Sorting out the
INTRODUCTION

Dementia is not a disease. It is a generic term that refers to the cognitive and behavioural disorder resulting from chronic brain disease or encephalopathy. Chronic encephalopathies may be non-progressive, occurring, for example, as a consequence of brain trauma or cerebral hypoxia, or progressive, arising as a result of an intrinsic, extrinsic or metabolic cerebral disorder. The primary focus of this article is the dementia syndromes that result from progressive degenerative disease. However, vascular disease will also briefly be addressed, because vascular dementia is relatively common and is an important cause of dementia.

The traditional view of dementia as a global loss of intellect is inaccurate. Cerebral diseases do not affect the brain uniformly, but preferentially affect certain brain regions and spare others. Moreover, psychological processes themselves are regionally organized in specific brain regions. Different cerebral diseases therefore are associated with distinctive and characteristic neuropsychological syndromes, whose identification can lead to a high degree of accuracy in clinical diagnosis. A useful empirical classification of progressive encephalopathies leading to dementia can be made on the basis of the predominant anatomical distribution of pathology within the brain: cortical, subcortical, cortico-subcortical and multifocal. These regional lesions lead to highly-distinct patterns of cognitive and behavioural change, neurological symptoms and signs, and findings on functional single-photon emission computed tomographic (SPECT) imaging, and electroencephalography (EEG). The process of syndrome analysis permits a differential diagnosis of the different forms of dementia.

CORTICAL ENCEPHALOPATHIES

Functional topography of the cerebral cortex

Psychological functions are regionally organized in the cerebral cortex (Fig. 1). The posterior hemispheres are critical for perceptual and spatial functions, that is, appreciation of the identity of visual percepts (e.g. objects in the environment) and of their spatial relationship with respect to each other and to the individual. Breakdown in visual perception leads to failure to recognize objects (agnosia) and faces (prosopagnosia), whereas spatial impairment leads to inability to navigate external surroundings (spatial disorientation). Language is dependent on the areas around the Sylvian fissure, extend-
ing from the frontal into the parietal and temporal lobes in the left hemisphere. Breakdown of language leads to an inability to express and comprehend spoken and written words (aphasia) and to communicate by gesture (gestural apraxia). Parietal lesions of the left hemisphere may be associated with an inability to calculate (acalculia). The superior parietal areas are important for the organization of skilled movements. Failure of executive motor functions leads to difficulties in the purposeful use of the limbs, face and mouth (apraxia). The medial portion of both hemispheres, designated the limbic system, which includes the hippocampus and amygdala, is essential for the acquisition and retention of information. Damage to limbic structures leads to a failure to learn new information and to recall past experience (amnesia). The anterior, or prefrontal, cortex is essential for the regulation of mental life, including strategic planning and monitoring, and evaluation of actions taking place over time. Breakdown in these regulatory or executive processes leads to aberrant personal and social behaviour, change in personality, and inability to conceiv of and successfully achieve behavioural goals.

Cortical encephalopathies give rise to distinct dementia syndromes, reflecting the topographical distribution of pathological change within anterior, medial and posterior cortices (Fig. 2).

Alzheimer's disease
Alzheimer's disease is a cortical dementia, with predominant involvement of the medial temporal and temporoparietal cortex (Cummings & Benson 1992) (Table 1). Patients have difficulty learning new information and are forgetful of day-to-day events. Information from the recent past may appear more affected than from the distant past. Visuospatial impairment leads patients to have difficulty aligning cutlery when laying a table, and orienting clothing when dressing. They have problems negotiating stairs because of impaired judgement of spatial depth. They become lost in their surroundings and eventually disoriented even in their own home. Spatial problems typically outweigh problems in visual perception. Nevertheless, in the later stages patients fail to recognize faces, including their own face in the mirror, and may misidentify objects secondary to visuoperceptual disorder. Breakdown of skilled movements of the arms and legs may be secondary to spatial disorientation, which results in difficulty in copying drawings and designs (constructional apraxia) and in dressing (dressing apraxia). However, apraxia disproportionate to perceptuospatial impairment may occur, impairing the manual use of objects and walking.

