Semantic dementia (SD), one of the main clinical variants of frontotemporal dementia, presents a unique combination of clinical and imaging abnormalities. We describe the epidemiological, cognitive, and radiological features of SD. The distinctive and consistent neuropsychological deficits in this disorder have had a major effect on current conceptions of the organisation of semantic memory and its links to episodic memory, language, and perceptual processes. Structural (MRI) and functional (fluorodeoxyglucose-PET) studies in SD emphasise the role of the temporopolar and perirhinal cortices. Unlike other frontotemporal dementia syndromes, the neuropathological findings in SD are fairly predictable: most patients have ubiquitin-positive, tau-negative neuronal inclusions.

From a nosological perspective, SD is regarded as one of the main clinical variants of frontotemporal dementia, sometimes also referred to as frontotemporal lobar degeneration. The umbrella term of frontotemporal dementia also includes progressive non-fluent aphasia and a behavioural or frontal variant. The justification for this grouping of seemingly diverse syndromes is threefold. The first is some shared clinical features: many patients with SD have the same behavioural changes as those with the behavioural variant of frontotemporal dementia. The second is a degree of anatomical overlap apparent on structural and functional brain imaging. The third, and perhaps most compelling, reason is the overlap in pathologies. Substantial advances have been made in each of these arenas, which will be discussed more fully below.

In addition to published research, we draw on our experience of 100 patients with SD studied in Cambridge, UK, over the past 17 years.

**Epidemiology and demography**

Little has been published specifically related to the epidemiology of SD but, because between a quarter and a third of patients with frontotemporal dementia have this disorder, some tentative extrapolations can be made. Depending on the clinic setting and the age range of the attendees, 5–20% of all patients with dementia have frontotemporal dementia. In our clinic, 10% of referrals have received this diagnosis, of whom a quarter have fulfilled criteria for SD (Hodges JR, unpublished). A study from Germany compared patients in different settings: two psychiatric hospitals versus the University of Regensburg Memory Disorders Clinic. Although behavioural disturbance was the most common reason for presentation in both groups, perhaps unsurprisingly, patients with language problems presented almost exclusively to the memory disorders clinic.

Prevalence studies based on defined populations have been done in Cambridgeshire, UK, London, UK, and the Netherlands. The two UK studies were in close agreement on the overall prevalence of early-onset dementia (80–100 per 100 000, 95% CI 60–120) and the prevalence of frontotemporal dementia, which was similar to that of AD in the 45–64 years of age group (15 per 100 000, 8–27). For undetermined reasons, the prevalence in the Netherlands was substantially lower (4–6 per 100 000, 3–8).
Many people view frontotemporal dementia, in all its forms, as a presenile disorder with onset typically between the ages of 45 and 65 years. Recent pathological and clinical studies have, however, reported onset after the age of 65 years in 20–40% of cases. In our series of 100 SD cases, the commonest age range at presentation was between 66 and 70 years, and 45% were aged over 65 years at diagnosis (figure 1). Men and women appear equally likely to be affected.

Up to 40% of patients with frontotemporal dementia are said to have a positive family history of a neurodegenerative disorder, but in many instances this is probably incidental. Patients with a strong familial tendency (early-onset dementia in one or more first-degree relative) are much rarer, perhaps accounting for 5–10%. Moreover, the familial rate seems unevenly distributed across frontotemporal dementia subtypes: SD has a lower rate than the other variants. This accords with our experience of 100 cases: 15 had a family history if late-onset dementia of any type is included, but only two had a clear family history of early-onset dementia or Pick’s disease.

Clinical features

The most prominent early feature and presenting complaint in typical SD is the reduction of expressive vocabulary, commonly described as a “loss of memory for words”. Although patients may also have non-specific memory impairment, this does not, in contrast to even early AD, reflect a true amnesia: memory for recent day-to-day events and topographical aspects of memory are relatively normal in patients with SD.

Another key and parallel impairment is the deterioration of receptive vocabulary. This change may not be immediately apparent in conversation, as at first the comprehension deficit affects only less common words, and normal conversation does not rely on every single word being understood. Hence, patients and even family members may not be aware of the extent of this impairment.

