Neurodegenerative diseases are a broad group of conditions that result in the death or dysfunction of nerve cells. The most common neurodegenerative diseases are dementias such as Alzheimer’s disease and Parkinson’s disease, which affect 800,000 and 120,000 people respectively in the UK. These conditions are generally considered diseases of the elderly, although early onset forms exist.

Other conditions such as motor neurone disease and Huntingdon’s disease also fit in to this category. These diseases are progressive, incurable and, although there have been advances in their treatment, currently available medications treat symptoms or delay progression rather than offering a cure.

Neurodegenerative disease, especially dementias, represent a significant health burden accounting for £23 billion a year in lost earnings and care costs in the UK, which is greater than the cost of cancer and heart disease combined, but funding for research into neurodegenerative conditions has lagged behind significantly. Dementia research is receiving less than 10% of the funding cancer receives.

The diagnosis of neurodegenerative diseases is based on clinical findings and is the preserve of neurologists and psychiatrists; traditionally the radiologist has played only a limited role in both diagnosis and monitoring of disease progression. Until the last decade, neuroimaging’s main role in neurodegenerative disease was to rule out other potentially treatable causes of symptoms, for example brain tumours or normal pressure hydrocephalus. In recent years advances in MRI methods and nuclear medicine techniques have made it possible to identify imaging biomarkers of neurodegenerative disease which aid in the diagnoses and with the monitoring of the effectiveness of treatment and progression.

In this short review we will outline the main imaging methods currently used clinically in the most common neurodegenerative diseases, Parkinson’s and Alzheimer’s, and the possible future roles of imaging biomarkers in the care of patients with these conditions; we shall also briefly discuss imaging in other rarer neurodegenerative conditions.

### Alzheimer’s disease

Alzheimer’s disease is a progressive neurodegenerative disorder and is the most common cause of dementia in elderly people. Its pathology is incompletely understood but the histological appearance is associated with accumulations of abnormal proteins amyloid-β. Alzheimer’s disease presents with progressive cognitive impairment with associated amnesia. The disease is preceded by a period of mild cognitive impairment (MCI) with an insidious onset. MCI usually progresses to Alzheimer’s disease or another form of dementia but in a small number of cases resolves. Current treatments for Alzheimer’s disease, such as donepezil (an anticholinesterase inhibitor), slow the progression of Alzheimer’s disease but do not regain lost cognitive function. A key goal of neuroimaging is to identify which patients with MCI will go on to develop Alzheimer’s disease so that appropriate medication can be started, promptly prolonging normal cognitive function.

Conventional anatomical imaging both with CT and MRI has a relatively low sensitivity in identifying Alzheimer’s disease and images may be within normal limits allowing for the patient’s age. Significant cortical atrophy is often seen in patients with dementia. Cortical atrophy patterns can be used to differentiate Alzheimer’s disease from other dementia types. Patterns of atrophy are specific for different causes of dementia, with hippocampal, temporal and parietal atrophy indicative signs of Alzheimer’s disease (see figure 1). Frontotemporal dementia has a frontal and temporal lobe atrophy preponderance. Lewy body dementia typically affects the parietal, occipital lobes and the cerebellum, which are usually spared in Alzheimer’s disease. Vascular dementia is vascular in origin and will show a patchy distribution of change.

Nuclear medicine imaging using FDG-PET shows reduced glucose metabolism in the parietal, temporal lobes and posterior singulate cortex. FDG-PET and SPECT both increase the sensitivity of the pathological diagnosis of Alzheimer’s disease combined with clinical criteria to 84% and 92% respectively, compared with 70% on clinical findings alone (see figure 2). Significant research effort has been applied to the quantifying atrophy in certain regions of the brain, such as the hippocampus, using MRI. Measurements of hippocampal atrophy, using computerised automated techniques such as voxel-based morphometry in patients with MCI, show a strong positive predictive value for them to go on to develop Alzheimer’s disease rather than other forms of dementia. The presence of imaging biomarkers of cerebrovascular disease such as previous infarcts, deep white matter lesions and, most sensitive, dilated Virchow-Robin spaces (enlarged perivascular spaces) have been shown to discriminate vascular dementia from Alzheimer’s disease (see figure 3). Diffusion weighted imaging (DWI) and diffusion tensor imaging (DTI) are MRI techniques that show information about the ability of water to move through the tissue imaged. In Alzheimer’s disease, DWI shows increased diffusivity in hippocampus, temporal and parietal lobes and these changes are apparent before significant atrophy is seen on conventional images (see figure 4).

