Disorders of semantic memory

Memory is a complex and multifaceted aspect of human cognition, as reflected by the broad range of neuropsychological deficits which present with complaints of "poor memory". We will review disorders of semantic memory, the component of long term memory which represents our knowledge of objects, facts, and concepts, as well as words and their meaning. The distinction between episodic and semantic memory was first drawn by Tulving on psychological grounds: episodic memory corresponds to the recollection of personally experienced episodes or events which are time and place specific. By contrast, semantic memory is culturally shared, usually overlearned, and not temporally specific. According to this dichotomy, remembering the details of a meal in a Parisian bistro on holiday last year depends on episodic memory systems, whereas knowing the meaning of the word “bistro” and that Paris is the capital of France, draws on semantic memory.

There is clearly a degree of interdependence between episodic and semantic memory: knowledge must first be acquired and is initially temporally specific, whereas all experiences must be understood at some level. Some theorists maintain, therefore, that they represent no more than the extremes of a spectrum of information acquisition. Yet examples of patients with profoundly impaired episodic memory and preserved general knowledge, such as Korsakoff amnestics, together with patients in whom semantic memory is selectively disrupted (see below), argue that these two systems are, at least partially, separable on neuropsychological grounds. From an anatomical perspective, the medial temporal structures, in particular

Figure 1  Representation of commonly tested input and output channels to and from semantic memory.
the hippocampal formation (hippocampus proper, dentate gyrus, subicular complex, and entorhinal cortex) are critical for the encoding of new episodic memories. Over time, it seems that such memories become independent of the hippocampal formation and that retrieval then depends on the frontal lobes and diencephalon (mammillary bodies and thalamus). The structural correlates of semantic memory remain more speculative, but evidence is accumulating to implicate the inferolateral temporal cortex in this role.

With the fast approaching prospect of disease modifying therapies, recognition of selective deficits in all forms of memory is becoming increasingly important to the diagnosis and staging of degenerative diseases. The principle underlying evaluation of semantic memory is the assessment of knowledge using verbal and non-verbal routes of input and output (fig 1). A pattern of consistency over testing sessions, together with item specific failure on a range of tests, suggests semantic memory impairment. Examples of such tests, and their relation to the input and output channels represented in fig 1, include the following:

- Category fluency: “Tell me the names of as many animals as you can think of in one minute.”
- Confrontation naming: “What does this picture show?”
- Naming to description: “What do we call the large African or Indian animal with a tough leathery skin and a trunk?”
- Picture sorting at superordinate, category, and subordinate levels: “Sort these pictures into living and man made items; land animals, birds, and water creatures; native and foreign animals etc.”
- Verification of semantic attribute questions: “Does an elephant have a trunk? Does an elephant lay eggs?”
- Word-picture matching: “Point to the elephant” (from an array of animals).
- Generation of verbal definitions: “How would you describe an elephant to somebody who had never seen or heard of one?”
- Tests of associative semantics such as the pyramids and palm trees test: the patient is asked to match a stimulus item (for example, an elephant) with one of two alternative targets (for example, a circus tent or a farm).
- The organisation and neural basis of semantic memory are subjects of much speculation, but insights can be gained by examination of patterns of breakdown in cross sectional and longitudinal studies of individual patients and populations. The remainder of this paper will focus on some of the important theoretical issues, in the context of specific conditions which give rise to semantic memory disturbance.

**Alzheimer’s disease: loss of knowledge or of access to knowledge?**

Episodic memory impairment is the earliest and most pervasive cognitive deficit in Alzheimer’s disease. Patients with Alzheimer’s disease show pronounced deficits in new learning as well as a temporally graded loss of remote autobiographical memory (relative sparing of older memories). Recent findings indicate that semantic memory loss may also occur early in the course of the disease, although it should be emphasised that, by contrast with semantic dementia (see below), this is never severe and is always overshadowed by the impairment in episodic memory. A study of patients with early presumed Alzheimer’s disease, some of whom had mini mental state examination scores above the traditional cut off score of 24 (out of 30), showed a subgroup with impairment on a range of semantic memory tasks, as well as a subgroup that performed flawlessly, although all had episodic memory loss.

The initial episodic memory impairment almost certainly results from functional disconnection of the hippocampus from incoming sensory information, as a result of the involvement of the transentorial region in the early stages of Alzheimer’s disease, whereas the semantic memory deficit is assumed to reflect spread of pathology into the temporal neocortex proper.

There has been a long debate as to whether the semantic deficit in Alzheimer’s disease reflects an actual loss of information or a deficit in information retrieval; the evidence reviewed below points to a breakdown at the level of semantic knowledge itself.

One of the most sensitive tests of semantic breakdown is category fluency, which is impaired early in the course of Alzheimer’s disease. This is, of course, a complex task that relies on several other components of cognition including attention, working memory, retrieval strategies, and phonological processes. Evidence of selective semantic loss comes from the finding that patients with Alzheimer’s disease show a reversal of the pattern seen in normal controls and in patients with subcortical dementias (Huntington’s disease, progressive supranuclear palsy, etc) who, although they perform poorly on both tasks, do relatively better on category than letter fluency (generating words beginning with a given letter). Moreover, recent work has shown that the order in which items are produced is abnormal in Alzheimer’s disease, reflecting semantic disorganisation.

