Neuropsychological features of dementia

Dr Ingrid C McGaughey MBBS

ABSTRACT

As our population ages, dementia is becoming increasingly prevalent in our society. This review paper highlights the neuropsychological features of the more common forms of primary dementia.

Dementia is a clinical syndrome characterised by acquired losses of cognitive and emotional abilities severe enough to interfere with daily functioning and the quality of life.[1] Occurring mainly later in life, the prevalence is around 1% at age 60 and doubles every five years, to reach 30–50% by age 85.[2,3] The diagnosis is usually made on a combination of careful history taking from the patient and carers and formal neuropsychological assessment.[4] Early neuropsychological assessment enables the memory and other cognitive and behavioural impairments to be characterised and give an indication of the likely underlying pathology. Testing can also be used to grade the severity of dementia and indicate the rate of cognitive decline.[5] Memory impairment is almost invariable. Alertness, attention, comprehension, learning, problem solving, judgement, mood and behaviour may also be affected. Dementia must be differentiated from delirium (an acute confusional state) and non-organic psychiatric disorders such as major depression and schizophrenia.[6]

The diagnosis of 'dementia' covers a number of conditions of varying etiology. The majority of pathologies causing dementia are primary, or non-reversible. However a small number, known as secondary or reversible dementia, occur in association with treatable conditions. Examples include toxic effects of antihypertensives, anticholinergic, psychotropic and antiparkinsonion medications. Metabolic disorders including hypothyroidism, hyperparathyroidism, Cushing's disease, Addison's disease and diabetes as well as depression are also implicated. Treatment of the underlying condition causes resolution of the dementia.

Some of the more common forms of primary dementia include:

- Alzheimer's disease
- Vascular dementia
- Frontotemporal dementia (including Pick's disease)
- Parkinson's disease and diffuse Lewy body disease
- Huntington disease.

Although there are numerous other causes of primary dementia, the proportion they contribute is not high and they will not be discussed further.

The primary dementia disorders may be subdivided into those that primarily affect the cerebral cortex (e.g. Alzheimer's disease) and those whose impact is on the subcortical structures (e.g. white matter diseases, Parkinson's disease and Huntington disease). Vascular dementia and Frontotemporal dementia commonly affect both cortical and subcortical structures. This division between cortical and subcortical dementias is useful as it gives an indication of likely neuropsychological features. Cognitive deficits can be detected several years before the clinical diagnosis of dementia.[5]

Alzheimer's disease

Alzheimer's disease is the most common dementing disorder, accounting for 70% of cases of dementia.[1] It has been estimated that between 1992 and 2016, the prevalence of dementia will increase in New Zealand by 96–100%, compared with a rise in the general population of 18–26%.[8] It is essentially a degenerative disease of the brain, characterised by a general loss of nerve cells, especially in the cortex of the brain resulting in a loss of synaptic connections; overall atrophy of the brain with shrinkage of the outer volume and enlargement of the inner ventricles; and degeneration of cell structure. Two distinct microscopic abnormalities have been identified: intracellular neurofibrillary tangles, and extracellular neuritic plaques (also known as senile plaques). While these may be present to a lesser extent in the brains of elderly non-demented patients, there appears to be a positive correlation between the number of neuritic plaques and tangles in the brain and the degree of dementia.[9]

Alzheimer's disease is a classical example of a cortical dementia. Generally the acquisition of cognitive and emotional impairments progresses in

predictable fashion through a number of stages outlined below. The history is usually one of progressive decline, although there may be short plateaus.

1. Early

Present from the earliest stages, the hallmark feature of Alzheimer's disease is progressive memory impairment, especially affecting episodic memory. Difficulty learning new information due to failure of encoding and rapid forgetting is apparent. Tests of delayed recall highlight the problem, with use of cues and provision of multiple choice alternatives of little benefit. As the disease progresses access to remote memory is affected. Interestingly there is a temporal gradient so early life memories are relatively spared. In the early stages, short term (working) memory is intact as demonstrated by normal digit span testing where patients are asked to repeat back progressively lengthening strings of digits in the same given order. Although language often appears superficially normal with relative sparing of phonology and syntax, cognitive assessment often reveals mild impairment of naming ability (anomia) and generation of exemplars on category fluency testing (e.g. listing as many animals as possible in a minute, less than 12 is considered suboptimal). Attention is intact with patients well oriented and frontal executive functions are relatively well preserved.[1,7,10]

