

# Imaging Strategies for Dementia

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Dementia is caused by a heterogeneous group of disorders which result in a progressive decline in higher functions of the human brain. Memory is the most common and easiest recognized of the impaired faculties, but changes in personality, judgment, language, abstract thought and visual recognition are also components of dementia syndromes (Tien 1993). It is becoming increasingly important for imagers to recognize the various dementia syndromes. As the population ages, the age-related prevalence of dementia increases. The prevalence of dementia in patients over 65 years of age is 5-6%. This figure doubles every 5 years beyond that (Tien 1993).

There are several classifications for dementia syndromes. A practical categorization scheme for clinicians and imagers classifies the causes as *cortical*, *subcortical* or *mixed types*. Cortical dementias include Alzheimer's dementia (AD) and Pick's disease. AD is the most common causes of dementia in developed countries (Jobst 1994). A clinical criteria for diagnosing this entity has a specificity of 75%, whereas imaging has a 90% or greater. Pick's disease is another form of cortical dementia, and it may be difficult to differentiate from AD on a clinical basis (Tien 1993). The predominance of personality changes and emotional lability early in the course of the disease may help distinguish it from Alzheimer's type. The cognitive decline and memory deficits occur later in the course of the disease. Intra-cytoplasmic Pick bodies, neuronal loss and cortical and subcortical gliosis are pathologic findings, with a proclivity to affect the temporal and frontal lobes.

The subcortical dementias include Parkinson's disease, Parkinsonian syndromes, Huntingtons chorea, chronic multiple sclerosis, and hydrocephalus. Patients with normal pressure hydrocephalus may present with dementia, unsteady gait, and/or incontinence as primary clinical features. These three signs constitute the triad classically described with this entity (George 1995). In symptomatic HIV positive patients, the AIDS dementia complex is one of the most common neurological disorders (Navia 1997).

Combined (cortical and subcortical) causes include the broad category of vascular dementia. Multi-infarct dementia, subcortical arteriosclerotic encephalopathy, and lacunar disease are included in this

category. Nonvascular causes of combined dementia include slow virus infections (Creutzfeldt-Jakob disease) and hypoxic encephalopathy.

## NEUROIMAGING

The primary role for imaging patients who present with dementia is to rule out treatable or reversible causes. Despite the fact that a minority of cases are treatable (Sandson 1996), it is extremely important that a diagnosis be made in a timely fashion in such cases, because a reversible etiology may progress to irreversible or high morbidity sequelae. Some potentially treatable causes of dementia include slow growing neoplasm such as meningioma (usually frontal lobe location which presents late after achieving significant size), extracerebral hematoma, Wernicke's disease, hypothyroidism, and some cases of hydrocephalus (Deleion 1995).

Structural abnormalities do not necessarily prove a dementia syndrome, but do provide insight regarding underlying pathologic changes (Lange 1995). A general screening examination can be accomplished with a noncontrast CT, which is sufficient to exclude an extra-axial fluid collection, hydrocephalus or a mass lesion. The multiplanar capabilities of MR allow a more detailed assessment of structures relevant to additional dementia etiology, such as Alzheimer's disease. Relevant structures such as the medial temporal lobe and hippocampal formation can be assessed using high resolution coronal images (Wahlund 1996).

In Alzheimer's dementia (AD) a characteristic pattern of temporal lobe and hippocampal atrophy is the most reliable anatomic finding (George 1995, Giacometti 1994). There may be increase signal on long TR images within the medial temporal lobes, but T2 value abnormalities have not proved valuable for the detection of AD (Campeau 1997). Semiautomated segmentation techniques have also been attempted for the early detection of AD. However, assessment for cortical gray matter loss is not sufficient to make a premorbid diagnosis (Tanabe 1997). Other measures of brain atrophy have been employed to assess for Alzheimer's dementia. Parameters such as bifrontal index, interhemispheric fissure width, interuncal distance and hippocampal atrophy have all been evaluated. Hippocampal atrophy

determinants include hippocampal height, choroid fissure width, and temporal horn width. The latter appears to be the best discriminator on an anatomic basis for Alzheimer's disease patients versus controls (Frisoni 1996). The interuncal distance is generally increased as well.

Pick's disease is far less common than Alzheimer's dementia. As opposed to selective atrophy of the hippocampal formations seen in AD, the anterior frontal and temporal lobes are primarily involved in patients with Pick's disease. Approximately half of patients have both frontal and temporal lobe atrophy, while the other half is relatively evenly divided between those who show predominately frontal or temporal lobe involvement. In addition to severe thinning of the cortex, there may be increased signal on long TR images, and decreased metabolism on functional studies.

Parkinson's disease may also be associated with a significant dementia component. Although this is usually a clinical diagnosis, there may be diminution of the pars compacta of the substantia nigra. The adjacent pars reticulata may show increased signal due to gliosis. The Parkinsonian (Parkinson's Plus) syndromes may show additional findings. For example, progressive supranuclear palsy (PSP) syndrome may show decreased AP diameter of the midbrain, increased signal intensity on long TR images within the tegmentum of the midbrain and pons, as well as the tectum and inferior olivary nuclei. Increased iron deposition in the putamen is characteristic, resulting in a reversal of the relative signal intensity compared to the globus pallidus. Patients with olivopontocerebellar atrophy may demonstrate hyperintensity on long TR images along the pontocerebellar pathways, in addition to the atrophic changes of the pons and cerebellum (Tien 1993).

