The neural and computational bases of semantic cognition

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Abstract | Semantic cognition refers to our ability to use, manipulate and generalize knowledge that is acquired over the lifespan to support innumerable verbal and non-verbal behaviours. This Review summarizes key findings and issues arising from a decade of research into the neurocognitive and neurocomputational underpinnings of this ability, leading to a new framework that we term controlled semantic cognition (CSC). CSC offers solutions to long-standing queries in philosophy and cognitive science, and yields a convergent framework for understanding the neural and computational bases of healthy semantic cognition and its dysfunction in brain disorders.

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Semantic cognition refers to the collection of neurocognitive mechanisms that support semantically imbued behaviours. We deploy our semantic knowledge not only to produce and understand language but also to support many non-verbal behaviours. Indeed, semantic knowledge transforms the sensory cacophony into a symphony of meaning, allowing us to recognize and make inferences about objects and events in the environment, and it provides the foundation for everyday behavioural acts. To spread jam on bread, for example, one must recognize the jam jar, the bread and the knife, infer their unobserved qualities (for example, bread is soft, knives are rigid and jam is sticky) and deploy the appropriate praxis (seizing the knife handle with a particular grip to allow the jam to be scooped out) — all tasks that require knowledge about both the objects and the actions. Accordingly, patients with semantic impairment as a result of brain disease have marked language and non-verbal disabilities that profoundly disrupt their everyday lives.

This Review examines a decade of research suggesting that semantic cognition relies on two principal interacting neural systems. The first system is one of representation, which encodes knowledge of concepts through the learning of the higher-order relationships among various sensory, motor, linguistic and affective sources of information that are widely distributed in the cortex. Conceptual representations are distilled within this system from lifelong verbal and non-verbal experience[1–4], and serve to promote knowledge generalization across items and contexts[5–7]. The second system is one of control, which manipulates activation within the representational system to generate inferences and behaviours that are appropriate for each specific temporal or task context[8–12]. We refer to this two-system view as the controlled semantic cognition (CSC) framework. In what follows, we review the converging evidence for each part of the CSC framework and consider how it reconciles long-standing puzzles from studies of both healthy and disordered semantic cognition.

Semantic representation

The hub-and-spoke theory

Around a decade ago, we and others proposed the 'hub-and-spoke' theory of semantic representation[6,7] (FIG. 1), which explained how conceptual knowledge might arise through learning about the statistical structure of our multimodal experiences[10], and also proposed some neuroanatomical underpinnings for these abilities, accounting for patterns of impairment that are observed in some semantic disorders[7,13]. The hub-and-spoke theory assimilated two important, existing ideas. First, in keeping with Meynert and Wernicke's classical proposal[14] and contemporary 'embodied' theories[1,15] (BOX 1), the hub-and-spoke model assumed that multimodal verbal and non-verbal experiences provide the core 'ingredients' for constructing concepts and that these information sources are encoded in modality-specific cortices, which are distributed across the brain (the 'spokes')[1,16]. Second, the model proposed that cross-modal interactions for all modality-specific sources of information are mediated, at least in part, by a single transmodal hub that is situated bilaterally in the anterior temporal lobes (ATLs). This second idea runs counter to some classical hypotheses and to contemporary 'distributed-only' theories of semantic representation, which have assumed that concepts arise through direct connections among modality-specific regions without a common transmodal region.

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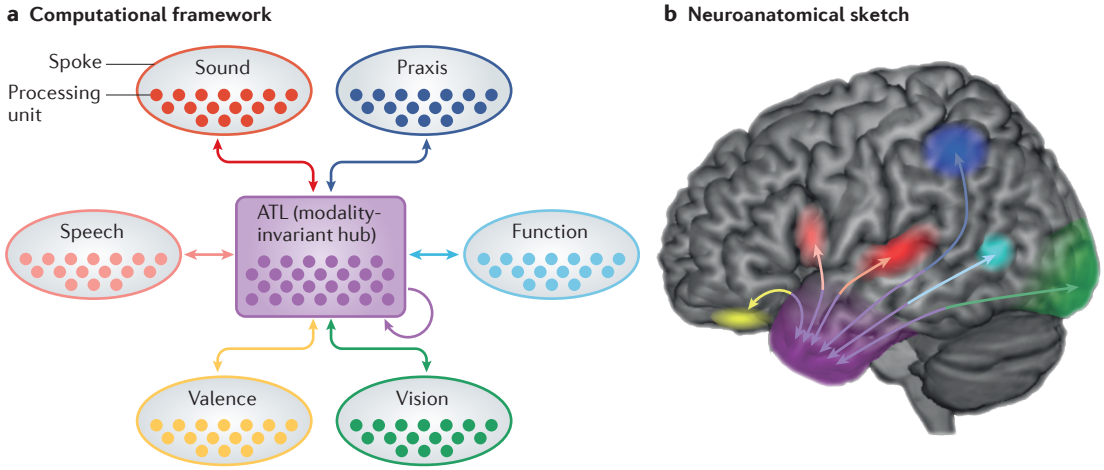

Figure 1 | **The original hub-and-spoke model. a** | The schematic illustrates the computational architecture for the original version of the hub-and-spoke model[7]. Modality-specific sources of information (spokes) are coded across a set of processing units within separate processing layers in the model. Each 'spoke' layer is reciprocally connected to a single transmodal 'hub'. The model is trained to take each of the spokes, in turn, as input and, through the hub, to reproduce the correct information across the other spokes. For example, the model is provided with the visual form of each item as input and is trained to reproduce the sounds, names, valence and other types of information that are associated with each item. The emergent result of this training is that the model forms generalizable semantic representations. The progressive, multimodal semantic impairment of patients with semantic dementia can be mimicked by gradually removing the hub connections. **b** | A neuroanatomical sketch of the location of the hub and spokes is presented. The hub is located within the anterior temporal lobe (ATL) region, whereas the modality-specific spokes are distributed across different neocortical regions (the same colour coding is used as for the computational model). Each spoke communicates bidirectionally with the ATL hub through short- and long-range white-matter connections (arrows). For examples of the multimethod convergent evidence for the crucial contribution of the ATL region in verbal and non-verbal semantic representation, as well as the representational division of labour across the hub and spokes, see Supplementary information S1,S3 and S5 (figures).

The ATL-hub view was motivated by both empirical and computational observations. The empirical motivation stemmed from cognitive neuropsychology. It was already known that damage to higher-order association cortices could produce striking transmodal semantic impairments, leading some researchers to propose the existence of multiple cross-modal 'convergence zones', possibly specialized to represent different conceptual domains[17]. However, a detailed study of the striking disorder called semantic dementia (SD)[18] (Supplementary information S1 (figure)) suggested that the ATL transmodal region might be important for all conceptual domains[19,20], as individuals with SD show semantic impairments across all modalities[21] and virtually all types of concept[13,22] (with the exception of simple numerical knowledge[23]). Several additional characteristics of the impairment in SD seem to be compatible only with disruption of a central, transmodal hub in this disorder. Notably, individuals with SD show markedly consistent patterns of deficits across tasks, despite wide variation in the modality of stimulus, response or type of knowledge required. Indeed, the likelihood that patients with SD correctly respond to a given item in a task requiring semantic knowledge can be consistently predicted by a combination of three factors: the familiarity of the item (high familiarity leads to better performance; Supplementary information S1 (figure)), the typicality of the item within a domain (typical items are associated with better performance; Supplementary information S2 (figure)) and the specificity of the knowledge that is required by the task (high specificity leads to worse performance)[24,25]. Unlike some forms of dementia (such as Alzheimer disease) that are associated with widespread pathology in the brain[26], SD is associated with atrophy and hypometabolism that are centred on the anterior ventral and polar temporal regions bilaterally[27,28] (Supplementary information S1 (figure)), suggesting that these regions serve as the transmodal domain-general conceptual hub.

