A QUICK GUIDE FOR NEUROIMAGING OF COMMON DEMENTIAS SEEN IN CLINICAL PRACTICE

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In conjunction with clinical history, structural neuroimaging with either computed tomography (CT) or magnetic resonance imaging (MRI) of the brain is important for the accurate diagnosis of a specific cause of dementia. Indeed, one of the proposed biomarkers helpful for the diagnosis of probable Alzheimer's disease is the presence of hippocampal atrophy.[1] Alzheimer's disease, dementia with Lewy bodies, frontotemporal dementia, and vascular cognitive impairment/vascular dementia – the most common dementias seen in clinical practice – all have specific findings on neuroimaging that can be readily identified in the clinical setting and do not always require specialized analyses. This article serves as a quick guide for the identification of these findings.

What to Look for on CT or MRI Scans

Although examining MRI or CT scans of the brain may appear daunting, there are just three simple rules to consider:

1. **Determine which anatomical plane of the brain is being viewed.** Regardless of whether CT or MRI is used, one of the various anatomical views of the brain – axial, coronal, or sagittal – can provide a better and easier visualization of certain areas of the brain (Figure 1).

2. **Determine if and where there are areas of brain atrophy.** Neurodegeneration, regardless of the specific pathological cause, usually causes atrophy of the brain. As an analogy, consider the healthy non-atrophic brain as appearing like a grape, with tight sulci and "plump" gyri/cortex. As the brain becomes atrophic, the sulci widen and become deeper while the gyri become smaller and more sharply defined (instead of having the usual rounded appearance), giving the brain the appearance of a raisin (Figure 2).

   To determine if an area of the brain has atrophy, look for asymmetry by comparing the anterior versus posterior regions of the brain and right versus left sides of the brain. In the dementias commonly seen in clinical practice, few areas of the brain – namely, the hippocampus and the temporal, frontal, and parietal lobes – are typically affected by clinical disease (Figure 3).

3. **Each dementia has a predilection for a part of the brain and can be seen on CT or MRI.** Specific to the cause of the dementia, there is usually a focal area of atrophy that is disproportionately affected before the rest of the brain. For example, in Alzheimer's disease, the hippocampus and parietal lobes usually are affected first and become atrophic compared to other lobes of the brain. In frontotemporal dementia, the frontal, temporal, or combination of the frontal and temporal lobes can be affected first. Compared to Alzheimer's disease, dementia with Lewy bodies is not commonly associated with any focal or significant atrophy of the brain. Finally, in vascular cognitive impairment or vascular dementia, there are identifiable areas of stroke or ischemic white matter changes.

Combing History and Neuroimaging for Diagnosis

Case. A 78-year-old man presents with a 7-year history of a dementia that initially presented with short-term memory deficits but progressed with the development of anomia, geographic disorientation, decreased hygiene, and ideomotor apraxia. He scored 18/30 on the Mini-Mental Status Examination, and his physical and neurological examination results were normal. The most likely suspected diagnosis is Alzheimer's disease, and an MRI scan of the brain is obtained (Figure 4).

Interpreting the neuroimaging and applying the rules. The axial MRI images (see rule 1, above) of the brain reveal predominant and progressive atrophy of the hippocampi (rules 2 and 3), the key neuroimaging finding in Alzheimer's disease (AD). The initial changes occur in the head of the hippocampus and subiculum and are followed by
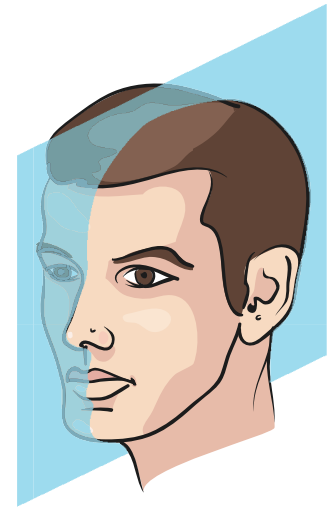
AXIAL
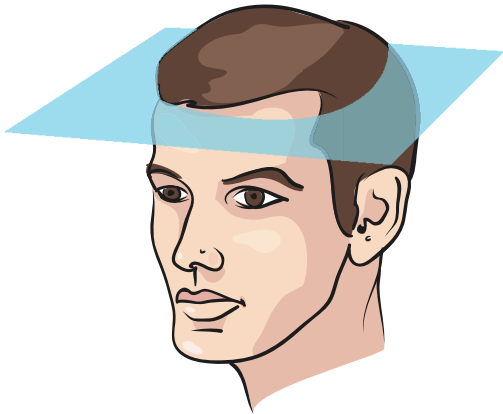
CORONAL

