

Fast Facts



# Fast Facts: Dementia

Lawrence J Whalley and John CS Breitner  
Second edition





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## **Declaration of Independence**

This book is as balanced and as practical as we can make it.  
Ideas for improvement are always welcome: [feedback@fastfacts.com](mailto:feedback@fastfacts.com)



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## Glossary of abbreviations

**ACh:** acetylcholine

**AChE:** acetylcholinesterase

**ACTH:** adrenocorticotrophic hormone

**ADL:** activities of daily living

**APP:** amyloid precursor protein

**ChAT:** choline acetyltransferase

**DSM-IV:** *Diagnostic and Statistical Manual of Mental Disorders*, fourth edition

**DSRS:** Dementia Symptom Rating Scale

**DZ:** dizygotic [twin]

**GABA:** gamma-aminobutyric acid

**ICD-10:** *International Statistical Classification of Diseases and Related Health Problems*, tenth revision

**MAP:** microtubule-associated protein

**MMSE:** mini mental state examination

**MRI:** magnetic resonance imaging

**MZ:** monozygotic [twin]

**NART:** National Adult Reading Test

**NFT:** neurofibrillary tangle

**NMDA:** N-methyl-D-aspartate

**NPI:** Neuropsychiatric Inventory

**NSAID:** non-steroidal anti-inflammatory drug

**PET:** positron emission tomography

**PHF:** paired helical filament

**ROS:** reactive oxygen species

**SPECT:** single photon emission computerized tomography

## Introduction

Whenever one of us lectures publically about dementia, someone in the audience is almost certain to ask, 'Is dementia the same as Alzheimer's disease?' And almost as often, someone will ask, 'What's the difference between ordinary forgetfulness in old age and dementia?' Or, 'Doesn't everyone get dementia if they live long enough?' Our answers are straightforward: Alzheimer's disease is one of the causes of dementia but there are many other less common causes. Dementia is different from normal age-related forgetfulness, both because memory loss is more severe and because other abilities such as language are affected. We don't really know the answer to the last question, so our carefully worded reply usually prompts more questions about the true nature of the dementias of old age. If pressed, we point to the typical degenerative changes that characteristically accompany most dementing illnesses, and we note that these changes almost always affect key brain areas that are critical for memory ('bottle-neck structures').

Nowadays, after enormous research efforts, it is true to say that more is known about the cause, course and treatment of the dementias than about any other psychiatric disorder. However, one research goal that remains unfulfilled – and is still a major worry and priority for many old people, public health doctors and politicians – is the early recognition of dementia, or more accurately the recognition of early dementia. Many predict that if dementia is ever to be prevented we will need the ability to identify patients at the very early stages of their illness or – better yet – those who are at greatest risk but who lack overt symptoms. So far, no hard and fast rules can reliably define the dementia 'prodrome'. Instead, the idea gaining currency is that the brain possesses 'cognitive reserve' ('brain reserve' or 'neural reserve') that enables it to withstand or buffer the presence of the early brain changes of dementia. Close study suggests that, like dementia itself, reserve consists of diverse parts that include education, original mental ability, accumulated stressful experiences and much more. If such reserve can be shown to have a sound biological basis, this discovery may lead to interventions and suggest novel approaches to the delay of dementia.

The holistic care of a person with dementia encompasses health and social elements. In developed societies, both have improved markedly over the past decades. In the USA, and possibly elsewhere in the developed world, there are established trends towards lower rates of disability and decreased mortality (especially among men) from acute myocardial infarction. These improvements attest to the impact of many innovations in risk factor reduction in primary and geriatric specialty care. These developments have relevance to dementia care.

First, public health strategies that lessen exposure to vascular risk factors reduce the frequency of acute vascular events. Examples include better control of hypertension, diabetes and lifestyle factors. In this sense, the association between mid-life vascular risk factors and late-onset dementia emerges as the single greatest opportunity to reduce the occurrence of dementia among the elderly.

Second, progress in social care of the elderly provides a sound basis for the claim that dementia care is improving, that quality of life is getting better and that, in step with improved geriatric care, the outlook for the elderly, including those with cognitive disabilities and dementia has improved. In time, these steps forward will lengthen with the growth of scientific knowledge. At present we are passing through a mature phase in the development of dementia services. We know that at our best what we do for persons with dementia can show our capacity for compassion to advantage, and that our standards of care help safeguard not only our own liberal values but also the independence of those with dementia.

