NEUROPSYCHOLOGY TODAY

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Mild Cognitive Impairment: Pre-Clinical Stage of Dementia

As the life expectancy continues to increase, the older segment of the US population is growing in size, and the research in the field of aging and dementia is accelerating rapidly. Even though the general public is quite familiar with such age-related condition as dementia, particularly Alzheimer's dementia, the awareness about Mild Cognitive Impairment (MCI), a neurocognitive syndrome that usually precedes dementia, is relatively low.[1]

Approximately 19% of people 65 years of age or older suffer from MCI, and the risk of developing MCI increases with age. Individuals with MCI experience subtle cognitive deficits, most frequently presenting with forgetfulness, with largely intact cognition and ability to perform daily tasks. The risk factors of MCI include older age, lower education, being African American, presence of apolipoprotein E (ApoE 4), cortical atrophy at neuroimaging, signs or symptoms of vascular diseases, and depression. The causes of MCI remain unknown, although studies suggest that there is a genetic component that contributes to its development.[1]

MCI lies on the continuum between normal aging and dementia. In other words, individuals with this neurocognitive syndrome present with cognitive symptoms that are not considered to be a part of normal aging,

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Inside:

Diagnosis and Assessment of MCI

The diagnostic criteria for MCI have been developed in order to identify individuals at pre-clinical stages of dementia. Early identification of MCI is critical, because interventions may still be effective in slowing cognitive deterioration and conversion to dementia, and in prolonging the individuals' independence and employability. Early identification also allows family and financial planning. Some researchers believe that a combination of cognitive tests and neuroimaging findings should be utilized in early detection of MCI.[2,4,5]

The diagnostic criteria for MCI are the following:

a) Abnormal cognitive functioning, but intact general intellect without dementia

b) Evidence of cognitive decline as assessed by *neuropsychological tests* and patient self-reports and caregiver reports

c) Preserved ability to perform activities of daily functioning, with minimal or no signs of impairment [1]

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Neuropsychological Findings in MCI

According to research, MCI may affect a wide range of the patients' neuropsychological functions. These include episodic memory (i.e. remembering events such as conversations and TV programs), executive functions (planning, reasoning, sequencing, decision making, problem solving, working memory, etc.), perceptual speed, visuospatial skills, and attention. Some language functions are also impaired in MCI, including verbal fluency (word finding ability), naming, and semantic and syntactic reasoning.[1,4]

It is not surprising that MCI-related cognitive deficits translate into daily difficulties for the patient. It has been found that compared to healthy individuals of the same age, people with MCI have more problems with shopping, medication intake, handling their finances, finding things at home, keeping appointments, and participating in- and remembering conversations. Such basic functions as bathing, feeding, and travelling are preserved in individuals with MCI.[1]

Importantly, individuals with MCI tend to have diminished awareness of their cognitive deficits, which not only complicates diagnosis, but also may have implications for various aspects of the patients' lives such as compliance with treatment, personal safety, financial autonomy, and caregiver burden. Research studies have demonstrated that cognitive rehabilitation (CR) neurocognitive symptoms can improve cognitive functioning and psychological well-being in patients with MCI (see "Treatment and Prevention of MCI on p.3).[1,7]

("Mild Cognitive Impairment: A Preclinical Stage of Dementia," continued from p.1)

but are viewed as a pre-clinical stage of dementia. After being diagnosed with MCI, the individuals' risk of developing dementia, including Alzheimer's disease, is about 6-7 times greater compared to older adults with normal cognition. For this reason, MCI is considered an important risk factor of dementia and Alzheimer's disease.[1,2,3,4]

A number of researchers have found that with some exceptions, MCI that affects memory (described as amnestic, most common type of MCI) is likely to evolve to Alzheimer's disease or vascular dementia, while MCI associated with a non-memory cognitive domain or with multiple domains usually converts to other types of dementia such as frontotemporal dementia, Lewy body dementia, primary progressive aphasia, etc.[4]

Research shows that the scores on neuropsychological tests of memory combined with the assessment of the volume of the hippocampus (a brain region linked to memory), as well as measurements of certain proteins found in the cerebrospinal fluid are among the strongest predictors of conversion from MCI to Alzheimer's disease. Other factors linked to converting to dementia include diminished ability to perform tasks of daily living, depressive symptoms, and motor problems.[1,2,4,5]

Some patients with MCI, however, never progress to dementia, or may even show some recovery from their deficits at the follow-up neuropsychological evaluation. Thus, MCI does not necessarily predict conversion to dementia or Alzheimer's disease, especially in younger individuals. Follow-up neuropsychological exams are needed to objectively evaluate the progression of MCI symptoms over time.[2,5]

