Mild cognitive impairment in adult: A neuropsychological review

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Abstract

Mild cognitive impairment (MCI) is associated with an increased risk of developing dementia. This is clinically relevant overt dementia can be prevented if treatment strategies are devised for MCI. Neuropsychological deficits in this condition are very common and are important clinically for treatment and outcomes. We aimed to review various neuropsychological deficits in MCI. Further, we have presented the current evidence for nosological status, neuroanatomical basis, and clinical outcome of this heterogeneous construct. All published papers on the topic of neuropsychological deficits in MCI on Medline and other databases were reviewed. A wide range of memory and executive function deficits are common in MCI patients. However, several studies are limited by either improper designs or inadequate sample sizes. Several neuropsychological impairments like memory function and executive functions can be diagnosed in MCI. The evidence base for the exact neuroanatomical basis of MCI is not robust yet. However, given the wide range of outcomes, controversies and debates exist regarding the nosological significance of the deficits. Hence, more studies are needed to specifically locate the impairments and further delineate the construct of MCI.

Key Words

Cognition, dementia, mild cognitive impairment

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Introduction

Dementia is been increasingly recognized as the leading cause of morbidity in elderly and includes Alzheimer's disease (AD), vascular dementia, parkinsonian dementia, and lewy body dementia. Mild cognitive impairment (MCI) represents a transitional state between healthy aging and dementia and is characterized by cognitive impairments that are out of proportion to the age of the individual. However, they do not meet the commonly accepted criteria for dementia. Studies have suggested that individuals with MCI tend to progress to dementia over a period of time.

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In this review, we have presented the neuropsychological dimension of MCI by focusing on various cognitive deficits, their progression, and their patho-physiological mechanisms. For simplification, we have not included other domains of MCI like co-morbidities and neurochemistry, although these aspects are equally important from the cognitive perspectives. We have included the controversial issues of nomenclature and diagnostic confusions and have attempted to give neuropsychological answers to these controversies.

For the purpose of review, Medline, Pub Med, and Google search for English language literature was carried out for the past 15 years (1998–Present) using MeSH heading "mild cognitive impairment/analysis" and additional search terms like "classification," "physiology," "pathology," "radiography," "memory," "executive function," "outcome," "amnestic MCI," "nonamnestic MCI," "therapy," etc.

The papers were evaluated for results, relevance, and originality of findings or approach. Thereafter, the information derived was collated and critically evaluated for the purpose of the review.

Names and Concepts – The Issue of Heterogeneity

The introduction of the term and concept of MCI by Petersen, was followed by a series of controversies regarding the same, which was generally believed to represent a transitional state between normal aging and dementia.[1] Specifically, the criteria were criticized for their inability to adequately encompass the spectrum of cognitive deficits often observed in patients with milder forms of cognitive impairment. Several researchers are of the view that MCI could be a heterogeneous construct neuropsychologically rather than a single homogeneous clinical syndrome.[2,3] Although MCI is currently one of the most widely studied concepts in the dementia literature, many differences and inconsistencies exist regarding its definitions and concepts used in different studies, and there is clearly a need for better characterization and clarification of the concept as a whole.[4-6] Petersen *et al*., proposed three different MCI subtypes (amnestic, multiple-domain, and single non-memory domain) in an attempt to provide a better classification to this rather heterogeneous group of cognitive deficits.[7-9] These groups were later re-divided to include two major subgroups (amnestic and nonamnestic MCI), with further subdivisions within each (single- and multiple-domain).

A community-based study in Kolkata, India, determined the rates of prevalence of amnestic MCI to be 6.04% and that of multiple-domain subtype to be at 8.85%, with males having a preponderance of amnestic MCI and female having multiple-domain MCI.[10]

Given the uncertainty inherent in the current clinical concept of MCI, along with the significance of better accuracy in identifying and detecting prodromes of different dementia syndromes clinically, it is imperative that MCI be defined with more clarity and to decipher whether the diagnosis primarily represents a risk factor for only AD or whether MCI is more accurately described as being composed of a heterogeneous construct that includes different pathologies, neuropsychological profiles, and/or neurological markers.[11-13]

Although this need seems to be urgent, strangely enough, there is a relative dearth of studies attempting to empirically validate and verify the existence of the recently proposed MCI subtypes. It has been postulated that MCI possibly represents a heterogeneous group of individuals with different pathologies and neuropsychological profiles.[11,13] It was expected that MCI would not represent a homogeneous population and, instead, would be better characterized as a heterogeneous group based on neuropsychological scores. Specifically, Petersen and Morris (2005) hypothesized that the following two major groups emerging from the data have to be (1) a subgroup demonstrating a neuropsychological profile consistent with amnestic MCI (specific cognitive deficits in memory) and (2) a subgroup with a cognitive profile consistent with the nonamnestic subtype of MCI (mild impairments in non-memory domains such as executive functioning or speed of processing).[7] If the groups significantly differed on neuropsychological test results as well as on neuroimaging findings like white matter lesions, then these can indicate different underlying pathologies and contribute to improving our clinical characterization of the MCI construct.