2. Middle

Short term working memory impairment and loss of general knowledge become increasingly obvious as do problems with attention resulting in temporal disorientation. Language becomes more vague with diminished vocabulary, word finding difficulty and increased use of automatic phrases in spontaneous conversations. Pauses in conversational speech become noticeable. Patients perform poorly on reading comprehension and verbal reasoning on formal testing.[5] Naming ability and generation of exemplars on category fluency testing deteriorates further. Problems with executive function become evident.[1,7] Difficulties with completing Part B of the Trail Making Test (e.g. connecting A-1-B-2-C-3...) become apparent. Visuospatial and perceptual deficits (e.g. figure-ground discrimination, detection of motion, recognising faces and misperceptions) also develop. In the clock drawing test, the accuracy of the fourth quadrant of the clock face shows the greatest sensitivity (87.5%) and specificity (82.3%) for dementia.[4]

3. Late

Marked dysfunction of intellectual function in all areas has occurred. Behavioural difficulties become increasingly apparent with extreme personality changes (ranging from passivity to hostility and aggression), depression and anxiety common. Wandering often occurs. Delusions, especially of a paranoid nature, are present in up to 50% of patients with Alzheimer's.[11]

Vascular disease is probably the second most common cause of dementia

Vascular dementia

Vascular disease is probably the second most common cause of dementia, accounting for 10–20% of all cases.[1] Three different contributing pathologies can be identified. Multi-infarct dementia is associated with multiple infarcts of varying size occurring in the cortex, subcortex or a combination of the two. These patients often give a history of recurrent strokes or trans ischemic attacks with stepwise mental deterioration after each event. It appears it is not so much the size of the infarct, but rather its location, which is predictive of the development of dementia.[12] Vascular dementia can also occur with a single infarct provided it is located in a strategically important area of the brain.

A third, more subtle type of vascular dementia, Binswanger's disease, is a dementing illness associated with diffuse, subcortical white matter damage often occurring in patients with chronic hypertension and/or severe atherosclerosis. The pathogenesis of Binswanger's disease is unknown.[10]

Table 1. Summary of features of cortical and subcortical dementias.[7]

Function	Cortical Dementia	Subcortical Dementia
Alertness	Normal	Marked 'slowing up' (bradyphrenia)
Attention	Intact in early stages	Impaired
Episodic memory	Severe amnesia	Forgetfulness due to poor encoding Recognition better than recall
Frontal 'executive' function	Normal until late	Typically impaired from onset
Personality	Preserved	Apathetic, inert
Language	Aphasic features	Normal, except for reduced output and dysarthria
Praxis	Impaired	Normal
Visuospatial/perceptual abilities	Impaired	Impaired

Subcortical features often dominate the clinical picture secondary to multiple lacunar infarcts in the basal ganglia and sub thalamic areas. These patients demonstrate psychomotor slowing, poor concentration, indecision and mental apathy.[12] In contrast, patients with predominantly cortical infarcts are more likely to have difficulties with memory, praxis and language. Motor speech abnormalities include dysarthria, reduced rate, and disruption of melody and pitch.[5] Often features of both cortical and subcortical dysfunction are present. Night time confusion and emotional lability are common.[7]

Frontotemporal dementia (including Pick's disease)

While most of the degenerative dementias will eventually involve the frontal and adjacent anterior temporal lobes, a few demonstrate early and selective involvement of this region. Dementia secondary to atrophy of the frontal or temporal lobes may represent 10 to 20% of persons with presenile dementia (onset before age 65).[10] Brain imaging studies usually show severe atrophy of the frontal and anterior temporal regions, reducing the gyri to a 'knife edge' appearance. Histological studies demonstrate gliosis and severe neuronal loss particularly affecting the outer layers of the cortex. Examination of the remaining neurons may exhibit a characteristic swelling (Pick cells) or contain Pick bodies (filamentous inclusions that are weakly eosinophilic but stain strongly with silver methods).[9] About 50% of patients with frontotemporal dementia have a strong family history, suggesting that this form of dementia is inherited in a autosomal dominant pattern.[13]

The clinical features depend on the area involved. In frontal lobe atrophy changes in personality, especially disinhibition, apathy, or agitation, and alterations in social behaviour are an early and prominent feature. Impairments of adaptive behaviour, mental flexibility, problem solving, planning and initiation are also common. Memory is relatively intact. Many neuropsychological tests that detect frontal impairment are unable to discriminate between Alzheimer's and Frontotemporal dementia. Counting backwards may be the most sensitive test for Frontotemporal dementia.[5] Most patients have little awareness of these changes and deny they have any problems (anosognosia).[1]

In temporal lobe atrophy disruption of semantic (general knowledge) memory causes difficulties with word finding (highlighted on category fluency and confrontational naming tasks) and loss of general knowledge. Speech remains fluent although diminished vocabulary and paraphasic errors are present.[7] Paraphasias (word substitution errors) may be meaning based (e.g. 'apple' instead of 'orange') or sound based. The latter may be real word approximations (e.g. 'stale' instead of 'snail') or neologisms (e.g. 'poot' instead of 'suit').