Computationally, the hub-and-spoke hypothesis provided a solution to the challenges of building coherent, generalizable concepts that have been highlighted in philosophy[29] and cognitive science[30–32] (for a more detailed discussion, see REFS 5,10,33). One challenge is that the information relevant to a given concept is experienced across different verbal and sensory modalities, contexts and time points. Another challenge is that conceptual structure is not transparently reflected in the sensory, motor or linguistic structure of the environment — instead, the relationship between conceptual structure and modality-specific features is complex, variable and nonlinear[5,20]. It is difficult to see how these challenges could be met by a system that simply encodes direct associations among the modality-specific information sources, but they can be solved by neural network models that adopt an intermediating hub for all concepts and modalities[10].

Concepts
Conceptual knowledge or semantic memory (typically treated as being synonymous terms in cognitive neuroscience) refers to our lifelong acquired, multimodal knowledge of, for example, objects, people, facts and words.

Semantic dementia
(SD). This is the temporal lobe variant of frontotemporal dementia and is characterised by progressive but relatively selective degradation of semantic knowledge and by hypometabolism and atrophy that are centred on the anterior temporal lobe (this is always bilateral, although often asymmetrical early in the disease).

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Box 1 | **Relationship to the embodied and symbolic accounts of semantics**

Over many years, multiple disciplines (for example, philosophy, behavioural neurology, cognitive science and neuroscience) have grappled with the issue of concept formation. Two recurring, contrasting theoretical positions can be found in each of these disciplines. Embodied theories assume that concepts are a direct reflection of our accumulated knowledge from language, non-verbal experiences, or both. Such experiential knowledge is often referred to as 'features' and was called 'engrams' by the nineteenth century neurologists[14]. Whether these experiential features are crucial only at the point of acquiring or updating a concept and whether they have to be reactivated each time the concept is retrieved are unresolved issues in contemporary embodied theories of semantic memory[15]. The alternative symbolic theories are based on the observation that features alone are insufficient for the formation of coherent, generalizable concepts, which might require manipulable, experientially independent symbols[143]. Although these symbolic theories provide an account for sophisticated concept processing and generalization, the solution fails to explain how concepts and their associated experiential features are linked or the genesis of the concepts themselves. Partially unifying theories have been proposed in philosophy[29] and cognitive science[31,32,144] that embrace the importance and centrality of verbal and non-verbal experience to concept formation but also posit additional representations that can map features to concepts and generalize knowledge. Likewise, the proposition of cortical convergence zones[17] also contains a related idea: modality-independent regions provide 'pointers' to the correct modality-specific features for each concept. The hub-and-spoke theory extends these unifying theories by providing a neurocomputational account for how coherent, generalizable concepts are built from experience, how the complex, nonlinear mappings between features and concepts are learnt, and also the neural instantiation of the processes.

New discoveries about the ATL hub

Various brain regions have long been a target of research in semantics (BOX 2), but the ATL received little prior attention. Indeed, although individuals with SD were reported more than a century ago, the link between semantic impairment and ATL damage only became apparent with modern neuroimaging techniques[19]. Classical language models were based on patients with middle cerebral artery stroke, which is unlikely to damage the middle to ventral ATL (and bilaterally)[34]. Likewise, a bias has existed in functional MRI (fMRI) studies that, owing to various methodological issues, has led to consistent undersampling of activation in the middle and inferior ATL[35]. Since the initial ATL-hub proposal, the role of this region in semantic processing has been extensively studied using various methodologies. Together, this work corroborates and extends several predictions of the hub-and-spoke model and clarifies the anatomical organization and functioning of the ATL region.

The cross-modal hub is centred on the ventrolateral ATL. Key postulates of the original hub-and-spoke model have been validated using various methods (Supplementary information S1 (figure) and Supplementary information S3 (figure)). The ATLs are engaged in semantic processing irrespective of input modality (for example, words, objects, pictures or sounds) and conceptual categories[36–39]. Although the hub is more strongly engaged for more-specific concepts[40,41] (for example, Pekinese), it also supports basic (for example, dog) and domain-level (for example, animal) distinctions[39,42]. Both left and right ATLs are implicated in verbal and non-verbal semantic processing[43,44] (BOX 3). ATL function is semantically selective insofar as these regions are not engaged in equally demanding non-semantic tasks[36,40,45].

These methods also provide important information that cannot be extracted from SD studies alone. Indeed, distortion-corrected fMRI in healthy individuals, cortical grid-electrode stimulation and electrocorticography in neurosurgical patients, and ^{18}F-fluorodeoxyglucose positron emission tomography in patients with SD (FIG. 2) all indicate that the ventral–ventrolateral ATL is the cross-modal centre-point of the hub for multimodal naming[46–48] and comprehension[36,39,44,46]. Moreover, as predicted by the hub-and-spoke model, multivoxel pattern analyses of fMRI[49] and electrocorticography[50] data have shown semantic coding and representational merging of modality-specific information sources[51] in the same area (Supplementary information S4 (figure)). Furthermore, in the ventral ATL, detailed semantic information is activated from 250 ms post stimulus onset (Supplementary information S4 (figure)), whereas coarse, domain-level distinctions may be available earlier (~120 ms post stimulus onset)[46,52–54]. Inhibitory transcranial magnetic stimulation (TMS) of the lateral ATL produces domain-general semantic slowing, whereas TMS of 'spoke' regions produces a category-sensitive effect[42] (Supplementary information S5 (figure)) — confirming the importance of both hub and spokes in semantic representation. In healthy participants, ATL regions exhibit intrinsic connectivity (as detected by resting-state fMRI) with modality-specific brain areas, and, in SD patients, the level of comprehension accuracy reflects both the degree of ATL atrophy and the extent of reduction in hub–spoke functional connectivity[28]. This body of work suggests that the cross-modal hub is centred on the ventrolateral ATL and also corroborates core predictions of the hub-and-spoke view: namely, that this region has an important, predicted role in coordinating the communication among modality-specific 'spokes' and that, in so doing, it encodes semantic similarity structure among items.

The broader ATL is graded in its function. The original hub-and-spoke model said little about different ATL subregions, partly because the distribution of atrophy in SD is extremely consistent (being maximal in polar and ventral ATL regions)[55] (FIG. 2C). Likewise, there is little variation in patients' multimodal semantic impairments, apart from small effects that are linked to whether atrophy is more severe in the left or right ATL early in the course of the disease (BOX 3). New evidence indicates not only that the ventrolateral ATL is the centre-point of the hub (as reviewed above) but also that the function varies in a graded manner across the ATL subregions (FIG. 2A,B).

The first clue for graded functional variation comes from cytoarchitecture. Brodmann[56] divided the anterior temporal region into several different areas, and modern neuroanatomical techniques have generated finer differentiations[57]. However, Brodmann also noted that cytoarchitectonic changes in the temporal cortex were graded: "to avoid erroneous interpretations it should again be stated that not all these regions are demarcated from

Electrocorticography
Implanted grid or depth electrodes that are used to record local field potentials.

^{18}F-fluorodeoxyglucose positron emission tomography
An imaging technique that is used to measure the rate of glucose metabolism across the brain.

Transcranial magnetic stimulation
(TMS). Electromagnetic coils are placed over the scalp to stimulate the underlying cortex. The frequency, intensity and duration of pulses can be varied to induce inhibition or excitation.

