The Brain in Older Persons With and Without Dementia: Findings on MR, PET, and SPECT Images

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Neuroimaging plays an increasingly important role in the evaluation of dementias of older adults. Although no unequivocal diagnostic test other than biopsy is currently available for Alzheimer’s disease and some other dementias during life, neuroimaging techniques are an integral part of the examination and follow-up of patients with dementia. This review describes findings in the brains of patients with normal aging and in elderly patients with dementia, as shown by MR imaging and MR spectroscopy, positron emission tomography (PET), and single-photon emission computed tomography (SPECT) and correlated with clinical and pathologic features.

Imaging Techniques

CT is commonly used in the assessment of neurodegenerative diseases. Although it is relatively inexpensive, is widely available, and has the advantage of rapid image acquisition with resultant diminished sensitivity to movement, CT still has limitations. Beam-hardening artifacts, limited imaging planes, and lack of sharply defined gray-white matter and CSF-bone interfaces mitigate the value of quantitative and qualitative measures.

MR imaging, with its faithful rendering of morphology, offers several advantages over CT. Age-related changes are better visualized with contiguous scanning, volumetric acquisitions, segmentation techniques, and pulse sequences that enhance differences in signal intensity of soft tissues [1, 2]. MR imaging is also more sensitive in detecting underlying pathologic changes related to dementia, including vascular disease (e.g., lacunar infarcts [3, 4], white matter lesions [5, 6]), and temporal lobe volume loss [1]. For evaluation of dementia, MR imaging offers exquisite structural information when conventional T1- and T2-weighted images are supplemented by newer volumetric and gradient-echo techniques.

MR qualitative assessments and grading systems for severity or pattern of atrophy developed in individual centers have met with some success in differentiating age-related changes from those associated with dementia [7, 8]. Controlled comparisons and pooling of data among medical centers, however, have proved difficult [9]. Semi-automated and volumetric MR sequences promise more quantitative, reproducible measurement of focal or generalized patterns of brain volume loss and other age-related changes [1, 2, 10–15]. One approach requires pulse sequences specifically designed to accentuate differences in tissue relaxation times; with this technique, reproducible volume measurements of tissues differing substantially in relaxation characteristics (e.g., CSF vs brain parenchyma) can be achieved [10–12]. Another approach requires observer-defined selection of anatomic boundaries; the areas defined are summed for volumetric measurements [13]. A semiautomated technique measuring computer-defined blocks of tissue in a reproducible manner reduces observer variability in choice of anatomic boundaries [14, 15]. Computerized MR segmentation techniques that differentiate brain from CSF on the basis of signal intensity accurately represent actual tissue volumes, although automated measurement of focal areas...
such as the hippocampus and caudate nucleus is more challenging. Although entirely automated observer-independent techniques such as computer-generated segmentation of tissue intensity solve many problems, even these automated methods have their limitations. These include lack of homogeneity of images, variation in scan angle, the occurrence of scanner drift over time, imprecision of partial volume averaging, and poor or inconsistent definition of anatomic landmarks.

The combination of structural imaging and metabolic mapping or functional imaging might ultimately provide the most meaningful information for evaluation of dementia. SPECT and PET provide information related to metabolism, as does MR spectroscopy, and for understanding pathogenesis, improving specificity, and possibly monitoring disease progression and therapeutic response.

Normal Aging

Age-related changes in older adults with normal cognition vary considerably. Loss of volume, diminution of brain weight, gyral atrophy, and ventricular dilatation differ widely. Brain weight and cortical thickness generally decrease with age, and small asymptomatic infarctions may be present [16]. Morphometric studies suggest that shrinkage of large neurons predominates with aging, resulting in an increase in small neurons and glia, particularly in the midfrontal and superior temporal cortices [17].

Some changes seen in the brains of older persons follow a topographic distribution similar to that seen in Alzheimer’s disease. A few neurofibrillary tangles, for example, are present in the brains of most persons without dementia who are more than 55 years old, most frequently in the entorhinal and perirhinal cortices and hippocampus and less commonly in the neocortex [18].

