-absent to successful-access trials was domain selective. Specifically, there was a greater increase for place-related trials compared with the other domains ($p = 0.002$), and there was no significant increase from unsuccessful-access to successful-access trials when only the three nonpreferred categories were considered ($p = 0.1$). In addition, place-selective regions exhibited a robust increase in response for unsuccessful-access trials relative to knowledge-absent trials ($p = 0.0002$), an effect that persisted when only nonpreferred stimuli were considered ($p = 0.004$), indicating a potential role of this network in the internal search for stored factual knowledge.

To assess the specificity of increased activity during unsuccessful compared with knowledge-absent access trials to the place-selective network, repeated-measures ANOVA was performed comparing the strength of the effect (unsuccessful – knowledge-absent trials) across the four networks. A significant effect of region ($F_{(3,69)} = 5.24, p = 0.003, \eta^2 = 0.19$) was driven by significantly stronger effects in the place-selective network than the person selective network ($t_{(23)} = 5.32, p < 0.0001$, Cohen’s

$d = 2.2$) and the object-selective network ($t_{(23)} = 3.09, p = 0.005$, Cohen’s $d = 1.3$), and stronger effects that approached significance in the scholastic knowledge domain-selective network ($t_{(23)} = 2.07, p = 0.050$, Cohen’s $d = 0.9$). These results confirm the greater involvement of the place-selective network in unsuccessful access.

While averaging across ROIs within a given network reduces multiple comparisons, it introduces the risk of mistaking local regional effects for global network-level effects. In a supplementary analysis, differences within the ROIs composing the knowledge domain-selective networks were assessed via repeated-measures ANOVA, following weighted averaging of the conditions to isolate the difference between successful versus unsuccessful access and between unsuccessful access versus knowledge-absent trials.

Comparing successful to unsuccessful access, interregional differences were limited to the person-domain network ($F_{(5,115)} = 6.01, p < 0.001, \eta^2 = 0.21$). *Post hoc* paired t tests revealed that this was driven by larger effects in ventromedial PFC (vmPFC) compared with other regions, with differences between vmPFC and left lateral anterior temporal lobe, right temporoparietal junction (TPJ), and left mid-MTG, surviving Bonferroni correction for multiple comparisons across regions (15 comparisons: adjusted $\alpha = 0.0033$). The response profile in vmPFC is consistent with the maximal response of this region when successful and unsuccessful access were contrasted independent of knowledge domain (Fig. 3B) and

may indicate a particular role of this region in successful access to semantic knowledge. However, each region individually showed greater responses for successful than unsuccessful access (p -values < 0.0001 , adjusted $\alpha = 0.0083$), indicating that, despite the variations across the network, all regions are contributing to the reported network-level effects. Comparing unsuccessful access to knowledge-absent trials, interregional differences in the object-elective ($F_{(5,115)} = 11.26, p < 0.001, \eta^2 = 0.33$) and scholastic ($F_{(2,46)} = 16.50, p < 0.001, \eta^2 = 0.15$) networks were both driven by a stronger response in the left IFG compared with other regions (object network: p -values $< 0.001, \alpha = 0.0083$; scholastic network: p -values $< 0.001, \alpha = 0.0167$). This pattern is consistent with the whole-brain analysis and role of this region in semantic control (Fig. 3A). Finally, differences in the place-domain network ($F_{(5,115)} = 4.13, p = 0.0017, \eta^2 = 0.15$) were driven by nonsignificant increases for unsuccessful access trial in right PPA, which were significantly smaller than the effects in left PPA and right TOS (p -values $< 0.0025, \alpha = 0.0083$), suggesting that the right PPA is less involved than other elements of this network in attempts to access semantic knowledge.

On the whole, these regional ANOVAs indicate a high degree of consistency between network-level analyses and the contribution of individual regions. They did reveal some additional nuances of regional effects within networks. While all regions of the person-selective network showed increases from unsuccessful to

