

## THE DIAGNOSIS OF MCI AND DEMENTIA

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The diagnosis of dementia is based on three criteria: disabling change in cognitive power, disease progression and exclusion of alternative pathologies. It is a clinical diagnosis. No single test – blood tests, neuroimaging, neuropsychological tests – is sufficient for making the diagnosis. The three criteria – disability, progression and exclusion – are sufficient.

### *A DISABLING LOSS OF COGNITIVE POWER*

One may not need to use a very sensitive test to establish that a patient is cognitively impaired, if the clinical situation has evolved to the point that dementia is suspected. In most clinical practices dementia is not suspected until the patient expresses some overt symptoms. When this happens, it means that the patient's natural compensatory mechanisms are being overwhelmed, and the pathology is well-entrenched. Cognitive impairment is usually demonstrable on any of the brief clinical screening batteries or rating scales that we reviewed in chapter X. A score below 24 on the MMSE is usually taken to indicate early or mild dementia, but failure to remember four words at five minutes is probably equally good.

On the other hand, if the goal of one's practice is to pick up cases of MCI at the earliest possible moment, then a battery of neuropsychological tests is necessary. At this point, the patient is likely to be asymptomatic. We have argued that computerized test batteries are most suitable for that purpose.

Patients with mild dementia are usually able to take a computerized test battery like CNS Vital Signs, although they may require a companion to explain the directions or to show them where the ENTER key is. Patients with MMSE scores under 20 usually have a great deal of difficulty with the test. It has always been discouraging to hear from neurologists – dementia specialists, in fact – who say, "My patients are much too impaired to take your test." We believe what they tell us, but it looks like they're seeing new patient pretty late in the game.

It may be harder to determine whether the impairment is disabling. Patients with early dementia may resist the idea that they are disabled, either for lack of insight, or determination to retain their independence. Whether they should continue to drive, for example, is often a matter of contention, and the opinions of family members may be discordant or biased.

Rating scales are perfectly suitable to measure a patient's functional status, but you can't rely just on the patient's response. Before you rely on the spouse's opinion, though, try to make sure that he or she isn't demented. We have more than one old couple who are both afflicted. Number one has a pretty advanced case, but number two has been her compensatory mechanism. Neither comes to clinical attention until number two starts to fail.

Measuring functional status is simple enough, with an 8 item scale like the IADL (Table X.01)

TABLE X.01 *instrumental Activities of Daily Living scale*

Activity	Need No Help (2 pts. each)	Need Some Help (1 pt. each)	Unable to Do At All (0 pts. each)
Using the Telephone			
Getting to Places Beyond Walking Distance			
Grocery Shopping			
Preparing Meals			
Doing Housework or Handyman Work			
Doing Laundry			
Taking Medications			
Managing Money			

## PROGRESSION

The most important thing to do for patients with MCI is to follow them serially. That is the only way to make the distinction between “converters” and “non-converters.” Converters will show gradual decline and ultimately will cross the line to disability. It is important to follow dementia patients, too, with serial cognitive tests, but one doesn’t wait six months or a year to make the diagnosis. Sufficient to establish that the patient’s current state represents a change from a past state.

## ETIOLOGY

Having established that the patient has dementia, it is appropriate to try to determine the etiology, but that is not always possible. In patients with a clinical diagnosis of dementia, the etiology can be inferred, but not “accurately predicted” during life. During life, there is no “gold standard” against which diagnostic validity can be measured. The diagnostic manual suggests the diagnosis of AD may be inferred if the patient has memory impairment accompanied by apraxia, agnosia, aphasia or impairment in executive function (DSM-IV). The diagnosis of CVD is based on a different neuropsychological profile/course: a “stepwise” rather than a progressive course, “patchy” distribution of neuropsychological deficits associated with focal neurological findings, and concurrent evidence of significant cerebrovascular disease. Frontotemporal dementia has a characteristic pattern of behavioral and cognitive disturbance. DLB has a unique and typical course. So it goes, for all of the dementias. Their clinical characteristics are typical, as long as the disorder occurs in pure form; in such cases, one can feel confident in the diagnosis. But mixed forms are not uncommon and the clinical characteristics overlap. The majority of community-dwelling older persons have brain pathology of some sort or another, and those with dementia most often have multiple brain pathologies.

So, it is nice to have an etiologic diagnosis for the demented patient, but it is not always possible. And at this stage of the art, it probably doesn't make much difference. Prognosis is more likely to be influenced by individual factors, and treatments, such as they are, are symptomatic and non-specific. It is defensible to scan a patient, for example, to look for signs of frontal or temporal atrophy, but what you're really looking for is a tumor, an old stroke, an abscess, etc. Functional imaging and CSF biomarkers may increase the accuracy of dementia sub-type diagnosis, but the cost-benefit tradeoff is wanting. The purpose of diagnostic studies has traditionally been to discover causes of reversible dementia, and this is still very much the case.