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Box 2 | **How does the angular gyrus contribute to semantic cognition?**

Classical neurological models of language suggested that the multimodally connected angular gyrus (AG) is the key neural location for semantic concepts[145]. More recent proposals have suggested that there might be a division of labour between the anterior temporal lobe (ATL) and AG hubs, with the latter processing thematic or combinatorial semantics[137,146]. Accumulating evidence seems to render the role of the AG in semantic processing less rather than more clear. Most functional MRI studies of semantic tasks find little or no AG activation[147], although comparisons such as words versus non-words or concrete versus abstract concepts reliably generate differences in the AG[148,149]. A recent large-scale meta-analysis[112] revealed that several cognitive domains (episodic tasks, sentence syntax and number fact recall) positively activate the AG, but, consistent with its contribution to the default mode network[150], the AG demonstrates task-related deactivation for multiple domains including semantics. In addition and potentially importantly, the level of AG deactivation is correlated with task difficulty. Although, as expected, the ATL semantic region exhibits deactivation for non-semantic tasks and positive activation for semantic tasks, direct comparison of the default mode and semantic networks[45] revealed that the AG shows task-difficulty-correlated deactivation for both semantic and non-semantic tasks. These findings raise the possibility that previous demonstrations of greater AG activation for words over non-words, concrete over abstract concepts, meaningful over novel-word combinations or any other contrast of easy over hard tasks might reflect generic task-difficulty differential deactivation. This alternative hypothesis is consistent with the observation that, when task instructions were changed to make decisions about concrete items harder than decisions about abstract items, the typical AG-activation difference was reversed[151]. Future targeted studies need to explore the circumstances in which the AG contributes to semantic tasks and whether its contribution can be more properly characterised in terms of non-semantic aspects of processing.

each other by sharp borders but may undergo gradual transitions as, for example, in the temporal and parietal regions" (REF. 56). This observation is replicated in contemporary cytoarchitectonic investigations[57], which indicate potentially graded patterns of functional differentiation across the ATL region.

The second insight arises from structural and functional connectivity. Consistent with the hub-and-spoke model, major white-matter fasciculi in both human and non-human primates converge in ATL regions[58,59]; however, their points of termination are only partially overlapping, leading to graded partial differentiations in gross connectivity across ATL subregions[58–60]. For instance, the uncinate fasciculus connects the orbitofrontal cortex and pars orbitalis most strongly to the temporopolar cortex; other prefrontal connections through the extreme capsule complex preferentially terminate in superior ATL regions, as does the middle longitudinal fasciculus from the inferior parietal lobule; and the inferior longitudinal fasciculus connects most strongly to the ventral and ventromedial ATL. The effects of these partially overlapping fasciculus terminations are made more graded through the strong local U-fibre connections in the ATL[58]. A similar pattern of partially overlapping connectivity has also been observed in resting-state and task-active fMRI studies[61,62]: in addition to strong intra-ATL connectivity, the temporopolar cortex shows greatest functional connectivity to orbitofrontal areas; the inferolateral ATL exhibits most connectivity to frontal and posterior regions that are associated with controlled semantic processing; and the superior ATL connects most strongly to primary auditory and premotor regions.

U-fibre connections
Short-range white-matter fibres that connect two local, neighbouring areas. The profile of such fibres is often a 'U' shape — hence the name. Such fibres contrast with white-matter fasciculi, which comprise large bundles of white-matter fibres that connect distant regions.

Third, data from recent neuroimaging results (which have addressed methodological issues related to successful imaging of semantic tasks in the ATL region[35,63]) are highly consistent with a graded connectivity-driven model of ATL function (FIG. 2A). As noted above, the ventrolateral ATL activates strongly in semantic tasks irrespective of input modality or stimulus category[36,39,44,64]. Moving away from this centre-point, the cross-modal semantic function of the ATL becomes weaker and is more tied to a specific input modality (FIG. 2B). Thus, more medial ATL regions show greater responsiveness to picture-based materials and concrete concepts than to other types of material[44,65,66]. The anterior superior temporal sulcus (STS)–superior temporal gyrus (STG) exhibits the opposite pattern, with greater activation for auditory stimuli, spoken words and abstract concepts[39,65,67], and an overlapping region of the STG has been implicated in combinatorial semantic processes[68,69]. Last, polar and dorsal ATL areas have shown preferential activity for social over other kinds of concept[70,71].

One possible explanation for these graded functional variations is that multiple mutually exclusive ATL subregions are dedicated to different categories or representational modalities[17,72,73]. However, there are two problems with this view. First, it is not consistent with the cytoarchitectonic, connectivity and functional data, all of which suggest that the ATL exhibits graded functional specialization rather than discrete functional regions. Second, such an account does not explain the role of the hub, which seems to support knowledge across virtually all domains and modalities. An alternative view is that the ATL hub exhibits graded functional specialization[33,58,74,75] (FIG. 2), with the responsivity of different subregions reflecting graded differences in their connectivity to the rest of the network. On this view, the neuroimaging findings that were noted above reflect the fact that neighbouring ATL regions contribute somewhat more or less to the representation of different kinds of information, depending on the strength of their interactions with various modality-specific representational systems.

Such graded functional specialization arises directly from the influence of connectivity on function[58,76]. In a close variant of the hub-and-spoke model, Plaut[76] introduced distance-dependent connection strengths to the modality-specific spokes. The importance of each processing unit in the model to a given function depended on its connectivity strength to the spokes. Central hub units furthest from all inputs contributed equally to all semantic tasks; units that were anatomically closer to a given modality-specific spoke took part in all types of semantic processing but contributed somewhat more to tasks involving the proximal modality. For instance, hub units situated near to visual representations would contribute more to tasks like picture naming but less to non-visual tasks (for example, naming items in response to their characteristic sound). The graded hub hypothesis extends this proposal by assuming that ATL functionality is shaped by the long-range cortical connectivity (FIG. 2A). Thus, the medial ATL responds more to visual or concrete concepts by virtue of having greater connectivity to visual than to auditory or linguistic systems; the anterior

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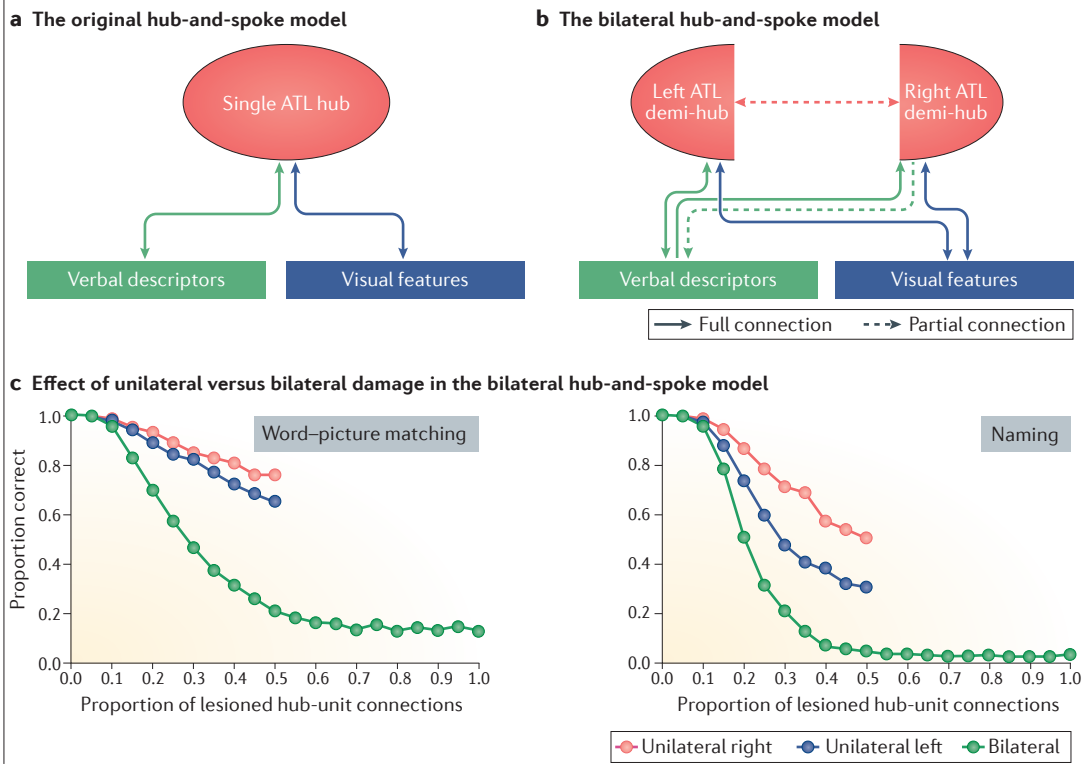
STS–STG contributes more to abstract concepts and verbal semantic processing by virtue of its greater connectivity to language than to visual systems; and the temporal pole contributes somewhat more to social concepts by virtue of its connectivity to networks that support social cognition and affect. The ventrolateral ATL remains important for all domains because it connects equally to these different systems.