Table 2. Significance, extent and location of regions showing differential responses for knowledge domain, as shown in Figure 5

| | | Cluster | | Peak | | |
|---------------------------|----------------------------|--------------------------|--------|----------|-------------------------------------|--------------|
| | | <i>P</i> (FWE-corrected) | Voxels | <i>T</i> | <i>x</i> , <i>y</i> , <i>z</i> (mm) | |
| Person | <i>Precuneus</i> | <0.001 | 2127 | 11.77 | 4, -54, 26 | |
| | <i>Left mid-MTG</i> | <0.001 | 2111 | 11.67 | -60, -14, -16 | |
| | <i>Left anterior MTG</i> | | | 7.36 | -48, 8, -30 | |
| | <i>Right mid-MTG</i> | <0.001 | 1700 | 10.28 | 58, -10, -16 | |
| | <i>Right anterior MTG</i> | | | 8.46 | 42, 12, -34 | |
| | <i>Right AG</i> | <0.001 | 1664 | 9.98 | 52, -68, 26 | |
| | <i>vmPFC</i> | <0.001 | 2345 | 9.34 | -6, 56, -14 | |
| | <i>mPFC</i> | | | 7.69 | -8, 54, 40 | |
| | <i>Right OFC</i> | <0.001 | 556 | 8.13 | 34, 34, -16 | |
| | <i>medial OFC</i> | 0.011 | 137 | 6.55 | -4, 24, -12 | |
| | <i>Left hippocampus</i> | <0.001 | 236 | 6.08 | -20, -10, -16 | |
| | <i>Right dlPFC</i> | <0.001 | 336 | 5.93 | 44, 20, 26 | |
| | <i>Right hippocampus</i> | <0.001 | 268 | 5.91 | 20, -8, -14 | |
| | <i>Right FG</i> | <0.001 | 341 | 5.78 | 38, -38, -24 | |
| | <i>Left AG</i> | <0.001 | 998 | 5.71 | -38, -70, 42 | |
| | <i>Right dlPFC</i> | <0.001 | 280 | 4.97 | 46, 10, 48 | |
| | <i>Left dlPFC</i> | 0.001 | 195 | 4.47 | -38, 14, 42 | |
| | Place | <i>Right RSC</i> | <0.001 | 6881 | 22.33 | 14, -54, 16 |
| | | <i>Left RSC</i> | | | 21.22 | -14, -60, 20 |
| <i>Left PPA</i> | | | | 16.8 | -28, -42, 32 | |
| <i>Left TOS</i> | | | | 13.25 | -36, -82, -10 | |
| <i>Right PPA</i> | | <0.001 | 1090 | 12.95 | 28, -34, -18 | |
| <i>Right TOS</i> | | <0.001 | 1299 | 11.86 | 38, -76, 36 | |
| <i>Left mid-cingulate</i> | | <0.001 | 618 | 8.2 | -4, -36, 40 | |
| <i>Left premotor</i> | | <0.001 | 374 | 7.47 | -24, 8, 50 | |
| <i>Right premotor</i> | | <0.001 | 418 | 5.97 | 26, 16, 46 | |
| <i>Left posterior MTG</i> | | 0.034 | 107 | 4.81 | -54, -62, -10 | |
| <i>Left posterior MTG</i> | | <0.001 | 1104 | 9.03 | -54, -66, 0 | |
| <i>Left latFG</i> | | | | 7.76 | -48, -50, -18 | |
| <i>Left IFG</i> | | <0.001 | 326 | 8.03 | -44, 34, 10 | |
| <i>Right IFG</i> | | <0.001 | 235 | 7.82 | 44, 38, 8 | |
| Object | <i>SMG</i> | <0.001 | 379 | 7.23 | -56, -32, 34 | |
| | <i>Left perirhinal</i> | 0.015 | 129 | 6.26 | -32, -10, -38 | |
| | <i>Left OFC</i> | 0.028 | 112 | 7.75 | -30, 38, -8 | |
| | <i>Right latFG</i> | <0.001 | 299 | 5.06 | 48, -44, -18 | |
| | <i>Right posterior MTG</i> | | | 5.03 | 54, -66, 0 | |
| | Scholastic | <i>Left IFG</i> | <0.001 | 872 | 6.52 | -52, 26, 2 |
| | | <i>Left MTG</i> | <0.001 | 1050 | 6.51 | -64, -50, 4 |
| | | <i>Right MTG</i> | <0.001 | 502 | 5.14 | 58, -38, 8 |

For large clusters spanning multiple regions, local maxima are listed separately. Italicized regions are incorporated in subsequent ROI analyses. AG, Angular gyrus; dlPFC, dorsolateral PFC; latFG, lateral fusiform gyrus; SMG, supramarginal gyrus.

successful access, this effect was enhanced in vmPFC, indicating that this region may play a particular role in successful semantic access. Analysis of unsuccessful access compared with knowledge-absent trials revealed a role of the IFG of both scholastic and object networks in the unsuccessful semantic access, consistent with the whole-brain analysis. Last, unlike other components of the place network, right PPA did not appear to be involved in unsuccessful semantic access.

