Magnetic Resonance Imaging of Dementia
Asim K. Bag, MD

Dementia is a state of serious cognitive impairment resulting in severe functional and emotional disability that is usually caused by neurodegenerative diseases. The major causes of dementia include neurodegenerative diseases. Brain parenchymal damage due to any cause can also result in dementia such as stroke, hemorrhage, infection and toxicity. Prion disease is another rare but important cause of relatively acute onset dementia.

Imaging plays crucial role in diagnosis of dementia. Most importantly imaging with CT and MRI is done to rule any structural cause such as prior insult to the brain, intracranial hemorrhage low-grade tumor etc. In the early stages of dementia due to neurodegenerative diseases there is no characteristic imaging findings. As the diseases progress over time selective areas more severe involvement gradually appears that may help in diagnosis.

Neurodegenerative diseases:

Alzheimer’s disease (AD)

AD is the most common cause of dementia. AD is more prevalent in the elderly and incidence increases with age. Annual incidence of AD is as low as 0.6% for individuals of 65–69 years of age to as high as 8.4% in individuals of ≥85 years of age. The incidence of AD is gradually increasing as the age of the general population is increasing. Pathophysiology, clinical features and management is beyond scope of this focused review.

Imaging of AD can be grossly classified as structural/ topographical imaging (computed tomography [CT] and MRI) or pathophysiologic imaging (FDG-PET, amyloid imaging). Please refer to the following article for detailed discussion of the functional/pathophysiologic imaging of AD.

Conventional neuroimaging with MRI is important as these often suggest clues suggesting AD, and also in excluding other diseases. CT scan can have a variable appearance depending on the stage of the disease. In early stage of AD, minimal brain atrophy is the usual finding, which is not possible to differentiate from normal aging pattern. With progression of disease, moderate to severe brain atrophy preferentially affecting the temporal lobes occurs. MRI of patients with AD often demonstrates diffuse cerebral volume loss predominantly in the parietal and temporal lobes, specifically the hippocampus.

Parietal and hippocampal volume loss can support a clinical diagnosis, but cannot definitely establish the diagnosis of AD as these findings often overlap with the variable degree of hippocampal atrophy. Predominant atrophy hippocampi are usually seen in patients with AD. Progressive atrophy of the hippocampi is associated with disease progression. There are many different quantitative softwares are available that can quantify the hippocampal volume and can be used as a guide to disease progression. These methods can be segmentation of the hippocampi from a high-resolution 3D T1 weighted images, or can be voxel –based morphometry. Longitudinal volumetry of a single patient can be used to identify progressive
atrophy of the hippocampi. However, quantitative volume analysis is usually used in the setting of research and clinical trials. Clinically, a visual scoring system is used for assessment of volume of the medial temporal lobe. There are many methods available for visual scoring system but the system described by Duara et al is the most widely accepted.

Figure Legends: Hippocampal atrophy in AD. Coronal MPRAGE reconstructed image through the level of the hippocampi demonstrates preferential severe atrophy of bilateral medial temporal lobes (Duara Grade IV). The left hippocampus is more severely affected.

There is a variant of the AD that predominantly affects the posterior aspect of the brain (posterior parietal, posterior temporal and occipital lobes), which is known as posterior cortical atrophy or Benson’s syndrome. This group of patients typically presents with visual problems due to atrophy of the primary visual cortex and association visual cortex.
Figure Legends: Posterior cortical atrophy. Axial MPRAGE reconstructed image through the level of the centrum semiovale demonstrates preferential severe atrophy involving bilateral posterior parietal lobes with relatively mild atrophy of the rest of the brain.

Dementia due to Lewy body disease:
DLB accounts for about 10%–22% of all dementia patients. Like AD, DLB is a disease of older age occurring after 65 years. There is a strong predilection for male patients. DLB is usually sporadic. However, familial DLB cases have been reported associated with mutation of the α-synuclein (SNCA) gene. In addition to neurocognitive decline, distinctive clinical features of DLB include visual hallucination, Parkinsonism, cognitive fluctuations, and autonomic dysfunction.
There is no specific finding on structural imaging to support the diagnosis of dementia due to Lewy bodies. Non-specific diffuse brain atrophy is seen but there is no characteristic pattern. However, dopamine transporter (DaT scan) imaging demonstrates loss of dopaminergic neurons at the striatum.
Frontotemporal dementia (FTD)

FTD is a group of neurodegenerative diseases resulting from the preferential involvement of the frontal lobe and temporal lobe in varying combinations. FTD is an extremely heterogeneous disease with wide variety of genetic abnormalities, clinical presentation, histopathologic and imaging findings. There are three well-known clinical syndromes categorized under FTD: behavioral variant (bv-FTD), which was classically described as Pick’s disease; progressive nonfluent aphasia (PNFA); and semantic dementia (SD).

Behavioral variant
Behavioral changes are the key clinical findings in bv-FTD. On histopathology, the frontal lobe is preferentially affected. On MRI, bilateral frontal lobe atrophy is the dominant imaging finding. In severe cases, the frontal lobe gyri become paper-thin.

Semantic dementia
In SD, typical clinical findings include fluent speech with prominent anomia and word finding difficulty. On histopathology, dominant temporal lobe is predominantly affected. On MRI, severe atrophy of the temporal pole of the dominant hemisphere is the key findings.