Senile plaques are present in some brains of nondemented older persons and of those with Alzheimer’s disease [16, 19]. Most neuropathologists recognize neuritic and diffuse senile plaques as major subtypes. Neuritic plaques display radially arranged abnormal distended neurites filled with lysosomes, paired helical filaments, and mitochondria and are surrounded by reactive astrocytes and microglia; these plaques often display central amyloid cores. Diffuse plaques, on the other hand, are more amorphous and lack the abnormal neurites and amyloid cores. Both plaque subtypes are seen in normal aging and in Alzheimer’s disease [20], although neuritic plaques are more closely associated with cognitive impairment.

Quantitative CT and MR grading systems developed for age-related changes and dementia focus on the pattern and severity of volume loss and the distribution and rate of ventricular enlargement. Coffey et al. [2] used observer-defined region-of-interest MR techniques to determine brain volumetric changes in 76 healthy adults. They found that the volumes of the cerebral hemisphere (0.23% per year), frontal lobe (0.55% per year), temporal lobe (0.28% per year), and amygdala-hippocampal complex volumes (0.30% per year) decrease gradually with age, consistent with autopsy results. Ventricular volumes increased at a rate of 2.8% per year for the third ventricle and 3.2% per year for the lateral ventricles, and subcortical hyperintensities of deep white matter (6.3% per year) and the pons progressed with age. Cognitively intact elderly persons typically have mild cortical atrophy, ventricular enlargement, and few white matter lesions [2]. In a study involving 55 healthy volunteers, Jernigan et al. [14, 15] used a semiautomated MR method of analysis of dual-echo sequences. They found significant age-related decreases in volumes of the caudate nucleus, anterior diencephalic structures (anterior hypothalamic gray matter, septal nuclei, basal forebrain nuclei), and cortical gray matter in most regions. T2 prolongation in hemispheric white matter with age was striking, without a reduction in overall white matter volume. Although volumetric changes varied widely in asymptomatic elderly persons, all cortical volumes decreased with age, with possibly greater mesial temporal involution.

Focal hyperintense white matter lesions seen on T2-weighted images in the deep subcortical and periventricular white matter (variously termed nonspecific white matter lesions, unidentified bright objects, and leukoaraiosis) have been the focus of considerable attention [5, 6, 21]. Although periventricular lesions occur with advancing age, more extensive or confluent white matter lesions are associated with memory loss and dementia [6, 22, 23]. Many cognitively intact adults have periventricular “halos” of white matter hyperintensity; these correlate poorly with increased CNS pressure and are an unreliable criterion for shunting in hydrocephalus [21].

The neuropathologic changes underlying these white matter hyperintensities have not been precisely defined. Differences in criteria for selecting patients, the mode of correlating pathologic and imaging findings (e.g., postmortem vs ante-mortem MR), and the variable location of white matter intensities studied have hampered a standard approach to this problem. An association has been found between autopsy findings of myelin pallor, diffuse vacuolation, gliosis, dilated perivascular spaces, and reduction of glial cell density and extensive signal changes in white matter on MR images. Deep cortical intensities generally correlate with varying degrees of white matter pallor without clear abnormalities of myelin or axons [5, 24–26]. Chronic vascular insufficiency has been proposed as an underlying factor. Alternatively, Munoz et al. [25] suggest that leakage of serum proteins from cerebral vessels may play a role. Other pathologic correlates include infarction, small vascular malformations, gliosis, demyelinating plaques, brain cysts, congenital diverticula of the lateral ventricle, dilated perivascular spaces, and vascular ectasia [26].

Vonch-Robin spaces or perivascular spaces are CSF-filled extensions of the subarachnoid space along the penetrating brain vasculature; these are most apparent coursing cephalad from the level of the anterior commissure or superficially from the leptomeninges, with diminution in size on successive sections of axial MR images [3, 27]. Enlargement of perivascular spaces correlates best with age, even when accompanying factors such as hypertension, dementia, or white matter lesions are considered [27].

Normal MR patterns of diminution of signal intensity in the red nucleus, substantia nigra, dentate nuclei, and globus
pallidus qualitatively correlate with tissue iron staining; signal intensities of the globus pallidus and putamen decrease with age [28, 29], as shown by high-field-strength T2-weighted spin-echo or gradient-echo techniques.

