

Where do you know what you know?

The representation of semantic knowledge in the human brain

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Abstract | Mr M, a patient with semantic dementia — a neurodegenerative disease that is characterized by the gradual deterioration of semantic memory — was being driven through the countryside to visit a friend and was able to remind his wife where to turn along the not-recently-travelled route. Then, pointing at the sheep in the field, he asked her “What are those things?” Prior to the onset of symptoms in his late 40s, this man had normal semantic memory. What has gone wrong in his brain to produce this dramatic and selective erosion of conceptual knowledge?

Semantic memory (also called conceptual knowledge) is the aspect of human memory that corresponds to general knowledge of objects, word meanings, facts and people, without connection to any particular time or place¹. Knowing that you ate Szechuan scallops at the Peking Restaurant in Cambridge last Thursday evening is episodic, not semantic, memory. Knowing that Szechuan refers to a province of China, that food from this region tends to be spicy and that scallops are sea-creatures that live in brittle bivalve shells are all forms of conceptual knowledge. Memory for episodic events is not only specific to times and places, it is also largely specific to an individual. Conceptual knowledge, on the other hand, is mostly shared across individuals in a given culture, although its precise scope depends on the individual's experience.

Only a few decades ago, one respectable position held that semantic memory might arise from ‘universal connectivity’ in the brain, and hence have no corresponding stable neural architecture². Because we now know that brain lesions can produce selective disruption of semantic memory, this hypothesis is probably no longer tenable; however, localizing the stable architecture of conceptual knowledge has proved difficult. Indeed, one researcher concluded that “The search for the neuroanatomical locus of semantic memory has simultaneously led us nowhere and everywhere...” (REF. 3) It is perhaps time for an assessment of what we do and do not know about the representation of conceptual knowledge in the human brain.

A semantic hub?

This Review focuses on one specific issue. Essentially all current theoretical positions about semantic memory share the view that much of the content of our semantic memory relates to perception and action, and is represented in brain regions that overlap with, or possibly even correspond to, the regions that are responsible for perceiving and acting^{4–6}. This view about the neural representation of how objects look, sound, move and so on therefore entails commitment to the idea that conceptual knowledge is a widely distributed neural network. Our knowledge of the scallop, for example, includes attributes such as its visual features, which will be represented in or near the brain regions that analyse visual form and colour; its manner of moving on the seabed, represented in or near the brain regions that respond to the perception of this kind of movement; its texture and taste, involving tactile and gustatory regions; the actions its edibility affords, such as cutting with a knife and fork or chewing, supported by frontal and parietal areas; its name or other descriptions that we could apply to it, represented in perisylvian language regions; and so on. The debate centres on the following question: are these distributed brain regions, along with the connections between them, the entire neural basis of semantic memory?

Many theories, forming a class that we refer to as the distributed-only view (FIG. 1a) offer a positive answer to this question. An alternative position, for which we argue here, is that the sensory-, motor- and language-specific aspects of conceptual knowledge are necessary but not sufficient: this is the distributed-plus-hub view

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doi:10.1038/nrn2277

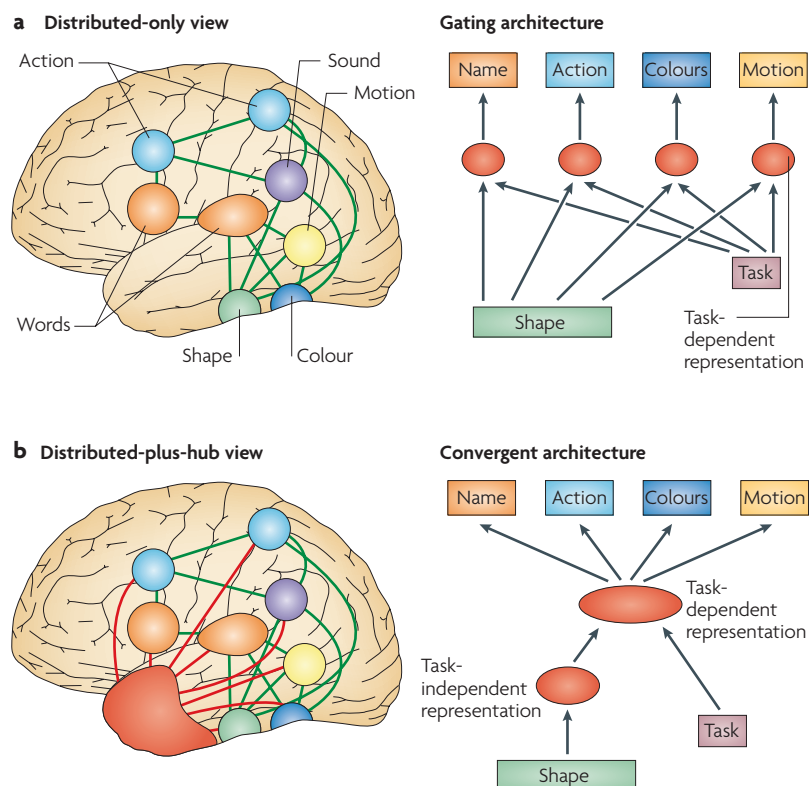


Figure 1 | Two theoretical positions regarding the neuroanatomical distribution of the cortical semantic network and schematic models based on these views.

Both positions hold, in agreement with most investigators, that the network is widely distributed and partly organized to conform to the neuroanatomy of sensory, motor and linguistic systems. **a** | The distributed-only view suggests that these widely distributed regions, along with the diverse connections between them (shown as green lines), constitute the whole semantic network. The flow of activation through this network can be 'gated' by a representation of the current task (right-hand panel): for instance, if the task is to name a line drawing of a familiar object, activation will flow from a representation of object's shape to a representation of its name. Associations between different pairs of attributes are encoded along different neuroanatomical pathways.

b | By contrast, the distributed-plus-hub view posits that, in addition to these modality-specific regions and connections, the various different surface representations (such as shape) connect to (shown as red lines), and communicate through, a shared, amodal 'hub' (shown as a red area) in the anterior temporal lobes. At the hub stage, therefore, associations between different pairs of attributes (such as shape and name, shape and action, or shape and colour) are all processed by a common set of neurons and synapses, regardless of the task. The right-hand panel (labelled 'convergent architecture') illustrates the model equivalent of the distributed-plus-hub view.

(FIG. 1b). The principal reason for this claim is that a central function of semantic memory is to generalize across concepts that have similar semantic significance but not necessarily similar specific attributes. Scallops and prawns have different shapes, colours, shell structures, forms of movement, tastes, names, verbal descriptions and so on, but semantically speaking, to seafood-eating humans they enter into similar scenarios and have substantial conceptual overlap. If semantic memory consisted only of the modality-specific content of objects (and the links between them), it is doubtful that we could ever achieve the higher-order generalizations on which so much of our semantic processing relies.