SAGITTAL

- Most common view provided
- Good for looking at all lobes of the brain
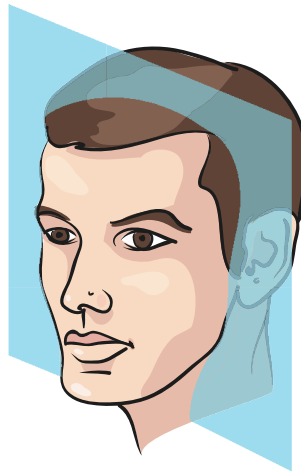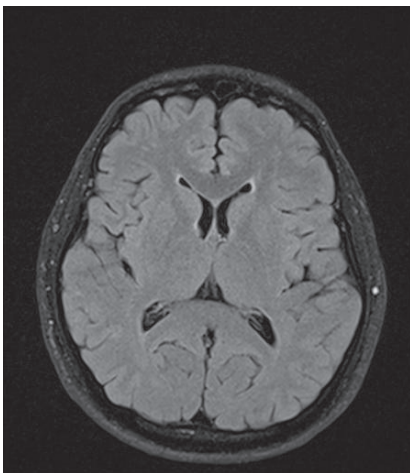
- Good for looking at temporal lobes (especially the hippocampus) and perisylvian fissures
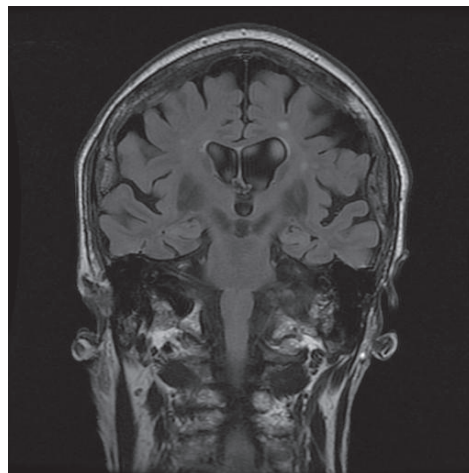
- Good for looking at midline and lateral structures