In addition to neurological and cognitive symptoms, individuals with MCI may present with psychological disturbances. It has been estimated that between 35% and 50% of MCI patients experience neuropsychiatric symptoms, including anxiety, depression, apathy, irritability, and agitation.[1]

("Diagnosis and Assessment of MCI," continued from p.1)

Currently, the diagnosis of MCI is mainly based on the results of an objective neuropsychological exam, which is necessary for several reasons. First, there is a tendency among the older individuals to under-report or over-report their cognitive difficulties. For instance, the elderly may mistake the effects of normal aging on their memory, attention, and processing speed for symptoms of dementia. Conversely, they may overlook cognitive decline by attributing it to aging, or may have diminished awareness of their cognitive symptoms due to the effects of cognitive impairment. Their caregivers also may not know where the line between normal aging and symptoms of cognitive dysfunction lies.[6]

Objective neuropsychological test scores accurately reflect the patients' cognitive functioning taking into account their age, educational level, and gender. Thus, when older adults undergo neuropsychological evaluation, their results are based on how their age group performs on each specific test. This allows differentiating the effects of normal aging on cognition from clinically significant cognitive decline.[1,6]

Neuropsychological evaluation involves objective assessment of different functions that may or may not be affected in MCI. It measures the extent of neurocognitive deficits and helps monitor their progression over time. Neuropsychological evaluation typically includes numerous cognitive tasks such as memorizing stories, words, and pictures, answering questions, arranging blocks, and identifying patterns. When it comes to bilingual patients or those who are not fluent in English, the neuropsychological exam can be conducted entirely or partially in their native language.[9]

In addition to objective neurocognitive measures, neuropsychologist administers tests of sensori-perceptual and fine motor functioning with scores that are also based on the patients' age group. This is done in order to ensure that the patients' performance on tests is not affected by poor eyesight, hearing, or weak pencil grip.[1,4]

Research shows that neurocognitive tests of long-term verbal recall, executive functions, and selective attention are most sensitive for detecting MCI. Objectively identified weaknesses in these skills among the older patients can be interpreted as "red flags" associated with a higher risk of MCI, and follow-up neuropsychological exams and brain scans are needed to monitor these high risk patients.[1,4]

Evidently, neuropsychological exam may help diagnose individuals with MCI, and subsequently, identify those at an increased risk for developing dementia. The sooner MCI is diagnosed, the sooner the appropriate interventions may occur, which may slow the progression of cognitive deficits and delay the onset of dementia.[1,4]

About Dr. Rimma Danov

Dr. Rimma Danov received her PhD in clinical psychology from Adelphi University in NY. She completed her internship in clinical psychology and neuropsychology at Harvard Medical School and postdoctoral fellowship in pediatric and adult neuropsychology in a private clinic affiliated with NJ Medical School and the Robert Wood Johnson Medical Center. She is an assistant clinical professor at Penn State University, Dept. of Kinesiology, and has served as an assistant clinical professor at NYU School of Medicine, Dept. of Neurology, and Adelphi University, Derner Institute. In the past, she worked as a neuropsychologist for the NJ Devils Hockey Team and was engaged as a co-investigator of TBI in boxers at the NYS Athletic Commission.

Presently, Dr. Danov maintains a full-time private neuropsychology practice where she examines neurocognitive and neurobehavioral functioning of patients 2-90 years of age with various neurological and neuropsychiatric disorders, such as MS, TBI, CVA, Parkinson's, Alzheimer's, dementia, ADHD, PDD, Autism, learning disabilities, seizures, and many others, using state-of-the-art neuropsychological techniques. Dr. Danov also conducts and publishes research in these areas. She is available for medico-legal consultations and testimony.

Structural and Functional Neurological Alterations in MCI

It is well established that MCI and dementias are caused by structural and functional brain abnormalities that may or may not progress with time. Autopsy studies have demonstrated that patients with MCI present with heterogeneous neuropathology, ranging from Alzheimer's-like pathology, to vascular damage, to lesions thought to be not associated with degenerative dementias, such as hippocampal sclerosis or argyrophilic grains.[5]

Similarly to patients with Alzheimer's disease, mostly medial temporal lobe structures are involved in MCI. The number of neurofibrillary tangles (characteristic of Alzheimer's disease) in MCI are related to memory loss, which supports the link between amnestic MCI and conversion to Alzheimer's disease.[1]

According to the imaging studies, patients with MCI tend to show atrophy in entorhinal and hippocampo-amygdala regions and alterations in parahippocampal white matter fibers, which may be seen very early in the disease course. Research suggests that hippocampal alterations contribute to memory disturbances in MCI and Alzheimer's disease, since incoming sensory information becomes partially disconnected from the hippocampus, which plays central role in memory.[1,4]