The distributed-plus-hub view is by no means the first to argue for unified conceptual representations that abstract away from modality-specific attributes^{7,8}. Most earlier proposals of this nature, however, were mute regarding the neuroanatomical basis for this central aspect of semantic processing. With a more specifically neuroanatomical focus, Damasio and colleagues^{9–13} proposed the existence of 'convergence zones' that associate different aspects of knowledge, and along with other researchers¹⁴, they have clearly articulated the importance of such zones for semantic processing. The convergence-zone hypothesis, however, differs in at least two respects from the distributed-plus-hub view illustrated in FIG. 1b. First, it proposes the existence of multiple specialized convergence regions: for example, one that encodes associations between visual representations of shape and corresponding actions, another that encodes associations between shape and object name, and so on. Second, it suggests that these zones become differentially important for representing different semantic categories. For example, because humans frequently interact with tools and other man-made objects, the zone that links object shape and action might be more important for knowledge of man-made artefacts than for knowledge of living things. Similarly, because animals move in characteristic ways, the zone that links shape to movement might acquire special salience for knowledge of animals. These two aspects of the convergence-zone hypothesis make it a variant of the distributed-only class of theories that is represented in FIG. 1a. By contrast, the distributed-plus-hub view proposes that, in addition to direct neuroanatomical pathways between different sensory, motor and linguistic regions, the neural network for semantic memory requires a single convergence zone or hub that supports the interactive activation of representations in all modalities, for all semantic categories.

Do the distributed-only and distributed-plus-hub positions result in different predictions? From the distributed-plus-hub perspective, damage to the hub should produce a semantic impairment that is independent of the modality of input (objects, pictures, words, sounds, tastes, and so on) and of the modality of output (for example, naming an object, drawing it or using it correctly). By contrast, from the distributed-only perspective, no form of focal brain damage would be expected to engender such a generalized impairment. We therefore start with two important empirical questions. Do selective but generalized impairments of semantic memory occur? And, if so, are they caused by relatively focal brain damage? The evidence pertinent to these questions comes from studies that have both investigated the performance of semantically impaired patients and attempted to determine the specific locus of their brain lesions. Following an overview of this evidence, we ask to what extent the resulting conclusions are consistent with, or challenged by, evidence from functional neuroimaging studies of healthy adults performing semantic tasks. Finally, we consider evidence from computational modelling that might help to explain why the cortical semantic network is apparently organized in a particular way.

Box 1 | The syndrome of semantic dementia

One of the most prominent symptoms of semantic dementia (SD) is anomia⁹¹: failure to name objects, concepts and people, whether in response to stimulus presentation or in spontaneous speech. Patients with other causes of anomia, and occasionally even healthy people, sometimes fail to name something because, although they know what it is, they cannot find the word for it at that moment. Anomia in SD does not result from this kind of word-finding difficulty but instead reflects degraded knowledge of the object or concept. When we asked one of our patients to name a picture of a zebra, she replied: "It's a horse, ain't it?" Then, pointing to the stripes, she added, "But what are these funny things for?"

For SD patients, the degree of success in naming (and, indeed, in any measure of conceptual knowledge) is largely independent of the modalities of input and output. Naming is most commonly assessed by presenting pictures and asking for a verbal naming response; however, SD patients are just as unsuccessful, indeed usually more so, if the stimulus is a description of the item to be named (for example, "What do we call the African animal with black and white stripes?"), or is the item's characteristic sound (for example, a telephone ringing or a dog barking), or if the patient is asked to write the name rather than say it.

The degree of success or failure in any semantic test in SD patients is determined by four principal factors^{72,92}: the severity or stage of progression of the disease; the familiarity of the object (the deficit is always more pronounced for less familiar things, words and concepts); the object's typicality (there are fewer successes for things that are atypical of their kind); and the specificity of information required by the task (for example, a patient might be able to identify an apple as something to eat without being able to identify it as an apple).

Most cognitive functions apart from semantic memory are reasonably well-preserved in patients with SD, at least until late in the disease. Thus — provided that the tests do not refer to or require access to semantic knowledge — SD patients have reasonably normal capabilities in general intelligence, problem solving, visuo-spatial function, short-term memory, episodic memory, simple calculation skills, and so on.

Acquired disorders of semantic memory

Impaired conceptual knowledge is associated with four principal neurological aetiologies: stroke; viral infection, most commonly herpes simplex virus encephalitis (HSVE); and two forms of neurodegenerative disease: Alzheimer's disease (AD) and the semantic variant of fronto-temporal dementia, typically called semantic dementia (SD). All four conditions give useful clues about the nature and organization of conceptual knowledge, but from different angles.

Semantic dementia. SD is one of the neurodegenerative conditions that belongs to the Fronto-Temporal Dementia spectrum¹⁵. Recent post-mortem analyses indicate that the typical neuropathology in SD is abnormal neuronal inclusions of the protein ubiquitin¹⁶, a form of pathology that is best known in motor neuron disease. SD is marked behaviourally by a progressive deterioration of expressive and receptive vocabulary and of knowledge about the properties of everyday objects, in the context of otherwise well-preserved cognition and memory for recent events (BOX 1). It was first reported in the modern era by Warrington¹⁷, Schwartz *et al.*¹⁸ and Snowden *et al.*¹⁹. As indicated in BOX 1, research on SD provides clear and positive answers to the two questions posed above. That is, SD represents a selective impairment to semantic abilities that affects all modalities of reception and expression, for all kinds of concepts, more or less equally (FIG. 2), and it is the consequence of relatively focal brain lesions. Degeneration of the anterior temporal lobes

(ATL) is invariably evident by the time that SD patients become symptomatic. Bilateral degeneration is the norm, although it is usually asymmetrical: in approximately two-thirds of cases the atrophy is greater on the left side than on the right. The typical pattern seen on structural MRI scans is one of well-defined atrophy of both the left and the right ATL, which is maximal at the temporal pole and on the adjacent rostral-inferior surface.

Alzheimer's disease. The most prominent cognitive deficit in typical AD is an impairment of episodic (autobiographical) memory: in particular, the ability to learn new information is progressively abolished. The original hypothesis, which attributed this phenomenon specifically to degeneration of the hippocampus²⁰, is now viewed not as wrong but as incomplete: functional brain imaging, even in patients with mild or early AD, reveals hypometabolism not only in the bilateral medial temporal lobes, but also in the thalamus, the posterior cingulate gyrus and other parts of the limbic system, which apparently constitute a network that is crucial for the formation of new memories²¹. Semantic memory is frequently affected in AD^{22,23}, but typically at a later stage and to a more modest extent than episodic memory. There are a few reported cases in which loss of conceptual knowledge was an early and significant symptom of AD. Where detailed neuroanatomical information was available in these cases, however, the pathology sometimes had a distribution that was atypical for AD and was in fact more similar to that seen in SD²⁴. It is the contrast between the prototypical distributions of degeneration in these two diseases that is most germane to the current Review, because the relatively widespread degeneration that is observed in AD apparently leads to a less consistent and usually less profound disruption of semantic memory than is observed in SD, where the pathology is relatively circumscribed within anterior temporal regions.

