Rapid review

Mild cognitive impairment in older people

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Context As public awareness of Alzheimer’s disease increases, more people are asking for help and advice about memory problems. Memory complaints may be secondary to psychiatric, psychological, and physical conditions and is an almost universal early symptom of dementia. The concept of amnestic mild cognitive impairment attempts to describe those people in whom memory loss is not of such severity to merit a diagnosis of dementia. The importance of this group of people is not just the need to develop interventions which ameliorate individual suffering but that they represent a population at high risk of developing dementia, especially Alzheimer’s disease, and are an appropriate target for dementia prevention strategies.

Starting point K Kantarci and colleagues (Dement Geriatr Cogn Disord 2002; 14: 198–207) looked at the diagnostic accuracy of magnetic-resonance hippocampal volumetry and spectroscopy in patients with mild cognitive impairment, in normal older people, and in patients with Alzheimer’s disease. Hippocampal volumes and N-acetyl aspartate/creatine spectroscopy were the most sensitive assessments discriminating people with mild cognitive impairment from Alzheimer’s disease. Combination assessments were better at discriminating these two groups from normal controls. The histological underpinning of cognitive symptoms in older people has been demonstrated by the Cognitive Function and Ageing study (Lancet 2001; 357: 169–75), which showed that a third of people with no clinical evidence of dementia had histopathological hallmarks of Alzheimer’s disease.

Where next? 25 million people across the world have dementia. Mild cognitive impairment, if a validated concept, represents an opportunity for preventing dementia. As more information becomes available about the cause of Alzheimer’s disease and prospects emerge for prevention, identification of predementia states offers considerable scope to reduce the individual and societal cost of the illness. Continued validation of the criteria for mild cognitive impairment and studies of intervention should be a priority. As more evidence becomes available highlighting the relatively arbitrary nature of dementia diagnosis (based largely on interference with activities) and interventions become available for the prevention of dementia, mild cognitive impairment and related conditions will become more important.

Mild cognitive impairment defines a transitional stage between normal ageing and dementia,¹ and reflects the clinical situation where a person has memory complaints and objective evidence of cognitive impairment but no evidence of dementia. Mild cognitive impairment is important in terms of recognising (and taking seriously) memory loss in older people as well as identifying a group of individuals at high risk of developing dementia and who may benefit from preventive strategies. With current publicity and awareness about the importance of dementia in general and Alzheimer’s disease in particular, people often present to their general practitioners, and to specialist services such as memory clinics, with complaints of memory loss and are less likely to accept the dismissal “it’s your age, what do you expect?” Several different labels have been ascribed over the years to what are broadly speaking the same concepts. Several conditions may have memory complaints as part of their presentation (eg, depression, anxiety, learning disability, delirium, chronic drug and alcohol use, physical illness) and these conditions should be excluded by clinical and mental state examinations and appropriate investigations.

The following descriptive terms are reserved for those clinical situations where no other cause for memory loss has been found. Benign senescent forgetfulness² was the first descriptor to make the distinction between memory loss which was benign and often associated with depressive symptoms, and that which was the harbinger of dementia. An awareness of memory problems, an inability to recall remote rather than recent events, and loss of memory for minor details were the hallmarks of the disorder compared with dementia. Age-associated memory impairment³ quantified the degree of memory impairment required for the diagnosis (a decline of at least one standard deviation below the scores for young adults) and a more severe form of impairment (late-life forgetfulness) which was defined as between one and two standard deviations below age-adjusted scores.⁴ Recognition that domains other than memory (eg, decision-making, executive functions) were affected was enshrined in the concept of ageing-associated cognitive decline.⁵ Whilst these conditions were regarded as being variants of normal ageing, disease classifications cited mild cognitive disorder (ICD10)⁶ and mild neurocognitive disorder (DSMIV)⁷ as conditions due to underlying disease and which occur at any age and involved symptoms other than memory loss. Cognitive impairment, as dementia, has been used in some studies.⁸

Mild cognitive impairment encompasses many of these concepts (panel). The full term, amnestic mild cognitive impairment, distinguishes the condition from the situation where cognitive domains in addition to memory are affected and where a single non-memory domain (eg, language) is affected and where progression to a dementia other than

Criteria for amnestic mild cognitive impairment¹

- Memory complaints preferably corroborated by informant
- Impaired memory function for age and education
- Preserved general cognitive function
- Intact activities of daily living
- No evidence of dementia

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Alzheimer’s disease could be expected. There are guidelines for the investigation and management of mild cognitive impairment.\(^8\)

Estimates of the prevalence of mild cognitive impairment (and related conditions) vary from 17% to 34%. Ritchie and colleagues\(^{19}\) reported the prevalence of mild cognitive impairment and ageing-associated cognitive decline in a representative population to be 3.2% and 19.3%, respectively.