PET and SPECT studies in the elderly show metabolic patterns similar to those of younger persons; correction for degree of atrophy facilitates interpretation of diminished activity in regional or focal areas [30]. Preliminary MR spectroscopic studies of mammalian brains indicate an age-related slight increase in phosphomonoesters and phosphodiester, and thus MR spectroscopy might be useful in differentiating normal aging from Alzheimer’s disease [31].

**Alzheimer’s Disease**

Although genetic evidence of familial patterns has been reported, most patients with Alzheimer’s disease do not have a clear-cut familial history; the genetic heterogeneity of Alzheimer’s disease is under investigation. The widely adopted consensus criteria for the clinical diagnosis of probable Alzheimer’s disease require confirmation of dementia by clinical examination and the Mini Mental Status Test, Blessed Dementia Scale, or similar test; deficits in two or more areas of cognition; progressive worsening of memory and cognitive function; no altered mental status; and absence of systemic or neurologic diseases that would account for the deficits. Currently, a diagnosis of definite Alzheimer’s disease requires histopathologic proof by autopsy or biopsy [32]. Despite the establishment of these criteria, the lack of standardized methods for assessing clinical, neuropsychiatric, neurologic, pathologic, and radiographic features of the dementias hinders comparisons or pooling of data among investigators. These problems are being addressed by the multicenter studies of the Consortium to Establish a Registry for Alzheimer’s Disease (CERAD) [9, 33, 34]. Although neuropathologists use microscopic criteria to diagnose Alzheimer’s disease, the brain often shows characteristic changes on gross examination [20, 34]. Cortical atrophy occurs to various degrees and generally is observed in the frontal, temporal, and parietal cortices [20, 34]. Frequently observed enlargement of the lateral and third ventricles is variable in degree [20, 34]. Disproportionate enlargement of the temporal horn of the lateral ventricle is common; it is usually accompanied by atrophy of the entorhinal (parahippocampal) cortex, amygdala, and hippocampus, structures invariably involved in Alzheimer’s disease [20, 34]. Pallor of the locus ceruleus is common in patients with Alzheimer’s disease who have long-standing dementia [20, 34]. The substantia nigra in the brains of patients with Alzheimer’s disease shows depigmentation in about one fifth to one third of cases, often in association with other changes of Parkinson’s disease [35, 36]. Some have termed cases of combined abnormalities of Alzheimer’s disease and Parkinson’s disease as the Lewy body variant of Alzheimer’s disease [37]. Alternatively, nigral degeneration with widespread neocortical Lewy bodies is seen in the absence of Alzheimer’s disease pathology [38].

The three major histopathologic hallmarks of Alzheimer’s disease are senile plaques (neuritic and diffuse), neurofibrillary tangles, and amyloid angiopathy involving meningeal and cortical blood vessels. Senile plaques of both subtypes are found in various proportions in Alzheimer’s disease in the neocortex, hippocampus, entorhinal cortex, amygdala, and other regions. Diffuse plaques predominate in the corpus striatum, hypothalamus, and cerebellum. Neurofibrillary tangles are found consistently in the entorhinal cortex, hippocampus, amygdala, nucleus basalis of Meynert, dorsal raphe nucleus, and other sites. Although the frequency of the neocortical tangles generally correlates with the severity of dementia [19, 39], neurofibrillary tangles are absent in the neocortex of some elderly persons with Alzheimer’s disease [40]. In addition to tangles, neuropi threads (thickened neurites within the neuropil) are associated with dementia [41]. Recently, synaptic density has emerged as a major correlate of cognitive impairment [42, 43]; many think this is a more reliable determinant of dementia than either tangles or plaques. Amyloid is deposited in the walls of meningeal and cortical blood vessels of persons with Alzheimer’s disease, as well as of cognitively intact elderly persons [44]. Although amyloid angiopathy is encountered in virtually all cases of Alzheimer’s disease, there is marked variation in the degree of this change.