Herpes simplex virus encephalitis. The most prominent cognitive consequences of typical HSVE are amnesia for earlier episodes in one's life and profound difficulty in learning new information. The impact on episodic memory can be attributed to the fact that this viral infection has a predilection for medial temporal lobe structures, including the hippocampus. Some patients with HSVE have no significant disruption to their conceptual knowledge, but have other cognitive deficits, most notably in the executive and control abilities that are associated with the frontal lobe. When semantic memory is affected, the deficit is often mild relative to the profound semantic deficits that are observed in SD. As in SD, however, semantic impairment in HSVE is associated with bilateral ATL lesions^{25,26}. Interestingly, the semantic deficit in HSVE is often category-specific, with relatively well-preserved knowledge of man-made things but impaired knowledge of living things. There is considerable debate in the literature as to whether these two domains of conceptual knowledge are represented separately in the brain²⁷, or whether this dissociation can be explained by some fundamental difference in the nature of the attributes that are

Expressive vocabulary

The set of words that an individual knows and can retrieve for referring to objects and other concepts in speech or writing.

Receptive vocabulary

The set of words that an individual can comprehend when hearing or reading them.

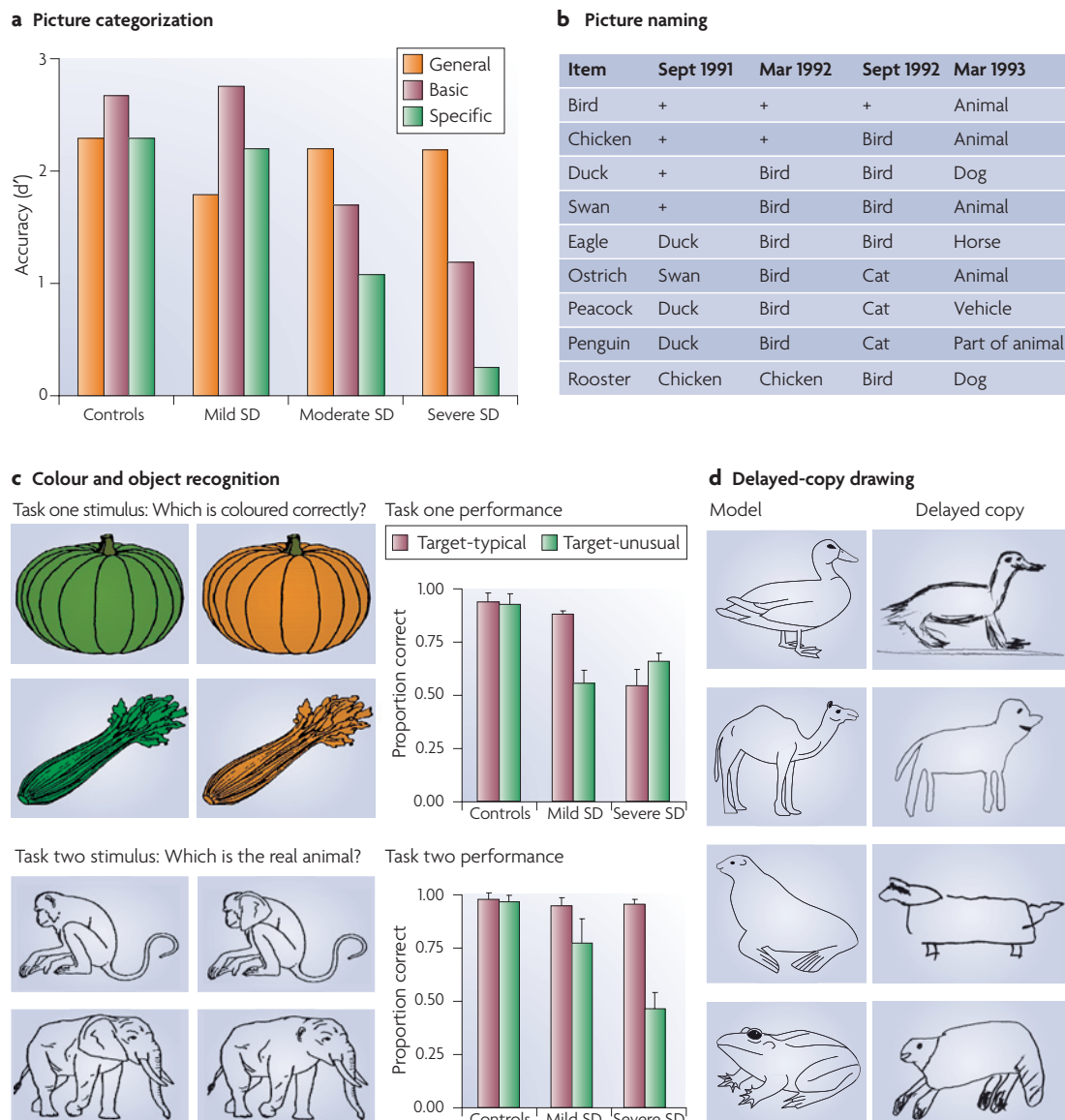


Figure 2 | Examples of impaired performance on semantic tasks in patients with semantic dementia. This figure illustrates the cross-modal nature of the impairment and the preservation of general relative to specific information in semantic dementia (SD). **a** | Accuracy at discriminating targets from distractors in a picture-categorization task for four groups of participants: healthy controls and patients with mild, moderate and severe SD⁷². Participants viewed a category label followed by a colour photograph and were asked whether the picture matched the label. Labels were either general (for example, 'animal'), basic-level (for example, 'dog') or specific (for example, 'Labrador'). **b** | Picture-naming responses for one SD patient who was assessed longitudinally⁶⁸. + denotes a correct response. **c** | Examples of stimuli and performance (for controls, mild and severe SD patients) on two recognition tasks. In the first task, participants judged which of two items was coloured correctly. Patients with milder SD performed well when the targets had a category-typical colour (for example, the green celery) but poorly when the items had an unusual colour (for example, the orange pumpkin). The judgements of patients with more severe SD were no better than chance (50%) in either condition⁸⁰. In the second task, participants judged which of two drawings depicted a real animal. Here, both the patients with mild SD and the patients with severe SD achieved normal levels of success for targets with relatively prototypical features (for example, the monkey which, like most animals, has small ears). For stimulus pairs in which the correct choice had unusual features (for example, the elephant, which has very large ears), the patients with mild SD were impaired and the patients with severe SD scored at chance levels⁷⁰. **d** | Delayed-copy drawings produced by SD patients⁷¹. The patients were shown a model picture which was then removed and, after a 10-second delay, they were asked to reproduce this picture from memory. Properties that are common to most animals, such as eyes and a tail, were preserved in the delayed drawings. Unusual properties that distinguish one animal from others — for example, the hump on the camel and the flippers on the seal — were frequently omitted. Some common properties were also incorrectly added to animals that lack them (for example, the four legs on the delayed drawing of the duck and the tail on the delayed drawing of the frog). Real animal pictures in part **c** reproduced, with permission, from REF. 97 © (1980) American Psychological Association.

Aphasia

Impaired language abilities resulting from brain disease or injury.