When temporoparietal areas around the perisylvian fissure are involved, language skills...
are affected. The patient’s speech is halting, reflecting difficulty in finding words, and failure to maintain a line of thought. Repetition is impaired, and patients have a reduced digit span and makesound-based errors in repeating polysyllabic word sequences. Comprehension is impaired, particularly at the sentence level. Reading, writing and calculation may all be impaired. Alexia, agraphia and acalculia are compounded by spatial difficulties, because the patient has difficulty tracking along a line when reading, or organizing written words and numerals in space.

In contrast to the severe cognitive deficits, social graces are well preserved and patients present a normal social façade because the frontal cortex is preserved. Failure on conventional neuropsychological ‘frontal lobe’ tests can typically be accounted for by the heavy demands of such complex, executive tasks on instrumental abilities of language, perceptuospatial skills and memory and do not reflect a primary disorder of frontal lobe function.

Neurological signs in Alzheimer’s disease consist of akinesia, rigidity, and myoclonus, which emerge with the gradual involvement of subcortical structures. Physical problems, however, are dwarfed by the momentous psychological disturbance and may be totally absent until the relatively late stages of disease.

The EEG shows progressive slowing of wave forms. Structural imaging reveals non-specific cerebral atrophy but functional imaging techniques, such as positron emission tomography (PET) and SPECT, reveal characteristic abnormalities of the parietal regions. Abnormalities may be present in the anterior regions, but typically these emerge relatively late in the disease and invariably in the context of posterior hemisphere deficits.

**Frontotemporal lobar degeneration**

Frontotemporal lobar degeneration is associated with circumscribed atrophy of the frontal and anterior temporal neocortex, with sparing of the posterior temporoparietal neocortex and the medial temporal limbic cortex ((Table 2) (Snowden et al. 1996; Neary et al. 1998). It encompasses distinct subsyndromes determined by the distribution of pathology within the anterior hemispheres (Fig. 3). Bilateral frontal and anterior temporal lobe involvement is characterized by the prominent behavioural disorder of frontotemporal dementia. Asymmetrical involvement predominantly of the left dominant anterior hemisphere leads to the syndrome of progressive non-fluent aphasia. Predominant involvement of both temporal lobes leads to a syndrome of fluent aphasia with associative visual agnosia (semantic dementia). Theses syndromes may be complicated by the development of the amyotrophic form of motor neurone disease.

**Frontotemporal dementia**

Frontotemporal dementia (FTD) accounts for approximately 20% of cases of primary cerebral