Many neuropathologists have adopted the consensus criteria reported by Khachaturian [45]; age-adjusted minimal senile plaque counts per low-power microscopic field and a clinical history of dementia are required for diagnosis of Alzheimer’s disease. Although adequate for most cases, these criteria do not allow characterization of less clear-cut cases. CERAD uses semiquantitative determinations of the frequency of neuritic plaques in the neocortex integrated with age and available clinical information to provide levels of certainty of diagnosis and to promote common terminology [34]. CT patterns of atrophy, particularly of the temporal lobe, help separate Alzheimer’s disease from normal age-related involution; these qualitative or perceptual techniques can be reasonably applied to MR images in the axial plane [7, 8] (Fig. 1). Various qualitative ratings of temporal lobe atrophy (e.g., size of the sylvian fissure, size of the temporal horn, size of the temporal sulcus, width of the suprasellar cistern) have been suggested to aid differentiation of Alzheimer’s disease from aging [8]. These ratings are based on images acquired with a scan angle parallel to or as much as 20° cephalic to the canthomeatal line. George et al. [7] found that enlargement of the choroid-hippocampal fissure on CT scans or MR images distinguishes Alzheimer’s disease from normal aging; this rating is based on images acquired with a negative scan angle (20° caudal to the canthomeatal line or parallel to the optic pathways). Enlargement of this fissure indirectly reflects atrophy of the hippocampus associated with Alzheimer’s disease (Figs. 2 and 3).

Although a variety of linear measurements determined on axial images have been used in Alzheimer’s disease, these are less reliable than volumetric techniques now obtainable with MR imaging [46]. Observer-drawn region-of-interest measurements based on thin-section coronal T1-weighted images are sensitive for detecting volume loss in the anterior
Fig. 1.—Diagrams show measurements that are helpful in differentiating Alzheimer’s disease from normal aging.

A, Width of temporal horn at three locations: 1 = anteroposterior width, 2 = border between temporal tip and body of temporal horn, 3 = width of temporal horn body; A and B indicate anteroposterior and transverse widths of sylvian fissure, respectively. Kido et al. [8] found that a temporal horn measurement greater than 3 mm at any of the indicated locations best distinguishes Alzheimer’s disease from normal age-related involution. (Angle of image plane is 15° positive to canthomeatal line.)

B, Enlargement of choroid-hippocampal fissure (arrow). George et al. [7] found that subjective grading of severity of enlargement is a sensitive and specific marker for Alzheimer’s disease. (Angle of image plane is 20° negative to canthomeatal line.)

Fig. 2.—80-year-old patient with probable Alzheimer’s disease. MR image (600/30, scan angle 20° negative to canthomeatal line) shows enlargement of choroid-hippocampal fissure (arrows). Hippocampal volume loss resulting in enlargement of choroid-hippocampal fissure is a sensitive marker for Alzheimer’s disease.

Fig. 3.—In contrast to Fig. 2, MR image (546/15) of cognitively intact 86-year-old man shows little evidence of hippocampal volume loss and far less enlargement of choroid-hippocampal fissures (arrows).

part of the temporal lobe and hippocampus [13, 47]. In a recent MR study, the best discriminators between persons with probable Alzheimer’s disease and healthy age-matched volunteers were atrophy of the entorhinal cortex (parahippocampal gyrus) and temporal neocortex; the next were enlargement of the temporal horn and atrophy of the hippocampal formation. The mean interrater reliabilities of atrophy ratings ranged from 0.50 to 0.78. Absence of temporal atrophy did not exclude early Alzheimer’s disease [48].

Quantitative volumetric MR studies show a greater CSF volume, smaller brain volume, and greater atrophy in patients with Alzheimer’s disease than in age-matched control subjects [12, 14, 15]. A study using inversion-recovery pulse sequences that optimize gray matter, white matter, and CSF separation for automated MR volumetric analysis found diminished gray matter in the temporal lobe, to a lesser extent in the parietal and occipital lobes, and in a central region including the corpus striatum and thalamus; no significant difference was found in white matter volumes in patients with Alzheimer’s disease compared with control subjects [10]. Other semiautomated MR analyses show findings of widespread loss of subcortical volume in patients with Alzheimer’s disease compared with control subjects, no reduction in white matter volume, and preferential thalamic atrophy [15].