Cross-modal

The term that is applied to representations or processes that operate across different kinds of sensory, motor and linguistic representations. For instance, representations and processes that receive input from and/or direct output to both visual and auditory representations would be considered cross-modal.

Anomia

The failure to name objects, concepts and people, whether in response to stimulus presentation or in spontaneous speech.

Volumetric MRI

A method that uses finely cut brain slices (usually less than 2 mm thick) to measure the volume of brain structures.

Voxel-by-voxel analysis

A method of whole-brain image analysis in which the brain scans of different individuals are fitted to a standard template (to minimize inter-individual differences in brain shape) so that brain regions can be compared systematically across subjects.

Lesion-overlap study

A method that seeks to define a common area of brain damage relevant to a given behavioural deficit by overlaying the scan-defined lesions of multiple subjects with the behavioural deficit in question.

PET activation paradigm

An experimental paradigm that uses PET to measure changes in cerebral perfusion in response to a stimulus.

characteristic of man-made and living things (for example, living things might be more heavily weighted towards sensory features and man-made artefacts might be more heavily weighted toward functional attributes)^{28,29}. Once again, the contrast between HSVE and SD in terms of both the severity of the semantic deficit (which is often either absent or mild in patients with HSVE, as opposed to progressive and ultimately profound in SD) and its pattern (which is frequently category-specific in HSVE, but very rarely so in SD) seems most telling in the current context. That is, because both diseases implicate the bilateral ATL in semantic processing, it must be the specific nature and/or distribution of the brain abnormalities in SD that produces the pervasive disruption — across all categories and all modalities — of conceptual knowledge that defines this condition.

Stroke. The most prominent impairment in stroke patients with extensive lesions in the left hemisphere is aphasia, but poor performance on non-verbal semantic tests as well as in verbal comprehension can result from left-hemisphere stroke, especially in a condition called transcortical sensory aphasia (TSA). At least in this cross-modal regard, TSA might resemble SD; however, there are important differences between the two patients groups. With reference to criteria designed to distinguish impairments of representation from problems in access or retrieval³⁰, some recent work suggests that the semantic deficit in TSA may be better described as an impaired ability to retrieve, select and manipulate semantic information in a task-appropriate fashion³¹, rather than the degradation of semantic representations themselves which is characteristic of SD. For example, the anomia that occurs in TSA readily benefits from cueing (for a patient struggling to name a picture of a violin, the cue might be, “It begins with a ‘v’”),³² whereas anomia in SD is largely unaided by cueing^{32,33}. There is essentially no overlap between the brain regions that are damaged in these two patient populations. Owing to the anatomy of the vascular system, stroke rarely, if ever, produces focal lesions in the ATL, and semantic deficits in TSA typically result from damage to either frontal or parietal regions (or both) that is restricted to the left hemisphere³⁴. In accordance with this view regarding the nature of the semantic impairment in TSA, there is substantial evidence from functional imaging of normal individuals that activation of prefrontal cortical areas is associated with selection or control processes^{35,36}.

Summary of semantic disorders. The range of aetiologies associated with impaired performance on semantic tasks reveals important similarities and differences. The cognitive and neuroanatomical abnormalities in SD, especially when contrasted with those from the other aetiologies reviewed above, provide trenchant evidence for the distributed-plus-hub view (FIG. 1b). The strength of this evidence hinges, however, on claims about the relatively focal nature of the pathology in SD. The remaining issue to be considered in this section is whether the selective conceptual impairment in SD can be securely attributed to circumscribed lesions of the ATL.

The suggestion that the cognitive syndrome in SD might result in part from structural and/or functional abnormalities elsewhere in the semantic network⁵ is challenged by recent findings with (¹⁸F)fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET). Three studies^{37–39} have confirmed bilateral anterior temporal dysfunction in SD, but no other area of hypometabolism was consistently observed: one reported more extensive hypometabolism along the length of the inferior left temporal lobe³⁷, the second observed additional hypometabolism in the left insula and orbito-frontal areas³⁸ and the third revealed no significant reduction in metabolism in any region except the rostral temporal lobes³⁹. In agreement with these studies of resting metabolism, volumetric structural imaging⁴⁰ indicates relative preservation of the posterior temporal lobe in SD^{38,39,41–43}. In the dorsal-ventral plane, the superior temporal gyrus is atrophic but also preserved relative to the inferior temporal gyrus⁴⁰. In other words, both structural and metabolic imaging studies of patients with SD suggest that the abnormalities are most pronounced in the anterior and inferior parts of the temporal lobes.

Of course, it is possible that the pathology is more widely distributed in SD, but that such further abnormalities are so subtle or variable across patients that they do not meet the standard for statistical significance in voxel-by-voxel analyses. A recent comparison of brain hypometabolism in patients with AD versus patients with SD suggests that this is not the case. Nestor and colleagues³⁹ demonstrated that hypometabolism is much more widespread in AD than in SD and, in particular, that it affects left frontal, occipito-temporal and temporo-parietal regions in AD — areas that have been implicated in the distributed cortical semantic network and which appear relatively normal in SD. Yet semantic impairment was much milder in AD patients than in SD patients, all of whom showed hypometabolism in the ATL (FIG. 3).

Other lesion studies also support the view that the ATL is important for semantic representation and/or processing. Perhaps the best known is a lesion-overlap study that tested picture naming in a large group of anomic patients with unilateral, stable, focal brain lesions¹¹. The stimuli included pictures of famous people — who must, of course, be named at a specific level (for example, ‘Princess Diana’ rather than ‘princess’ or ‘woman’) — and pictures of animals and tools, which are usually named at the basic level (for example, ‘elephant’ or ‘hammer’), which does not distinguish individual category members from one another. Impaired naming of famous faces was associated with the ‘tightest’ lesion overlap, centred on the left temporal pole, whereas impaired animal naming correlated with lesions in the anterior, inferior left temporal lobe. Poor tool-naming revealed the lowest degree of lesion overlap and was associated with damage in the posterior, lateral left temporal lobe as well as in the temporo-occipito-parietal junction. Lesion-symptom correlation thus implicated the left ATL in naming for two of the three categories tested. When healthy participants named the same items in a PET activation paradigm, all three stimulus