Metacognitive judgments of knowledge confidence

To examine the neural correlates associated with the metacognitive judgment of the degree of confidence with which inaccessible knowledge was believed to be possessed, we compared ToTs and FoKs to unknown responses in the metacognitive stage of the trial. Both ToTs and FoKs activated prefrontal control regions bilaterally and medially (Fig. 7). There was a graded response, with greater responses to ToTs than FoKs. Specifically, all regions showing a response to FoKs also exhibited a response to ToTs, and activation of control circuitry was more expansive

for ToTs than FoKs and was significantly stronger in bilateral IFG and the right middle frontal gyrus (MFG), indicating that it was possible to distinguish ToT from FoK states within the current paradigm. ToTs additionally activated representational components of the semantic system in the lateral mid-MTG bilaterally and the left temporoparietal junction. Despite longer reaction times for FoKs than ToTs, no region responded more strongly to FoKs than ToTs, indicating that these effects are not driven by reaction time differences or general level of difficulty.

Influence of the inclusive mask on reported results

The inclusive mask was included to clarify the exposition of these results and focus analyses on regions previously implicated in semantic processes and did not impact the statistical significance of any reported results. While excluded regions were predominantly centered in reward regions (caudate, insula, substantia nigra), the mask did diminish the extent of some clusters. In particular, when unsuccessful access was compared with knowledge-absent trials, the dmPFC cluster was more extensive and the RSC/PPA cluster extended posteriorly into the lingual gyri and cuneus. Comparing successful to unsuccessful access, additional clusters were evident in sensorimotor cortices, the posterior planum temporale, and cerebellum. These clusters were associated with a deactivation compared with fixation baseline and may result from faster reaction times for successful than unsuccessful access judgments. Notably, these clusters did not persist when successful access > knowledge-absent trials (which were matched for RT) were included as a conjunction. Locations, significance, and extent of all excluded clusters are presented here: <https://figshare.com/s/194aa97ca67800f4c658>.

Discussion

In this work, we examined the neural processes underlying successful and unsuccessful access to stored semantic knowledge. Using this paradigm, we were able to identify neural processes associated with the search for possessed knowledge and those involved in access to the relevant piece of factual information. The internal search for factual knowledge was associated with the activation of both prefrontal circuitry associated with semantic control and the recruitment of cortical regions traditionally associated with place-related processing. Successful access was associated with increased activation in representational subcomponents of the semantic system.

Recruitment of semantic control systems during successful and unsuccessful semantic access

Relative to knowledge-absent trials, unsuccessful attempts at semantic access resulted in increased activation in regions consistently implicated in semantic control: opercular and triangular sections of the IFG, and the dmPFC-SMA, consistent with a cognitive process where attempts are being made to guide selection toward the elusive lexicosemantic representation. While whole-brain analysis showed minimal difference between successful and unsuccessful access, ROI analysis indicated increased recruitment of the pars orbitalis during successful semantic access and the dmPFC-SMA during blocked access. A more general role for the dmPFC-SMA in cognitive control may partially account for the observed dissociation. The dmPFC-SMA ROI falls within the multiple-demand network, while the left IFG ROIs do not (Fedorenko et al., 2013) and dmPFC-SMA shows parametric modulation by both working memory and semantic control demands, while left

Table 3. Significance, extent, and location of regions during the recall event, as shown in Figure 7