Although the degree of white matter signal abnormalities in patients with vascular dementia does not correlate with severity, the prevalence of white matter disease does correlate with the presence of dementia (Skoog 1994, Tanabe 1997). It has also been noted that white matter lesions contribute to cognitive decline in both demented and nondementia elderly patients (Skoog 1996). Deep white matter lesions are associated with depression in the elderly, versus periventricular white matter lesions, which are more commonly associated with dementia (O'Brien 1996).

Abnormal signal intensity within the basal ganglia (increased signal on long TR images) have also been described in association with Creutzfeldt-Jakob disease, Wilson's disease and Leigh's disease. Although Creutzfeldt-Jakob disease is a rare cause of dementia, characteristic imaging findings can help make early diagnosis in this rapidly progressive form of dementia. Basal ganglia signal abnormalities include increased signal intensity on long TR images within the putamen and caudate, which do not enhance. Within four months of symptom onset, profound volume loss in the cerebral hemispheres and cerebellum is evident (Finkenstaedt 1996, Tzeng 1997). Demyelination may also be present on follow-up studies in such patients several months after the onset of symptoms.

## Imaging Technique

Anatomic imaging may be tailored to demonstrate the anatomic features described above. T1-weighted sagittal and long TR spin echo axial images are supplemented with high resolution coronal images (3D SPGR) to provide high resolution assessment of the medial temporal lobes to include the hippocampal formations. Conventional long TR dual echo axial images provide assessment of the anatomic features of the posterior fossa structures and the cerebrum, in addition to the contrast resolution required to assess for abnormalities of brain iron deposition. In general, contrast is not needed unless an abnormality is detected on the precontrast studies. This does not necessarily enhance sensitivity for detecting underlying etiologies for dementia, but it does allow further assessment of any lesion that is detected. In general, any neoplastic process that would give rise to dementia symptoms would be detectable without the addition of contrast agents.

## FUNCTIONAL IMAGING

Structural chemical and physical changes accompanying pathologic states in dementia may be visualized with various MR techniques (Gilberto 1996). Perfusion and metabolic abnormalities may perceive anatomic abnormalities in dementia syndromes (Giacometti 1994). An early diagnosis can best be affected by combining anatomic and functional imaging (Julin 1997). To the extent that ongoing studies are able to demonstrate the ability to make a preclinical diagnosis and treatment based on this diagnosis can be refined to achieve clinical benefit, functional imaging will continue to evolve as an important contributor to the evaluation of dementia

patients.

Developments in quantitative imaging techniques are improving our ability to distinguish physiologic and biochemical changes in dementia patients from the normal elderly patient. Normative data must be considered when evaluating dementia patients, due to the presence of underlying changes detected in the normal aging population. Current assessments of functional tests performed at rest and with cognitive tasks are used to distinguish the various types of dementia.

Multiple modalities are utilized to assess perfusion and metabolic parameters in various regions in the brain. The pattern of perfusion and metabolic deficiencies lend specificity to the identification of the various causes of dementia. Nuclear medicine studies include 99 Tc-HMPAO SPECT (single photon emission computed tomography), positron emission tomography (PET). Biochemical assessment using magnetic resonance spectroscopy (<sup>1</sup>H-MRS) and dynamic susceptible contrast MRI can be used to assess perfusion (Harris 1996, Parnetti 1996, Masterman 1997). MR spectroscopy may show decreased NAA in the temporal lobes of Alzheimer's patients (Parnetti 1996). Caution must be employed when evaluating mesiotemporal lobe metabolic abnormalities, as they may overlap those seen in healthy elderly adults (Jagust 1996). Some investigators maintain that it is the decreased metabolic and perfusion parameters in the lateral temporal lobe which distinguish Alzheimer's disease from normal aging (Cohen 1997). Some investigators are advocating the combination of functional brain imaging with genetic assessment for the preclinical detection of Alzheimer's disease. For example, apolipoprotein E-4 allele appears to represent a marker for the later development of clinical Alzheimer's dementia (Small 1996). We are just beginning to realize the potential of combining anatomic, functional and biological evaluation for a number of disease processes.

Due to localization of physiological abnormalities, the diagnostic accuracy may be better for presenile than senile dementia using functional imaging studies (Herholz 1995). And although patients with Parkinson's disease with dementia and Alzheimer's disease may both demonstrate decreased metabolic processes in the lateral, parietal and temporal lobe, Parkinson's disease patients tend to show involvement of the visual cortex relative preservation of the medial temporal lobes (Vanderborght 1997).

Patients with vascular dementia demonstrate scattered foci of cortical and subcortical

hypometabolism, as opposed to the temporoparietal predominance seen in Alzheimer's dementia (Kumar). The volume of these metabolic abnormalities generally correlates with the severity of dementia.

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