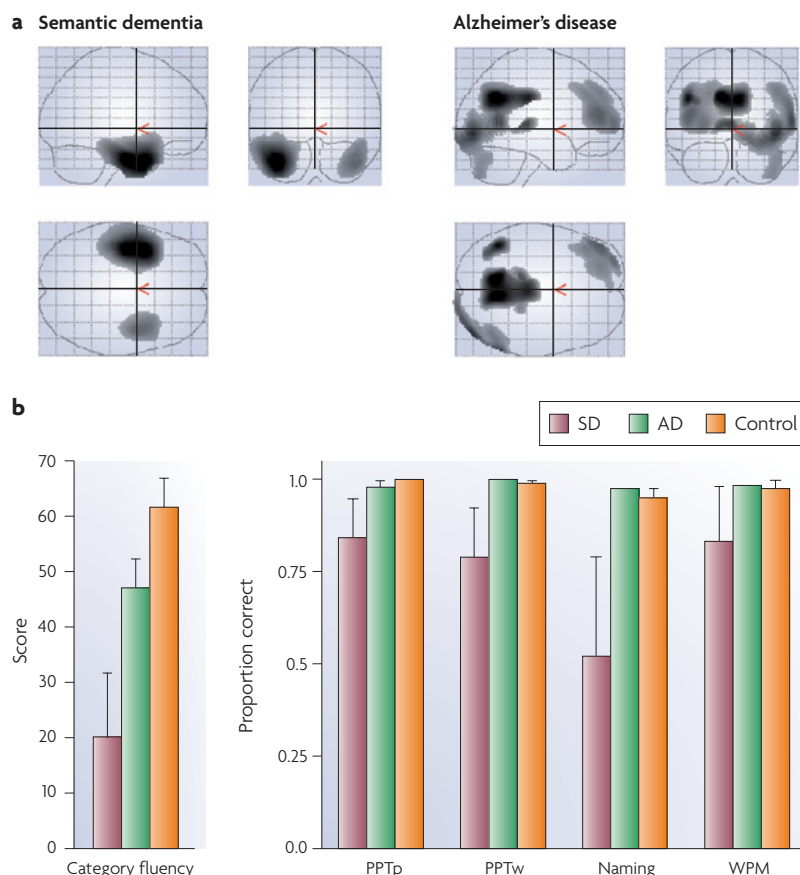


Figure 3 | Differences between semantic dementia and Alzheimer's disease in measures of brain function and semantic memory. **a** | The areas of reduced metabolism (shown as graded grey areas), are widespread in patients with Alzheimer's disease (AD) and include some regions that are implicated in the cortical semantic network (see FIG. 1). In the AD cases shown, however, there was little evidence of any abnormality in anterior temporal regions, which show substantial and focal hypometabolism in patients with semantic dementia (SD). **b** | The performance of AD and SD patients, as well as of a group of age-matched healthy controls, on a range of semantic tasks. The SD patients were significantly more impaired than the AD patients on all tasks, even though the brain abnormalities in the AD patients were more widespread. In category-fluency tasks, participants are given 1 minute to list as many examples of a semantic category as they can. PPTp and PPTw indicate the picture and word versions, respectively, of the Pyramids and Palm Trees test of semantic association⁹⁸. Naming indicates performance on a simple picture-naming task and WPM indicates performance on a 10-alternative, forced-choice word-to-picture matching task. Parts **a** and **b** modified, with permission, from REF. 39 © (2006) Academic Press.

types yielded significant blood-flow increases (relative to a control condition) in the left temporal pole, with further activation of the right temporal pole during face-naming and similar but discernibly different activation patterns in the posterior left temporal regions for animal- versus tool-naming¹¹.

Taken together, the neuropsychological literature suggests that the selective but amodal semantic impairment in patients with SD is attributable to relatively focal pathology in the ATL and not to widespread damage in the cortical semantic network. Such data strongly support the distributed-plus-hub view shown in FIG. 1b, and further suggest that the 'hub' part of the semantic network is located in the bilateral ATL (BOX 2).

Magnetoencephalography (MEG). A method of measuring physiological activity across the cortex by detecting perturbations in the magnetic field that is generated by the electrical activity of neuronal populations.

Evidence from functional neuroimaging

This conclusion from neuropsychological evidence might seem surprising to researchers who are familiar with functional brain-imaging studies of semantic abilities in healthy individuals. Although there have been more than 40 published reports of ATL activation by a wide variety of semantic tasks (FIG. 4), these reports constitute a relatively small proportion of the functional imaging studies of semantic memory in the literature of the past decade. According to both primary sources^{44–49} and review articles^{3,5,50,51}, imaging studies more often implicate some combination of frontal, posterior temporal, temporo-parietal and parietal regions in the cortical semantic network. In this section we consider whether these results are genuinely at odds with the neuropsychological data discussed above, and suggest two ways of reconciling the apparently conflicting sources of evidence.

The anterior temporal lobe is 'shy' to functional MRI.

In standard acquisition protocols for functional MRI (fMRI), which has largely replaced H₂¹⁵O-PET for functional neuroimaging purposes, the signal-to-noise ratio diminishes substantially near the temporal poles, owing to their proximity to air-filled sinuses (the so-called 'susceptibility artefact'). One study compared the functional activation revealed by PET and by fMRI (using a standard whole-brain acquisition sequence) in a group of people performing a semantic categorization task⁵². Although both methods showed substantial semantic-related activity in ventral posterior temporal lobes, only PET revealed that this activation extended all the way rostrally to the temporal pole. Other PET evidence has demonstrated significant ATL activation during the semantic tasks of category fluency⁵³, object naming⁵⁴, category verification⁵⁵ and word recognition⁵⁶. Perhaps most saliently — because what could more clearly exemplify the essence of semantic processing? — the tasks of comprehending connected speech versus various forms of distorted (and hence meaningless) speech, and of reading coherent text versus a meaningless visual control condition, seem to engage the left temporal pole when measured by both PET^{57,58} and fMRI⁵⁹.

Other functional imaging methods similarly implicate the ATL in semantic processing. For instance, an elegant experiment was performed with anatomically constrained magnetoencephalography (MEG) in which subjects made semantic judgements about spoken or written words⁶⁰. As expected, the brain's initial responses to words were detected in the appropriate sensory areas for each modality; however, from approximately 400 ms after stimulus onset, the MEG responses for both modalities converged on the ATL.

Specificity of semantic processing. In the PET component of the object-naming study cited above¹¹, the strongest ATL activation was observed when participants were required to recognize and name famous people. A subsequent study from the same group⁶¹ proposed that the temporal pole might have a special role in the recognition and identification of unique concepts

Box 2 | Why the anterior temporal lobe?

This Review summarizes evidence for the hypotheses that, first, semantic generalization requires a single amodal hub and, second, that the neuroanatomical site of this hub is the anterior temporal lobe (ATL). Assuming, for the moment, that these hypotheses are valid, why is the ATL a neuroanatomically sensible place for the semantic hub? One reason that is sometimes offered is the fact, known from non-human primate physiology⁹³, that many primary sensory and motor areas, along with their related association cortices, connect to the ATL. This is true, but not a unique feature of the ATL: the 'tri-state' junction of the temporal, parietal and occipital lobes, including the angular gyrus, has the same feature of being well connected to input from multiple modalities, and indeed some researchers have ascribed a similar cross-modal mapping function to this area^{14,94}. It is worth noting that cross-modal is not the same as a-modal: the region around the angular gyrus might serve to combine information from several modalities but still not have the genuinely amodal function of a semantic hub.

Two neuroanatomical facts about the ATL region might make it an appropriate candidate for extracting amodal conceptual information. First, it is neuroanatomically proximal to the amygdala and to other limbic structures, as well as to the orbito-frontal cortex — regions that are known to be important for the processing of emotion and reward⁹⁵. Given that affective response to some extent pervades everything that we perceive, do and know, ATL regions might be well suited to computing associations between affect and more value-neutral sensory, motor and linguistic aspects of conceptual knowledge. Second, the ATL regions that seem so crucial to semantic memory are immediately adjacent to the anterior parts of the medial temporal lobe memory system — a system that is critical for rapid learning of new episodic information. As episodes must contribute to the gradual acquisition of new conceptual knowledge, it makes sense for episodic and semantic systems to be situated in close proximity.