Carers may report subtle behavioural changes, though these should not dominate the early clinical picture. There is, however, substantial overlap of behavioural abnormalities between SD and the behavioural variant of frontotemporal dementia. Degraded social functioning results from a combination of emotional withdrawal, depression, apathy, or irritability; restriction of food preferences or bizarre food choices are more common than overeating. Clockwatching and rigidity are common, and some patients develop an intense interest in jigsaw puzzles or word search puzzles. Emotional coldness and a lack of empathy are distressing for carers.

Spontaneous speech is consistently characterised by anomia, which is made especially salient by its embedding in relatively normal phonology and grammar. When a word cannot be retrieved, word-finding pauses do occur; but more often, and increasingly with progression, specific terms tend to be replaced by commoner, more general terms: “thing” instead of “kettle”, “place” instead of “Cambridge”, and “doing” instead of “cooking” or “gardening”. On formal assessment, naming of line drawings and pictures of objects is seriously and increasingly impaired, and this clearly reflects a general, central, and hence amodal problem. The patients are, if anything, more anomic if asked to put a name to a description (eg, “what do you call a bird that lives on water and quacks?”) or to write rather than speak the object’s name. As the disease progresses, many patients are left with just a few stereotypical expressions and, in speech comprehension, may appear “word deaf”.

The aspects of word knowledge that are preserved or impaired in SD are thrown into sharp relief by asking the patients first to repeat long, low-familiarity words with complicated sound sequences, such as “hippopotamus” or “chrysanthemum”, and then to say what the words mean. Repetition is almost invariably perfect, but the definitions offered are either generalised and lacking in detail (eg, “Hippopotamus, can you say that?”, “Yeah, hippopotamus”; “What is a hippopotamus?”, “A big animal”) or simply absent (“I think I’ve heard of a hippopotamus but I can’t say what it is”). Patients with progressive non-fluent aphasia typically show the opposite pattern (ie, an advantage for defining over repeating these long words). A few patients with SD, however, develop some features similar to those in progressive non-fluent aphasia, such as problems with repetition, which further emphasises the overlap between frontotemporal dementia syndromes.

As a disorder of concepts, SD also affects knowledge of object use, although this is often subtle at the beginning.
Carers usually report that the patients function normally at home and are still able to use objects correctly despite being unable to name them.

A deficit in person knowledge is consistently a feature of SD, at first affecting the ability to name people, then to generate information from their faces or names, and eventually even to identify whether someone is familiar or famous. Whether person knowledge is a special and especially vulnerable category of knowledge, or whether it is simply a kind of semantic knowledge that must be retrieved at a very specific level is unclear. Specificity has a profound impact on semantic performance in SD; when asked to verify that a picture of a robin is an animal, a bird, or a robin, success in patients with SD might decrease from near perfect for the first, to moderately impaired for the second, to near chance for the third of these judgments. There is some indication that the neuroanatomical representation of person knowledge is special given that patients with SD with right temporal atrophy almost invariably have a gross loss of person knowledge. In a study of patients with SD with either left or right predominance, at the time of first presentation to the clinic, language-related deficits, namely anomia and impaired comprehension, were more common in the former; by contrast, patients with right predominance had a higher prevalence of person recognition problems, social awkwardness, and poor insight (table 1).

In contrast to AD, orientation in time, simple calculation, and drawing skills are all well preserved in SD. This pattern of preservation and loss can be revealed with simple bedside testing instruments, such as the Addenbrooke’s Cognitive Examination, which is sensitive to both early AD and SD. Little work has been done on the practical effect of SD but two recent studies have emphasised that the considerable burden and effect on quality of life caused by caring for patients with SD and other forms of frontotemporal dementia is even greater than in AD.

**Neuropsychological findings**

The Cambridge semantic memory battery has formed the core of our assessment of patients with suspected SD. The guiding principal underlying the battery is the use of the same target items from selected categories of living (32 animals, birds, and fruit) and man-made (32 tools, household objects, and vehicles) things, across a range of tasks designed to probe input to and output from a central semantic knowledge base. The following subtests comprise the battery: category fluency, picture naming, word–picture matching, sorting of pictures and words at different levels of specificity, and generation of word definitions.