AXIAL

CORONAL

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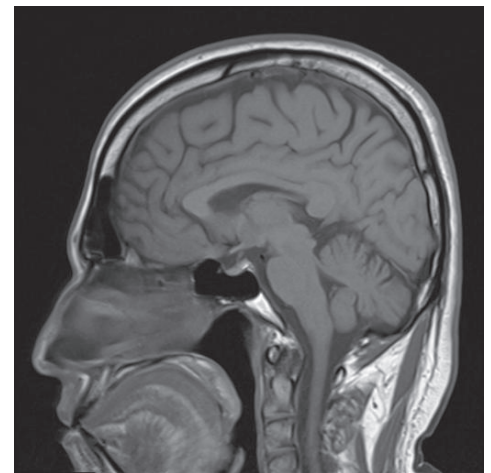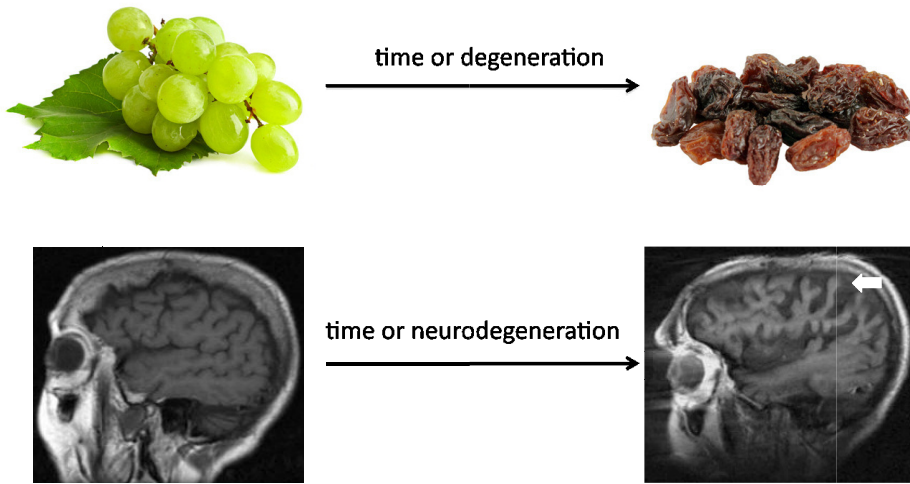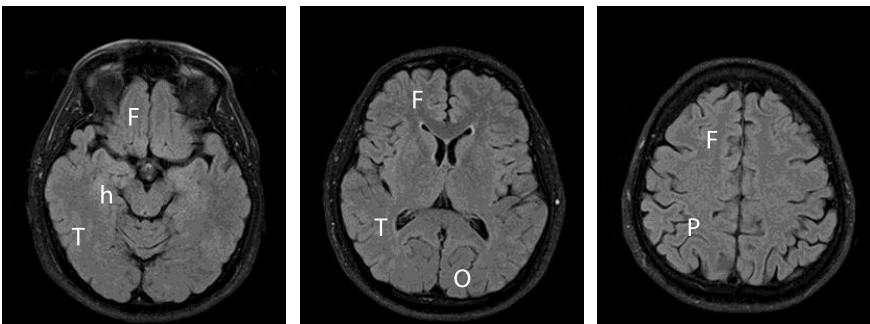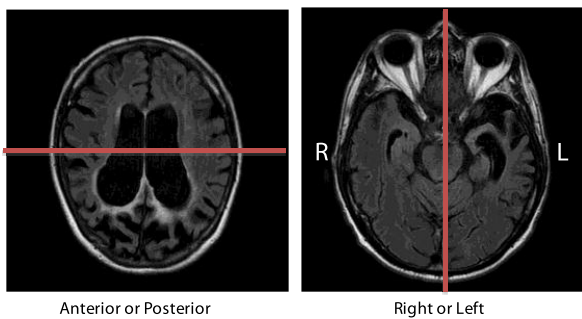

Figure 1. Views of the brain and the usefulness of each view.

Figure 2. Analogy for the identification of atrophy of the brain.
With atrophy, there is enlargement of the cerebral sulci *(arrow)* and ventricles, associated with a loss of cortical volume.

time or degeneration

time or neurodegeneration

Anterior or Posterior   Right or Left

Figure 3. Locations of atrophy in the brain: anterior or posterior region, right or left side, and specific areas.

Common areas/lobes of brain atrophy: frontal (F), temporal (T), hippocampus (h), occipital (O), parietal (P)