— individual people and famous buildings being two prominent examples. A number of functional imaging studies, using both PET and fMRI, have since supported this idea, showing ATL activation related to the recognition of familiar versus unfamiliar buildings⁶², faces^{62,63}, names^{64,65} and even voices⁶⁶.

Semantic dementia patients are profoundly impaired at recognizing famous individuals from photographs, names and verbal descriptions⁶⁷; this impairment, however, appears to be one notable manifestation of a more general sensitivity to the specificity with which an item must be recognized or categorized. Across a wide array of semantic tasks (FIG. 2), the patients might perform well as long as accurate performance requires only a relatively coarse or general categorization of the stimulus. Thus, severely impaired SD patients can sometimes call a picture an 'animal', without being able to name it 'chicken' or even 'bird'⁶⁸; they can accurately sort pictures or words into categories such as 'animal' versus 'man-made object', but not 'car' versus 'boat'⁶⁹; they will correctly judge — when offered two pictures of a donkey, one with and one without a hump on its back — that 'the real one' is the humpless exemplar, but will make the same humpless (and therefore more 'animal prototypical', but incorrect) choice for the camel, to which humps are specific⁷⁰; they will copy-draw a line drawing of a real humped camel a mere 10–15 seconds after studying it, but omit the hump⁷¹; and so on. This pattern does not arise simply because tasks that require precise classification are more difficult. For example, Rogers and Patterson⁷² showed that, whereas healthy controls are faster and more accurate at classifying items at the basic level (for example, 'dog') relative to a more general level (for example, 'animal'), patients with SD show the reverse pattern: they have greater impairment on the more precise basic-level classification. Such findings suggest that semantic tasks that require the distinctive classification of a stimulus place particularly strong demands on the ATL regions that are affected in SD.

Functional imaging studies may likewise indicate that the ATL is most strongly recruited not just by recognition of unique items (such as the Eiffel Tower or Princess Diana), but by any form of specific semantic processing. One of several PET studies that support this view used a task in which normal participants were asked to verify, by answering yes or no, whether the stimulus shown in a colour photograph belonged to a particular category⁵⁵. For example, in trials designed to receive 'yes' responses, participants judged on different occasions whether the photo of a robin depicted an animal (superordinate level), a bird (basic level) or a robin (subordinate or most specific level). Relative to a control condition, all three semantic-judgement conditions activated the bilateral posterior fusiform gyrus and the occipito-temporal cortex, but the subordinate condition, when contrasted with both superordinate and basic levels, activated the ATL bilaterally. The ATL activation peaks aligned closely with the areas that showed the strongest grey-matter reduction in a voxel-based morphometry analysis of atrophy in SD patients⁴². The ATL activation peaks for the subordinate condition also matched those from another PET study that contrasted the naming of unique items with the (basic-level) naming of common objects⁷³. Similar results have been reported using fMRI^{74,75}. A conjunction analysis of results from four different PET studies of semantic processing, two with words as stimuli and two with pictures, highlighted activation of the inferior ATL; the authors concluded that this region supports a polymodal or amodal network of semantic representations that is recruited when more specific conceptual information is required⁵⁶ (BOX 3).

This brief Review suggests that activation in ATL regions during semantic tasks is not as scarce as an initial survey of the literature might suggest, especially if one takes into account the low signal-to-noise ratio that is achieved by standard fMRI methods in these regions and the fact that the amount of signal generated in ATL regions is related to the specificity of semantic process-

Voxel-based morphometry

A voxel-by-voxel analysis of structural-image data, most commonly the grey-matter segments extracted from T1-weighted MRI.

Conjunction analysis

A statistical method used in functional brain imaging research for identifying brain regions that are significantly activated in two or more separate experimental conditions.