| | ToT > knowledge-absent | | | | FoK > knowledge-absent | | | | Tot > FoK | | | |
|-------------------|------------------------|--------|------|----------------|------------------------|--------|------|----------------|------------------|--------|------|----------------|
| | Cluster | | Peak | | Cluster | | Peak | | Cluster | | Peak | |
| | $p_{(FWE-corr)}$ | Voxels | t | x, y, z (mm) | $p_{(FWE-corr)}$ | Voxels | t | x, y, z (mm) | $p_{(FWE-corr)}$ | Voxels | t | x, y, z (mm) |
| Left IFG | <0.001 | 2027 | 8.69 | −50, 18, 0 | <0.001 | 1099 | 5.07 | −52, 16, 4 | <0.001 | 530 | 4.58 | −50, 18, 0 |
| Left anterior IFG | | | 7.2 | −44, 42, −4 | | | 5.84 | −44, 42, 0 | | | | |
| dmPFC-SMA | 0.001 | 191 | 6.8 | 2, 26, 46 | 0.003 | 165 | 5.93 | −4, 18, 50 | | | | |
| Left anterior PFC | 0.017 | 120 | 7.05 | −40, 52, 4 | 0.027 | 109 | 5.09 | −3, 2, 60, 6 | | | | |
| Left premotor | <0.001 | 610 | 6.9 | −42, 10, 38 | <0.001 | 469 | 5.69 | −38, 8, 42 | | | | |
| Right MFG | <0.001 | 2193 | 6.73 | 46, 22, 32 | <0.001 | 288 | 4.93 | 44, 40, 28 | | | | |
| Right IFG | | | 6.41 | 40, 24, −8 | 0.022 | 114 | 5.03 | 40, 24, −8 | <0.001 | 586 | 4.49 | 42, 40, 2 |
| Left IPS | <0.001 | 1297 | 6.68 | −48, −48, 48 | <0.001 | 784 | 5.87 | −26, −56, 38 | | | | |
| Right mid-MTG | <0.001 | 628 | 6.75 | 46, −30, −2 | | | | | <0.001 | 443 | 5.81 | 54, −28, −2 |
| Left mid-MTG | <0.001 | 855 | 6.13 | −60, −36, −6 | | | | | 0.003 | 163 | 4.27 | −58, −34, −6 |
| Right IPS | 0.014 | 125 | 4 | 44, −60, 52 | | | | | | | | |
| Left cerebellum | 0.002 | 173 | 6.35 | −32, −62, −32 | | | | | | | | |
| Left cerebellum | 0.044 | 97 | 6.82 | −8, −78, −30 | | | | | | | | |
| Left TPJ | | | | | | | | | 0.004 | 161 | 4.18 | −54, −44, 32 |
| Right TPJ | | | | | | | | | 0.036 | 102 | 4.43 | 60, −54, 20 |

For large clusters spanning multiple regions, local maxima are listed separately. IPS, Intraparietal sulcus.

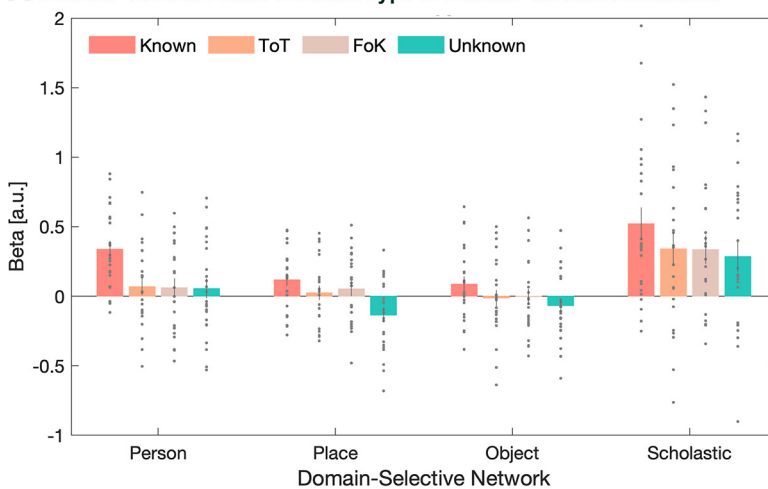
IFG exhibits modulation only by semantic control demands (Gao et al., 2021). These suggest a relatively more diverse role in cognitive control in dmPFC-SMA, which may be involved in additional extrasemantic working memory and control processes associated with blocked semantic access (Maril et al., 2005). On the other hand, the orbitalis may be more closely linked to semantic, and potentially lexical, processes, possibly through a perisylvian language-supported semantic subsystem (Xu et al., 2016, 2017).

Further recruitment of control systems in the subsequent metacognitive judgment were observed in the present study. ToT and FoK judgment activated prefrontal systems more than knowledge-absent judgments. As in previous work, this occurred in a graded manner, with ToT judgments producing greater responses than FoK judgments (Maril et al., 2005). These effects extended beyond classically semantic prefrontal regions to the right IFG, MFG, and anterior PFC, consistent with previous studies and potentially reflecting additional prefrontal cognitive processes, such as response selection or conflict resolution (Maril et al., 2001, 2005).