Normal Brain   Alzheimer's Disease

Year 1   Year 6   Year 7
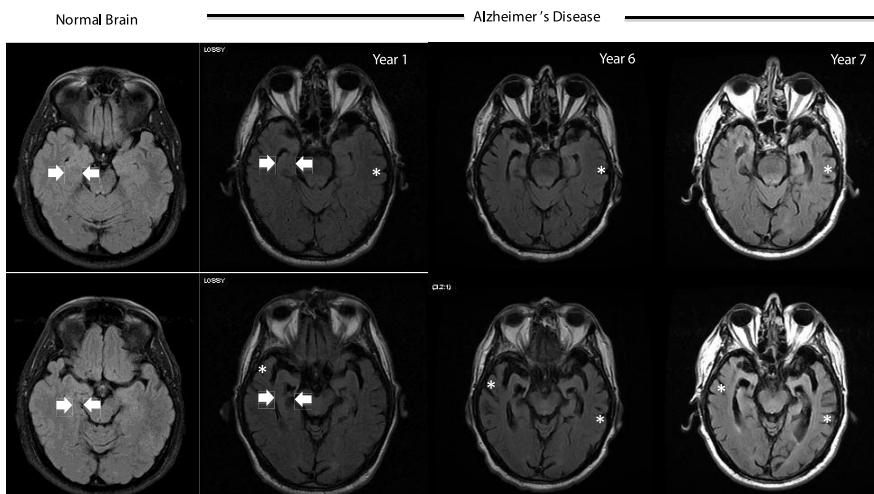
Figure 4. Magnetic resonance imaging (MRI) scans of a normal brain and a brain in Alzheimer's disease.
The scans of a normal brain ("grape" appearance) show that hippocampal atrophy is not present (*arrows* indicate the right hippocampus). The scans of the brain of a person with Alzheimer's disease show progressive atrophy of both hippocampi in following years (*arrows* indicate the right hippocampus) and compensatory dilation of the temporal horn of the lateral ventricles. Progressive atrophy of the bilateral temporal lobes (*stars*) is also noted with deepened sulci ("raisin" appearance).
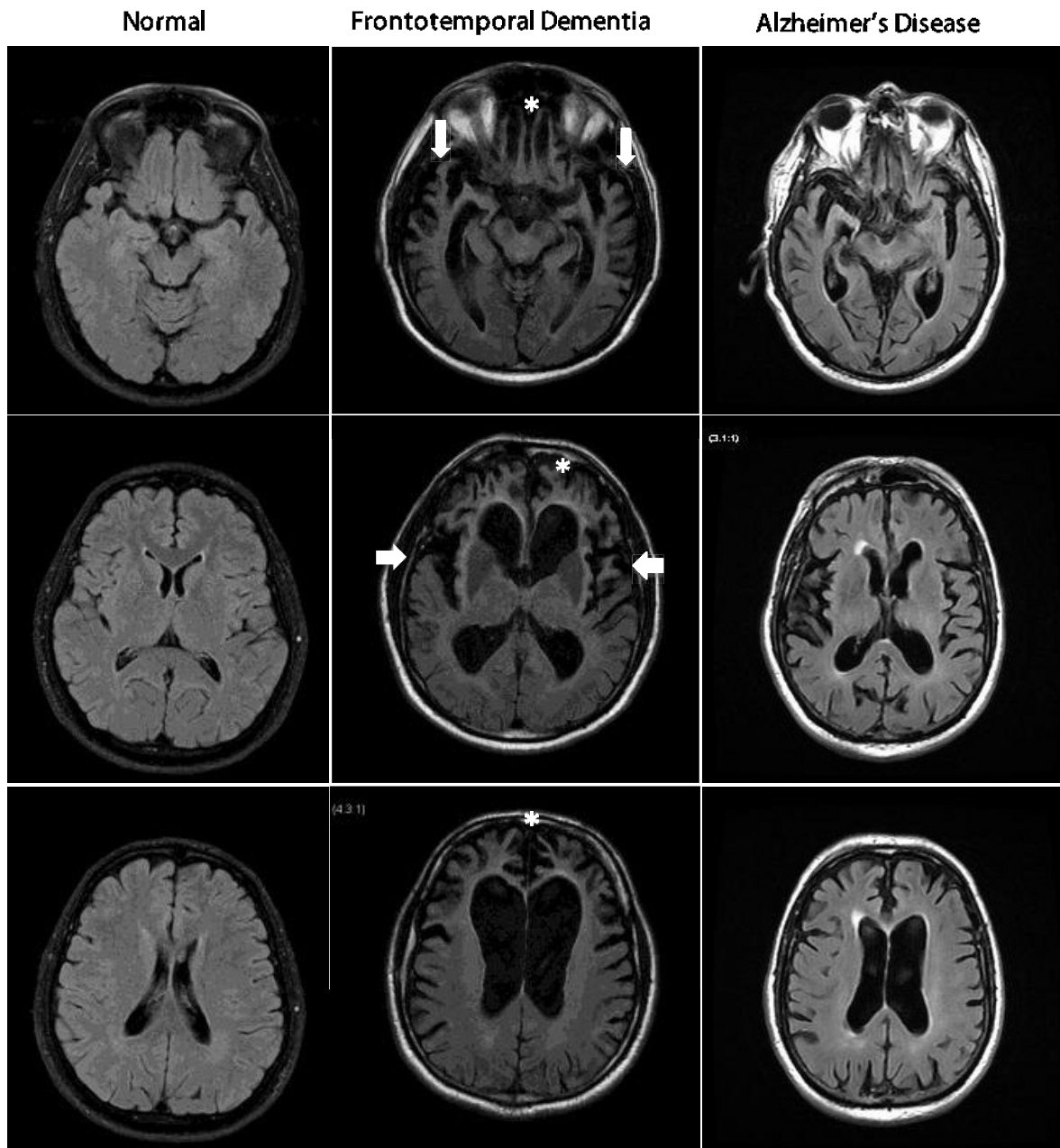
Figure 5. Frontotemporal dementia.
Magnetic resonance imaging (MRI) scans demonstrating frontotemporal dementia (middle panel) show preferential atrophy of the frontal lobes (*stars*) and temporal lobes (*arrows*) when compared with MRI scans of the normal brain (left panel) and the brain in Alzheimer's disease (right panel).

