Neuroimaging for dementia diagnosis

Guidance from the London Dementia Clinical Network

Authors
Dr Stephen Orleans-Foli
Consultant Psychiatrist, West London Mental Health NHS Trust

Dr Jeremy Isaacs
Consultant Neurologist, St George's University Hospitals NHS Foundation Trust
Deputy Clinical Director, Dementia Clinical Network, NHS England (London Region)

Laura Cook
Quality Improvement Manager, Dementia Clinical Network, NHS England (London Region)

Contents

Introduction

The 2016 London Memory Service Audit[1] highlighted wide variation in the use of neuroimaging investigations in patients undergoing assessment for dementia by memory assessment services. The percentage of patients in each service who had any type of brain scan varied from 42 to 87 per cent, with the percentage of people who had an MRI scan ranging from 0 to 64 per cent and a CT scan from 2 to 58 per cent.

Two of the challenges contributing to timely diagnosis are the increasing number of referrals to memory services; and the demographic growth in the population aged over 85 (in whom the prevalence of dementia is approximately 30 per cent). Many memory services experience long waiting times for externally provided CT and MRI scans, while access to functional imaging modalities is highly variable and associated with high cost. Furthermore, as patient age increases, neuroimaging tests lose specificity, significantly reducing their diagnostic accuracy, thus increasing the likelihood of false positive or false negative results[2,3].

The updated NICE clinical guideline on dementia[4], published in June 2018, states: 'Offer structural imaging to rule out reversible causes of cognitive decline and to assist with subtype diagnosis, unless dementia is well established and the subtype is clear'. The revised guideline also includes recommendations on the use of functional imaging.

The aim of this document is to support good clinical care and a reduction in variation in imaging practice between memory services by setting out a rationale for the pragmatic use of neuroimaging in this setting, and promoting a consistent approach to its use in the assessment of people with suspected dementia.

Considerations prior to requesting a scan

The below questions can help guide clinical decision making prior to requesting a scan.

1. Why are you doing a scan?

Is a scan being requested to *exclude* a potentially treatable disorder which may mimic the signs of a dementia (such as hydrocephalus), or is it being performed to determine the subtype of dementia?

2. Will doing a scan change your management?

There may be no clinical purpose in accurate subtype diagnosis. For example, the management of mixed vascular/Alzheimer type dementia is the same as for Alzheimer's disease (AD). In both cases an acetylcholinesterase inhibitor (AChEI) and/or memantine is indicated and in both vascular risk factors should be appropriately managed. The presence of white matter changes may or may not have a cognitive correlate and will not necessarily alter your management.

3. What are potential effects of a scan on your patients?

Patients will receive a dose of radiation from a CT scan or several unpleasant, noisy and claustrophobic minutes in an MRI scanner. A scan may also delay a diagnosis and cause delays for other patients in your service for whom a scan might be considered a more essential part of a clinical work up. These risks may be justified but it is important to consider them as part of your decision-making *before* you order a scan.

4. When should a scan be requested?

- The decision to refer a patient for neuroimaging should be a clinical decision and take into account patient preference.

- Having a CT scan or MRI in primary care must **not** be a requirement before referral to a memory service. This leads to unnecessary neuroimaging.

- During triage, check if the patient has had a brain scan within the lifetime of the cognitive symptoms. If so, source the scan and ask for it to be re-reported (if required), ideally providing the radiologist with up to date clinical information.

  If the information from clinical assessment together with the previous scan do not enable you to provide a diagnosis **and** the patient's symptoms have progressed since that scan then it may be appropriate to request a second scan of the same modality, to determine whether there has been any interval change.

- Services may choose to refer patients for neuroimaging at the point of triage, as long the triage process is robust enough to identify for whom a scan is appropriate and what the most likely dementia subtype is.

- The majority of patients referred to memory services who are under the age of 60 do not have dementia. These patients should have a thorough assessment before a clinical decision is made on whether to refer for neuroimaging.

Determining the suitability of patients to scan

Patients who might not need neuroimaging for a dementia diagnosis

1. **Older people with a history of gradual cognitive decline occurring over a year or more, with moderate or severe cognitive impairment with a pattern of symptoms and signs typical for AD (eg early episodic memory deficits), no history of other neurological symptoms, and where the clinician believes AD is the only likely diagnosis.**

Rationale: A diagnosis of AD is essentially based on a good clinical history and examination. AD should not be ruled out based solely on the results of CT or MRI scans[4], so a normal scan in this situation wouldn't over-ride the diagnostic significance of a clear history of cognitive decline. Whilst in theory a reversible cause might be present, the absence of localising neurological symptoms or signs in the context of a typical presentation of AD makes this highly unlikely. Additionally, practitioners should consider, on an individual patient basis, whether neurosurgical intervention (which has its own risk/benefit analysis) for structural pathology would be justified. If not, then there is little to be gained from performing neuroimaging.