This fully updated second edition of *Fast Facts: Dementia* begins with a review of the basic neuroscience, followed by a discussion of brain aging and its relationship to neurodegenerative disease. It then considers the cause, course and treatment of the common illnesses that can provoke dementia syndrome. Our aim is to equip the primary care physician and other members of the healthcare team with an understanding of the basic causes of dementia, particularly Alzheimer's disease, the clinical characteristics of dementia, and the basic principles of its evaluation and management. We hope that, in the process, readers will learn some of the steps that will improve the long-term care of patients with dementia or perhaps even prevent dementia.

Although the presence of dementia does not always imply the existence of an identifiable brain disease, it usually does so. A basic knowledge of some of the principles of neuroscience and the anatomy and physiology of the brain is therefore essential to a basic understanding of dementing illness.

### Simple functional anatomy of the brain

An adult human brain weighs approximately 1.3 kg. The central nervous system of the adult brain is divided into six main parts: the spinal cord; the medulla, pons and midbrain that together comprise the brainstem; the diencephalon; and the two cerebral hemispheres (Figure 1.1).

The largest components are the two cerebral hemispheres, which are principally responsible for the higher intellectual functions that distinguish humans from non-human primates. They consist of the cerebral cortex and three deep-lying structures:

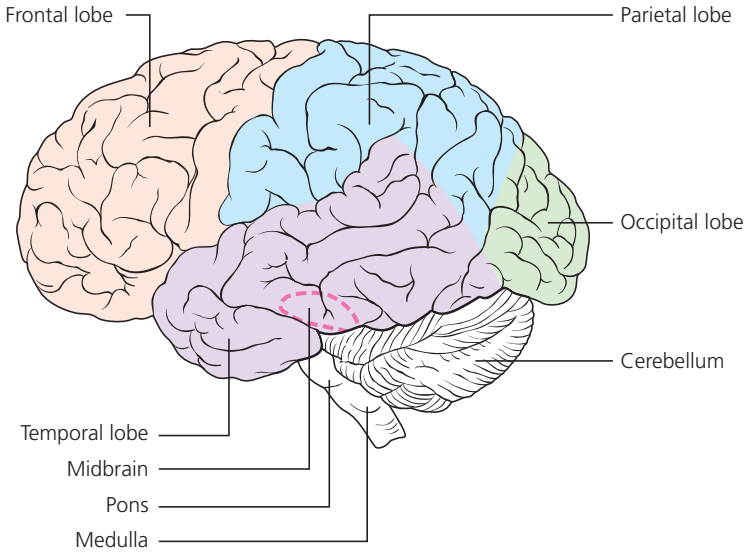
- the basal ganglia, involved with regulation of activity and motor performance
- the hippocampi (singular hippocampus), involved with memory
- the amygdaloid nuclei, involved with linkage of nervous and hormonal responses to emotions.

Deeper and older in evolutionary terms are the diencephalon and brainstem. The diencephalon contains two structures:

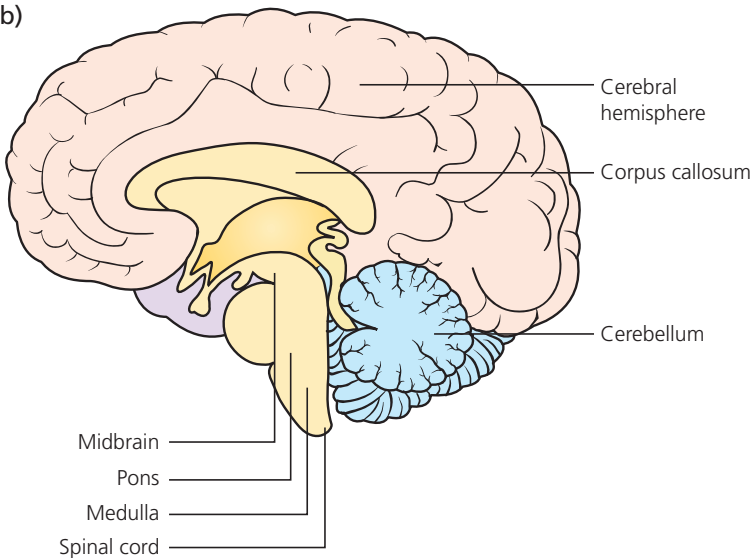
- the thalamus, which acts principally as a relay station for information passing to the cerebral cortex from the rest of the nervous system
- the hypothalamus, which regulates hormonal, autonomic and other basic body functions such as temperature control, salt and water balance, thirst and appetite.