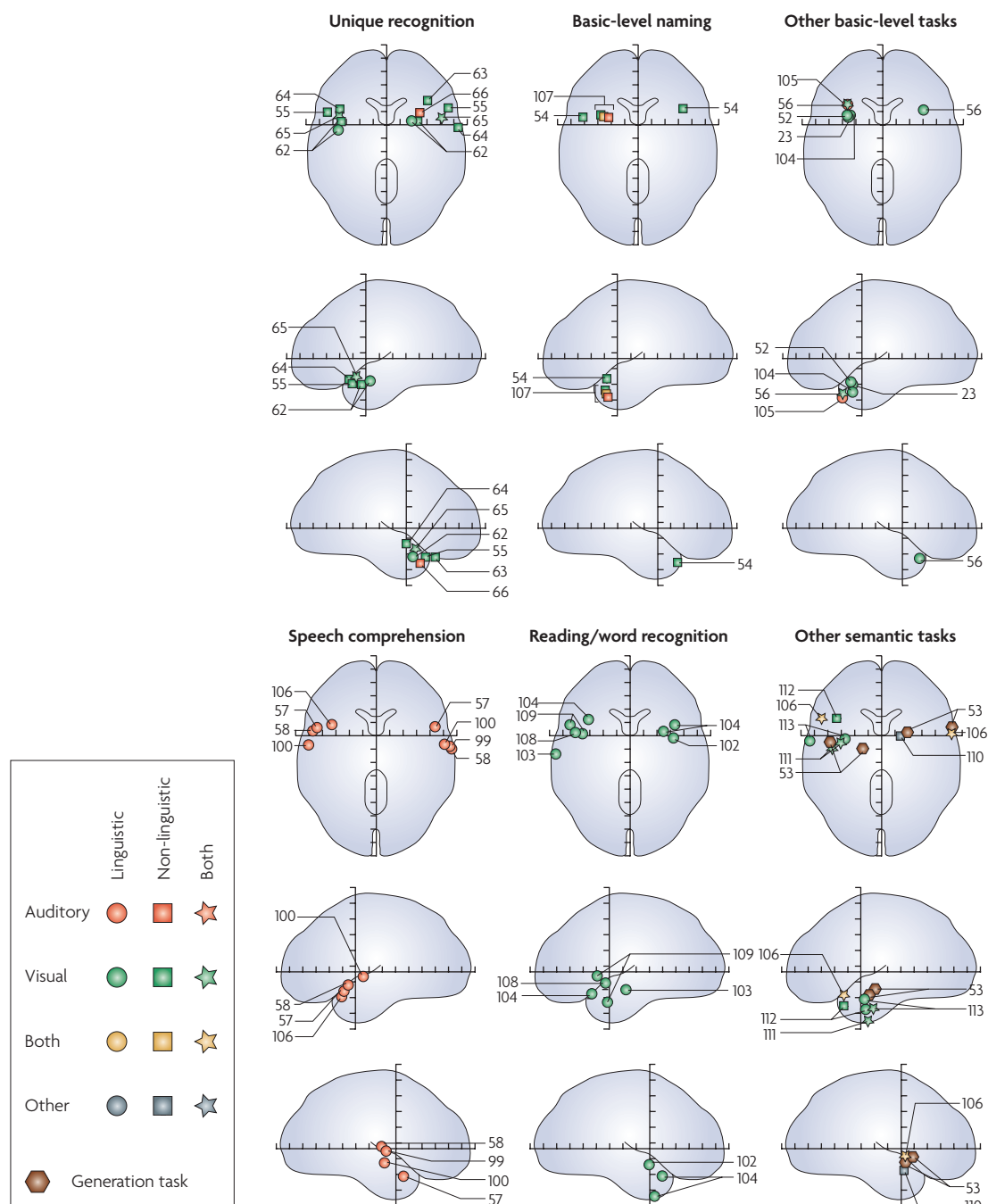


Figure 4 | ATL activation in functional imaging studies of semantic processing. This figure shows the most anteriorly located temporal-lobe activation peaks (plotted in Talairach space) reported in 28 different studies of semantic-task performance in healthy individuals. More than 40 of such studies using a variety of imaging methods, have been published; this set includes those studies that used either positron emission tomography or functional MRI and reported coordinates of anterior temporal lobe (ATL) peaks in either Montreal Neurological Institute (MNI) or Talairach standardized spaces. Peaks originally reported in MNI coordinates were transformed to Talairach space using the transformation described by Brett and colleagues¹¹⁴. The studies varied in the modality of stimulus presentation, the nature of the particular task that was being performed, whether or not the stimuli were linguistic, and the specificity of the categorization that was required for successful task performance. Despite these variations in methodology, the different studies showed activation in remarkably similar regions of the ATL. The numbers indicate the studies from which the data were taken, as numbered in the reference list (see REFS 52–58,61–66,99–113). The shape and colour of the plotted areas indicate the nature of the stimulus that was used in the experiments, as shown in the legend. Where multiple points are plotted for the same study, these represent the most anteriorly located activation peaks in the temporal lobe from different contrast conditions in the same study. For instance, for a study that used both words and pictures as stimuli, and that reported separate anterior-temporal peaks corresponding to the two stimulus sets, both peaks are shown.

ing demanded by the task. Of course, a review of the functional imaging literature performed with a different 'filter' might reach a different conclusion, especially if it excluded PET studies and included only fMRI studies that lacked techniques designed to maximize the signal in the 'hard-to-get' rostral temporal lobes. Indeed, much of the evidence from such imaging studies supports the view that semantic processing involves mainly frontal or posterior-temporal loci, and of course our own position also implicates these regions in the larger semantic network.

The current Review is selective in that our primary aim was to determine whether the scarcity of reported ATL activation in the literature to date is sufficient to refute the conclusion drawn from lesion studies, which unambiguously point to ATL regions as being crucial for semantic processing. To paraphrase a recently-departed United States Secretary of Defense, we do not believe that the seeming absence of evidence constitutes, in this case, evidence of absence.

Why does the semantic network need a hub?

The above considerations support a view of human semantic cognition that raises at least two questions. The first question is why a single region of the brain should contribute to learned associations among widely distributed sensory, motor and linguistic representations. For example, visual representations of objects are apparently coded in the posterior inferior/middle temporal cortex, and knowledge about action is probably supported by frontal and parietal regions^{76,77}. Surely then, the knowledge that allows one to brush one's hair with a hairbrush and one's teeth with a toothbrush could be coded in direct associations between object-recognition regions in

the posterior-temporal cortex and motor plans in frontal and parietal areas, perhaps via the dorsal visual processing stream? Yet the ATL focus of damage in SD, which is far removed from these sites and does not lie between them, seems to disrupt knowledge about characteristic object use^{78,79}. Furthermore, damage in the same region impairs knowledge of the colours that are characteristic of certain object shapes (for example, grey for an elephant and orange for a carrot)^{80,81}, even though shape and colour are two manifestly visual forms of information that are thought to be supported by neighbouring regions in the posterior ventral occipito-temporal cortex. Again, why are there not just direct connections between these two modality-specific regions? That is, why the need for a single hub?

The second question relates to the fact that was noted earlier regarding scallops and prawns: conceptual similarities between items are not necessarily apparent from their perceptual features. For instance, in one of the simple tasks used in studies with healthy and semantically impaired individuals, called 'category fluency', a person might be asked to name as many different fruits as possible in one minute. A typical sequence of responses might be "Apple, orange, banana, pear, grapes, lemon..." and so on. These six objects are very different from one another in colour, shape, texture, how they grow, how they are eaten, *et cetera*. Yet normal individuals can (whereas SD patients definitely cannot) perform this task with ease, because knowledge of conceptual similarity allows these objects to be grouped as fruits, even though they have few sensory/motor properties in common. The second question is therefore: how does the semantic system acquire representations that capture such conceptual similarity relationships?

Box 3 | Sensitivity to specificity in the anterior temporal lobe

Both neuropsychological and functional imaging data suggest that anterior temporal lobe (ATL) regions are especially taxed by tasks that require very specific recognition or classification of a stimulus. What accounts for this sensitivity to specificity?

One possibility is that a specificity gradient exists in the temporal lobes, such that the greater the specificity with which an item must be recognized or categorized, the more rostral the activation in the temporal lobes will be⁹⁶. The data in FIG. 4, however, challenge this hypothesis: the ATL regions that are engaged by recognition of unique entities (top left of FIG. 4) are no more anterior than those that are activated by tasks that require discrimination of (non-specific) basic-level categories (top middle and top right of FIG. 4) or other semantic tasks (bottom section of FIG. 4).

The distributed-plus-hub view offers a different explanation. It suggests that ATL regions encode the similarity relations among various concepts, so that semantically related items (for example, various different birds) are coded with similar patterns across ATL neurons. According to this model, naming a particular bird as a 'robin' requires the ATL hub to instantiate the robin representation almost exactly, as the name does not apply to other kinds of birds, many of which nevertheless have representations that are very similar to the robin. To name the same item 'bird', however, the robin pattern need not be instantiated exactly. Because the name applies to all birds and all birds share similar representations, it is only necessary for the hub to find a representation that is sufficiently 'bird-like' to activate the name. Thus, small distortions of the 'robin' representation — perhaps resulting from ATL atrophy — will prevent the network from retrieving the robin's specific name (and other properties that differentiate it from other birds) without disrupting the retrieval of properties that are common to birds. A similar explanation extends to the interpretation of the functional imaging results, if one assumes that a stronger metabolic response in the ATL occurs in tasks that require the differentiation of highly overlapping representations.

Evidence from computational modelling. The two questions posed above might seem unrelated, but evidence from neural-network models suggests that they are not. Computer simulations with such models have shown that networks that adopt a convergent architecture — in which all forms of information about concepts are, at some point, processed through the same population of neurons and synapses — exhibit functional properties that explain how the semantic system is able to learn conceptual similarity relationships⁸². An example of such a convergent architecture is illustrated in the right-hand panel of FIG. 1b. Contrasting with this is what might be called a 'gating' architecture, illustrated in the right-hand panel of FIG. 1a.