We note here that this type of graded function is not unique to the ATL-hub region or semantic processing. Indeed, other cortical regions and types of processing (for example, the visual and auditory processing streams) also demonstrate graded functional profiles[77,78], which follow the underlying patterns of connectivity[79]. Connectivity-induced graded functions may therefore be a general principle, and information arriving at the ATL

Box 3 | **The bilateral ATL hub: role of left versus right ATL in semantic representation**

Individuals with semantic dementia always have bilateral anterior temporal lobe (ATL) atrophy (although, at least early in the disease course, the atrophy is often strikingly asymmetric) (Supplementary information S1 (figure)), suggesting that both left and right regions contribute to conceptualisation. Patients with unilateral ATL damage generally have much better semantic abilities than patients with bilateral ATL damage, although, with more sensitive assessments, semantic deficits following unilateral lesions can be observed[152–154], which is consistent with findings from left versus right ATL transcranial magnetic stimulation (TMS) studies[43]. Likewise, classical comparative neurological investigations revealed chronic multimodal semantic impairment in non-human primates after bilateral but not unilateral ATL resection[155,156], which was replicated in a rare human single-case neurosurgery study[157]. A bilateral version of the hub-and-spoke model explored these differences across patient groups[129]. The original model connected visual and verbal sources of information through a single transmodal hub (see the figure, part **a**). The new, bilateral model split this into two demi-hubs (to mimic left and right ATL regions) (see the figure, part **b**). This updated model demonstrated the same performance difference as patient and primate data — namely, that bilateral damage is more disabling than unilateral lesions, even when the volume of damage is equated[129] (see the figure, part **c**). There are currently different hypotheses regarding the contribution of each ATL to semantic representation[74,128,158,159]. One possibility is that a single functional transmodal hub might be supported by a bilateral, interconnected ATL neural network, making the resultant system robust to damage[129,160] and able to upregulate the contribution of and interaction with the contralateral ATL after unilateral damage, as demonstrated in combined TMS–functional MRI (fMRI) studies[130,131]. Neuropsychological studies also indicate that there may be important variations across the hemispheres in terms of input or output modality and category of information[159,161,162], with the most robust, reliable findings being that left ATL damage leads to greater anomia, whereas right ATL damage leads to greater prosopagnosia[153,161,162]. Furthermore, a recent large-scale fMRI meta-analysis indicated that the ATL-hub system seems to be primarily bilateral but with left hemisphere predilection for speech production and written word stimuli[75]. Following the connectivity-constrained-hub hypothesis (see the main text), this combination of a primarily bilateral system with graded asymmetries is captured by computational models that include a bilateral transmodal hub with graded differences in the white-matter connectivity to input and output systems[129,160]. Parts **b** and **c** are reprinted from REF. 129 by permission of the MIT Press.



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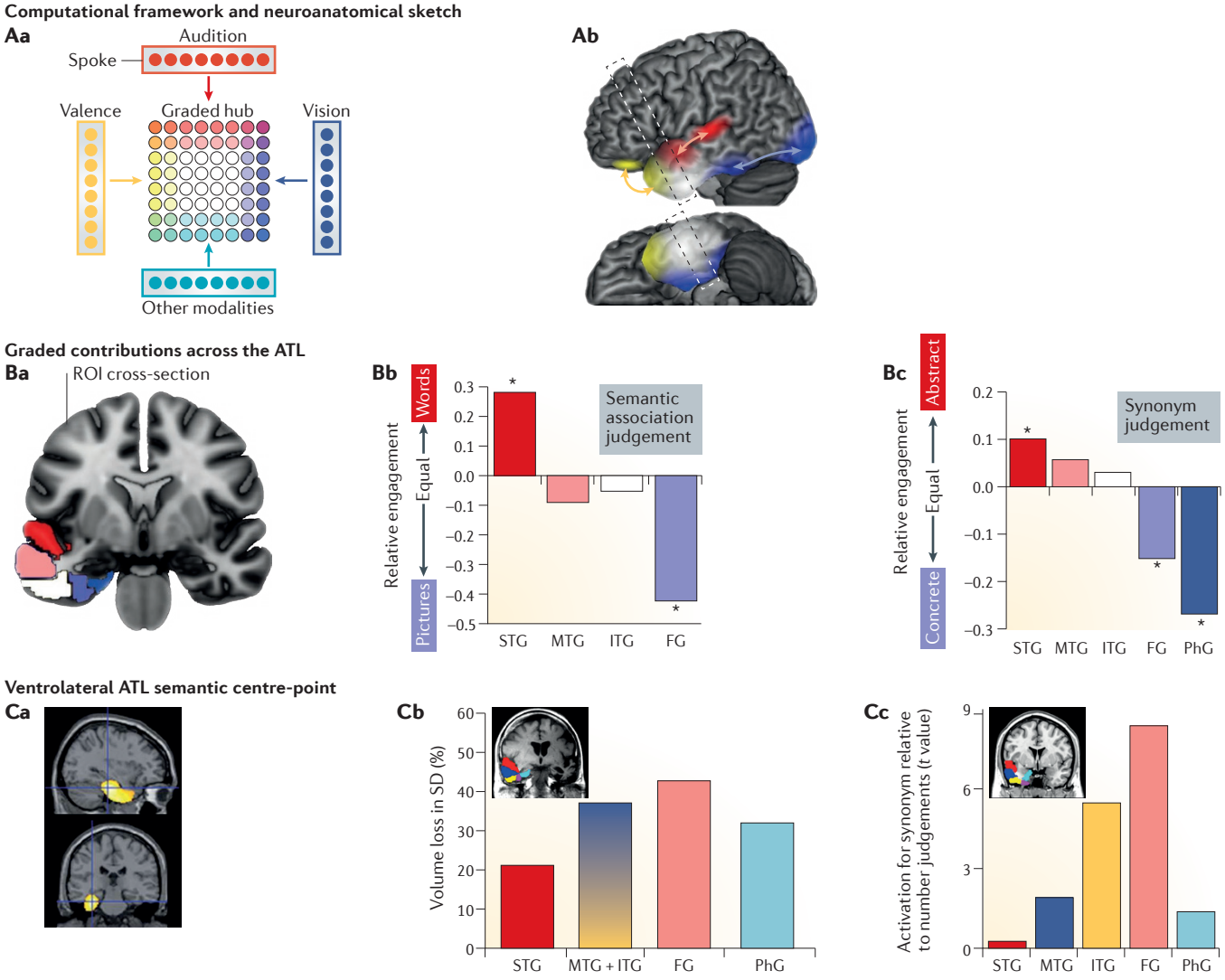