Patients with Alzheimer’s disease and persons who are cognitively intact both have punctate deep white matter or confluent white matter findings on MR images; in contrast,
more extensive periventricular and subcortical foci suggest vascular disease with or without dementia [22, 23]. Although longitudinal CT studies have shown faster progression of atrophy and ventriculomegaly in patients with Alzheimer's disease compared with control subjects, overlap is too great to warrant the use of these measurements as predictors of dementia in individual cases [49].

Functional neuroimaging (PET, SPECT, and MR spectroscopy) may yet be most informative for imaging in Alzheimer's disease and may be useful in early diagnosis. Cortical regional hypometabolism can be perceived on PET scans before cortical atrophy can be seen on CT or MR images [50]. Although patients with Alzheimer's disease characteristically have a biparietotemporal pattern of decreased glucose metabolism on PET scanning (Fig. 4), correction of PET data based on MR evidence of brain atrophy suggests that regional hypometabolism detected with PET can be overestimated if not corrected for brain volume loss [12]. A blinded assessment of PET in the diagnosis of Alzheimer’s disease found a sensitivity of 0.38 and specificity of 0.88, suggesting that the primary role of PET might be in differentiating among otherwise similar dementias [51].

SPECT blood flow imaging, as well as PET metabolic imaging, might offer improved specificity in the diagnosis of Alzheimer’s disease. The probability of diagnosis of Alzheimer’s disease with SPECT was reported by Holman et al. [52] as 19% for patients with memory loss and normal SPECT perfusion patterns, 82% when abnormal perfusion patterns coincided with memory loss, 77% if the abnormal pattern was bilateral temporoparietal deficiency, 57% with unilateral temporoparietal deficiency, 43% with deficiencies confined to the frontal regions, and 0% for abnormalities that were small and confined to the cortex (Fig. 5). Cognitive activation models are used with SPECT to enhance its diagnostic sensitivity; these include comparative SPECT studies before and after memory testing to identify measurable quantitative differences in temporoparietal activity. In patients with Alzheimer’s disease, no differences on scans are seen with memory activation [53].

Preliminary reports suggest that phosphorous and hydrogen MR spectroscopic studies also offer valuable information about brain biochemical activity that may aid in the diagnosis of Alzheimer’s disease [54, 55].

Vascular Dementia

The role of vascular disease as a cause of dementia remains controversial. Patients with pure vascular disease and combined Alzheimer’s and vascular disease constitute a substantive subset of patients with dementias in some studies [56]. On the other hand, many patients clinically diagnosed as having vascular dementia are proved at autopsy to have predominantly or coexistent pathologic changes of Alzheimer’s disease. Recently, two groups [57, 58] have proposed clinical and radiographic criteria for the diagnosis of vascular dementia. Neuroimaging (T1-weighted MR or CT) demonstration of vascular lesions is considered supportive evidence of vascular dementia. Conversely, the absence of vascular lesions on T1-weighted MR images or CT scans is sufficient to exclude a diagnosis of vascular dementia.

In general, clinical features of vascular dementia include a stepwise deterioration with focal neurologic signs and symptoms and historical, physical, or laboratory evidence of significant cerebrovascular disease. Infarcts occupying more than 50 ml in volume are often associated with dementia, although both volume and location of these lesions may be critical factors [59]. Garcia and Brown [60] found vascular dementia associated with focal infarcts in strategic regions (i.e., angular gyrus on the left, caudate nuclei, and both medial thalami), large or multifocal cortical infarcts in an arterial or a watershed distribution, or disease primarily or exclusively of the hemispheric white matter. Imprecise nomenclature used for subcortical vascular disease that is typically associated with long-standing hypertension includes multiinfarct dementia, lacunar dementia, subcortical leukoencephalopathy, and Binswanger’s disease. In multiinfarct dementia, multiple foci of softening and/or cystic change can occur, most frequently involving the deep gray matter of the thalamus and basal ganglia and often affecting the cerebral white matter as well. Ventrices can be enlarged, often asymmetrically, reflecting the loss of brain tissue. Although the definition of Binswanger’s disease remains
controversial, associated neuropathologic changes include diffuse pallor of myelin with multiple small infarcts in the white matter and thickening of penetrating arteries and arterioles. Ventriculomegaly as a consequence of white matter loss is common, and the cortex usually is spared.