Increased recruitment of representational semantic regions in successful semantic access

Compared with unsuccessful semantic access, successful access resulted in the increased recruitment in cortical regions previously associated with domain-general semantic representation, specifically, bilateral mid-MTG, the left angular gyrus, and vmPFC (Binder et al., 2009; Lambon-Ralph et al., 2017). The greatest increase was seen in vmPFC, a region

A Domain-General Effect of Recall Type in Domain-Selective Networks



B Response to Preferred and Non-Preferred Stimulus Domains

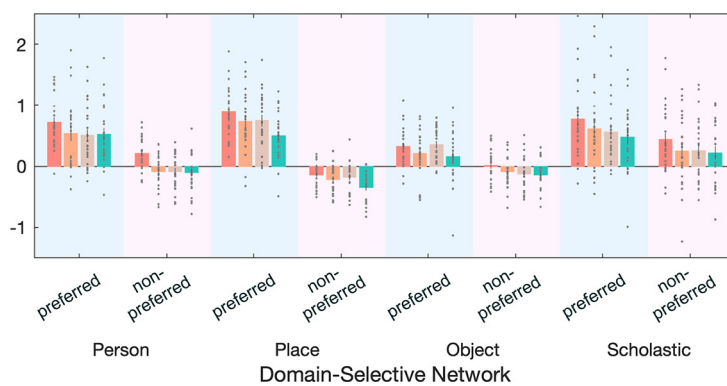


Figure 6. Effect of recall type within knowledge domain-selective cortical networks. **A**, Effect of recall type for all stimulus domains. **B**, Effect of recall type for the preferred (e.g., person-related questions in person-selective regions) and nonpreferred stimulus domains of each network (e.g., the average of place-, object-, scholastic-related questions in person-selective regions). Error bars indicate ± 1 SEM. Dots indicate the regional fMRI response of individual participants in each condition.

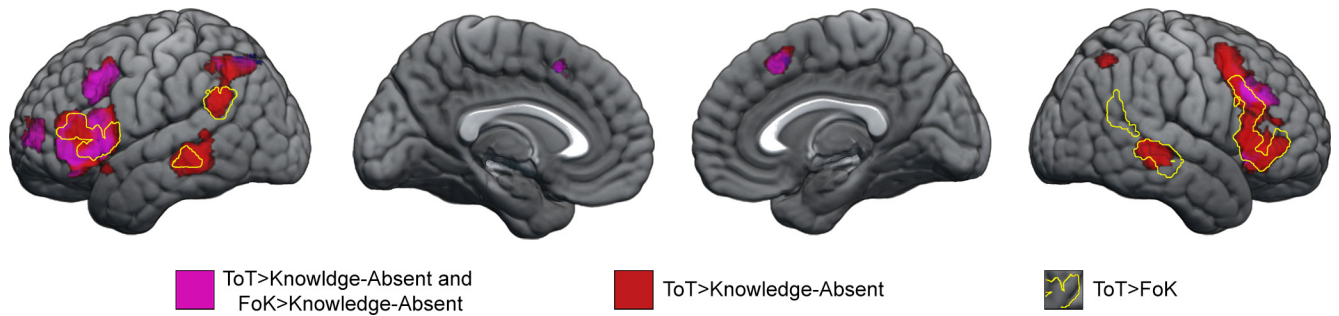


Figure 7. Whole-brain analysis of metacognitive judgment comparing ToT, FoK, and knowledge-absent responses. Brain maps are initially thresholded at a voxel-wise threshold of $p < 0.001$ and cluster-level corrected $p_{FWE} < 0.05$ (Table 3, significance, extent, and location of clusters).

that also exhibited statistically stronger increases than other elements of the person-selective network. The reason for the more pronounced involvement of this region in successful semantic access is uncertain but may stem from the role of this region in higher-level semantic representation (Frankland and Greene, 2020; Acunzo et al., 2022). Encompassing these regions and extending over additional temporal, parietal, and prefrontal areas, we observed robust selectivity for the four knowledge domains that were used, to a much greater extent than is seen with single-word stimuli (Fairhall and Caramazza, 2013a). This pronounced sensitivity of sentence-level stimuli to knowledge domain is consistent with the effects seen in previous work (Rabini et al., 2021) but notably were extended to show a person-selective response in a section of the right lateral fusiform gyrus anatomically overlapping the fusiform face area, a region that seldom shows person selectivity for person-related word stimuli (Bi et al., 2016), and an object-selective response in perirhinal cortex, a region showing multivariate sensitivity to the semantic relationship between objects (Bruffaerts et al., 2013; Liuzzi et al., 2015). The scholastic knowledge domain selectively activated core regions of the semantic system that were either implicated in control (left IFG) or in semantic representation (bilateral mid-MTG; Lambon-Ralph et al., 2017). Selective recruitment of left IFG is certainly consistent with scholastic information requiring additional control, and IFG ROIs within both scholastic and object-selective networks showed distinct increases during unsuccessful-access trials. However, the tiled nature of selectivity for scholastic, person, and object knowledge domains across the left and right IFG makes it unlikely that this reflects overall differences in demands for semantic control. This pattern may indicate partial representation of semantic content within these regions or that semantic control systems are anatomically organized into subsystems that interact with different domain-selective semantic representations.