**Predictors of cognitive decline and Alzheimer’s disease**

Factors which predict the development of dementia in the normal population include raised systolic blood pressure and high cholesterol,\(^{11}\) impairments on tests of memory and executive function,\(^{12}\) white-matter lesions on magnetic resonance scans,\(^{13}\) and the possession of the apolipoprotein e4 allele.\(^{14}\)

Follow-up studies have reported the rates at which people with mild cognitive impairment (or states akin to mild cognitive impairment) develop dementia (usually Alzheimer’s disease) at follow up. Annualised rates of conversion from mild cognitive impairment to dementia range from 4%\(^{16}\) to 25%.\(^{17}\) Most other studies have rates of between 10% and 15%.\(^{18}\) Where domains in addition to memory loss are affected, the rates are higher\(^{19}\) and where there is evidence of associated vascular or parkinsonian disease, the rates are similarly increased.\(^{20}\) Even within the diagnosis of mild cognitive impairment, it is possible to delineate and operationally define degrees of severity, with the more severe form representing a group of people who later develop Alzheimer’s disease.\(^{21}\) In a representative survey, Ritchie and colleagues\(^{19}\) showed that the rates of conversion for people satisfying criteria for ageing-associated cognitive decline were three times those for mild cognitive impairment.

**Assessment**

One of the biases inherent in the assessment of mild cognitive impairment is that the same scales developed to document Alzheimer’s disease are used to estimate rates of conversion to Alzheimer’s disease, creating a self-fulfilling prophesy.\(^{22}\) Memory complaints are the core feature of mild cognitive impairment, but the measurement of cognitive functions in addition to memory is important, not least to show that they are normal. There are two clinical screening instruments which allow for a broad assessment of mild cognitive impairment—the CAMCog (part of the CAMDEX)\(^ {23}\) and the SISCO (part of the SIDAM).\(^ {24}\) The mini-mental state examination\(^ {25}\) is the most widely used cognitive test and while this test is a good indicator of cognitive impairment, it is necessary to reach a consensus of a single marker of a single scale. The possession of one or two apolipoprotein e4 alleles predicts decline.\(^{26}\)

**Treatment**

There is no evidence at present that mild cognitive impairment is amenable to treatment but several agents used to treat Alzheimer’s disease are being tested in mild cognitive impairment.\(^{27}\) Treatments which stabilise or reverse deposition of amyloid plaques or abnormal phosphorylation of tau protein (the basis of the neurofibrillary tangle) will have a bigger role in impeding the progression of the disease than neurotransmitter-replacement therapies.

**Spectrum of cognitive disorders in older people**

Alzheimer’s disease is the endpoint of a decline in cognitive and psychosocial function. The presence of objective and measurable cognitive loss is the hallmark in those people who develop Alzheimer’s disease but there is now good evidence that even earlier stages can be defined where subjective complaints in themselves predict the development of mild cognitive impairment.\(^ {28}\) It is possible to postulate an even earlier asymptomatic stage, where subtle cognitive changes occur over time, indistinguishable from normal ageing and where there is no evidence of cognitive impairment but there are neuropathological changes in keeping with a histological diagnosis of Alzheimer’s disease.\(^ {29}\)

Since there are many related concepts of mild cognitive impairment, it is necessary to reach a consensus of a broad but rigorously defined category of mild cognitive impairment which will act as a platform for interventions. We postulate a continuum (figure), starting with the histopathological changes of Alzheimer’s disease in the absence of clinical symptoms, the presence of subjective cognitive complaints but without evidence of objective impairment, the development of measurable decline (mild cognitive impairment), and, finally the early stages of dementia.\(^ {30}\) This is obviously an oversimplification of a
complex process, and it is unknown whether there is a linear progression from one stage to another, how best to identify and diagnose people at different stages across the spectrum, and whether there are any treatment options or implications attached to these labels. Cerebrovascular disease can give rise to symptoms of memory loss, so-called vascular cognitive impairment.12

Conclusions
Mild cognitive impairment is a term in evolution, and while it still seeks precise nosological definition, the term reflects an important clinical entity. Mild cognitive impairment has been defined by phenomenological, epidemiological, clinical, neuropsychological, and biological variables, with its core characteristics drawn from concepts of dementia. Other terms describe related clinical and pathological states, but amnestic mild cognitive impairment relates to a pathological state which differs from normal ageing, there is objective evidence of memory impairment, and patients are more likely to develop Alzheimer’s disease than the normal population. At present, research in mild cognitive impairment is suffocated by too many heterogeneous definitions. A consensus is required to corral these definitions but which is rigorously broad enough to include not only memory impairments but also other cognitive impairments and vascular and extrapyramidal signs. Current research shows evidence that pre-stages of mild cognitive impairment can be defined where subjective complaints in themselves predict mild cognitive impairment and it is possible to postulate an even earlier (asymptomatic) stage with subtle cognitive changes with neuropathological changes only.

In some people, mild cognitive impairment may represent the very early stages of Alzheimer’s disease, but there is a reluctance to make that diagnosis because of its individual ethical and legal implications, fuelled by the fact that, until recently, no effective treatment was available for Alzheimer’s disease and coupled with a reluctance to medicalise what is still regarded by many as a normal experience. It is analogous to the situation up until the 1970s where dementia in older people was regarded than an inevitable consequence of atherosclerosis, and attracted therapeutic nihilism. Mild cognitive impairment needs to be defined with its own variables and not simply borrowing (and often not even adapting) measures used for the characterisation of dementia. Mild cognitive impairment has clinical and nosological utility, and the spirit of the concept should be embraced, not only to provide help and advice to individual patients but also as a vehicle by which to address the prevention of dementia in general and Alzheimer’s disease in particular.

Conflict of interest statement
The authors have received honoraria from pharmaceutical companies involved in the development of antidementia drugs.

References
30 Jorm AF, Christensen H, Korten AE. Memory complaints as a precursor of memory impairment in older people: a longitudinal analysis over 7–8 years. Psychol Med 2001; 31: 441–49.