As for the functional brain studies, MCI has been recently linked to reduced glucose metabolism in the hippocampus (see Image below). Some researchers believe that hippocampal glucose levels should be used as part of the diagnostic procedures in MCI.[1]

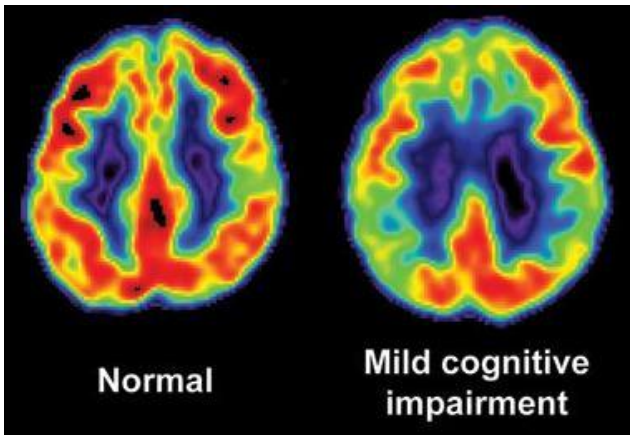
Additionally, MCI is associated with elevated levels of tau protein (t-tau) and several hyperphosphotylated isophorms (p-tauX, p-tau181, etc.) in the cerebrospinal fluid. These abnormalities which are also found in individuals with Alzheimer's disease. It is generally accepted that elevated t-tau levels reflect the degree of neuronal damage in the cortical regions typically affected in Alzheimer's disease.[8]

Treatment and Prevention of MCI

Early treatment is associated with better long-term outcomes in MCI, and treating this condition may be the most effective method of delaying progression to Alzheimer's disease. However, to date, no pharmacological interventions proven to treat MCI are available. Clinical trials involving the use of cholinesterase inhibitors (donepezil, rivastigmine, and galantamine), anti-inflammatory drugs (rofecoxib), and nootropics (piracetam) did not provide promising results. Some studies suggest that antioxidants (Gingkgo Biloba, selegiline, and vitamine E) may slow progression from MCI to dementia.[1]

It has been proposed that addressing vascular risk factors and depressive symptoms may be helpful in slowing the progression of MCI. Additionally, research shows that socially integrated lifestyle, as well as physical, and particularly, cognitive exercising in late life protect against dementia and Alzheimer's disease. In fact, cognitive rehabilitation (CR) can improve such functions as memory, attention, processing speed, mood, and psychological well-being and slow further cognitive decline in patients with MCI, which calls for increased use of this type of non-pharmacological treatment in MCI.[7]

Individual CR involves a customized program that includes various verbal and non-verbal exercises than may or may not be pencil-and-paper based to improve cognitive functions or compensate for them. It is recommended that before the beginning of CR, each patient's neurocognitive functioning is assessed by neuropsychological tests to objectively measure the extent of cognitive deficits. This allows designing an individual CR program that focuses on the specific deteriorated cognitive functions (memory, attention, information processing, reasoning), as well as subjectively reported difficulties with daily tasks (organizing work and chores, managing finances and medication intake, keeping appointments, etc.). The effectiveness of CR may be evaluated at the mid-point of the program and/or upon its completion by re-administering the neuropsychological tests.[5,9]



The PET scan above shows lower glucose metabolism levels (yellow and orange regions) in a patient with MCI compared to a normally aging individual.

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Editor

Dr. Rimma Danov, Ph.D.

Layout:

Natalia Shtompel, M. A.
Research Coordinator

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Languages

We are very much open to diverse cultures in this practice and value the quality of a bilingual neuropsychological exam performed in the patient's native language. Dr. Danov is a native Russian speaker. Her current clinical staff include native ***Russian***, ***Spanish*** and ***Hebrew*** speakers.

For ALL appointments and questions call: 718-667-5530

Office Locations:

Staten Island: (main office, forward **all** correspondence)
65 Kelvin Ave.
Staten Island, NY 10306

Brooklyn:
95-11 Shore Rd., Suite C
Brooklyn, NY 11209

Manhattan:

139 Fulton St., Suite 215
New York, NY 10038

Queens:

7613 113 Street, Suite 1F
Forest Hills, NY 11375

Long Island:
2900 Hempstead Tpke, Suite 217
Levittown, NY 11756

Dr. DANOV NEUROPSYCHOLOGIST, P.C.

65 Kelvin Avenue
Staten Island, NY 10306

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