Recent imaging studies support earlier observations that dementia is related to the extent of cerebral infarction [61–63]. In an evaluation of patients with vascular dementia, patients with strokes without dementia, and healthy control subjects, the strongest MR factors favoring vascular dementia, in descending order, were total area of white matter lesions as seen on T2-weighted images, area of white matter lesions in the left hemisphere, ratio of lateral ventricular area to total brain area on axial images that included the
largest ventricular size, area of white matter lesions in the right hemisphere, age, area of cortical infarction in the left hemisphere, area of infarction in the left parietal lobe, and total area of infarction [61] (Fig. 6). Ischemic lesions involving the occipital, temporoparietal, or temporoparietal cortex are more often associated with dementia [62]; other areas implicated in vascular dementia are the territory of the posterior cerebral artery and the left cerebral hemisphere. In contrast, other investigators [63] have found that the volume of white matter lesions correlates with age and chronic vascular disease, but have observed no correlation between the severity of these white matter lesions and decline in neuropsychological function independent of age-related changes.

MR findings associated with chronic vascular insufficiency and long-standing hypertension with or without clinical evidence of vascular dementia include multiple lacunar infarcts of the deep gray matter and brainstem, diffuse deep white matter abnormalities, moderate ventriculomegaly with irregular ventricular borders, and coalescent central pontine hyperintensities [4] (Fig. 7). Although the term Binswanger's disease has been used to describe generic MR findings associated with long-standing hypertension, radiologic criteria for differentiating vascular insufficiency without dementia from this uncommon variant of vascular dementia have not been established.

A reduction in cerebral metabolism and regional blood flow in vascular dementia has been confirmed by PET findings that showed focal asymmetric and variable regions of diminished metabolism and perhaps crossed cerebellar diaschisis. Defects shown on PET or SPECT scans are often larger than those seen on structural imaging studies; this finding might be important for differentiating ischemia from infarction for therapeutic purposes or for early diagnosis of vascular dementia [64]. Also, other investigators [65] found that the total volume of metabolically impaired tissue was directly related to the severity of dementia in patients with presumed vascular dementia; these patients had larger areas of hypometabolism than did patients with Alzheimer's disease, particularly in the deep gray matter and cerebellum.

**Parkinson's Disease and Related Disorders**

Parkinson's disease is eventually accompanied by dementia in approximately 15–40% of affected patients [66]. The brains of patients with Parkinson's disease who have dementia show not only the neuropathologic changes of

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**Fig. 6.—**65-year-old man with multiinfarct dementia. MR image (2270/90) shows two adjacent large infarcts (arrows) involving at least 50 ml of brain volume.

**Fig. 7.—**Older adult with long-standing hypertension.

A–C, MR images (2200/90) show characteristic findings of long-standing hypertension: central area of hyperintensity in basis pontis without clinical evidence of brainstem infarction (arrow, A), deep gray matter lacunar infarcts (arrows, B), and ventriculomegaly associated with prominent periventricular white matter disease (C).
idiopathic Parkinson's disease but often also those of coex-
istent Alzheimer's disease. Extrapyramidal signs unrelated
to medication can subsequently develop in patients with pri-
mary dementia diagnosed as Alzheimer's disease, and over-
lapping pathologic features of Alzheimer's disease and
Parkinson's disease can also manifest. Although these coex-
istent clinical features may represent overlap of two common
neurodegenerative diseases of the elderly, the association
between the two disorders may be more than coincidental.

Classic neuropathologic changes associated with idiop-
atic Parkinson's disease include loss of cells and gliosis of
the pars compacta of the substantia nigra and the presence
of Lewy bodies in pigmented nuclei (substantia nigra, locus
ceruleus, and dorsal vagus nucleus), the nucleus basalis,
and other sites. Neurons may contain one or more Lewy
bodies in their cytoplasm [66]. Although varied terminology
is used for primary dementias with combined pathologic fea-
tures of Alzheimer's disease and Parkinson's disease (e.g.,
diffuse Lewy body disease, Lewy body variant of Alzheimer's
disease), clinicopathologic studies have suggested distinc-
tions among these entities.