Figure 2 | **The graded ATL semantic hub. A** | These panels show the computational framework (part **Aa**) and a neuroanatomical sketch (part **Ab**) of the graded hub-and-spoke model[39,44,58,74]. The eight-by-eight unit grid of coloured circles represents a computational instantiation of the anterior temporal lobe (ATL) hub with reciprocal connectivity to the modality-specific spoke layers (each spoke layer is represented by a differently coloured strip of eight units). In the original hub-and-spoke model, all hub units made equal contributions to semantic representation irrespective of the modality of input. By contrast, in this updated model, the contribution of the hub units to semantic representation is gradedly different, reflecting the varying pattern of connectivity to the spoke layers (for example, the function of the hub units with stronger connection to the visual input layer (dark blue) becomes weighted towards this information source (denoted by the blue colour of these hub units). At the centre-point, there is equally weighted connectivity to all inputs, and thus the function of the units remains evenly transmodal (denoted by their white colour). The neuroanatomical figure sketches how this graded hub might map onto the human ATL. Three example input sources (orbitofrontal 'valence' (yellow); primary auditory cortex (red); and visual cortex (blue)) project (coloured arrows) into the ATL. The semantic function varies across the ATL according to the strength of these inputs: subregions closest to each input become tuned more to that information source (denoted by the corresponding colour), whereas the ventrolateral region (white) remains equally engaged by all input types. The dashed boxes represent the cross-sections that are shown in part **B**. **B** | These panels show empirical evidence for a graded ATL. The graded semantic differences across the ATL are shown in the coronal cross-section (part **Ba**): the superior temporal gyrus (STG) shows relatively greater semantic activation for words than for pictures and for abstract than for concrete words (parts **Bb**,**Bc**); the middle temporal gyrus (MTG) and inferior temporal gyrus (ITG) exhibit the strongest (see part **C**), and equal, involvement across modalities and categories of concept, whereas the contribution of the frontal gyrus (FG) is somewhat greater for pictures than words and for concrete than abstract words[44,65] (parts **Bb**,**Bc**). The asterisks denote an activation difference that is significantly greater from zero. **C** | The paramount importance of the ventrolateral ATL transmodal region to semantic function overall is shown. Hypometabolism in this region correlates with semantic function in patients with semantic dementia (SD)[47] (part **Ca**). Likewise, the greater contribution of ventrolateral regions (MTG, ITG and FG) to semantic processing is mirrored in the distribution of gyral atrophy in such individuals[55] (part **Cb**) and in the variation of semantic activation that is observed in distortion-corrected functional MRI (dc-fMRI) in healthy participants[36] (part **Cc**). PhG, parahippocampal gyrus; ROI, region of interest. Part **Ca** is adapted from Mion, M. *et al.*, What the left and right anterior fusiform gyri tell us about semantic memory, *Brain*, 2010, **133**, 11, 3256–3268, by permission of Oxford University Press. Parts **Cb** and **Cc** are adapted from Binney, R. J., Embleton, K. V., Jefferies, E., Parker, G. J. M. & Lambon Ralph, M. A., The ventral and inferolateral aspects of the anterior temporal lobe are crucial in semantic memory: evidence from a novel direct comparison of distortion-corrected fMRI, rTMS, and semantic dementia, *Cereb. Cortex*, 2010, **20**, 11, 2728–2738, by permission of Oxford University Press.

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hub has already been partially processed in these graded non-ATL regions and through the interaction between the ATL and modality-specific regions[52,80].

Category-specificity and the graded hub

Theories of semantic representation and its neural basis have been strongly influenced by two sets of neuropsychological and functional neuroimaging data, leading to two different theoretical positions. One literature has focused on the general semantic impairment that is observed in some types of brain disease, demonstrating largely equivalent disruption across types of knowledge. Such data support proposals — including the hub-and-spoke model — that the cortical semantic system is widely distributed and interactive but needs a transmodal component to capture coherent, generalizable concepts[5,7]. The second literature focuses on 'category-specific' variations in performance in which different categories of knowledge can be differentially disrupted in neurological disorders or yield differential activation in specific healthy brain regions. Perhaps the most commonly studied, although by no means the sole, contrast is between living things versus man-made items[81,82]. Such evidence has been used to argue that anatomically distinct and functionally independent neural systems have evolved to support knowledge about different conceptual domains (for example, animals, tools, faces and scenes)[83,84].

Recent empirical and computational investigations have enhanced the hub-and-spoke framework into a unified theory that may account for both sets of data. In the neuropsychological literature, several large case-series investigations provide contrastive patterns of semantic impairment and clear information about critical neural regions. For example, patients with SD with bilateral ATL atrophy have generalized semantic impairment and largely similar performance levels across different categories of knowledge (once other important performance factors, especially stimulus familiarity and typicality, are controlled)[25,85]. By contrast, patients with posterior ventral occipito-temporal lesions can present with relatively poor identification of natural kinds[86], and patients with anteromedially centred temporal-lobe damage following an acute period of herpes simplex virus encephalitis (HSVE) show strikingly poorer knowledge of natural kinds than of man-made items[13,87]. Last, patients with temporo-parietal damage show greatest deficits for praxis-related man-made items[88,89]. These contrastive behavioural–anatomical associations for general versus category-specific semantic impairments find counterparts in convergent evidence from other techniques, including functional neuroimaging and inhibitory TMS in healthy participants and cortical electrode studies of neurosurgical patients[36,42,46,82,90].

All these findings can be captured by the connectivity-constrained version of the hub-and-spoke model[91]. The first key notion, which was already expressed but is worth reiterating, is that semantic representations are not just hub based but reflect collaborations between hub and spokes[42] (Supplementary information S5 (figure)). The second is that, consistent with embodied semantic models[1], modality-specific information (for example, praxis) will be differentially important for some categories (for example, tools). It follows that the progressive degradation of the ATL transmodal hub in patients with SD will generate a category-general pattern, whereas selective damage to spokes can lead to category-specific deficits. Thus, impaired praxis or functional knowledge is deleterious for manipulable man-made items[89,92], whereas reduced high-acuity visual input is particularly challenging for differentiating between animals given their shared visual contours[86,93]. The differential contributions of the hub versus spokes in semantic representation have been demonstrated using TMS in neurologically intact individuals. Indeed, a study showed that such individuals exhibit a category-general effect following lateral ATL stimulation but a category-specific pattern, with slower naming of man-made objects, when the praxis-coding parietal region was directly stimulated[42]. The connectivity-constrained hub-and-spoke model also offers insights into other empirical observations that were noted above. For example, the medial ventral occipito-temporal region exhibits greater activation for man-made items, in part because it is directly connected to the parietal praxis-coding regions[94]; and an explanation in these terms[91] accounts for the evidence that congenitally blind participants show greater activation for man-made items than for animate things in this 'visual' region[84].

A remaining challenge is to explain the difference between semantic impairment in HSVE and SD. Despite highly overlapping areas of ATL damage in these conditions (albeit damage is more medially focused in HSVE)[95], individuals with HSVE commonly show better knowledge for man-made artefacts than for natural-kind concepts[4,95]; this finding is rarely observed in individuals with SD[13]. However, a crucial factor in this particular category effect has been acknowledged in one form or another by virtually all researchers who have studied it. Recall that concepts can be categorised at superordinate (for example, animal or tool), basic (for example, dog or knife) or specific (for example, poodle or bread knife) levels. Most semantic research has focused on the basic level, and, at this conceptually salient level, animate or natural-kind concepts tend to be visually and conceptually more similar to one another, and hence more confusable, than man-made things[13,66,96]. It is therefore an extremely important explanatory clue that the artefact versus animate performance difference in HSVE holds for the basic level but is eliminated at the subordinate level, at which cases with HSVE are equally and severely impaired for both categories[13]. The obvious interpretation, although this requires more empirical testing, is that the medial temporal lobe region that is typically damaged by the herpes virus is crucial not for distinguishing between living things but for distinguishing between visually or semantically confusable things[86,95,97], which include different types of knife and different breeds of dog. This possibility is compatible with the graded hub-and-spoke hypothesis and the existing evidence of graded, connectivity-driven differential contributions to representation of abstract and concrete concepts across ATL subregions[65] (FIG. 2B), with a preference for concrete items in the medial ATL[58,59].

Herpes simplex virus encephalitis
(HSVE). An acute or subacute infection in the brain that is often transmitted via the olfactory nerve and typically causes damage to the anterior temporal lobes.