All patients but those with the very earliest stages of SD score poorly on simple naming tests, with a highly characteristic pattern of progression over time (table 2). The target object may be named initially as a semantically similar category coordinate (eg, zebra → “giraffe”), then as a much higher-familiarity member of the category (eg, zebra → “horse”), subsequently as the superordinate category name (eg, zebra → “animal”), and finally, in the

<table>
<thead>
<tr>
<th>Round 1</th>
<th>Round 2</th>
<th>Round 3</th>
<th>Round 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mammals</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pig</td>
<td>+</td>
<td>On farms</td>
<td>Dog</td>
</tr>
<tr>
<td>Elephant</td>
<td>+</td>
<td>Horse</td>
<td>Horse</td>
</tr>
<tr>
<td>Squirrel</td>
<td>Cat</td>
<td>Chicken</td>
<td>Cat</td>
</tr>
<tr>
<td>Birds</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chicken</td>
<td>+</td>
<td>+</td>
<td>Bird</td>
</tr>
<tr>
<td>Ostrich</td>
<td>Swan</td>
<td>Bird</td>
<td>Cat</td>
</tr>
<tr>
<td>Insects</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ant</td>
<td>Bird</td>
<td>Bird</td>
<td>Cat</td>
</tr>
<tr>
<td>Bee</td>
<td>Bird</td>
<td>Animal</td>
<td>Don’t know</td>
</tr>
<tr>
<td>Water creatures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alligator</td>
<td>Small dog</td>
<td>Fish</td>
<td>Cat</td>
</tr>
<tr>
<td>Lobster</td>
<td>For eating</td>
<td>Don’t know</td>
<td>Don’t know</td>
</tr>
<tr>
<td>Fruit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orange</td>
<td>Apple</td>
<td>Apple</td>
<td>Don’t know</td>
</tr>
<tr>
<td>Pineapple</td>
<td>Food</td>
<td>Food</td>
<td>Growing</td>
</tr>
<tr>
<td>Body parts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hand</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Lips</td>
<td>+</td>
<td>To eat</td>
<td>A hole</td>
</tr>
<tr>
<td>Household</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chair</td>
<td>+</td>
<td>+</td>
<td>Table to sit on</td>
</tr>
<tr>
<td>Cooker</td>
<td>Radio</td>
<td>Radio</td>
<td>Box</td>
</tr>
<tr>
<td>Envelope</td>
<td>+</td>
<td>Letter</td>
<td>Book</td>
</tr>
<tr>
<td>Musical instruments</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Violin</td>
<td>Music</td>
<td>Music</td>
<td>Music</td>
</tr>
<tr>
<td>Trumpet</td>
<td>Music</td>
<td>Blow it</td>
<td>Music</td>
</tr>
<tr>
<td>Clothing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sock</td>
<td>Boot</td>
<td>Boot</td>
<td>Shoe</td>
</tr>
<tr>
<td>Waistcoat</td>
<td>Shirt</td>
<td>Jacket</td>
<td>Jacket</td>
</tr>
<tr>
<td>Tools</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scissors</td>
<td>+</td>
<td>+</td>
<td>To cut things</td>
</tr>
<tr>
<td>Screwdriver</td>
<td>Un +</td>
<td>Knife</td>
<td>Knife</td>
</tr>
</tbody>
</table>

Table 2: Naming responses to line drawings of common animals and objects

Adapted with permission from the American Academy of Neurology.
late stage, with no information at all (zebra → “I don’t know”). There are sometimes circumlocutions revealing partial knowledge (eg, kangaroo → “It’s from Australia”).

There is a notable decrease in the ability to generate words, either from a specified initial letter or from a particular category. Category fluency drops dramatically, often to just a handful of words, whereas letter fluency (at least early in the disease) is relatively spared.59 If tested on a range of categories, patients with SD have particularly meagre output for more specific categories such as “breeds of dog” or “types of boat” compared with that for animals or vehicles.60

Patients with SD invariably have impaired comprehension of content words, such as nouns, verbs, and adjectives (as tested by word–picture matching, generation of definitions, and synonym tasks), and this deficit is strongly graded by word familiarity. In parallel with the nature of spontaneous speech, where patients have severe anomia but produce fairly well structured sentences, their comprehension shows the same dissociation between many failures on single specific content words but good ability to understand sentences—sometimes even syntactically complex ones—if they know what the content words in the sentences mean.60–62

Given that the diagnostic criteria for SD specify multimodal semantic deficits spanning non-verbal as well as verbal domains, the patients are impaired on non-verbal tests of semantic knowledge; but documenting and characterising this deficit is non-trivial, partly because some of the most helpful tasks are not in routine clinical usage. In the pyramids and palm trees test,63 the patient is asked to select one of two response pictures on the basis of its association to a third target picture (eg, on one trial, the correct choice to go with the tree is the apple