Within the brainstem, the midbrain controls many sensory and motor functions such as eye movements and coordination of visual and auditory reflexes. Nerve tracts in the pons convey information about movement from the cerebral hemispheres to the cerebellum, which

(a)



(b)



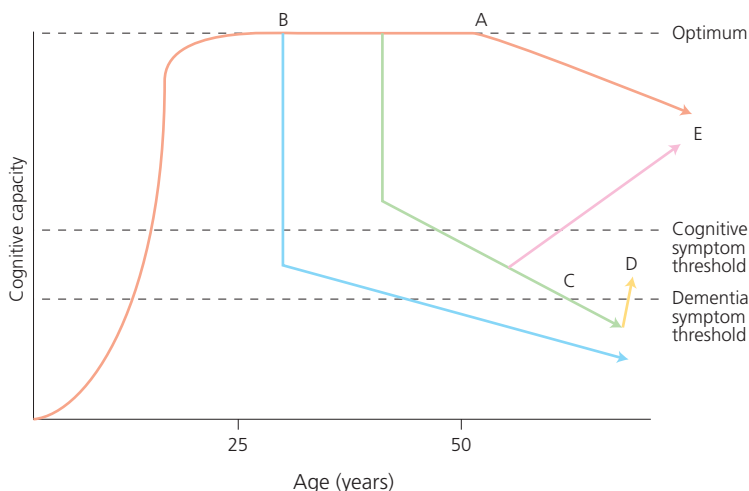
**Figure 1.1** Schematic views of the brain: (a) lateral view; (b) midsagittal section.

### 3 Symptoms, signs and course

Neurodegenerative brain changes at the molecular, subcellular, cellular or tissue levels can reach a threshold level of severity at which cognitive capacities are lost. Some neurodegenerative conditions such as Alzheimer's and Parkinson's diseases may represent exaggerations of 'normal' aging processes (see previous chapter), but many certainly do not. Certain broad principles that apply are described below.

#### The 'threshold–decompensation' model

The 'threshold–decompensation' model of symptom formation that applies to many organ systems can also be applied to cognitive decline, as illustrated in Figure 3.1. Cognitive capacities normally grow through infancy and childhood so that optimal functional capacity is attained in early adulthood (left-hand, ascending portion of curve). The measure of this optimum cognitive capacity may be influenced by genes and also by



**Figure 3.1** Trajectories of cognitive development and decline (see text for explanation).

childhood illnesses, education, nutrition or exposure to neurotoxins. Exposure to severe harmful influences may limit brain development so that optimum functional maturity is not attained, as is seen in neurodevelopmental disorders. Upon attaining optimum development, the 'normal' cognitive capacity curve typically begins to decline slowly, several decades after reaching its optimum, at about 50 years of age (point A in Figure 3.1). However, a catastrophic event (point B) such as a traumatic brain injury or stroke can suddenly disrupt brain integrity or function beyond the critical symptom threshold, below which cognitive symptoms appear. Such injury can result in cognitive disability. Other injuries may be insufficient to cause an observable cognitive syndrome but nonetheless may reduce the brain's cognitive reserve so that the 'normal' aging trajectory now proceeds from a lower starting point (green line). Accelerated decline in the trajectory now crosses the symptom threshold in relatively early old age (point C). In some instances, functional integrity may be re-established with treatment of (or recovery from) the insult, leading to a partial recovery (point D) or complete restitution of capacities (point E). Then, the age when obvious cognitive symptoms appear is affected minimally, if at all.

### **Cognitive disorders: delirium, dementia and focal syndromes**

Insults that cause disarray in the functional capacity of the brain may result in different cognitive syndromes.

- Fulminant neurodegenerative processes (rarely) or severe alterations of the brain's metabolic milieu (more commonly) can provoke delirium.
- Slow neurodegenerative processes or more chronic injury states typically provoke dementia.
- Focal neurological injuries may provoke monofocal cognitive deficits.

Although these syndromes share the cardinal feature of cognitive decline, they are otherwise distinct.

**Delirium.** The hallmark of delirium is clouding of consciousness. Other common features include abnormalities of emotion, perception and behavior, as well as cognition. The terms 'delirium' and 'confusion' are