Progressive nonfluent aphasia
PNFA preferentially affects the perisylvian area of the dominant hemisphere. Patients with PNFA have difficulty in understanding language. On MRI, there is severe peri-Sylvian atrophy of the dominant hemisphere.

Figure Legends: PNFA. Sagittal T1 weighted image through the level of the left Sylvian fissure in a right-handed male patient demonstrates preferential severe atrophy involving peri-Sylvian regions.
FTD associated with motor neuron disease

Approximately 15% of patients with bv-FTD have associated motor neuron disease. This variant is recognized as a special subtype of FTD (FTD-MND) as it has a specific genetic linkage. In patients with predominant amyotrophic lateral syndrome, diffusion restriction as well as FLAIR hyperintensity can be seen along the corticospinal tracts.

Vascular dementia:

Vascular dementia (VaD) is the second most common cause of dementia after AD. VaD is defined as dementia with a decline in memory and intellectual ability that causes impaired functioning of daily living associated with objective evidence of cerebrovascular disease. Most importantly, there is a temporal relationship between the cerebrovascular insult and the onset of dementia. VaD may be subclassified as secondary to large vessel disease or secondary to small vessel disease.

Secondary to large vessel disease
Dementia secondary to large vessel disease is associated with multiple infarcts of the major arterial territories of the brain or strategic infarction in areas such as the angular gyrus, thalamus, and basal forebrain.

Secondary to small vessel ischemic disease
Small vessel disease involves the innumerable perforating arteries supplying the subcortical structures (the deep brain nuclei) and long medullary arteries supplying the deep cerebral white matter (centrum semiovale, corona radiata). Dementia secondary to small vessel disease can be due to numerous small vessel pathologies but hypertension, diabetes and chronic renal diseases are the most common causes. Imaging manifestations could be lacunar infarcts due to sudden complete occlusion of the small arteries or confluent areas of white matter T2/FLAIR hyperintensity due to prolonged hypoxia associated with critically narrowed small arterioles.

Cerebral amyloid angiopathy

Cerebral Amyloid Angiopathy (CAA) is also a disorder of abnormal amyloid deposition but amyloid is preferentially deposited in the cortical and leptomeningeal blood vessel sparing the more central blood vessels. As a result of abnormal amyloid deposition, there is fibrinoid degeneration, necrosis, and end-vessel microaneurysm formation resulting in hemorrhages. Most commonly hemorrhages are microscopic but frank lobar hemorrhage is also common. Superficial siderosis is another common imaging finding due to chronic subclinical subarachnoid hemorrhage. All these findings can be easily seen on GRE or SWI sequence.
Figure Legends: CAA. Axial GRE image through the level of the lateral ventricles demonstrate tiny focus of hypointensities in the superifical brain of right temporal lobe and hypointensity along the sulci (superficial siderosis) involving bilateral occipital lobes.

**CADASIL**

Cerebral autosomal-dominant arteriopathy with sub- cortical infarcts and leukoencephalopathy (CADASIL) is an autosomal dominant disease due to mutations of the NOTCH 3 gene, located on chromosome 19. Classic presentation of CADASIL includes subcortical ischemic events, dementia, migraine with aura, mood disorder, seizures, and motor abnormalities. Unlike CAA, typical of chronic small vessel arteriopathy involves both penetrating cerebral and leptomeningeal arteries.

MRI abnormalities can be see as early 10–15 years before clinical symptoms. The most common MRI abnormality is confluent areas of T2/FLAIR changes in the deep cerebral and periventricular white matter. Abnormal T2/FLAIR abnormality at the white matter of the anterior temporal lobe is the characteristic imaging abnormality. In later stage of the disease there is involvement of the external capsule. Diffusion imaging may demonstrate focal or multifocal diffusion restriction. Microhemorrhages on GRE and SWI sequences are another common MRI abnormality.
Prion diseases:

Unlike the previously mentioned neurodegenerative disease, Prion diseases are a cluster of neurodegenerative diseases due to abnormality in protein folding that progresses very rapidly over several months instead of years. On histopathology, there are characteristic spongiform brain changes (presence of small vacuoles in the neuropil) with neuronal loss, glial proliferation without any evidence of inflammation. Creutzfeldt–Jakob Disease (CJD) is the most common type of human prion disease presenting with dementia. This is a rare disease with an annual incidence of 0.25–2 cases per million populations. Most cases of CJD are sporadic (up to 95%). CJD can be also be variant, familial and iatrogenic. MRI is highly sensitive and specific for the diagnosis of CJD. Diffusion restriction in the caudate head, putamen, globus pallidus, thalamus, and cerebral and cerebellar cortices are the key imaging abnormality. Diffusion restrictions can predominately involve the peripheral cortices or the basal ganglia or mixture of the two. Even though there is diffuse cortical involvement, the primary sensorimotor cortex is almost always spared even in late stage of the disease FLAIR and T2 hyperintensity in the areas of diffusion restriction is almost always seen although the diffusion weighted sequence is more sensitive and specific. Enhancement with contrast is not an imaging feature due to absence of inflammation.

Figure Legends: sCJD. Axial diffusion weighted images through the basal ganglia (A) and the central semiovale (B) demonstrate diffusion restriction involving bilateral insular cortices, bilateral frontal lobe, and bilateral cingulate cortex.

However, FLAIR sequence is more sensitive than diffusion weighted imaging in the variant CJD that is transmitted via animal (Mad cow disease). Thalamus and basal ganglia is predominantly affected in variant CJD.