![Figure 2: Tests of non-verbal semantic knowledge developed in Cambridge, UK, for use in studies of SD](http://neurology.thelancet.com)
rather than the onion). This test reveals deficits in moderately impaired patients with SD. To show that the semantic impairment even early in SD represents deterioration of central, amodal knowledge, we have developed a range of other non-verbal assessments (figure 2), including: a more difficult version of pyramids and palm trees (the camel and cactus test); matching of object pictures to their characteristic sounds; matching of man-made artefacts (like a vegetable peeler or a hammer) to their typical recipients or to other objects that could be used for the same purpose; colouring in of line drawings of objects with characteristic colours; selection of the correctly coloured animal or object; selection of the correct version of a pictured object or animal from two alternatives when one has been altered in some way (eg, an elephant with normal-sized rather than large ears); and delayed copying of line drawings. Patients with even early SD, who have minimally impaired performance on easy semantic tasks, such as picture-to-word matching, invariably show deficits on many of these non-verbal tasks.84–86

Assessments designed to probe object knowledge and use86–87 have provided a likely explanation for the apparent discrepancy between patients’ ability to use objects at home and their readily measurable impairment of object use in the clinic. First of all, the success of patients with SD is strongly modulated by familiarity: they are more likely to succeed on formal assessment with objects that they use at home everyday, such as combs and forks, but they typically do poorly with less familiar things, such as corkscrews or stethoscopes. Secondl, appropriate use of something that is familiar as a particular “token” of its type (eg, a person’s own corkscrew with a black plastic body that is always to be found in the dining room cabinet) can be maintained by day-to-day episodic and procedural memory. One essential signature of functioning semantic memory is generalisation from one token to another of the same type: with disrupted semantic memory, a patient might not be able to generalise from the wood-and-metal corkscrew presented in the testing room to the black-bodied corkscrew in his cabinet at home.

As already indicated, patients with SD are not amnesic; but documenting the preservation of everyday memory function is also non-trivial.84,85,67 Comprehension of test instructions can be a problem, and even more so is any assessment requiring spoken output. Performance is better on memory tests that use non-verbal materials, such as recall of the Rey complex figure. Tasks requiring recognition memory for objects or colour pictures are unproblematic, even when patients can no longer identify the object or famous face, provided that the stimulus picture is identical at original and subsequent presentation. If the original stimulus is altered at test to a different photograph of the famous person, or a different exemplar of a telephone, or even a differently coloured telephone of the same kind, shape, or size, recognition memory in SD is definitely impaired.26,70 In other words, the decline in the patients’ conceptual knowledge forces greater reliance on perceptual characteristics of the things that they encounter.

On tests of autobiographical memory, patients with SD show a unique pattern. Patients with the amnesic syndrome resulting from hippocampal damage (after anoxic brain damage or in the early stages of AD) typically have significantly impaired memory for their recent life events but relatively preserved autobiographical memory for earlier phases of their lives:86 patients with SD, by contrast, commonly show a reversal of this typical temporal gradient, with memory for very recent events least affected,72,77,81 although the latter finding has not been replicated by all researchers.82

Implications for theoretical models of semantic memory

Research on SD has had a major effect on neural and computational models of normal semantic memory. In brief, such work supports the view that, although separable and widespread brain regions represent individual domains of knowledge about an object (its shape, colour, sound, characteristic movement, etc), the bilateral anterior temporal lobes play a key part in linking and coordinating this information, in enabling a whole range of conceptual knowledge about an object to be retrieved on the basis of receiving just fragments of information about it in a single mode, and in enabling both generalisation across and differentiation between similar concepts.85