atrophy of the lateral body of the hippocampus. In addition, patients with AD have atrophy of the parietal lobes (not shown). As the disease progresses, there is progressive atrophy of the other parts of the brain; however, the hippocampi remain primarily and severely affected.[2–5]

Case. A 65-year-old man presents with a 3-year history of progressively odd behaviour characterized by saying any thought that comes to mind, rubbing the backs of strangers, and joking and appearing not to care at a funeral. He scored 28/30 on the Mini-Mental

Status Examination. Physical and neurological examination results were normal. Given the presentation of disinhibition, the most likely diagnosis is frontotemporal dementia, and an MRI scan of his brain is obtained (Figure 5).
Interpreting the neuroimaging and applying the rules. The axial MRI brain scans (rule 1) show symmetrical atrophy of the anterior portion of the brain (rule 2), mainly in the frontal lobes (orbitofrontal, dorsolateral, and medial frontal areas) and anterior temporal lobes (rule 2), with compensatory dilation of the frontal horns of the lateral

|	Semantic Dementia	Non-fluent Primary Progressive Aphasia
Clinical characteristics	Initial presentation is a fluent speech by marked with an anomia (no proper nouns are used), loss of word>object meaning, phonetic spelling and reading (surface agraphia and surface alexia, respectively)	Initial presentation of a non-fluent, agrammatical speech with preserved single-word comprehension
Neuroimaging characteristics	Focal left anterior temporal atrophy	Left inferior frontal/perisylvian/insular atrophy
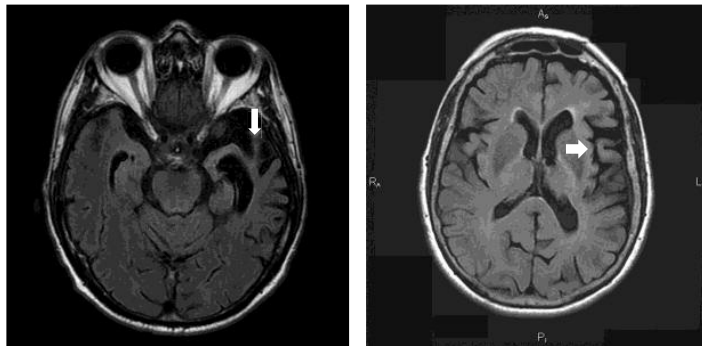
Figure 6. Progressive aphasic variants of frontotemporal dementia, and clinical and neuroradiological findings of the language presentation of frontotemporal dementia.