In the gating architecture, the associations between different kinds of attributes are encoded in different neuroanatomical pathways: one pathway stores the association between an item's shape and its name, another stores the association between an item's shape and the usual action associated with the item, and so on. A representation of the current task determines the pathway through which activation will flow. If the task is to name a line drawing of an object, then activation will flow from the shape representation to the name representation. If the task is to demonstrate how an object is used, then activation will flow along a different path,

Connectionist model

A form of computational model used to understand cognitive processes by simulating the flow of activation among simple, neuron-like processing units through weighted, synapse-like connections.

Normative property-listing studies

Studies in which participants are given the name of a category or item (for example, 'bird' or 'robin') and asked to list as many properties as they can think of that characterize it. The proportion of participants that list any particular property serves as an index of the property's importance to the concept.

Drawing-to-name

A non-verbal method of investigating a person's knowledge of objects in which the participant is given a concept name (for example, 'camel') and asked to draw the corresponding object.

from the shape representation to a representation of action. In this architecture, the same input activates separate pathways, depending on the task at hand — thus, the task representation 'gates' the flow of activation through the network.

By contrast, in the convergent architecture, the associations between a given input (for example, a shape representation) and all other kinds of attribute are stored in the same neuroanatomical pathway. As FIG. 1b illustrates, the task-dependent representation can still shape the flow of activation through the network, so that the same stimulus can differentially activate various attributes depending on the task demands. In this kind of model, however, the neurons and synapses that comprise the task-independent representations contribute to the processing regardless of whether the task is to name an object, use an object or identify an object's characteristic colour (when seen in black and white).

Computer simulations of learning and processing in networks with these architectures suggest that the convergent architecture is better able to learn conceptual similarity relationships than the gating architecture⁸³. To understand this, consider how the gating model might encode information about a pear. The pathway that stores associations between shape and name will learn an intermediate representation that reflects both visual and phonological similarity to other known objects. Thus, a pear and a light-bulb will generate somewhat similar representations in this pathway because they have similar shapes; a pear and a bear will generate somewhat similar representations because they have similar-sounding names; and a pear and a banana will generate rather different representations because they have different shapes and different-sounding names. The gating architecture will not encode conceptual similarity relationships, which should capture the fact that pears and bananas are semantically related whereas pears and light-bulbs or pears and bears are not.

It might seem as though such problems can be solved simply by attributing greater weight or salience to some sensory or motor features than others. For instance, if similarity of taste is more salient than similarity of shape or word-sound, then bananas and pears, which are both sweet, might be judged more similar to one another than pears and light-bulbs or pears and bears. The problem with this approach is that the salience of a given feature varies from one semantic category to another: colour, for example, is important for categorizing fruits (consider lemons versus limes), but is irrelevant for categorizing toys⁸⁴. Thus, there appears to be a chicken-and-egg problem: to determine the salience of a given sensory, motor or linguistic feature, one must know to which category the item belongs, but the item is difficult to categorize without knowing the salience of its observed features^{85–87}. In other words, there is no single salience for a given property that will correctly capture semantic similarity for all concepts.

In a convergent architecture, however, where the same intermediate units that code the association between shape and name must also learn to code relationships between shape and colour, shape and action, shape and

texture, and so on, as well as complementary mappings (that is, mappings in the other direction) between these surface representations, the internal representations that emerge look very different. They are not dominated by the similarities expressed in any individual modality (or pair of modalities), but instead reflect the similarity relationships that is apparent across all of the modality-specific representations taken together. In other words, the intermediate representations that arise in the hub can capture the 'deep' structure of concepts and hence can promote generalization across items that are conceptually related, even if they do not happen to have similar shapes, colours, associated actions, and so on. These representations are amodal in that they can be generated from any individual receptive modality and can be used to generate behaviour in any individual expressive modality. They are semantic in that they express the conceptual similarity relations among concepts that are critical to semantic generalization and induction, even though, in themselves, they have no retrievable content⁸².

Rogers *et al.*⁸⁸ demonstrated the appeal of this idea using a fully recurrent connectionist model that was trained to map between simple visual representations of objects, verbal descriptions of the objects, and the objects' names. The information contained in the verbal descriptions and visual representations was derived from normative property-listing studies⁸⁹ and a study of drawing-to-name⁸⁸. The internal representations that were learned by the model captured the gross similarity relations among the items in the corpus. More interestingly, they also captured aspects of similarity structure that were not apparent when considering the verbal descriptions or the visual representations alone. For instance, considering just visual similarities, fruits and vegetables share many properties with man-made objects whereas, considering just the verbal descriptions, fruits and vegetables are quite distinct from both animals and man-made objects, although they share a few properties with animals. When trained on these patterns, the model acquired internal representations in which the fruits and vegetables were distinct from animals and man-made objects, but were actually more similar to man-made objects. Thus, the model made the counterintuitive suggestion that fruits and vegetables, although they are 'natural' and not man-made, might be represented as being more similar to artefacts than to other natural things (like animals) in the human semantic system. Consistent with this suggestion, when asked to sort pictures of apples and other fruits and vegetables into one of three categories — plant (correct), animal, or man-made artefact — SD patients mis-assigned a number of fruits and vegetables to the artefact category, despite making few errors when the choice categories for the apple were fruit, bird or land animal⁸⁸.

Concluding remarks

We return to Mr M, driving through the countryside with his wife, retrieving the several-years-old memory that they will have to turn left ahead. His view from the car window includes not just the cues to this preserved route knowledge (knowledge that many people with normal brains would find difficult to retrieve), but one

of the most familiar scenes in the British countryside: a flock of sheep. The sheep are a puzzle to Mr M: not only does he not know what to call them, he no longer knows what they are. He wears a wool jacket when it's cold and eats roast lamb for Sunday lunch, but would not be able to say that "those things" out there are the source of these products. He would succeed in matching a photograph of a sheep taken from the side to one taken from the front, because this task — which people can perform on meaningless objects that they have never seen before — relies on visual perceptual abilities rather than semantic ones⁹⁰. If asked whether the photograph of a sheep is an animal, he would probably say yes, but if asked what other animal is similar to it, he would look blank. This striking combination of preserved and disrupted cognition has now been documented in hundreds of patients

with SD in dozens of neurology clinics in many different languages and countries. Not every such patient has had detailed structural and/or functional brain imaging but, for those who have, the resulting neuroanatomical profile is as consistent as the cognitive profile: the selective but generalized semantic degradation that occurs in SD goes hand-in-hand with focal degeneration of the bilateral ATL. Specific features of conceptual knowledge are almost certainly represented elsewhere and in a widely distributed network; but people's ability to receive information in one modality and express it in another, to generalize across conceptually similar entities that differ in almost every specific modality, and to differentiate between entities that resemble each other in many modalities — all quintessentially semantic abilities — seem to depend on the ATL.

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Acknowledgements

We gratefully acknowledge help from E. Copper-Pye in preparation of the manuscript.

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