Picture naming is also consistently impaired, but at a later stage than category fluency. Evidence that this is due to a semantic, rather than a phonic, deficit comes from analysis of naming errors, which tend to be semantically related to the target (for example, superordinate—animal for elephant, or category coordinate—giraffe for elephant). Perceptual errors also occur as the disease progresses.

Work from our group, among others, has also shown impairment on other verbally based tests of semantic knowledge such as verification of semantic attributes and the production of verbal descriptions in response to the name of an item (see above for a full description of these tasks); performance on the second also correlates highly with the ability to name pictures of the same items.

The abnormal performance on non-verbal based tasks, such as picture sorting and the pyramids and palm trees test, is also strong evidence in favour of a central semantic disorder.

**Semantic dementia: insights into the organisation of semantic memory**

Although recognised in Japan in the 1940s under the title of Gogi (word meaning) aphasias, selective impairment of semantic memory was not described in the English literature until 1975, when Warrington reported three patients with progressive anomia and impaired word comprehension. Many subsequent patients, however, were classified as cases of primary progressive aphasias—a term introduced by Mesulam to describe the syndrome of isolated aphasias in the absence of other cognitive deficits. Over the past decade it has become clear that patients with this syndrome fall into two broad groups: progressive non-fluent aphasias, who have prominent deficits in non-semantic (phonological and grammatical/syntactic) processes, resulting in a Broca’s type aphasias, and fluent aphasics, in whom the language disorder usually reflects a breakdown in the semantic components underlying-
ing language production and comprehension. The term semantic dementia was introduced to describe the second group, and to convey the concept of profound and pervasive semantic deterioration which disrupts factual knowledge and object recognition as well as language processes. Patients with semantic dementia present with loss of memory for words and increasing difficulty recognising familiar objects and people. Their spontaneous speech is characteristically empty, with word finding difficulties and occasional semantic errors, but is fluent, with normal articulation, phonology, and syntactic structure. By contrast with patients with Alzheimer’s disease, their memory for day to day events is strikingly well preserved, as reflected by their good recall of recent events and preserved orientation. Formal testing of language discloses a severe anomia, impaired comprehension of single words, both spoken and written, greatly reduced generation of exemplars on category fluency tests, and an impoverished fund of general knowledge. By contrast, comprehension of syntactic structures remains unaffected. Visuospatial skills, frontal “executive” functions, and non-verbally based problem solving are also intact. Analysis of reading typically shows a pattern of surface dyslexia—a tendency to regularise the pronunciation of words with irregular spelling-to-sound correspondences (for example, pint, to rhyme with hint, flint etc).

Brain MRI discloses atrophy of the inferolateral portion of the temporal lobe, and functional imaging studies have also implicated this region as the principal site of pathology. Controversy exists regarding the necessity for bilateral disease, but at least some patients have shown left sided changes only. To date, relatively few have come to postmortem, but of those examined, all have shown either non-specific degeneration or more often the intracellular inclusions typical of Pick’s disease.

The psychological changes in semantic dementia are particularly relevant to debates about the organisation of semantic knowledge. A common finding is that the finer-grained (subordinate) aspects of these patients’ knowledge seem to be more vulnerable than higher order information. For instance, a patient may fail to show any specific knowledge about elephants but still know that an elephant is an animal. It is easy to imagine how this superordinate information might be deduced from a picture, but the same finding also applies to words. Furthermore, there is an orderly progression to the naming errors over time in semantic dementia, which evolves from circumlocutions to category coordinates to superordinate labels; for instance in response to a picture of an elephant: “big African animal” → “horse” → “animal”. Some commentators interpret these findings as evidence for a hierarchical structure of knowledge. According to this account, the mental representation of a concept is analogous to a branching tree, the origin of which corresponds to the most collective and the periphery to the most selective designation of an item (fig 2A). The idea of a degenerative process “pruning back the semantic tree” has an obvious intuitive appeal, but an alternative model, the distributed feature network, predicts the same phenomenon in a different way. According to this theory, the basic units of semantic representation are properties, and concepts reside in unique patterns of activation across these units (fig 2B). A degraded network would still be more likely to contain units common to whole categories than units critical for the identification of individual instances. Judgements about category membership would therefore continue to be supported long after more fine grained knowledge had disappeared. Adjudication between these competing theories is one of the major goals of current research in the field of cognitive neuroscience.