Normal Brain — Dementia with Lewy Bodies — Alzheimer's Disease
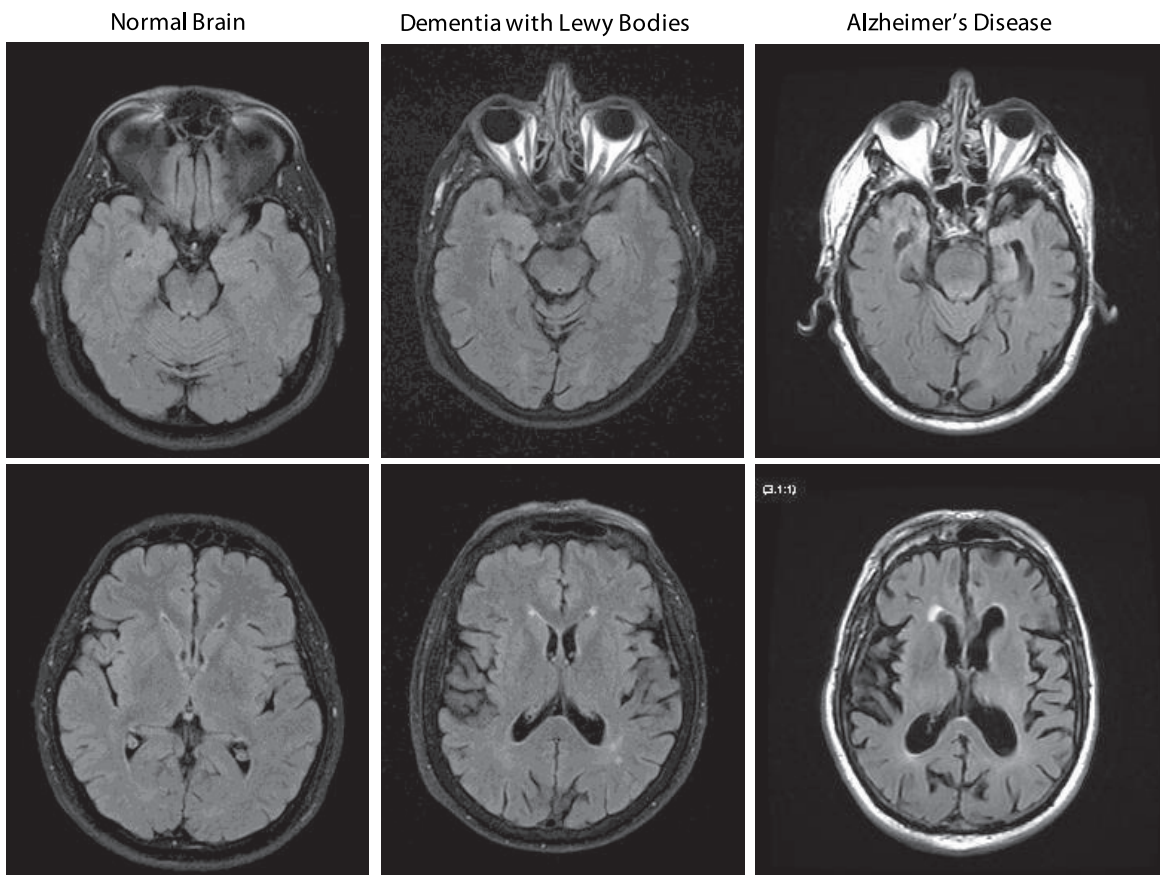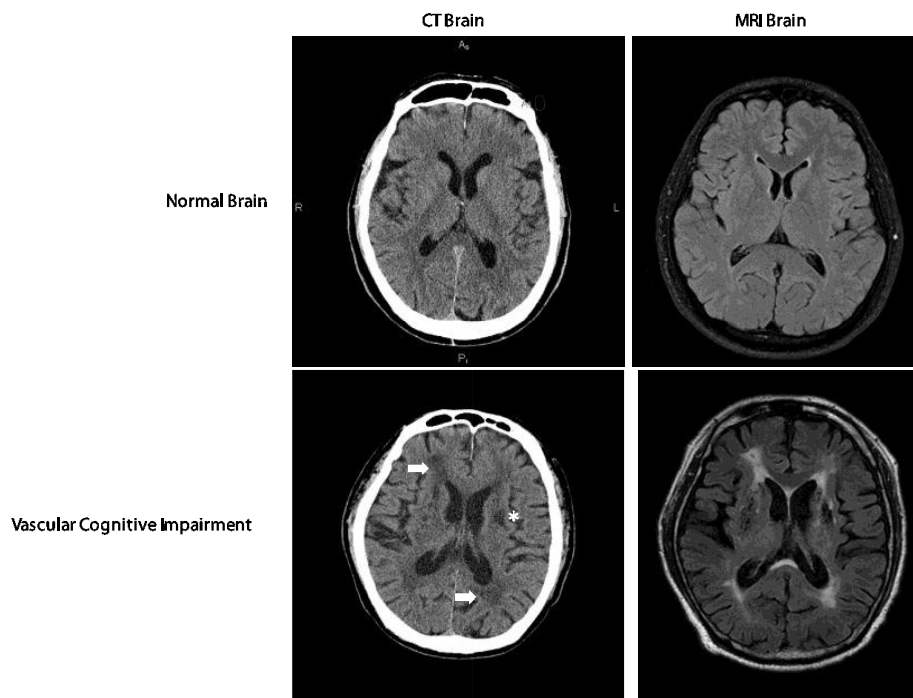

Figure 7. Dementia with Lewy bodies.
In comparison with to the magnetic resonance imaging (MRI) scan of a normal brain (left panel), minimal atrophy is shown on the MRI scan of a person with dementia with Lewy bodies (DLB) (middle panel). Note the lack of hippocampal atrophy and significant generalized cerebral atrophy in DLB as opposed to Alzheimer's disease (right panel).