<table>
<thead>
<tr>
<th>Table 2 Frontotemporal lobar degeneration: demographic features, clinical profile, pathology and genetics</th>
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<tbody>
<tr>
<td><strong>Age of onset</strong></td>
</tr>
<tr>
<td>Usually 45–65 years, range 21–75.</td>
</tr>
<tr>
<td><strong>Sex ratio</strong></td>
</tr>
<tr>
<td>Equal males and females.</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
</tr>
<tr>
<td>Variable, median 8 years, range 2–20.</td>
</tr>
<tr>
<td><strong>Main clinical features</strong></td>
</tr>
<tr>
<td>Behavioural change or circumscribed cognitive disorder.</td>
</tr>
<tr>
<td><strong>Gross pathological features</strong></td>
</tr>
<tr>
<td>Atrophy particularly affecting the frontal and/or temporal lobes. Bilateral frontal lobe and anterior temporal atrophy (frontotemporal dementia). Asymmetrical atrophy of left hemisphere, particularly involving frontal and temporal regions (progressive non-fluent aphasia). Bilateral atrophy of temporal lobes (semantic dementia).</td>
</tr>
<tr>
<td><strong>Histopathology</strong></td>
</tr>
<tr>
<td>Affected areas of cortex show loss of pyramidal cells, microvacuolation of outer cortical laminae, and mild astrocytosis. No inclusion bodies or swollen neurones.</td>
</tr>
<tr>
<td>or:</td>
</tr>
<tr>
<td>Affected cortex shows severe loss of pyramidal cells with severe astrocytosis, sometimes with inclusion (Pick) bodies and swollen (Pick) neurones</td>
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<tr>
<td><strong>Genetics</strong></td>
</tr>
<tr>
<td>Up to 50% of patients have a positive family history of dementia and autosomal dominant inheritance is demonstrable in the majority. Some familial cases with Parkinsonian features show mutations in the tau gene on chromosome 17. Cases of frontotemporal dementia with motor neurone disease have shown linkage to chromosome 9.</td>
</tr>
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</table>
atrophy occurring in the presenium (Gustafson 1987; Neary et al. 1988). The striking characteristics are of changes in personality and social and personal behaviour. Patients rapidly become incapable of managing their own affairs and lose their jobs through irresponsibility and impaired judgement. They may appear apathetic, lacking in motivation and emotionally blunted, or overactive, disinhibited and fatuous. Insight is lost and, in contrast to those with Alzheimer’s disease, patients show no distress or concern when confronted with task failures. Patients show reduced capacity to demonstrate both primary emotions, such as happiness, fear and surprise, and social emotions such as sympathy, empathy and embarrassment. Stereotyped and perseverative behaviours may occur, ranging from simple repetitive actions such as hand rubbing to complex rituals surrounding activities of daily living. Gluttony, food fads and a preference for sweet foods are common. The diagnostic importance of these behavioural characteristics is exemplified by the finding that changes in emotion and insight, combined with the presence of behavioural stereotypes and altered dietary habits, and an absence of any spatial localization problem, distinguishes FTD from Alzheimer’s disease with an accuracy of 95% (Bathgate et al. 2001).

Speech in FTD is economical and concrete, and verbatim copying of what is said by others (echolalia) and repetition of their own responses (perseveration) may occur, particularly in more apathetic patients. Patients eventually become mute. Severe difficulties in abstraction, mental set shifting, organizational and strategic skills are elicited on psychological tests sensitive to frontal lobe dysfunction, and responses are concrete and perseverative. Despite the severity of their behavioural disorder, patients are not clinically amnesic and remain orientated in their environment. Inefficiencies on formal memory tests are secondary to inattention and impairments in strategic and organization skills. Patients show no visuospatial abnormalities until the terminal stages of the disorder, due to sparing of the posterior cortices, and even when patients are mute and formally untestable they may spatially align objects and negotiate their environment without difficulty. Neurological signs are minimal and consist of primitive reflexes in the early stages. Akinesia and rigidity do occur, but typically very late in the disease. Myoclonus, seen in Alzheimer’s disease, does not occur.

The routine EEG is normal. CT confirms cerebral atrophy, which may be more evident in the frontal regions. Preferential involvement of frontal and anterior temporal lobes is typically demonstrable on magnetic resonance (MR) imaging. SPECT confirms selective abnormalities in the frontal and temporal lobes.

**Progressive non-fluent aphasia**

In this syndrome, progressive decline in language production occurs in the relative absence of other psychological deficits (Mesulam 1982). Speech is non-fluent, effortful and lacking in prosody. Repetition, series speech (reciting well-rehearsed verbal series, such as the days of the week) and reading aloud are also impaired, with effortful production and phonemic paraphasic errors (e.g. ‘tig’ for ‘big’). Anomia is prominent. Writing and oral spelling are impaired. Comprehension is relatively preserved.

Structural brain imaging with CT and MRI reveals atrophy of the left cerebral hemisphere. Left hemisphere abnormalities are also apparent on SPECT imaging. The EEG may be normal or show slow waves over the dominant cerebral hemisphere.