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One further factor meriting mention is the fact that SD is a neurodegenerative disease, yielding steady degradation of the ATL and, consequently, of conceptual knowledge. Although patients with SD continue to be surrounded by the multimodal experiences that continuously reinforce and extend conceptual knowledge in a healthy brain, the slow-but-constant deterioration of semantic knowledge in SD is largely incompatible with relearning. By contrast, successfully treated HSVE is an acute illness that is followed by some degree of recovery and relearning. These differences can be mimicked in the hub-and-spoke computational model by comparing progressive degradation against *en masse* hub damage followed by a period of retraining: the former generates a category-general effect, whereas the latter results in better performance on man-made than on animate concepts. The latter outcome arises because, with reduced representational resources, the model struggles to recapture sufficient 'semantic acuity' to differentiate between the conceptually tightly-packed animate items and subordinate exemplars.

Semantic control

What is semantic control?

In everyday life, the activity within the network for semantic representation must often be controlled to ensure that the system generates representations and inferences that are suited to the immediate task or context. Some tasks may require one to accentuate subordinate meanings, focus attention on non-dominant features or suppress strong associates of a given concept. Furthermore, the crucial aspects of meaning can change for the same concept over time, both in language and in non-verbal behaviours. Imagine, for example, the different uses of the same knife when making a cheese and chutney sandwich: packet opening, bread cutting, butter spreading, cheese slicing, chutney scooping, and so on. Each use requires different, specific aspects of the properties of the knife to be brought to the fore, one by one, while the most commonly listed property of cutting often has to be inhibited. In the case of scooping, the canonical functions of the knife (such as cutting open, slicing and spreading) have to be disregarded altogether and replaced by a function that is typically served by another object (a spoon). In addition, the semantic representations that are evoked by objects and words must be shaped to align with the immediate context — for instance, to overcome the moments of ambiguity or confusion[9,11,12] that follow when new inputs are hard to integrate with the meaning of the established or evolving context[98] (returning to the sandwich-making example that was described above, imagine the semantically related problem solving that is required if you discover that there is no bread but a supply of rye crackers).

According to the CSC framework, control of semantic cognition is implemented within a distributed neural network that interacts with, but is largely separate from, the network for semantic representation. Consistent with extensive work on cognitive control generally[9,99–101] and its role in semantic retrieval specifically[11,12], the control network is thought to support working memory and executive representations that encode information about the temporal, situational and task context relevant to the current behaviour. These executive mechanisms constrain how activation propagates through the network for semantic representation. In well-practised contexts in which the relevant information is robustly encoded, the representation network needs little input from semantic control to produce the correct response. Contexts requiring retrieval of weakly encoded information, suppression of over-learned responses, emphasis of uncharacteristic features, and so on, depend more strongly on input from the control network. As with the hub-and-spoke model, this perspective on controlled semantic processing has both converging empirical evidence (see below) and computational motivations (BOX 4).

Disorders of semantic control

Head[102] and, later, Luria[103] investigated patients with disordered semantic processing arising from penetrative missile wounds to the temporoparietal region. They noted that the patients had difficulties in manipulating and using knowledge rather than loss of semantic knowledge and that this deficit co-occurred with other types of 'symbolic' processing deficits. Head coined the term semantic aphasia (SA) to describe this pattern. A similar profile was also reported by Goldstein[104] for a subset of patients with post-stroke aphasia. Later, Warrington and colleagues[105,106] contrasted the consistent semantic 'store' deficits in SD with the inconsistent semantic 'access' deficits that are found in some patients with global aphasia after large middle cerebral artery stroke. Detailed case-series comparisons of SD and SA[8,25] have recently delineated several qualitative differences between the two patient groups in both verbal and non-verbal domains[107,108]. In contrast to individuals with SD, patients with SA exhibit the following: poorest performance on the most executively demanding tasks and stimuli (Supplementary information S6 (figures)); inconsistent performance across tests; insensitivity to the frequency or familiarity of stimuli (Supplementary information S7 (figure)); a strong influence of the ambiguity or semantic diversity of word meanings (with poorer performance on words with multiple and varying meanings such as 'bark', 'pen' and 'chance') (Supplementary information S7 (figure)); strong effects of cueing and miscuing on task performance (Supplementary information S8 (figure)); poor inhibition of strong competitors and associated items (for example, falsely selecting a jar of marmalade when intending to make cheese-on-toast); associative, as well as coordinate and superordinate, semantic errors in naming (associative errors, such as saying 'milk' in response to a picture of a cow, are essentially never observed in SD); and a tendency in category and letter fluency to produce strong associates of prior responses that fall outside of the target category (for example, for the category of animals, a patient with SA might give the examples of "cat, dog, horse, saddle, whip …")[8,25,107–110].

The cueing and miscueing effects are a striking exemplar of the group differences between patients with SD and those with SA[108,110]. Given a picture of a tiger, for example, both patient groups will probably fail to name it. However, with presentation of the phonological cue "t", patients with SD still fail but patients with SA will

Semantic aphasia
(SA). A condition affecting patients who, after acute brain damage (usually from stroke), show deficits in verbal but also non-verbal semantic tasks, as well as in other cognitive domains that require executively linked manipulation of internally represented knowledge.

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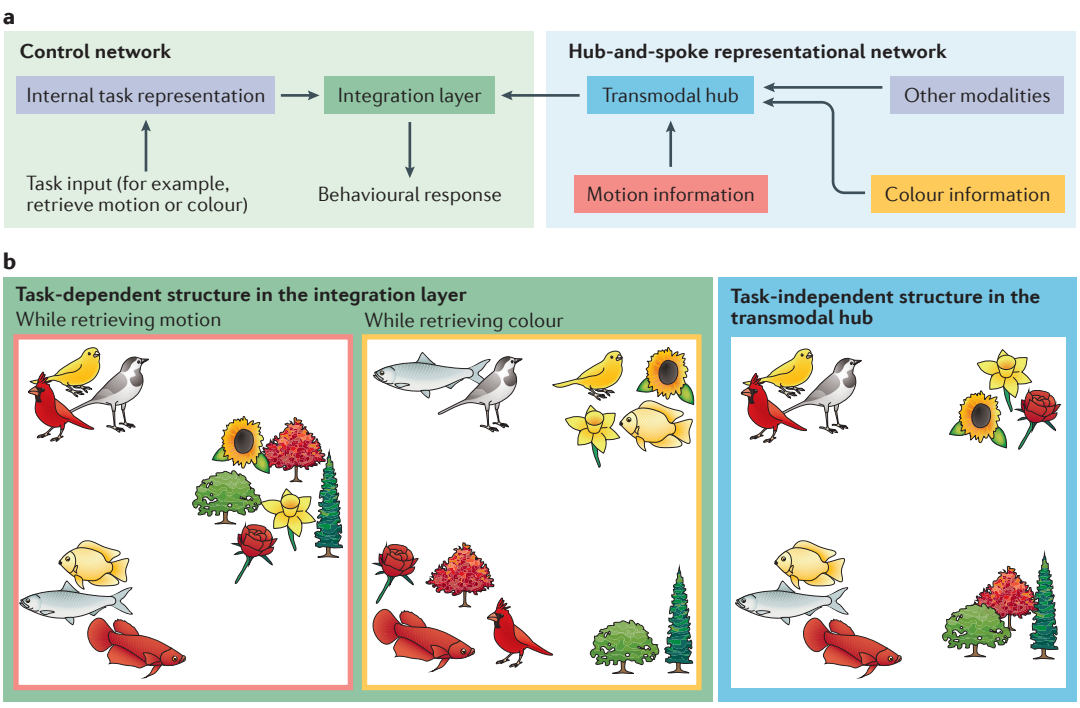
often succeed. Moreover, given the same picture plus the cue "l", individuals with SD again may say nothing but individuals with SA will often produce "lion". All these differences are consistent with the view that the impairment in SD arises from degradation within the network for semantic representation, whereas the impairment in SA reflects disordered control of activation within that network.