One of the most striking features of cognitive behaviour under the conditions of a degraded semantic system is the patients’ increasing tendency to respond correctly only to things (objects and words) that are typical of their class, and to make “typicalisation” errors on words or objects with an atypical structure, especially if these are not the most familiar items. This phenomenon is observed across a whole range of tasks, including reading aloud (where patients will correctly pronounce typical words such as “new” but will read “sew” as “sue”),84 spelling of spoken words (correct spelling of typical words like “stem” or “blink” but errors like “blood” spelled “blud” or “scissors” spelled “sizzers”),81 and generation of the past tense forms of verbs (correct inflection of typical verbs like “talk” as “talked” but typicalisation errors to irregular verbs; thus, the past tense of “drink” becomes “drinking” instead of “drank”).85 This kind of typicalisation error has an equivalent in the object domain. For example, when a patient with SD was asked to copy a drawing of a peacock with the stimulus picture present, he showed good copying skills (figure 2). On a different occasion, the patient looked at the stimulus picture for 5 seconds but it was then withdrawn and he counted from 1 to 15 before being asked to draw the picture. In this situation, the patient remembered that there was something odd at the back end, but the response now had a body shape more appropriate to a
mammal than a bird plus the four legs typical of most familiar animals. Other drawings where patients with SD must wait briefly before reproducing the target reveal camels lacking their humps, rhinos lacking their horns, and seals with legs rather than flippers.87

Neuroimaging findings
Patients with even early-stage SD show bilateral, though typically asymmetrical, atrophy of the anterior temporal lobes; as the disease progresses, the degeneration extends either caudally into the posterior temporal lobes or rostrally into the posterior, inferior frontal lobes, or both. These changes are readily seen on coronal MRI (figure 3) but can be missed on CT, and even on MRI without coronal cuts.88,89 Quantitative MRI studies, with both manual methods and automatic voxel-based morphometry, have refined these observations by showing consistent and extreme atrophy (commonly 50–80% grey matter loss) of the polar and perirhinal cortices and the anterior fusiform gyri.90–95 Moreover, the degree of atrophy of these regions correlates with the degree of semantic memory impairment on cognitive testing.90,91 The involvement of the polar–perirhinal cortex is of theoretical interest given lesion studies in non-human primates showing that this region has a particular role in the binding of high-level sensory information that underlies object recognition.97,98

Early non-quantitative observations suggested sparing of the more medial parts of the temporal lobe in SD; but objective measures have shown that the hippocampus and the entorhinal cortex are, in fact, substantially involved in the pathological process.90,91 Unlike in AD, however, there is a rostral–caudal gradient in SD, with anterior portions most affected. Medial temporal degeneration might seem mysterious in the context of the relative preservation of episodic and autobiographical memory in SD (though mainly for non-verbal stimuli in the former and mainly for recent events in the latter). Recent metabolic imaging has shed some light on this enigma. A comparison of patients with SD and very early AD that involved combined structural (MRI) and metabolic (fluorodeoxyglucose-PET) imaging revealed hippocampal atrophy and hypometabolism in both groups. The main difference came in the form of strikingly reduced metabolism in the posterior cingulate cortex in patients with AD99 that was not present in those with SD, suggesting that the status of this region has an important bearing on episodic memory100 (figure 4).

Another recent observation is that regional atrophy and hypometabolism are closely coupled in SD but not in AD. That is to say, in SD the anterior temporal regions are both atrophic on MRI and hypometabolic on PET, with changes typically confined to this region and to the closely connected orbital frontal cortex. AD, by contrast, is characterised by much more extensive hypometabolism in regions that are not obviously atrophic.100 At present, there are few data on longitudinal changes in SD although a recent study that involved tensor-based morphometry showed substantial contralateral temporal grey matter loss in patients with initially lateralised atrophy together with volume loss in ventromedial frontal and insular regions.88

Neuropathology
The neuropathology of frontotemporal dementia, once thought mainly to be a tauopathy, has become increasingly complex with the identification of three basic patterns.44,103,104

First, there are tau-positive disorders, including: classic Pick's disease with tau-positive and ubiquitin-positive spherical inclusions most numerous in the hippocampal dentate gyrus and frontotemporal cortex; familial frontotemporal dementia with parkinsonism, with associated mutations in the MAPT gene on chromosome 17, characterised by tau-positive inclusions in neurons and glial cells; corticobasal degeneration with tau-positive inclusions in cortical layer II with swollen acentric...
Figure 4: Fluorodeoxyglucose-PET findings in patients with mild cognitive impairment and SD superimposed on MRI coronal images
Top: In mild cognitive impairment there is posterior cingulate and parietal hypometabolism. Bottom: In SD, hypometabolism centres on the temporal pole and perirhinal cortex, but with sparing of the posterior cingulate region. By convention, the left side of the brain is shown on the right.