Although many of these biomarkers are still at a development stage, upcoming revisions of diagnostic criteria are considering including imaging biomarkers. Drug companies are beginning to use structural biomarkers to indicate progression of disease. An important point to remember is that, for an imaging biomarker of neurodegenerative disease to be valuable, it has to provide information above that which can be obtained clinically. A biomarker is of no use if it is able to differentiate only between a young healthy individual and a patients with Alzheimer’s disease; this adds nothing to observations a health care professional could make at the clinic. Biomarkers have to be able to distinguish patients with similar signs and symptoms but with different types of disease.

### Parkinson’s disease

Parkinson’s disease is a progressive movement disorder. Its clinical diagnosis is based on the presence of muscle rigidity, tremor, a slowing of physical movement. It is caused by the loss of dopaminergic neurons in the substantia nigra and their connecting neurons within the basal ganglia. Symptomatic treatment exits in dopamine replacement (L-dopa) but treatment loses effectiveness gradually over time. Conventional anatomical MR brain imaging is usually normal. Inversion recovery MR sequences can show volume and...
signal loss within the substantia nigra.\textsuperscript{11}

Nuclear medicine DAT scan (a Ioflupane labelled radioactive isotope of iodine, which has similar binding properties to dopaminergic) in patients with Parkinson’s disease reveals decreased uptake in the basal ganglia especially the putamen. This is of clinical use when the diagnosis of Parkinson’s disease is unclear clinically.\textsuperscript{12}

Advanced MR imaging techniques are under investigation for the early identification of patients with Parkinson’s disease and different sub-types of the condition. Magnetisation transfer imaging has shown promise in identifying abnormalities in the substantia nigra which appear normal on conventional MR imaging.\textsuperscript{11} Anosmia (loss of smell) is a common early symptom of Parkinson’s disease; MRI diffusion weighted MRI shows increased diffusivity in olfactory tracts. Computer-aided volume methods, such as Voxel-based morphometry, shows cortical atrophy in patients with Parkinson disease with dementia.\textsuperscript{13}

Functional MRI looking at areas of the brain active during motor tasks show hypoactivation in basal ganglia, supplemental motor area and hyperactivation cerebellum and motor cortex in patients with Parkinson’s disease compared with control subjects.\textsuperscript{14}

These techniques, although still experimental, may be able to diagnose Parkinson’s disease at an earlier stage, allowing medications that slow the progression of the disease to take effect before symptoms begin to manifest.

Other neurodegenerative diseases

Other neurodegenerative diseases include Huntington’s disease, which is a genetic movement disorder that has a variable age of onset. Neuroimaging of patients with Huntington’s disease shows genetic abnormality before the onset of symptoms with DWI; MRI shows increased diffusion in the striatum and may be able to indicate when symptoms will start.\textsuperscript{15} PET studies also show areas of hyperfusion in the basal ganglia. Motor neuron disease or Amyotrophic Lateral Sclerosis is a progressive disease causing the destruction of motor neurons. MRI imaging can show T2 hyperintensities along the corisocipital tract or T2 hypointensities in the precentral gyrus.\textsuperscript{16}

Neuroimaging is advancing in its role of neurodegenerative disease and these conditions are moving away from purely clinical diagnoses. The ability to map the progression of these diseases using imaging biomarkers opens up the prospect of monitoring the effectiveness of novel therapies. As in other areas of neuroradiology, such as stroke and tumour, imaging advanced imaging methods such as diffusion weighted MRI and PET are likely to play an ever-increasing clinical role in neurodegenerative diseases.

References

*Suggested reading


FIGURE 1
(A) Normal subject, (B) Alzheimer’s disease. Atrophy of the hippocampus and temporal lobe entorhinal cortex occurs in 80-90% of AD cases but only 5-10% of control subjects.

FIGURE 2
SPECT, using Tc-hexamethylpropyleneamine oxime (HMPAO) showing (A) a normal scan, as seen in control subjects, (B) Alzheimer’s disease and (C) dementia with Lewy bodies.

FIGURE 3
Axial inversion recovery MR images showing Virchow-Robin spaces (VRS) as linear structure passing through the basal ganglia (arrows) the presence of high numbers of VRS in the basal ganglia is a sensitive indicator of a diagnosis of vascular dementia.

FIGURE 4
(A) Normal subject. (B) MCI, (C) Alzheimer’s disease. Diffusion tensor imaging (DTI) maps of fractional anisotropy (FA), a measure of the directionality of random water diffusion in brain tissue. Arrows point to regions of diminished FA signal in the parahippocampus (top row) and posterior cingulate (bottom), indicating disintegration of white matter fibres.