The influence of semantic access within these domain-selective regions is complex but informative. In an ROI analysis, we compared the fMRI response averaged across key elements of networks exhibiting a selective response for person, place, object, and scholastic knowledge domains. While all networks showed overall increases in activity during successful compared with unsuccessful semantic access, in networks selective for person, object, and scholastic knowledge domains, this effect was present for both preferred and non-preferred domains and was enhanced for the non-preferred domain, and this pattern persists in networks that are inactive for the non-preferred categories relative to baseline during unsuccessful-access or knowledge-absent trials (i.e., place and

object networks; Fig. 6B). Thus, while it may be intuitive to expect increases associated with semantic access to be domain selective in domain-selective networks, the data indicate that successful access is associated with a relative broadening of the accessed semantic representations—increased recruitment of representational regions selective for both the preferred and non-preferred domain. One cognitive interpretation of this broadening is that successful access to the fact results in access to knowledge that is not only specific to the domain but also brings with it a generalized set of associated knowledge extending to other knowledge domains. The place-selective network represented an exception to this pattern. In addition to showing a selective increase in response to place stimuli, these regions showed greater responses to unsuccessful-access trials than knowledge-absent trials, for both preferred and non-preferred domains. This indicates that, unlike the other knowledge domain-selective regions, PPA, TOS, and RSC are involved in searching for the knowledge. These regions are implicated in knowledge-based navigation, such as locating a particular street within a university campus (Epstein et al., 2007) or locating a particular city, the provenance of a famous person, or even a traditional food-dish within a country (Fairhall, 2020), and in making semantic judgments about kinds of people (e.g., professions; Fairhall and Caramazza, 2013b). The present result extends the particular profile of place-selective semantic regions to show that they are also involved in the search for semantic information, both when access is successful and when the searched-for-fact is elusive. The reason for the particular involvement of these scene-selective and spatially selective regions in the search for knowledge is uncertain. An increasing body of evidence has emerged to suggest that neural mechanisms for spatial navigation in the entorhinal cortex (“grid cells”) are repurposed to allow navigation across nonspatial dimensions, such as olfactory or pitch spaces (Aronov et al., 2017; Bao et al., 2019) and extending to navigation across certain conceptual spaces (Constantinescu et al., 2016; for review, see Bottini and Doeller, 2020; Viganò and Piazza, 2020). One intriguing possibility is that the involvement of place-selective regions in navigation to complex factual information is derived via the interdependence between these regions and entorhinal cortices in spatial processing. However, this is an unexpected and preliminary finding, and future work is needed to determine whether these results reflect navigation across conceptual spaces.

Lexical access may contribute to the observed cortical activations, both when the answer is successfully accessed, and in unsuccessful-access trials in the form of partial

lexical information (Brown and McNeill, 1966; Brown, 1991; Caramazza and Miozzo, 1997). Internally guided lexical access in verbal fluency paradigms (retrieving words starting with a specific letter or from a specific semantic category) predominantly recruit IFG and dmPFC (Wagner et al., 2014), while picture-cued lexical access may additionally recruit posterior aspects of the inferior/middle temporal gyri and superior temporal sulcus when lexical access is more challenging (Price, 2012). Lexical (as well as semantic) processes may influence responses in these regions. On the other hand, increased responses in place-selective PPA, RSC, and TOS, and other, particularly right hemispheric, knowledge domain-selective regions are less likely to reflect lexical processes. However, lexical and semantic processes are deeply entangled in the brain, and the results reported here are best considered as “lexicosemantic” in nature. Future studies are needed to better decouple the contributions of lexical and semantic processes from the current results.