In Parkinson's disease, separation of the hypointense red
nucleus from the pars reticulata of the substantia nigra can
be inapparent on MR images; this finding results from vol-
ume loss in the pars compacta of the substantia nigra (Fig.
8). Currently, no pattern of MR findings allows confident
differentiation of patients with idiopathic Parkinson's disease
from age-matched control subjects. MR patterns of basal
ganglia and midbrain hypointensity tend to be accentuated
in related disorders such as multisystem degenerations that
include striatonigral degeneration or olivopontocerebellar
atrophy, as well as in other forms of drug-resistant parkin-
sonism [67, 68]. PET studies of patients with Parkinson's
disease have shown increased glucose metabolism in the
basal ganglia early in the disease; some patients with Par-
kinson's disease and dementia have reductions in parietal
lobe metabolism similar to those seen in Alzheimer's dis-
ease. In Parkinson's disease with or without dementia and in
other parkinsonian disorders, reduced striatal uptake of L-
dopa labeled with fluorine-18 is observed on PET scans [69].

Patients with progressive supranuclear palsy may have
mild dementia or symptoms that mimic Alzheimer's disease.
Grossly, enlargement of the aqueduct of Sylvius usually is
apparent, resulting from involvement of the periaqueductal
gray matter and colliculi. Variable enlargement of the third
and fourth ventricles is seen and can be prominent in long-
standing cases. Atrophy of other commonly involved regions
(e.g., the globus pallidus or subthalamic nucleus) may be
detected grossly. The microscopic hallmark of progressive
supranuclear palsy, the globuse neurofibrillary tangle, is
present in characteristic subcortical structures in concert
with variable neuronal loss and gliosis.

MR findings of progressive supranuclear palsy parallel the
neuropathologic changes. Focal midbrain atrophy, particu-
larly of the tectum, with enlargement of the cerebral aque-
duct, quadrigeminal plate cistern, and posterior third
ventricle is observed. Accentuated hypointensity of the basal
ganglia and midbrain on T2-weighted images is variable
[70]. Frontal hypometabolism predominates on 18F-fluorde-
oxyglucose PET studies in progressive supranuclear palsy.

Corticobasal ganglionic degeneration with neuronal achro-
masia [71] may be associated with mild dementia, and
occasionally is clinically diagnosed as Alzheimer's disease.
The brains of persons who have this disorder may exhibit
distinctive, often asymmetric atrophy of the perirolandic gyri.
On microscopic examination, these atrophic regions show
neuronal loss, gliosis, and variable numbers of ballooned or
achromatic neurons. Other regions such as the basal gan-
glia, thalamus, substantia nigra, and cerebellum are involved
to various degrees.

In corticobasal ganglionic degeneration, asymmetric corti-
cal atrophy may be detected on MR studies, particularly as
the disease progresses [72]. PET studies in patients with
corticobasal ganglionic degeneration with neuronal achro-
masia have shown decreased oxygen utilization in involved
regions of the cortex and subcortical structures.

Hydrocephalus in Elderly Persons

A clinical constellation of gait apraxia, urinary inconti-
nence, and dementia supports a diagnosis of normal-pres-
sure hydrocephalus, although gait disorders alone are also
associated with hydrocephalus in the elderly. The response
to shunting is best in patients with a history of prior menigi-
tis or subarachnoid hemorrhage and resultant communicat-
ing hydrocephalus. Patients who have no prior events
etiologically associated with communicating hydrocephalus
have a less favorable response to ventricular shunting; even
with careful selection of patients, lack of response to shunt-
ing, surgical complications, shunt malfunction, and clinical
deterioration are substantial [73]. Because chronic and
hypertensive vascular disease is associated with ventricu-
lomegaly and white matter abnormalities, radiographic crite-
ria to distinguish this from normal-pressure hydrocephalus
require further refinement [74].