Figure 8. Vascular cognitive impairment/vascular dementia.
In the computed tomography (CT) brain scan of a patient with vascular cognitive impairment, microvascular disease is shown with hypodensities within the white matter that appear as dark gray (*arrows*) and strokes that appear as black holes (*star*). The normal appearance of white matter on CT is light gray (top left). The equivalent magnetic resonance imaging (MRI) scan of the same patient shows ischemic white matter changes (white areas) and strokes (black holes).
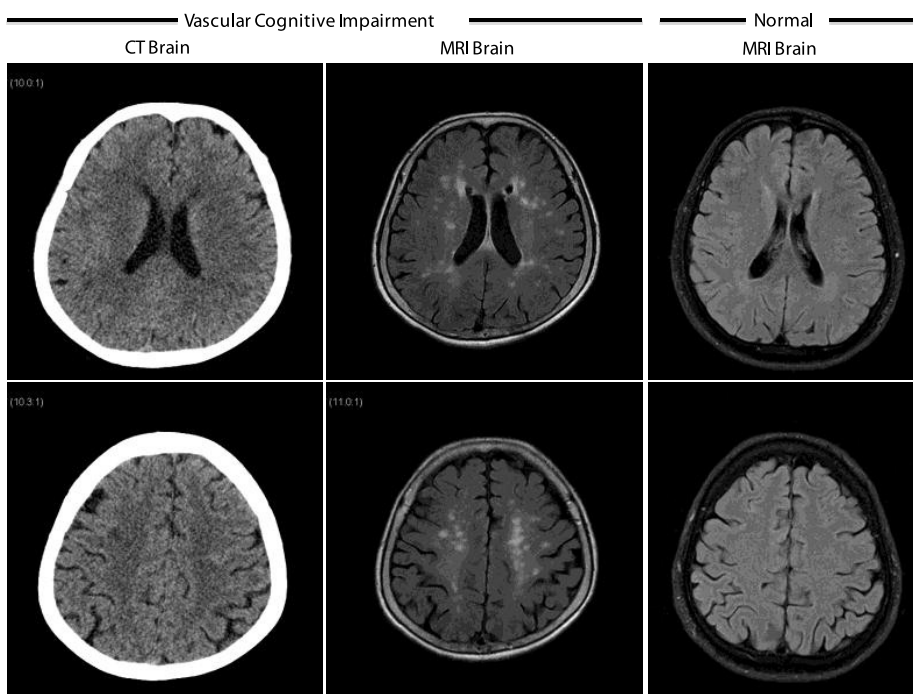
Figure 9. Computed tomography (CT) versus magnetic resonance imaging (MRI) in vascular dementia.
MRI is more sensitive than CT in detecting ischemic white matter disease in a patient with vascular cognitive impairment (VCI). In these equivalent sections of a patient with VCI who underwent both CT and MRI, the MRI scans (middle panel) demonstrate ischemic white matter changes (shown as bright white dots) that are not readily seen on the CT scans (left panel). MRI scans of the normal brain (right panel) do not show these changes.

ventricles. As the disease progresses, there is involvement of the amygdala and hippocampus. However, the degree of atrophy affecting the frontal and temporal lobes is different from that seen in patients with AD (see Figure 5, middle versus right panels). These findings are typical of the behavioural variant of frontotemporal dementia (rule 3).

Frontotemporal dementias (FTDs) represent a spectrum of disorders with varied clinical presentations but involvement of the frontal and temporal lobes. In addition to the behavioural presentation of FTDs as described, there are two distinctive language presentations: semantic dementia and progressive non-fluent aphasia. The neuroimaging findings for these disorders are similarly distinct and are shown in Figure 6.[2,6,7]

Case. A 64-year-old woman presents with a 5-year history of rapid eye movement sleep behaviour disorder. During the past year, she has developed a shuffling gait, micrographia, stooped gait, bradyphrenia, and spontaneous non-threatening visual hallucinations. She scored 24/30 on the Mini-Mental Status Examination and had difficulties on serial "7s" and copying the pentagons but preserved three-word recall. Physical examination results were normal; however, neurological examination revealed parkinsonism that was affecting the right side more than the left side. In this case, the most likely suspected diagnosis is dementia with Lewy bodies (DLB), and an MRI scan of her brain is obtained (Figure 7).