Figure 5: Pathological changes in a patient with SD
A: Lateral view showing striking atrophy of the left anterior temporal lobe. B and C: Coronal slices through the temporal pole and body of the temporal lobes. D: Ubiquitin-positive inclusions in the dentate gyrus of the hippocampus. E: A section through the temporal neocortex that shows severe neuronal loss, spongiosis, and ubiquitin-positive staining of remaining neurons.
neurons and astrocytic plaques; and argyrophilic grain disease.

Second, there is frontotemporal dementia with ubiquitin-positive, tau-negative inclusions, which were initially reported in the context of motor-neuron disease but subsequently found in vivo in many patients with frontotemporal dementia without motor-neuron disease. These inclusions are typically found in cortical layer II and hippocampal dentate granule cells; also included in this pattern are familial cases with recently identified mutations in the progranulin gene (GRN) who typically have lentiform intranuclear inclusions. A very recent development has been the identification of a major pathological protein in familial and sporadic cases with ubiquitin-positive inclusions known as TAR DNA-binding protein 43 (TDP-43).4,104-107

The third basic pattern is of microvascular degeneration and gliosis lacking distinctive inclusions.

Because some of these variants have been recognised only very recently, information about the relations between clinical syndromes and pathology is relatively scarce. Relative to some of the other clinical frontotemporal dementia syndromes, however, SD seems to have a predictable pathological basis—most patients have ubiquitin-positive, tau-negative inclusion pathology (figure 5).108-111 Our SD series to date comprises post-mortem samples of 20 patients: 14 with this pathology, four with tau-positive Pick's disease, and two with AD pathology.112-114

There have been substantial advances in understanding the genetics of frontotemporal dementia with the discovery of two major gene defects (MAPT and GRN both on chromosome 17) plus two much rarer loci.115-118 Although the pathological basis of SD is predominantly tau-negative, ubiquitin-positive, these inclusions do not have the characteristic morphology of familial cases (lentiform intranuclear inclusions) and accordingly cases with GRN mutations have yet to be described in association with SD. Another intriguing and unresolved issue is the degree of overlap between SD and motor-neuron disease. The pathological findings in SD resemble those found in patients with frontotemporal dementia associated with motor-neuron disease,102,103,120 but, to date, very few cases with SD and clinical motor-neuron disease are known. We have now seen three such cases with the very late development of amyotrophy.

Prognosis

Early reports of prognosis in frontotemporal dementia based on cases coming to post-mortem suggested a median survival in SD of 8 years (range 3–15 years).119 This was probably an underestimate and distorted by those dying within a few years. In our series of 100 cases, 32 of whom have died, the median survival from diagnosis is 12 years. There is, however, considerable variability in the speed of progression in SD, and the factors influencing this are currently unknown.

Management

SD, in common with other forms of frontotemporal dementia, is a devastating illness that affects all family members, and therefore the management of patients and their carers requires a multidisciplinary team with input from clinical psychology, clinical genetics, and specialist nurses. Information and support for patients with frontotemporal dementia and their carers are vital. Most dementia literature is on AD, but there are now extremely useful frontotemporal dementia carer-support organisations in the UK and North America. There is no known treatment to delay the progression of frontotemporal dementia, although environmental and pharmacological interventions may help symptomatically with behavioural management. Irritability, agitation, and bizarre eating behaviour may respond to treatment with selective serotonin reuptake inhibitors, although the results of trials in frontotemporal dementia have been mixed.122,123

Conclusions

As this review illustrates, a great deal has been learnt about SD over the past decade with advances in cognitive neuroscience, imaging, and pathology. There is still a need for cross-disciplinary longitudinal studies, because clinico-pathological analyses are still scarce. In-vivo markers of pathology are urgently required, because disease-modifying therapies will target specific pathological processes. In the absence of more radical therapies, attention should be given to cognitive rehabilitation strategies to ameliorate patients' and carers' distress.

Contributors

JRH and KP reviewed and prioritised articles for inclusion. JRH wrote the first draft. JRH and KP contributed equally to the final version.

Conflicts of interest

We have no conflicts of interest.

References

1012

Review

19 Harvey RJ, Skelton-Robinson M, Rossor MN. The prevalence and causes of dementia in people under the age of 65 years. J Neurol Neurosurg Psychiatry 2003; 74: 1206–09.


64 Ikeda M, Patterson K, Graham KS, Lambon Ralph MA, Hodges JR. “A horse of a different colour”: do patients with semantic dementia recognise different versions of the same object as the same? Neuropsychologia 2006; 44: 566–75.