Semantic control network

Converging evidence for a distributed semantic control network. Beginning in the late 1990s, results from a series of seminal fMRI studies suggested that, although prefrontal regions do not encode semantic representations per se, they have crucial roles in accessing, retrieving and executively manipulating semantic knowledge[9,11,12]. For instance, semantic tasks requiring participants to select a response from among many potentially correct options or to retrieve infrequent semantic associations elicit increased activation in parts of the prefrontal cortex (PFC). Juxtaposed with earlier patient work, this discovery generates a potential conundrum, given that SA was classically associated with damage to the temporoparietal cortex but not to the PFC. This discrepancy has begun to be resolved as evidence has amassed across methodologies (FIG. 3a). SA is now known to arise from either prefrontal or temporoparietal lesions (or both), with only small differences in the behavioural profile between patient groups[8,111]. Likewise, recent meta-analyses of fMRI studies (FIG. 3b) identified regions other than the lateral PFC in which cortical responses correlate with semantic control demands, including the posterior middle temporal gyrus (pMTG), the intraparietal sulcus (IPS), the pre-supplementary motor area and the

Box 4 | **Controlled semantic cognition**

Computationally, separate but interacting networks for semantic control and representation resolve a long-standing puzzle. On the one hand, concepts must generalize across contexts (for example, canaries, like other birds, lay eggs). On the other hand, we are often required to retrieve diverse conceptual properties to complete different tasks (for example, colour (yellow) versus motion (hops) when either spotting or catching a canary). Both challenges are solved by implemented computational models that have separate but interacting networks for control and representation[10] (see the figure, part **a**). As per the hub-and-spoke framework, modality-specific information interacts with a transmodal hub to form generalizable concepts. As part of a separate executive control network, a region represents the current task context. These two components interact through an integrative system, which dynamically and transiently reshapes the multidimensional similarity structure arising in the context-independent hub to generate task-, time- and context-relevant behavioural responses. Thus, if two contrastive tasks (for example, spotting versus catching a canary) require focus on colour versus movement properties, then the integrative layer generates context-relevant internal representations that are congruent with the target behaviour (see the figure, part **b**; left and middle panels). Because the hub is not directly connected to task or context information, it learns representations that capture the structure that is independent of the various and idiosyncratic contexts encountered, providing the core computational basis for cross-context conceptual generalization (see the figure, part **b**; right panel). The same computational characteristic does not arise in models that blend task or context and perceptual inputs, immediately, within a single intermediating hub[10]. Thus, although this computational model was initially advanced solely to account for cognitive phenomena, it leads to the conclusion that semantic cognition requires separate and interacting neural networks for representation and control.



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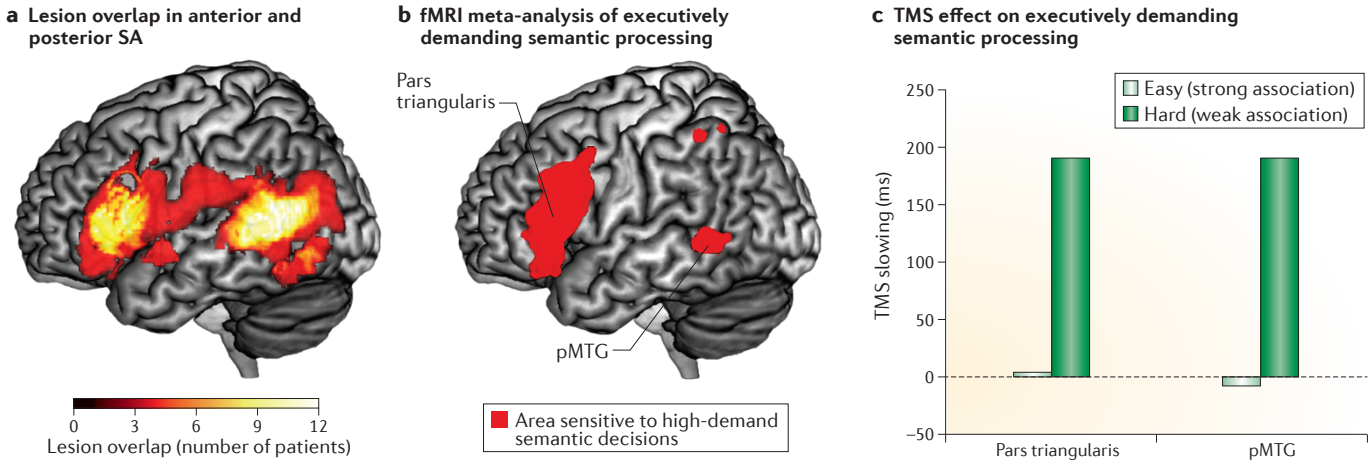

Figure 3 | **The neural basis of semantic control.** Various studies have provided strongly convergent evidence for the regions that are crucial for executively controlled semantic processing. **a** | Determination of lesion positions in cases of semantic aphasia (SA)[119] highlighted the involvement of both prefrontal and temporoparietal areas. **b** | A meta-analysis of functional MRI (fMRI) studies conducted in healthy participants[113] also revealed the involvement of the prefrontal cortex, posterior middle temporal gyrus (pMTG) and intraparietal sulcus. **c** | Last, in healthy participants, inhibitory transcranial magnetic stimulation (TMS) to the left prefrontal cortex (pars triangularis) or pMTG (the same areas as the peaks identified in the fMRI meta-analysis and lesion overlap in patients with SA) produced selective slowing of executively demanding semantic decisions. For more information on the nature of the semantic impairment in patients with SA and how this differs to semantic dementia, see Supplementary information S2,S6–S8 (figures). Part **b** is reprinted from REF. 113 by permission of the MIT Press.

anterior cingulate–ventromedial PFC[112,113]. Inhibitory TMS applied to the left inferior frontal region, pMTG or IPS transiently disrupts semantic functioning, particularly in conditions that tax cognitive control[114–117] (FIG. 3c), suggesting that these regions jointly have a crucial role in the successful completion of executively demanding semantic tasks. Of course, the proposal that the PFC and parietal regions function together to support cognitive control is familiar from theories of executive function and working memory more broadly (see below).

Graded functional specialization within the control network. Is the distributed semantic control network functionally homogeneous or are there important functional subdivisions? With regard to the prefrontal versus temporoparietal distinction that was noted above, only relatively subtle differences are observed — for instance, anterior lesions are more likely to produce refractory effects (accumulated proactive interference from one trial to the next) in both verbal and non-verbal tasks, as well as a higher rate of perseverative errors. Both phenomena may arise from an inability to inhibit previously generated responses, which may be more seriously compromised by prefrontal damage[8,111,118,119].

Other recent convergent evidence suggests a superior–inferior functional specialization of the control network. For instance, blood-oxygen-level-dependent (BOLD) responses in more dorsal and posterior aspects of the inferior frontal sulcus (IFS) correlate with executive demands across multiple domains[120,121], whereas responses in more ventral and anterior aspects of the IFS correlate more specifically with executive demands of controlled memory retrieval — potentially supporting the promotion of relatively weak representations in both semantic and episodic memory systems[9,108,122]. A similar superior–inferior gradation has been observed for semantic retrieval when the nature and demands of the tasks are carefully varied[9,123,124]: the ventral PFC (vPFC) and pMTG show increased activation during the retrieval of weak semantic associations, whereas the dorsolateral PFC and IPS areas show increased responses when selection demands are high. Activation in the intermediate middle–lateral PFC correlated with both demands, suggesting that the PFC exhibits graded specialization. Studies of functional and anatomical connectivity tell a similar story: both vPFC and pMTG robustly connect to the ATL, whereas superior aspects of the control network do not[58,62,125]. Likewise, inhibitory TMS applied to the vPFC and pMTG (inferior network components) selectively slows semantic judgements[114,115], whereas application to the IPS (superior component) slows both difficult semantic and non-semantic decisions[116]. Together, these results suggest a graded organization of the semantic control network in which more inferior regions, by virtue of their connectivity to the network for semantic representation, boost retrieval of weakly encoded information and more superior regions, alongside the pre-supplementary motor area and anterior cingulate cortex, contribute to more domain-general control[120].