The presence of a highly selective disorder of language in progressive aphasia contrasts with the range of cognitive deficits typical of Alzheimer’s disease. Nevertheless, Alzheimer’s disease may sometimes present with a language disorder so that the two can be confused in the early stages. Typically, however, in Alzheimer’s disease other deficits emerge with progression of disease, particularly visuospatial impairments.
Semantic dementia
Patients with semantic dementia lose the meaning of words, and of face and object identity (Snowden et al. 1989, 1996; Hodges et al. 1992). Spontaneous speech is fluent, effortless and grammatically correct, but empty of content and there are semantic paraphasias (e.g. ‘dog’ for ‘pig’). There is profound anomia and impaired comprehension of spoken and written words. Patients can repeat what is said to them, albeit without understanding. They can also read aloud and write to dictation, provided that words have regular pronunciations and spellings. They fail to recognize objects and to identify faces, despite preserved ability to copy accurately and match objects and faces (associative agnosia).

Visuospatial skills and day-to-day memorizing are well preserved, contrasting with the striking loss of semantic knowledge. However, patients perform poorly on traditional formal memory tests, which typically employ words or pictures that the patient may not understand. Behavioural alterations are common, but less severe than in frontotemporal dementia, and have a more compulsive quality.

Brain CT reveals either non-specific cerebral atrophy or widening of the Sylvian fissures, suggesting temporal atrophy. Prominent temporal lobe atrophy is invariably detected by MRI. This is bilateral, but often asymmetrical. In patients with a left temporal emphasis, the initial presenting symptoms are in the realm of lanugage, whereas in patients with right temporal emphasis the earliest deficit is in face recognition. SPECT shows reduced uptake of tracer in the anterior regions, which may be asymmetrical. The EEG is normal.

Semantic dementia is most commonly confused with Alzheimer’s disease, not least because patients and their relatives tend to frame the patient’s deficits in terms of memory (e.g. ‘I can’t remember things’). However, what the patient cannot remember is the meaning of words, the identity of faces and the significance of objects (semantic memory). Memory for day-to-day, autobiographical events that is so characteristically impaired in Alzheimer’s disease is notably spared in semantic dementia. The presence of profound anomia or prosopagnosia in the presence of preserved orientation and autobiographical memorizing ought to alert the physician to the presence of semantic dementia.

Frontotemporal lobar degeneration and motor neurone disease
Frontotemporal lobar degeneration, in particular the syndrome of frontotemporal dementia can be complicated by the development of motor neurone disease (Neary et al. 1990). This is of the amyotrophic form with bulbar palsy, weakness, wasting, and fasciculations of the limb muscles, in the absence of significant spasticity of the muscles. Typically the neurological symptoms and signs appear after the development of the dementia and lead to death within 3 years from respiratory complications. In longer-surviving patients, extrapyramidal signs seen in the latest stages of frontotemporal dementia may make an appearance. Electrophysiologic studies demonstrate widespread denervation of muscles.

SUBCORTICAL ENCEPHALOPATHIES
Several diseases predominantly affect subcortical structures with relative sparing of the cerebral cortex. These include degenerative disorders such as Parkinson’s disease, Huntington’s disease, progressive supranuclear palsy and rare late onset leucodystrophies in young people. Subcortical structures and their projections to the cerebral cortex exert a quantitative and regulatory effect on the pace and organization of psychological functions (Cummings 1990). Patients with subcortical disorders show slowness and rigidity of thinking (bradyphrenia) with inflexibility and difficulty in switching responses (perseveration). Although forgetful they do not have a severe amnesia. Rather they have difficulties in planning and sequencing mental events and may fail on tests sensitive to frontal lobe dysfunction, thus showing similarities to patients with frontal cortical disease. They do not, however, show the specific abnormalities of language, visual perception and spatial functioning seen in cortical disorders. Nor do they typically show the gross behavioural disorder of frontal cortical disease. The exception to this is Huntington’s disease in which personality change and bizarre behaviour are not uncommon (Harper 1996). Progressive supranuclear palsy represents the prototypical subcortical dementia (Albert et al. 1974).