Herpes simplex encephalitis: category specific loss of semantic memory

Recovery from herpes simplex virus encephalitis (HSVE) may be followed by various cognitive deficits. As the major locus of damage is the medial temporal lobe, a profound amnesic syndrome is the commonest deficit, but destruction of the inferolateral temporal lobe is also common with resultant loss of semantic memory. An intriguing feature of these patients is their tendency to evince a preferential loss of information about living things relative to artefacts. It has been argued that this finding may reflect nothing more than a test artefact consequent on uncontrolled linguistic variables such as word frequency, but the reports of a few patients with the opposite pattern favours the idea that the phenomenon is a true reflection of functional specialisation within the cerebral cortex. At the simplest level, this could be translated into the notion

Figure 2 (A) Representation of part of a hierarchical network concept. (B) Representation of part of a distributed feature network showing emergent concepts of elephant (solid line) and tiger (broken line).
that the neural representations of different categories are located in separate cortical regions. An alternative hypothesis is that living things have many more perceptual features which are critical for their identification, whereas representations of man made items are more heavily weighted towards functional features. Comparing the process of deciding whether an animal is a tiger or a leopard, with that of determining whether a vessel is a vase or a bowl, is a striking illustration of this idea.

Support for the second explanation comes from various sources. Firstly, in an extensive series of tests employing many different semantic categories in patients with a selective loss of natural kinds knowledge, Warrington and McCarthy found that not all categories respected the living-man made distinction. In particular, body parts were found to segregate with artefacts, whereas musical instruments, fabrics and precious stones behaved more like living things. Further support came from computational neural network models, in which it was found that a loss of living things could be induced by selectively "lesioning" nodes that represent perceptual features.

In anatomical terms, the living-man made dissociation seems to respect a fairly constant anatomical division between the ventral temporal structures that are vulnerable in HSVE and frontoparietal lesions, usually resulting from large middle cerebral artery territory infarcts. This distinction has parallels with results of experiments on the poststriate visual pathways of rhesus monkeys, showing that the perceptual task of object discrimination is dependent on ventral projections terminating in the inferior temporal cortex, whereas the task of object localisation and grasping are subserved by more dorsal pathways. In support of this distinction, recent PET studies have also shown differential activation of ventral and more dorsal regions during semantic tasks involving animals and objects respectively.

The phenomenon of category specificity is also important to the debate about whether there are single or multiple knowledge systems. It has been argued that the delayed appearance of language, in both phylogenetic and developmental terms, necessitates at least two separate systems. McCarthy and Warrington have reported a series of patients who show a significantly different level of performance on semantic tasks depending on both the category of the item (living things vs artefacts) and the modality of presentation (pictures vs words). On the basis of these findings they postulate multiple meaning systems (verbal and visual systems for living things and artefacts).

The doctrine of multiple meaning systems, and the redundancy of information that it entails, has been questioned by some theorists, who argue instead for a single, all purpose meaning system, and attempt to explain away modality effects as arising from a difference in the information inherent in pictures and words. Cases with an advantage for words over pictures are regarded as representing a disconnection at a presemantic stage of processing. In an effort to resolve these anomalies a third model has been proposed, in which a rapid, visually accessed "identification semantics", is coupled to an amodal store of associative knowledge.

Conclusions

The breakdown of semantic memory is common in Alzheimer's disease, in which it occurs in the context of more widespread cognitive decline. Isolated semantic memory loss gives rise to a clinically distinct syndrome (semantic dementia). Category specific deficits occur most commonly in the setting of HSVE. Recognition of these phenomena is important in the differential diagnosis of cognitive disorders, as well as in understanding and explaining a patient's difficulties at a practical level. From a theoretical stance, a number of important issues regarding the organisation of semantic knowledge remain uncertain, but will hopefully be resolved by combining experimental neuropsychological methods with structural and/or functional brain imaging.

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NEUROLOGICAL STAMP

Wilhelm Griesinger (1817-68)

Griesinger's great contribution to psychiatry was his recognition that there were certain different categories of mental disease. He considered that the brain was responsible for mental disease and that mental illness had a definite physical basis. In 1845 he published his Pathology and therapy of psychic disorders, which accurately described clinical syndromes based on pathological studies and psychological analyses. Griesinger succeeded Romberg as Professor of Psychiatry and Neurology at Berlin University in 1865. In 1868, the year of his death, he founded the Archiv Für Psychiatrie, known also as Griesinger's Archives. Apart from his work in psychiatry, between 1857 and 1864 he published monographs on infectious diseases in which he discussed typhus, typhoid, relapsing, and malarial fevers. Griesinger's disease is ancylostomiasis or hook worm disease.

He is also remembered eponymously by Griesinger's sign, the oedematous swelling behind the mastoid process occurring with thrombosis of the transverse sinus. Griesinger also contributed to the muscular dystrophies and the clinical features were summarised in his monograph of 1865. Duchenne dystrophy was also known as Duchenne-Griesinger disease but it was Duchenne who initially separated and classified various muscle diseases.

He was postally honoured in 1960 by the German Democratic Republic (East Germany) to commemorate the 250th Anniversary of the foundation of the Charité Hospital in Berlin where Griesinger had been appointed head of the neurological and psychiatric clinic in 1866 (Stanley Gibbons E531, Scott 254).

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