In this work, we sought to determine the processes that distinguish successful and unsuccessful semantic retrieval. By proxy, this approach allowed us to dissociate the neural processes associated with the search for a piece of knowledge from access to that knowledge. We observed that prefrontal semantic control regions are involved in the search for information and are supported by cortical regions involved in scene and spatial knowledge (PPA, TOS, and RSC) for all stimulus domains. We saw that access to knowledge recruits representational systems and does so broadly, recruiting both regions selective for the relevant knowledge domain and those selective for other domains. Collectively, these results suggest that prefrontal semantic control systems and classical spatial knowledge-selective regions work to locate relevant information and that access to a fact brings with it a broad range of associated memories incorporating other knowledge domains, rather than a narrowing to retrieved information to that most relevant to the specific knowledge domain.

References

- Aruno DJ, Low DM, Fairhall SL (2022) Deep neural networks reveal topic-level representations of sentences in medial prefrontal cortex, lateral anterior temporal lobe, precuneus, and angular gyrus. *Neuroimage* 251:119005.
- Aronov D, Nevers R, Tank DW (2017) Mapping of a non-spatial dimension by the hippocampal-entorhinal circuit. *Nature* 543:719–722.
- Bao X, Gjorgieva E, Shanahan LK, Howard JD, Kahnt T, Gottfried JA (2019) Grid-like neural representations support olfactory navigation of a two-dimensional odor space. *Neuron* 102:1066–1075.e5.
- Bi Y, Wang X, Caramazza A (2016) Object domain and modality in the ventral visual pathway. *Trends Cogn Sci* 20:282–290.
- Binder JR, Desai RH, Graves WW, Conant LL (2009) Where is the semantic system? A critical review and meta-analysis of 120 functional neuroimaging studies. *Cereb Cortex* 19:2767–2796.
- Bottini R, Doeller CF (2020) Knowledge across reference frames: cognitive maps and image spaces. *Trends Cogn Sci* 24:606–619.
- Brown AS (1991) A review of the tip-of-the-tongue experience. *Psychol Bull* 109:204–223.
- Brown R, McNeill D (1966) The “tip of the tongue” phenomenon. *J Verbal Learning Verbal Behav* 5:325–337.
- Bruffaerts R, Dupont P, Peeters R, De Deyne S, Storms G, Vandenberghe R (2013) Similarity of fMRI activity patterns in left perirhinal cortex reflects semantic similarity between words. *J Neurosci* 33:18597–18607.
- Caramazza A, Miozzo M (1997) The relation between syntactic and phonological knowledge in lexical access: evidence from the “tip-of-the-tongue” phenomenon. *Cognition* 64:309–343.
- Carreiras M, Mechelli A, Price CJ (2006) Effect of word and syllable frequency on activation during lexical decision and reading aloud. *Hum Brain Mapp* 27:963–972.
- Constantinescu AO, O’Reilly JX, Behrens TEJ (2016) Organizing conceptual knowledge in humans with a gridlike code. *Science* 352:1464–1468.
- Epstein RA, Parker WE, Feiler AM (2007) Where am I now? Distinct roles for parahippocampal and retrosplenial cortices in place recognition. *J Neurosci* 27:6141–6149.
- Fairhall SL (2020) Cross recruitment of domain-selective cortical representations enables flexible semantic knowledge. *J Neurosci* 40:3096–3103.
- Fairhall SL, Caramazza A (2013a) Brain regions that represent amodal conceptual knowledge. *J Neurosci* 33:10552–10558.
- Fairhall SL, Caramazza A (2013b) Category-selective neural substrates for person- and place-related concepts. *Cortex* 49:2748–2757.
- Fedorenko E, Duncan J, Kanwisher N (2013) Broad domain generality in focal regions of frontal and parietal cortex. *Proc Natl Acad Sci U[S]A* 110:16616–16621.
- Fernandino L, Binder JR, Desai RH, Pendl SL, Humphries CJ, Gross WL, Conant LL, Seidenberg MS (2015) Concept representation reflects multimodal abstraction: a framework for embodied semantics. *Cereb Cortex* 26:2018–2034.
- Fiebach CJ, Friederici AD, Müller K, Von Cramon DY (2002) fMRI evidence for dual routes to the mental lexicon in visual word recognition. *J Cogn Neurosci* 14:11–23.
- Frankland SM, Greene JD (2020) Concepts and compositionality: in search of the brain’s language of thought. *Annu Rev Psychol* 71:273–303.
- Friston KJ, Rotshtein P, Geng JJ, Sterzer P, Henson RN (2006) A critique of functional localisers. *Neuroimage* 30:1077–1087.
- Gao Z, Zheng L, Chiou R, Gouws A, Krieger-Redwood K, Wang X, Varga D, Ralph MAL, Smallwood J, Jefferies E (2021) Distinct and common neural coding of semantic and non-semantic control demands. *Neuroimage* 236:118230.
- Hart TJ (1965) Memory and the feeling-of-knowing experience. *J Educ Psychol* 56:208–216.
- Jackson RL (2021) The neural correlates of semantic control revisited. *Neuroimage* 224:117444.
- Kikyo H, Ohki K, Miyashita Y (2002) Neural correlates for feeling-of-knowing. *Neuron* 36:177–186.
- Lambon-Ralph MA, Jefferies E, Patterson K, Rogers TT (2017) The neural and computational bases of semantic cognition. *Nat Rev Neurosci* 18:42–55.
- Liuzzi AG, Bruffaerts R, Dupont P, Adamczuk K, Peeters R, De Deyne S, Storms G, Vandenberghe R (2015) Left perirhinal cortex codes for similarity in meaning between written words: comparison with auditory word input. *Neuropsychologia* 76:4–16.
- Liuzzi AG, Bruffaerts R, Peeters R, Adamczuk K, Keuleers E, De Deyne S, Storms G, Dupont P, Vandenberghe R (2017) Cross-modal representation of spoken and written word meaning in left pars triangularis. *Neuroimage* 150:292–307.
- Liuzzi AG, Aglinskis A, Fairhall SL (2020) General and feature-based semantic representations in the semantic network. *Sci Rep* 10: 8931.
- Liuzzi AG, Ubaldi S, Fairhall SL (2021) Representations of conceptual information during automatic and active semantic access. *Neuropsychologia* 160:107953.
- Lydling V, Stemle E, Borghetti C, Brunello M, Castagnoli S, Dell’Orletta F, Dittmann H, Lenci A, Pirrelli V (2014) The PAISA Corpus of Italian Web Texts. In *Proceedings of the 9th Web as Corpus Workshop* (Bildhauer, Felix & Schäfer, Roland, eds): pp 38–43, Gothenburg, Sweden.
- Maril A, Wagner AD, Schacter DL (2001) On the tip of the tongue: an event-related fMRI study of semantic retrieval failure and cognitive conflict. *Neuron* 31:653–660.
- Maril A, Simons JS, Weaver JJ, Schacter DL (2005) Graded recall success: an event-related fMRI comparison of tip of the tongue and feeling of knowing. *Neuroimage* 24:1130–1138.