In subcortical disorders the neuropsychological deficits are overshadowed by profound and characteristic neurological symptoms and signs: akinesia, rigidity and tremor in
Parkinson's disease; involuntary and purposeless movements in Huntington's disease; and paralysis of eye movements in progressive supranuclear palsy. The EEG may be normal or show slight slowing of waveforms but is of no diagnostic significance. Brain CT and MRI may both be normal or show just non-specific cerebral atrophy. In progressive supranuclear palsy, PET and SPECT reveal abnormalities in frontal cortex similar to those of frontotemporal dementia.

Vascular dementia
Recurrent completed strokes lead to an accumulated neurological and psychological deficit. Their sudden onset, together with evidence of multiple infarctions or haemorrhages on brain imaging, is not likely to lead to diagnostic confusion. But, when vascular lesions predominantly affect the subcortical white matter, a characteristic subcortical syndrome (subcortical arteriosclerotic dementia) emerges that is progressive without stroke-like clinical events (Table 3). This syndrome requires differentiation from subcortical neurodegenerative diseases and from communicating hydrocephalus.

Neurological symptoms and signs reflect subcortical white matter lesions with dysarthria, dysphagia, pyramidal weakness, rigidity, ataxia and gait disorder (marche à petits pas). Subcortical lesions in the cerebrum are predominantly anterior and periventricular so that behavioural changes together with failure on psychological tests of frontal executive function can lead to diagnostic confusion with frontotemporal dementia.

Cortical Lewy body disease
Lewy body disease—dementia with Lewy bodies—is a disorder of the elderly that is usually sporadic (Table 4) (McKeith et al. 1996). Mental changes develop before or after parkinsonian symptoms and signs of akinesia, rigidity and tremor, which are responsive to the administration of L-dopa. Changes in the cerebral cortex may give rise to cortical symptoms of aphasia, agnosia and apraxia akin to those seen in Alzheimer's disease. However, the dominant feature of the illness is a fluctuating mental state with visual illusions and hallucinations leading to secondary delusions. Such fluctuations, which are presumably due to simultaneous disorder of cortex and subcortex, are highly diagnostic, because they are not characteristic of the cortical or subcortical encephalopathies. Dementia with Lewy bodies can also be distinguished qualitatively from Alzheimer's disease by the presence of distractibility, incoherence in line of thought, confabulatory responses, perseverations and intrusions (Doubleday et al. 2002).

Table 3 Vascular dementia: demographic factors, clinical profile, pathology, and genetics

<table>
<thead>
<tr>
<th>Age of onset</th>
<th>Usually after 40 years. Most common in elderly</th>
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<tbody>
<tr>
<td>Sex ratio</td>
<td>Males affected more often than females</td>
</tr>
<tr>
<td>Duration</td>
<td>Variable, up to 12 years</td>
</tr>
<tr>
<td>Main clinical features</td>
<td>Physical and mental change</td>
</tr>
<tr>
<td>Gross pathological features</td>
<td>Multiple infarcts in cerebral cortical and subcortical grey matter and internal capsule</td>
</tr>
<tr>
<td></td>
<td>White matter demyelination, often with lacunes, usually in frontal and temporal lobes. Incomplete infarction.</td>
</tr>
<tr>
<td>Histopathology</td>
<td>Completed infarcts, many cases with histopathology of Alzheimer's disease</td>
</tr>
<tr>
<td></td>
<td>Fibrous and hyaline degeneration of small artery walls. Microcystic degeneration around blood vessels, sometimes confluent leading to incomplete infarction of white matter. Reactive astrocytosis.</td>
</tr>
<tr>
<td>Genetics</td>
<td>No associations except with atherosclerosis of extracerebral arteries, or hypertension and cigarette smoking</td>
</tr>
</tbody>
</table>

Structural and functional brain imaging reveals asymmetrically distibuted focal lesions in the white matter of the cerebral hemispheres.

Cortico-subcortical encephalopathy
Two degenerative disorders show features of both cortical and subcortical syndromes because of the spread of pathology to both structures. In Lewy body disease the distribution of pathology is relatively symmetrical whereas in corticobasal degeneration it is highly asymmetrical.

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The EEG characteristically reveals severe slowing of wave forms and sometimes periodic wave complexes. Brain CT reveals cerebral atrophy. SPECT shows reduced uptake in the cerebral cortex especially in the posterior hemispheres.