Additionally in patients over 80 years old, neuroimaging changes are less specific, with greater overlap between normal ageing and the radiological hallmarks of AD and vascular dementia[2]. In this age group, neuroimaging may not add to the clinical assessment so should be considered for 'rule in' purposes on an individual basis rather than being automatically requested.

2. **People who have had a scan within the lifetime of the presenting cognitive symptoms.**

Rationale: The scan should be reviewed or re-reported if required. A second scan may be appropriate only if: the previous scan together with clinical information does not support you to make a diagnosis **and** the patient's symptoms have progressed since that scan.

3. **People with severe dementia with a clear history of decline over several years (eg nursing home residents who require assistance with activities of daily living).**

Rationale: Subtype diagnosis is less important in severe dementia where commencement of AChEIs is not indicated and imaging is more likely to cause distress. The DiADeM[5] (diagnosis of advanced dementia mandate in care homes) is a useful tool for the primary care led assessment and pragmatic diagnosis of these patients, which is also helpful for memory services covering care home populations.

4. **People with severe chronic physical illness or those with a terminal illness.**

Rationale: These patients are likely to find undergoing a scan distressing and it is unlikely to alter your management, which should be focused on the primary medical condition.

5. **People with schizophrenia who present with the typical neurocognitive deficits and negative symptoms of schizophrenia, such as impaired attention and concentration, apathy, or with sedative side effects of their psychiatric medication.**

Rationale: The neurocognitive profile of schizophrenia should be determined by clinical history, physical examination and neuropsychological assessment, to help differentiate the diagnosis from a progressive neurodegenerative condition. The structural neuroimaging changes associated with AD can also be present in chronic schizophrenia, so these images would be less useful in determining a diagnosis.

Patients who almost always require neuroimaging

1. Younger patients where there is a clinical presentation of cognitive deficits in the absence of a significant mood or anxiety disorder or clinical features to suggest a functional cognitive disorder.
2. Any patient with these symptoms:
    - Seizures (or transient loss(es) of consciousness in which seizures cannot be excluded)
    - Signs and symptoms of raised intracranial pressure
    - Acute or rapid onset of symptoms
    - Any other focal neurological symptoms or signs not explained by past medical history (eg limb weakness, ataxia, etc)
    - A non-amnestic pattern of cognitive deficits (eg dysphasia, behavioural presentations, prominent visuospatial or praxis deficits)

Which scan: CT or MRI?

Modern CT scanners have similar ability to MRI in detecting characteristic patterns of atrophy (eg global cortical atrophy and medial temporal lobe atrophy) and major cerebrovascular pathologies[6]. Most reversible causes of dementia that show up on brain imaging will be satisfactorily demonstrated on a CT scan. Therefore, unless there is a very atypical history, such as a rapidly progressive dementia, the preferred 'rule out' imaging modality is CT. There are cases, discussed below, in which even showing potentially reversible pathology won't alter management, and so brain imaging in these circumstances might not be in a patient's best interest.

CT scans have the added advantage of lower cost in many centres. However, the radiation exposure associated with CT results has a less favorable risk/benefit ratio in younger patients, especially those with mild symptoms in whom repeat imaging might be required.

Therefore, CT is a suitable option for most older patients (even if MRI is available), particularly those with clear-cut presentations, and is the preferred option for those who are frailer, agitated, claustrophobic and less able to tolerate the longer imaging protocols. MRI is contraindicated for patients who have a pacemaker or metallic implants.

The only major dementia subtype in which MRI has been shown to be superior to CT at 'ruling in' is vascular dementia. This is because cortical and subcortical ischaemic lesions are better demonstrated on MRI and some vascular pathologies, such as microbleeds, cannot be seen on CT. Therefore, if the dementia subtype is uncertain and vascular dementia is suspected, MRI is the preferred modality[4].

There is a limited group of rarer pathologies in which MRI has clear advantages over CT. These include prion disease, non-degenerative causes of rapidly progressive dementia such as central nervous system (CNS) lymphoma or gliomatosis, inflammatory diseases of the CNS such as multiple sclerosis or limbic encephalitis, metabolic disorders such as mitochondrial disease, CADASIL and CNS infections such as HIV and progressive multifocal leukoencephalopathy.

Instances when the need for a scan may be unclear

It may not be clear whether or not some patients require a scan, such as:

- An 85 year old with a two year history of cognitive decline very suggestive of AD. On examination, she has a moderate gait dyspraxia which her family reports has started within the past year.
- A 40 year old presenting with moderate depression and minor attentional and executive deficits but who has a very strong family history of early onset AD.