Imaging studies in elderly individuals with both normal-
pressure hydrocephalus or gait impairment–associated
hydrocephalus show variable disproportionate ventriculome-
galy compared with sulcal size, rounding of the anterior third
ventricle or frontal horns, enlargement of the temporal horns
and sylvian fissure, and an increased ratio of the maximum
frontal horn ventricular width to the transverse inner diame-
ter of the calvaria [73–75]. Additionally, MR findings associ-
ated with normal-pressure hydrocephalus include a prominent
CSF flow void within the cerebral aqueduct and adjacent
third ventricle and extensive white matter foci that have
been attributed to deep white matter infarction [74, 75]
(Fig. 9). Clinical evaluation, CSF findings, and response to
spinal tap and removal of CSF are factors considered in the
selection of patients for shunting.
Fig. 8.—60-year-old man with signs and symptoms of Parkinson’s disease. MR image (2015/90) shows symmetric bilateral loss of separation between hypointense signal of red nucleus (straight arrow) and that of pars reticulata (curved arrow) of substantia nigra, indicating volume loss in pars compacta region of substantia nigra, as seen in Parkinson’s disease and other similar disorders.

Fig. 9.—78-year-old woman with clinical features suggestive of normal-pressure hydrocephalus. A and B, Proton density–weighted MR images (250/20) show a prominent third-ventricular flow void (arrow, A) and disproportionate ventricular enlargement compared with sulcal size (B). MR findings described in normal-pressure hydrocephalus include a prominent CSF flow void within cerebral aqueduct and adjacent third ventricle.

Pick’s Disease

Pick’s disease, a rare dementia of mid to late adulthood, causes prominent atrophy of the frontal or temporal lobes that may be asymmetric; relative sparing of the posterior two thirds of the superior temporal gyrus is common. Silver staining usually reveals characteristic cytoplasmic Pick bodies in neurons of involved regions. Subcortical nuclei also can be affected. Pathologic confirmation is required to differentiate Pick’s disease from other dementias with predominant frontal lobe atrophy.

MR and CT findings mirror the neuropathologic findings. Imaging studies reveal atrophy of the frontal or temporal lobes with widening of the interhemispheric fissure frontally and compensatory enlargement of the frontal horn. This may be difficult to differentiate from changes of other frontal lobe dementias, Alzheimer’s disease, or normal aging (Fig. 10). Pick’s disease is associated with diminished fluorodeoxyglucose metabolic activity in the frontal lobes on PET scans and diminished blood flow on PET or SPECT scans [76]. Often, the pattern of decreased deoxyglucose utilization on PET images is dramatic in its demarcation between normal cortical uptake and impaired uptake in the anterior frontal lobe (Fig. 10).

Summary

Our understanding of neuroimaging correlates of normal aging and dementias of the elderly continues to evolve. At present, the most consistent MR findings in Alzheimer’s disease are those reflecting volume loss in the medial temporal lobes. These include enlargement of the temporal horn and, with a reverse scanning plane angle, enlargement of the cisterns and fissures medial to the hippocampus. These findings are reliable for discriminating Alzheimer’s disease from normal changes of aging, but their reliability in differentiating Alzheimer’s disease from other dementias is uncertain. The predominantly periventricular white matter changes tend to be relatively minor or mild in Alzheimer’s disease and normal aging. MR evidence of extensive subcortical white matter disease and infarction typifies changes of vascular dementia; criteria for differentiating persons with vascular disease from those with associated dementia have not been developed. MR criteria for diagnosis of other dementias and mixed dementias await further definition.

Quantitative imaging techniques promise more reproducible measures of atrophy and white matter lesions, and these may facilitate our ability to differentiate among various causes of dementia on a case-by-case basis. Although new functional imaging techniques promise to expand our understanding of the pathophysiologic features of the brain in patients with neurodegenerative diseases, the techniques still have relatively restricted application for diagnosis in individual cases. Merger of metabolic imaging tools such as PET, SPECT, and MR spectroscopy with the detailed structural anatomic findings on MR images, however, should facilitate early diagnosis,
improve diagnostic accuracy, and allow monitoring of therapeu tic interventions in neurodegenerative disease.

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