**Corticobasal degeneration**
Corticobasal degeneration is a rare condition in which a cortical neuropsychological syndrome (apraxia) is superimposed on a subcortical dementia and neurological signs of basal ganglia disorder (Rinne et al. 1994). There is significant left-right asymmetry in the severity of neurological signs and extent of apraxia, reflecting an asymmetrical distribution of pathology within cortical and subcortical sites.

Asymmetrical akinesia and rigidity affect predominantly the upper limbs, which are also the site of tremor, dystonic movements and myoclonus. Psychologically there is slowing, inflexibility and perseveration consistent with a subcortical syndrome. The cortical syndrome is characterised by a profound, asymmetrical apraxia, typically most marked in the upper limbs, but gradually involving buccofacial, lower limb and whole body movements. The limbs progressively lose all executive functions and may develop autonomous movements (alien limb). Additional features of parietal lobe disease, namely visuospatial deficits, may also emerge.

Brain CT reveals cerebral atrophy. Functional imaging (PET and SPECT) reveals asymmetrical abnormalities of the basal ganglia and associated frontoparietal cortex. EEG changes are of non-specific asymmetrical slow waves.

**MULTIFOCAL ENCEPHALOPATHY**
Subacute spongiform encephalopathies (prion diseases), such as Creutzfeldt-Jakob disease, are rapidly progressive disorders with a low familial risk, and are often terminal within about six months (Matthews 1985; Kretzschmar et al. 1996). Longer survival may occur in familial disease forms such as the Gerstmann-Straussler-Scheinker syndrome and in the new variant form of Creutzfeldt-Jakob disease in young people (Will et al. 2000).

The aggressive disease process seems not to respect anatomical boundaries or functional systems so that a wide variety of psychological and neurological deficits rapidly emerge (Fig. 4). Some patients present with neurological symptoms such as a cerebellar syndrome, cortical blindness, sensory motor deficits, myoclonus and epileptic seizures. Focal psychological syndromes such as aphasia may herald the onset of the disease. When thalamic structures are preferentially involved the pre-
dominant picture may be one of progressive somnolence. In contrast to cortical encephalopathies, in Creutzfeldt-Jakob disease psychological impairment occurs together with the rapid march of neurological disorder and in an unpredictable manner. However, in the new variant form of Creutzfeldt-Jakob disease, linked to the epidemic of bovine spongiform encephalopathy, a ‘psychiatric’ presentation with depression, withdrawal, apathy or psychosis may precede the onset of ataxia, rigidity and myoclonus for prolonged periods, making early diagnosis difficult (Lowman et al. 2001). In the final stages of Creutzfeldt-Jakob disease, episodes of unresponsiveness increase in frequency and duration until akinetic mutism supervenes.

The severe neurological and psychological disorder is reflected in the grossly disturbed EEG in which there is profound slowing of wave forms, and characteristic periodic triphasic wave complexes emerge. Brain CT is either normal or reveals non-specific cerebral atrophy. SPECT imaging reveals a patchy reduction of uptake of tracer in the cerebral cortex.

**DIAGNOSTIC CONSIDERATIONS**

Cortical, subcortical, cortico-subcortical and multifocal dementias differ with respect to the relative prominence of the associated mental and physical changes during the evolution of disease (Table 5), providing an important framework for differential diagnosis of these disorders. Cortical dementias are characterised by profound mental changes and the relative absence of early neurological signs, whereas subcortical dementias are associated with striking physical signs while mental changes may be of relatively lesser significance and tend to emerge later in the disease. In cortico-subcortical and multifocal dementias, physical symptoms and signs emerge along with the psychological disturbance.

In the case of cortical dementias, the dearth of neurological signs means that differentiation is more crucially dependent on cognitive and behavioural characteristics elicited from the history and neuropsychological evaluation. Differential characteristics of the two prototypical cortical dementias, Alzheimer’s disease and frontotemporal dementia, are shown in Table 6. Comparisons with subcortical vascular dementia, also shown in the table, demonstrate that frontotemporal dementia shares affinities with subcortical vascular dementia. The principal distinctions lie in the greater preponderance of physical symptoms and signs in vascular dementia but with less personality and behavioural change.

