

MILD COGNITIVE IMPAIRMENT, A TRANSITIONAL ZONE BETWEEN NORMAL COGNITIVE FUNCTION AND DEMENTIA

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Mild cognitive impairment (MCI) is defined as a transitional or preclinical state between the cognitive decline of normal aging and the cognitive decline due to Alzheimer's dementia. It involves problems with memory, language, thinking and judgment that are greater than is expected for one's age. General cognitive functions remain preserved and changes are not severe enough to interfere with daily life and usual activities. A person with MCI may be aware of memory function problems as well as his family and close friends who may also notice a change.

The annual prevalence of MCI in the USA is estimated to 3-4% in the eighth decade of life in the general population, and 19.2% for ages 65-74 years, 27.6% for ages 75-84 years, and 38% for ages 85 years and older [1-3]. In the Mayo Clinic Study of Aging a prevalence of MCI in men was found [4].

There are two different subtypes of MCI: amnesic and nonamnesic MCI. In the amnesic form of MCI memory impairment predominates. This subtype of MCI is more often a precursor to clinical Alzheimer's disease. In the nonamnesic subtype of MCI the most common cognitive impairment is probably the damage of the executive functions. This form of nonamnesic MCI may be associated with cerebrovascular disease or with frontotemporal dementia [5]. A considerable percentage of persons with MCI progresses to dementia, about 10-15% per year [6].

There have been discussions about whether MCI must be viewed as a separate nosological entity at increased risk of dementia or a prodrome of Alzheimer's disease. The concept of MCI was defined by Petersen and all. in 1997, and was restricted to only memory

impairment leading to the identification of people at a high risk of progression to Alzheimer's disease [7]. Some patients with MCI regain normal cognitive function, some remain stable and some show a progression to different types of dementia. Due to this heterogeneity of the clinical presentation, as well as the outcome of numerous MCI subjects, Petersen extended his previous concept to a syndrome-type classification: amnesic MCI which is characterised by the following criteria: -complaining about memory, preferably corroborated by an informant or by the subjects themselves;- objectively impaired memory function in relation to the age and education;- preserved general cognitive function;- intact basic activities of daily life; and- no dementia [8].

Several medical conditions and lifestyle factors may be linked to an increased risk of cognitive change although the evidence for these risk factors is less clear-cut. These risk factors include: diabetes, smoking, depression, high blood pressure, elevated cholesterol, lack of physical exercise, infrequent participation in mentally or socially stimulating activities.

For the objective measurement of cognitive deterioration standard neuropsychological tests are applied, in which poor performance on delayed recall and executive functions indicate a high risk of progression towards AD [9,10]. Those tests are complimentary to the mini-mental state examination. Supplementary information from a knowledgeable informant (e.g. a family member) concerning the individual's memory abilities can be particularly helpful as some patients may be unaware of their cognitive changes [11]. Many patients with MCI suffer from anxiety and depres-

sion, thereby it is sometimes difficult to make the correct diagnosis. Other disorders, such as frontotemporal dementia, Lewy body dementia or vascular origin of cognitive impairment might be suggested.

Biomarkers in the cerebrospinal fluid are helpful to differentiate between MCI and normal ageing and to identify patients at risk for progression to AD. The markers that have been studied include total tau, phosphorylated tau and beta-amyloid 1–42 [12,13]. Follow-up studies performed by Hansson et al. demonstrated that concentrations of these markers in MCI patients were strongly associated with further development of AD [14]. The consistent feature of numerous studies points out that increased total tau and phosphotau concentrations are highly sensitive.

Investigations with magnetic resonance imaging (MRI) have demonstrated medial temporal lobe atrophy in people with MCI compound who were cognitively normal individuals, and this atrophy is predictive of progression to dementia [15–18]. Longitudinal hippocampal volume losses in these patients are closely associated with increasing hyperphosphorylated tau [19].

On Positron emission tomography (PET) changes of regional cerebral metabolic rate for glucose (CMRGlc) were found in many subjects with MCI. These changes were predictive of clinical progression to Alzheimer disease within a follow-up period of more than a year [20–23]. The reduction of CMRGlc in AD typical brain regions were related to elevated phosphor-tau levels and combined to assessment of the APOE genotype improved identification of high-risk patients [24,25]. Acetylcholine esterase activity as a marker of cholinergic activity is reduced in AD [26]. The cholinergic system is important for memory functions, and therefore the decrease in AChE activity might be a predictor of conversion from MCI to AD.

Another promising tracers for detection of deposition of amyloid are ¹¹C-labelled arylbenzothiazoles, known as „Pittsburgh Compound-B“ [27]. In cortical areas PIB retention was increased in AD and correlated inversely with cerebral glucose metabolism [28].

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