Pick's disease is a subset of frontotemporal dementia. It usually presents with a combination of both frontal and temporal lobe dementia although some patients present with predominant frontal or predominant temporal dementia. Behavioural disturbances including apathy, hypersexuality and psychomotor slowing as well as abundant unfocused speech (logorrhea), echolike spontaneous repetition of words or phrases (echolalia) and compulsive repetition of phrases (palilalia) are characteristic.[1,7]

Parkinson's disease and diffuse Lewy body disease

The presence of Lewy bodies (cytoplasmic neuronal inclusions) in the substantia nigra and locus ceruleus is a feature of Parkinson's disease. Lewy bodies can also be found in other areas of the brain, e.g. the cerebral cortex, in some patients who have had Parkinson's disease for many years. Cortical Lewy bodies are also associated with a form of severe, rapidly evolving dementia. When associated with changes typical of Alzheimer's disease (e.g. extracellular neuritic plaques) it is termed the Lewy body variant of Alzheimer's disease. When the Lewy bodies occur without the changes typical of Alzheimer's disease the condition is known as diffuse Lewy body disease.

Approximately 20–30% of patients with Parkinson's disease eventually develop dementia.[1] The risk of dementia is much higher in patients with Parkinson's disease than those without at the same age. It is unclear whether the dementia develops secondary to degeneration of the substantia nigra with subsequent loss of connections to limbic and frontal association areas, the presence of cortical Lewy bodies or coincidental Alzheimer's disease.[14] Treatment with L-dopa neither accelerates nor prevents this process.[10]

Key Points

- Occurring mainly later in life, the prevalence [of dementia] is around 1% at age 60 and doubles every five years, to reach 30-50% by age 85.
- It has been estimated that between 1992 and 2016, the prevalence of dementia will increase in New Zealand by 96-100%, compared with a rise in the general population of 18-26%.
- Delusions, especially of a paranoid nature, are present in up to 50% of patients with Alzheimer's.
- Dementia secondary to atrophy of the frontal or temporal lobes may represent 10 to 20% of persons with presenile dementia (onset before age 65).
- Approximately 20-30% of patients with Parkinson's disease eventually develop dementia.

This type of dementia displays many features suggestive of frontal lobe damage. Marked impairment of executive functions is common. The Wisconsin card sorting test, which determines ability to form concepts, shift set, monitor one's responses and benefit from feedback is particularly sensitive in detecting the patterns of executive dysfunction seen in this group.[14] General psychomotor slowing, apathy, impairment of visuospatial skills and verbal fluency as well as delusions and hallucinations are also early features.[1] Poor performance on all memory measures is also noted, although in contrast to Alzheimer's, memory impairment is characterised by severely impaired retrieval of stored information rather than poor encoding and rapid forgetting. Free recall is low, but use of cues and multiple choice alternatives enhance performance. Retention of memory between immediate and delayed testing is relatively preserved. Cognitive loss typically fluctuates daily, or even hourly.[14]

Huntington disease

Huntington disease is an autosomal dominant inherited disorder which usually manifests itself between 20 and 50 years of age. It is characterised by progressive choreiform movements, psychiatric disturbances (including impulsivity, apathy, depression and schizophrenia like disorders), and dementia. The dementia has features similar to that associated with Parkinson's disease. The degree of cognitive impairment is variable and there is a correlation with age of onset, with younger age being associated with a more severe and rapidly progressive course.[14]

Conclusion

Dementia is a devastating disease. The impact upon individuals, their families and society is huge. There are many types of dementia. Only a few of the more common, primary forms have been discussed in this paper. Early diagnosis, usually through a combination of careful history taking and formal assessment of cognitive decline is of benefit. While these dementias are progressive and irreversible, early recognition of dementia and use of pharmacological and non pharmacological treatments can enhance quality of life for the patient and in turn lessen the burden of care on the family.

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