Examination of the cerebrospinal fluid is unhelpful, except in sporadic Creutzfeldt-Jakob disease when there may be high levels of 14.3.3 proteinase inhibitor proteins, released from damaged neurones. The EEG can be of diagnostic significance. In Alzheimer’s disease, the standard EEG often shows mild slowing of waveforms in the moderately advanced stages of the disease. Frontotemporal dementia is unique in that a normal record is preserved until the latest stages of the disease. Gross slowing of waveforms and periodic complexes are characteristic of the subacute spongiform encephalopathies (with the exception of new variant Creutzfeldt-Jakob disease) and also of cortical Lewy body disease.

Whereas brain CT is useful in delineating structural changes such as the presence of infarcts or hydrocephalus, it is less useful in differential diagnosis in neurodegenerative disorders because scans may be normal or reveal just non-specific cerebral atrophy. However, high-resolution brain MRI may be useful in highlighting prominent areas of atrophy, complementing the clinical and SPECT findings.

SPECT imaging demonstrates functional change in the brain, which is of high diagnostic value in the neurodegenerative disor-

**Table 5** Nature and relative severity of psychological, neurological and electroencephalographic (EEG) changes associated with various forms of dementia

<table>
<thead>
<tr>
<th>COGNITIVE DISORDER</th>
<th>NEUROLOGICAL DISORDER</th>
<th>EEG</th>
</tr>
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<tbody>
<tr>
<td>Cortical</td>
<td>Severe, specific</td>
<td>Mild, specific</td>
</tr>
<tr>
<td>Subcortical</td>
<td>Mild, specific</td>
<td>Severe, specific</td>
</tr>
<tr>
<td>Cortico-subcortical</td>
<td>Severe, specific</td>
<td>Severe, specific</td>
</tr>
<tr>
<td>Multifocal</td>
<td>Severe, non-specific</td>
<td>Severe, non-specific</td>
</tr>
</tbody>
</table>

AD, Alzheimer’s disease.
ders, because the abnormalities on imaging closely reflect the topographical distribution of pathology within the cerebrum (Table 7). In frontotemporal dementia the characteristic abnormality in the frontotemporal lobes contrasts strikingly with the bilateral parietal defects seen in Alzheimer’s disease (Fig. 5). An asymmetrical dominant hemisphere defect characterises progressive non-fluent aphasia (Fig. 5), whereas predominantly bitemporal defects underlie the ‘semantic’ dementia of fluent aphasia and associative agnosia. Subcortical disorders, such as progressive supranuclear palsy, have an anterior cerebral defect that is less severe than in lobar atrophy. An asymmetrical frontoparietal defect is seen in corticobasal degeneration, whereas multifocal lesions are demonstrated in subacute spongiform encephalopathy.

Advances in neurogenetics have permitted the diagnosis from blood samples of specific genetic mutations, accounting for Huntington’s disease (huntingtin gene, chromosome 4) and familial Creutzfeldt–Jakob disease (prion gene, chromosome 20). However, mutations in the presenilin genes in presenile Alzheimer’s disease, and in the tau gene on chromosome 17 in frontotemporal dementia, account for only small numbers of affected families and so cannot be the basis, as yet, of diagnostic tests. Moreover, the detection of risk factors for late onset Alzheimer’s disease, such as the apolipoprotein e4 genotype, cannot be used diagnostically.
CONCLUSIONS
Dementia is a generic term embracing a number of neuropsychological syndromes characteristic of different brain diseases that affect different parts of the brain. Dementia is not a non-specific end-stage intellectual failure, nor is it a synonym for brain disease. Hierarchical descriptions at the levels of neurological and psychological behaviour, taken together with the results of brain imaging and electrophysiology, permit a rational classification of disorders leading to the various forms of dementia.

REFERENCES