Interpreting the neuroimaging and applying the rules. The axial MRI scan (rule 1) reveals no significant cortical atrophy (rule 2) or ischemic vascular disease. When compared to MRI scans of the normal brain and the brain in AD, scans of the brain in DLB typically show no focal areas of brain atrophy but show a generalized cortical atrophy. Furthermore, more recent studies have determined that the presence of significant cortical atrophy (especially the hippocampus) in a patient with a history consistent with DLB also suggests concomitant AD pathology.[2,8]

Case. A 72-year-old man with hypertension, angina, hypercholesterolemia, diabetes, and a history of previous strokes presents with a progressive dementia characterized by memory loss, geographic disorientation, and problems using appliances. He scored 18/30 on the Mini-Mental Status Examination. Physical examination results were normal; however, neurological examination revealed a mild right hemiparesis, right hyperreflexia, and a right Babinksi sign. Given the cerebrovascular risk factors and focal neurological examination findings, the most likely cause of the dementia is vascular dementia, and an MRI brain scan is obtained (Figure 8).

Interpreting the neuroimaging and applying the rules. The axial CT and MRI scans (rule 1) do not show any significant focal atrophy (rule 2) but do demonstrate both ischemic white matter changes and frank small-vessel infarcts.

There are three neuroimaging findings for vascular cognitive impairment: (1) small vessel disease (microangiopathy [the ischemic white matter changes] and/or lacunar infarcts), (2) large vessel disease (macroangiopathy – larger arterial strokes, appearing as dark wedges [not shown]), and (3) microhemorrhages. Small vessel disease on CT images appears as hypodensities (darker gray, as compared to normal white matter) and/or small lacunes (small black holes). Small vessel disease on MRI, using fluid-attenuated inversion recovery sequences, appear as hyperintensities (bright white areas) within the white matter and/or lacunar infarcts that appear as small black holes. The degree of small vessel disease (mild to severe) and the strategic location of lacunar infarcts can also contribute to dementia. Infarcts that affect the hippocampus, anterior thalamus, or caudate head can acutely cause changes in cognition and/or dementia. Microhemorrhages can be shown only with MRI with a specific gradient echo sequence (GRE sequence); they appear as black dots or areas (not shown). The presence of microhemorrhages can be due to either systemic hypertension or the presence of cerebral amyloid angiopathy, a condition in which amyloid is deposited in the blood vessel walls and that is associated with a risk of lobar intracranial hemorrhage and AD.[2–10]

Ordering Neuroimaging
CT or MRI?
Neuroimaging with CT is adequate for the majority of uncomplicated cases of dementia such as AD. The focal areas of atrophy specific to the type of dementia, such as hippocampal atrophy in AD, can readily be determined with either CT or MRI. However, for atypical presentations of dementia, rapidly progressive dementias, or suspicion of vascular dementia, MRI is generally recommended since it is more sensitive than CT in detecting ischemic white matter changes (Figure 9), changes with the cerebral cortex, infection, and microhemorrhages.

How to Order
When ordering either CT or MRI for the evaluation of dementia, it is helpful to ask the neuroradiologist to comment on a particular area that is pertinent to the diagnosis. For example, if AD is suspected, the neuroradiologist's comments on the presence of hippocampal atrophy will help with diagnosis. Similarly, if FTD is suspected, comments on the presence of frontal and anterior temporal lobe atrophy for behavioural variant or left anterior temporal lobe atrophy for the semantic dementia variant will be helpful. Vascular cognitive impairment is characterized by the degree or amount of ischemic white matter changes and/or the presence of strokes, so the neuroradiologist should comment on the degree of white matter changes (mild, moderate, or severe).

Key Points
- *Structural neuroimaging of the brain by computed tomography (CT) or magnetic resonance imaging (MRI) is important for the accurate determination of the specific causes of dementias.*
- *Each common dementia has a predilection for a particular part of the brain, usually manifest as a focal area of atrophy that is disproportionately affected before the rest of the brain and that can be shown by CT or MRI.*
- *In examining neuroimages, first determine which anatomical plane of the brain is being viewed, then determine if and where there are areas of brain atrophy.*
- *When ordering CT or MRI for the evaluation of dementia, ask the neuroradiologist to comment on the particular areas that are pertinent to the suspected diagnosis.*

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