There is no right or wrong in these cases; discuss with the patient and family the pros and cons of a scan and order one if it seems the right thing to do.

Specialist imaging

Specialist imaging should only be considered if it would help to diagnose a dementia subtype **and** knowing more about the dementia subtype would change management[4].

Specialist imaging includes fluorodeoxyglucose positron emission tomography (FDG-PET), single proton emission CT (SPECT) and I-FP-CIT SPECT (DAT scan).

FDG-PET is a proxy indicator of neuronal activity and can reveal characteristic regional patterns that can help differentiate the subtypes of dementias due to neurodegenerative disease[7].

FDG-PET in Alzheimer's disease

Cerebral regions more typically affected in early AD are the parieto-temporal and posterior cingulate cortices. Normal ageing is associated with a greater than 25 per cent reduction of cerebral glucose metabolism at 80 years of age, but tends to spare the medial temporal lobes and temporo-occipital cortex[8]. FDG-PET therefore, has the potential to differentiate patients with AD from patients who do not have AD or have other causes of dementia, and should be considered if the diagnosis is uncertain. SPECT imaging can be considered if FDG-PET is unavailable, however SPECT has longer scan times and produces low-resolution images that are prone to artifacts and attenuation.

FDG-PET in frontotemporal dementia (FTD)

Where structural imaging does not show the expected regional atrophy and the diagnosis remains unclear, FDG-PET scan may be considered. It is more specific and sensitive than MRI earlier in the course of the disease.
It is important not to rule out FTD solely on the basis of a normal FDG-PET scan.

DAT scan in dementia with Lewy bodies (DLB)

DAT scans have high specificity and sensitivity in distinguishing Parkinsonian syndromes from other neurodegenerative disorders such as AD and FTD. FDG-PET and SPECT scans can also be used to assist in the diagnosis of DLB, albeit with less accuracy than DAT scans; these demonstrate hypometabolism and hypoperfusion respectively in the occipital lobes with relative sparing of the medial temporal lobes. However, a typical history, with cognitive fluctuations, visual hallucinations, anosmia, rapid eye movement sleep behaviour disorder and Parkinsonism is so specific for DLB that a 'rule in' DAT scan to confirm the diagnosis should not be necessary. The international consensus criteria for dementia with Lewy bodies[9] should be used to guide clinical judgement[4].

Summary

Services need to consider the rationale behind neuroimaging requests for dementia diagnosis particularly in patients who:

- are frail;
- have had a previous scan within the lifetime of the cognitive symptoms;
- have severe dementia;
- are in later life, have classical symptoms of moderated to sever AD and without any atypical cognitive or neurological features.

CT scans are a suitable option in most cases, but in uncertain cases of vascular dementia and atypical presentations MRI might be more appropriate. Functional imaging modalities have a role only where the diagnosis is uncertain following expert clinical assessment and structural imaging.

---

[1] London Dementia Clinical Network (2016) London Memory Service Clinical Audit http://www.londonscn.nhs.uk/wp-content/uploads/2017/03/dem-audit-150317.pdf [accessed January 2018].

[2] O'Brien JT (2007) Role of imaging techniques in the diagnosis of dementia. British Journa4)l of Radiology 80: S71–7.

[3] Sullivan, V., Majumdar, B., Richman, A. and Vinjamuri, S., 2012. To scan or not to scan: neuroimaging in mild cognitive impairment and dementia. Advances in psychiatric treatment, 18(6), pp.457-466.

[4] NICE 2018 [NG97] 2018. Dementia: assessment, management and support for people living with dementia and their carers https://www.nice.org.uk/guidance/ng97 [accessed June 2018].

[5] Yorkshire and Humber Dementia Clinical Network (2016) DiADeM Tool – Diagnosing Advanced Dementia Mandate (for care home settings) http://www.yhscn.nhs.uk/mental-health-clinic/Dementia/Diagnosis.php#DEARGP [accessed January 18].

[6] Wattjes M, Wouter J. P. Henneman, et al , Radiology Diagnostic imaging of patients in the memory clinic. Radiology 2009 253 p174-18.

[7] Mosconi L. Glucose metabolism in normal aging and Alzheimer's disease: methodological and physiological considerations for PET studies. Clinical and Translational Imaging. 2013;1:217–233.

[8] Kalpouzos G, Chetelat G, Baron JC, et al. Voxel-based mapping of brain gray matter volume and glucose metabolism profiles in normal aging. Neurobiology of Aging. 2009;30:112–124.

[9] McKeith I et al 2017. Diagnosis and management of dementia with Lewy bodies: Fourth consensus report of the DLB Consortium. Neurology 2017 Jul 4;89(1):88-100.