- Price CJ (2012) A review and synthesis of the first 20 years of PET and fMRI studies of heard speech, spoken language and reading. *Neuroimage* 62:816–847.
- Rabini G, Ubbaldi S, Fairhall SL (2021) Combining concepts across categorical domains: a linking role of the precuneus. *Neurobiol Lang (Camb)* 2:354–371.
- Rubin TN, Koyejo O, Gorgolewski KJ, Jones MN, Poldrack RA, Yarkoni T (2017) Decoding brain activity using a large-scale probabilistic functional-anatomical atlas of human cognition. *PLoS Comput Biol* 13:e1005649.
- Schacter DL (1999) The seven sins of memory: insights from psychology and cognitive neuroscience. *Am Psychol* 54:182–203.
- Schuster S, Hawelka S, Hutzler F, Kronbichler M, Richlan F (2016) Words in context: the effects of length, frequency, and predictability on brain responses during natural reading. *Cereb Cortex* 26:3889–3904.
- Viganò S, Piazza M (2020) Distance and direction codes underlie navigation of a novel semantic space in the human brain. *J Neurosci* 40:2727–2736.
- Wagner S, Sebastian A, Lieb K, Tüscher O, Tadić A (2014) A coordinate-based ALE functional MRI meta-analysis of brain activation during verbal fluency tasks in healthy control subjects. *BMC Neurosci* 15:19.
- Xu Y, Lin Q, Han Z, He Y, Bi Y (2016) Intrinsic functional network architecture of human semantic processing: modules and hubs. *Neuroimage* 132:542–555.
- Xu Y, He Y, Bi Y (2017) A tri-network model of human semantic processing. *Front Psychol* 8:1538.
- Yarkoni T, Poldrack RA, Nichols TE, Van Essen DC, Wager TD (2011) Large-scale automated synthesis of human functional neuroimaging data. *Nat Methods* 8:665–670.