The CSC and other theories

The CSC framework is, to our knowledge, unique in providing a joint account of representation and control within the human semantic system — an essential step towards a fuller understanding of semantic cognition and its disorders. Of course, there are already rich, separate literatures on, and alternative theories of, these aspects of semantic memory. Here, we briefly note the relationship between these approaches and the CSC framework.

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Executive-semantic processing

The semantic control processes that we described are intimately related to cognitive control frameworks that seek to explain the interaction between goals (coded in the dorsal PFC) and posterior perceptual or knowledge systems (for example, Fuster's perception–action cycle[126] and Braver's dual control framework[127]). The top-down application of a task set or goal is proposed to engage the multiple-demand network, including the IFS and IPS, irrespective of the type of representation (for example, visual, motor or semantic) that has to be controlled. In the CSC, additional regions such as the pMTG and vPFC that are specifically implicated in semantic control may allow the interaction of domain-general control processes with semantic representations[123], for example, by allowing current goals to influence the propagation of activation within the hub-and-spoke representation network. In turn, the CSC theory would also anticipate strong recruitment of the pMTG and vPFC when activation within the semantic system itself triggers the engagement of control, for example, when inputs or retrieved meanings are ambiguous or unexpected[98,112].

We also note that studies of semantic representation and semantic control have often advanced independently of one another. The joint consideration of both aspects is important for at least three reasons. First, there are multiple, distinct ways in which semantic knowledge can be difficult to deploy (for example, in the case of weak, impoverished representations or ambiguous meanings, or if there is inconsistency between concepts and contexts). These situations may require different types of executive support[9,98]. Second, semantic representation and control are probably highly interactive — very little is known so far about, for instance, the circumstances and neural systems that recruit semantic control. Third, the nature of this interaction will change if one or more of the CSC components is compromised by damage or neural stimulation; therefore, a full understanding of these effects requires a framework addressing both control and representation.

Semantic convergence zones

Other researchers have proposed that the transmission of information across distributed modality-specific systems of representation flows through multiple discrete, neural regions that are known as 'convergence zones' (REFS 17,73). By virtue of their connectivity to input and output systems, different zones are proposed for receptive versus expressive semantic tasks and for different semantic categories. These ideas resonate with key proposals of the CSC framework: first, the semantic network is organized around a cross-modal hub, and second, network connectivity shapes functional specialization in this network. However, the two views differ in other key aspects.

Convergence zones are characterized as 'pointers' that bind together modality-specific sources of information that are distributed throughout the cortex, although the pointers do not represent semantic structure. By contrast, the hub has a crucial role in discovering cross-modal similarity structures that allow for generalization across conceptually similar items[5,7]. The proposal that multiple discrete zones exist for different tasks and categories makes it difficult to understand the now-widely documented task- and domain-general contributions of the ATL to semantic cognition. The graded hub proposal of the CSC framework accounts for both domain- and modality-general patterns of impairment and other types of semantic disorder in which some modalities or domains are more impaired than others[72,73,128]. Finally, whereas the idea of convergence zones proposes differentiation of expressive functions across hemispheres[72,73,128], the CSC framework proposes a functionally integrated bilateral hub. Computational explorations[129], combined TMS–fMRI[130,131] and patient fMRI[132] studies all suggest that bilateral interaction is crucial to preserving semantic performance after brain damage or dysfunction (BOX 3).

Distributed domain-specific hypothesis

Like the CSC framework, the proposal by Mahon and Caramazza[92] states that different parts of the semantic neural network become tuned towards a domain as a result of their differential patterns of functional connectivity. Thus, both accounts emphasize that local function is strongly influenced by connectivity, and this can explain patterns of category-specific deficits or differential fMRI activation. However, the distributed domain-specific hypothesis is silent on the need for an additional transmodal hub to form coherent, generalizable concepts, an explanation of the multimodal, pan-category semantic impairment in SD and, relatedly, the important, general role of ATL regions in semantic representation.

Fully distributed feature-based views

The CSC theory in common with both classical neurological models[14] and other contemporary theories[1], proposes that semantic representations involve the parallel reactivation of multiple modality-specific sources of information that are distributed across the cortex. Contemporary methods including large-scale semantic feature data sets collected using crowd-sourcing[16] and state-of-the-art multivariate decoding of neural signals[133] have reinforced this view by probing the relative weighting of different sources of information in semantic representation and mapping their neural locations. Although little consensus exists regarding exactly which cortical regions encode which kinds of properties, most investigators seem to endorse a distributed feature-based view of semantic representation. The CSC theory substantially elaborates this general view in proposing a specific architecture through which modality-specific representations interact, how network connectivity shapes graded functional specificity and a framework for understanding how semantic control shapes the flow of activation in the network to generate context-, task- and time-appropriate behaviour.

Future directions and questions

The hub-and-spoke model assumes that concepts reflect both hub and spoke representations and their interaction. However, there is a long way to go before we understand the relative contributions of the hub versus spokes to the overall semantic representation and the nature and time

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course of their interactions in the process of settling on a stable semantic representation; for example, are the core components of a concept available when the hub is first activated or do they require an ongoing interaction between the hub and spokes?

As summarized in this Review, considerable advances have been made in understanding normal and impaired semantic representation and control. Although the core computations of such representation and control can be cognitively and neurally separated, all semantic behaviours require a synchronised interaction between these two components (BOX 4). We still know little about the nature of this interaction or, in patients, how this changes after damage to one of the systems. Progress will require elucidation of the computational mechanisms that underpin semantic control, as well as their integration into the graded hub-and-spoke model.

Future investigations are needed to improve our understanding of how abstract, emotional and social concepts are represented across the graded hub-and-spoke neurocomputational framework and the challenges that they present to the control network. These next steps will build on recent investigations that include the demonstration that the abstract–concrete distinction is multidimensional[134] and the importance of context and semantic control in processing abstract meanings[65].

Feature-based approaches to semantic representation struggle to account for knowledge about the relationship between features and concepts. For instance, the relationship between 'car' and 'vehicle' (class inclusion) is qualitatively different from the relationship between 'car' and 'wheels'. Different relationships support very different patterns of inductive generalization: the proposition 'all vehicles can move' should generalize to 'car' by virtue of the class-inclusion relationship, but the proposition 'all wheels are round' does not generalize to 'car' (as cars are not round) because this kind of induction is not supported by a possessive relationship. Other relationships, such as causal or predictive relationships among attributes, have been a focus of study in cognitive science for decades[135,136]. An early articulation of the CSC theory addressed such influences at length[10], but cognitive neuroscience has only started to explore the neural bases of different types of semantic relationship (for example, taxonomic versus thematic or associative)[61,137,138]. A comprehensive understanding of the neural systems that support relational knowledge awaits future work.

What is the relationship between item-based concepts (for example, animals, objects, abstract and words) and item-independent concepts (such as numbers, space or location, schema and syntax)? There is clear evidence from neuropsychology and fMRI studies that these two types of concept dissociate[36,139,140]. One set of computationally informed hypotheses[112,141,142] suggests that there are two orthogonal statistical extraction processes in the ventral (temporal) and dorsal (parietal) pathways. The ventral pathway may take our ongoing verbal and non-verbal experiences and integrate over time and contexts to extract coherent, generalizable item-based concepts. The dorsal pathway may, conversely, integrate over items to extract generalizable information about syntax, time, space and number, which are types of structure that are largely invariant to the items. As well as exploring this issue, future research also needs to investigate how these fundamentally different types of concept interact and collaborate to generate time-extended, sophisticated verbal (for example, speech) and non-verbal (for example, sequential object use) behaviours.

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Competing interests statement
The authors declare no competing interests.

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