The "diagnosis" of MCI is based on the unequivocal identification of cognitive impairment, relative to the patient's age, level of education, and premorbid neurocognitive status; unaccompanied by disabling changes in the patient's personality, emotional or behavioral state, or activities of daily living. But MCI, like dementia, is simply a description of the patient's functional state. When a patient presents with a mild cognitive problem, it should be the occasion of a differential diagnosis. "Progression" is not essential for the diagnosis, since the occurrence of MCI does not necessarily indicate progressive deterioration. Many cases of MCI are stable, and some cases remit when testing is repeated after a few months.

Everyone agrees that an older patient with complaints of cognitive weakness, or demonstrated cognitive impairment on a neurocognitive screening test, should have a comprehensive medical, neurological and psychiatric examination. Essential studies ought to include a complete blood count, comprehensive metabolic profile and a CT scan. No one would argue with serial neurocognitive testing for such patients, at six-month intervals, or at least annually.

#### **DIAGNOSTIC TESTS**

##### *IMAGING*

Cranial CT (without contrast) is necessary to rule out structural lesions that can cause or aggravate dementia, like neoplasms or extradural fluid collections. The yield may be low, but the cost of missing such a lesion is high. If the neurological examination is nonfocal, the yield may be no more than 4%. It is arguable that CT is not an essential part of the dementia workup. The consensus, however, is that "a neuroimaging procedure should be performed once in all cases of dementia."

MRI can detect small strokes or ischemic changes that cannot be visualized on CT. The absence of cerebrovascular lesions on MRI is strong evidence against a vascular etiology of the patient's dementia. Their presence, however, is not evidence against the diagnosis of AD.

PET scanning is used in some centers to identify patterns of hypometabolism characteristic of different forms of dementia. It is an extremely expensive test, intrusive, and not widely available. SPECT scanning is less expensive and more widely available. The clinical utility of functional imaging has not been established.

##### *EEG*

Electroencephalography is not routine, but is sometimes used to detect toxic or metabolic disorders, Creutzfeldt-Jacob disease, or subclinical seizures. Quantitative EEG (e.g., BEAM) does not have an established role in the dementia work-up.

*CSF*

This is a special test, and only for atypical cases, e.g.: dementia in a patient less than 55, cancer, suspected CNS infection, connective tissue disease, hydrocephalus, reactive serology, immunosuppression, or rapidly progressive dementia.

*GENETIC TESTING*

Apolipoprotein E alleles: ApoE4 indicates vulnerability, especially to AD, while ApoE2 indicates relative protection. At the present time, it is a very expensive test. It is not a diagnostic test, by any means, and sometimes it raises more questions than it answers. If a patient with mild cognitive impairment is  $\epsilon$  4 positive, is one committed to a more aggressive approach to treatment? And what, exactly, should such an approach comprise?

*FORMAL NEUROPSYCHOLOGICAL TESTING*

Detection of mild deficits in a screening neurocognitive battery may indicate the need for a standard neuropsychological evaluation. Patients with MCI ought to be given a complete test battery. Evaluation for premorbid ADD or learning disabilities is essential. On the other hand, little is to be gained if the patient presents with overt dementia; for example, an MMSE score less than 24. Unless the neuropsychologist is to be engaged in counseling or cognitive remediation, expensive and arduous testing may not be useful.

*LABORATORY TESTS*

The cost-effectiveness of comprehensive serologic testing has been questioned. The likelihood of identifying a reversible form of dementia by such methods is about 11% (8% partially reversible, 3% fully reversible).

<i>TABLE X.02 LABORATORY TESTING FOR MCI</i>	
ROUTINE LABORATORY TESTS	
	CBC & Differential
	LFT's, BUN, Creatinine
	Calcium, Electrolytes
	Thyroid profile
SPECIAL LABORATORY TESTS	
	B <sub>12</sub> levels, Folate
	Methylmalonic acid
	VDRL, HIV
	Heavy metals
	Lyme serology
	Toxicology screen
	ApoE alleles
INFLAMMATORY MARKERS	
	C Reactive Protein
	Homocysteine
	Interleukin-6
	ESR
	Anti-nuclear antibody
	Extractable nuclear antigen
	Anticardiolipin antibodies
	Lupus anticoagulant
	Paraneoplastic autoantibody panel