Cognitive Deficits in Mild Cognitive Impairment: Memory

The accepted criteria for MCI include the presence of a memory complaint, impaired performance on age-adjusted memory tasks, intact general cognitive function, an absence of significant functional repercussions, and an absence of dementia.[1] Given the seminal role of memory impairment as the first basic criteria for MCI, the figures for prevalence necessitate extrapolation from non-amnesic, which averaged 16.77% (17-38%) in different studies.[14]

Nature of deficit

Memory deficits are the core problems in MCI. These memory deficits are not only important for treating MCI but also because cases of amnestic MCI (65-80%) convert to Alzheimer's dementia at a rate of 38 per 100 person-years.[15,16] It is however difficult to derive a universal equation of these memory problems given the various types of memory-related functions and diversity in the classification prevalent in the literature. Conceptually, for encoding of any form of memory, attention is the most important prerequisite. It is being increasingly recognized that attention deficits are prevalent in MCI. A direct impact of these attention deficits is on the working memory and other neuropsychological functioning of both AD and MCI. Saunders and Summers found that MCI group displayed deficits in attention processing, working memory, and semantic language along with impairments in verbal and visual memory.[17] Similar deficits in WM and executive attention functions have been observed in AD and MCI by Belleville *et al*.[18]

One of the most prevalent memory deficit encountered in amnestic MCI is the reduction in episodic memory that has adverse consequences on functioning of the subjects. Irish *et al*., (2011) attempted to study the relevance and impact of deficits in episodic memory, especially about routine events using a plethora of tasks relevant to daily functioning.[19] They found impairment in measures of acquisition, delayed recall (story-memory), and associative memory (face-name pairings), followed by everyday memory (for everyday mundane events) and spatial memory tasks (route learning and recall). Further, delayed associative memory performance at the baseline was a potential predictor of subsequent conversion to AD on exploratory logistic regression analyses revealed that delayed associative memory performance at baseline was a potential predictor of subsequent conversion to AD.

Information that needs to be remembered is rapidly lost over time in MCI, as demonstrated by poorer performance on longer retention intervals in the Brown–Peterson (BP) procedure and inter-trial forgetting of items on a word list learning task, although the extent of the deficit in MCI is not as extreme as in AD.[18,20]

Prospective memory (PM) is another important cognitive domain that can serve as an early sign of memory failure in MCI-AD. While retrospective memory is the ability to recall information or events from the past, PM is the ability to remember and perform an intended action at an appropriate point in the future.[21]

Remembering to do a designated task in future such as taking medication, paying bills by due date, and visiting doctor on the day of appointment are examples of PM. PM is relevant for social functioning, treatment adherence, and all instrumental activities of daily living.[22,23]

PM may be a more pronounced deficit than retrospective failure in MCI, probably reflecting the greater self-initiated retrieval demands involved in the PM task used. The relationship between the prospective retrieval and retrospective memory functioning in MCI has been studied and both the prospective component and the retrospective component are impaired in MCI.[24] Declarative memory dysfunction results in impairment of retrospective memory, while deficits in executive abilities or reflexive mechanisms explain the impairment in PM.

Both familiarity based memory and recollection have been found to be impaired in amnestic MCI.[25] A well-designed study was conducted by Alqarabel.[26] His results indicated that recollection decreases with age and neurological status, while familiarity remains stable in the elderly normal controls (NC). In contrast, both recollection and familiarity are deficient in MCI. Alqarabel found that specific encoding situation generated deficits in recollective and familiarity mechanisms of retrieval occur in subjects with MCI. Other amnestic cognitive deficits in MCI include impairment in fluid intelligence, working memory, semantic fluency, design fluency, and category fluency.[27,28] Not all of these are strictly memory deficits and include elements of executive dysfunction as well.

Verbal learning memory is another domain that has been studied in detail in MC patients. Ribeiro *et al*., (2007) used the California verbal learning test to details memory performance in MCI patients and compared them with normal and AD patients.[29] They found that less semantic clustering was found in the MCI group, but both MCI and controls showed benefit from semantic cueing. Poorer semantic clustering and lower strategy use as well as decreased control beliefs to compensate memory deficits have also been found.[30] These studies show that MCI patients have difficulties in all the stages of verbal memory processing including acquisition, consolidation, and recall stages.

These memory deficits are not limited to the amnestic MCI, but are also present in non-amnestic MCI, albeit at lower intensities. In individuals with non-amnestic MCI, episodic memory and other cognitive domains were impaired.[31,32] The PM Test (PMT) event-based PM, the Symbol Digit Modalities Test Accidental Memory, Stick test (ST) [visuo-constructional memory, and Working Memory components] were impaired; however, these were better than the impairments seen in amnestic MCI. However, semantic memory was affected to a degree comparable with that in amnestic MCI.

However, subjects with MCI are often aware of their memory deficits.[33] They are also able to assess the demands of an externally driven meta-memorial situation adequately and also update memory self-knowledge accurately based on experience. Preserved metamemory skills can be utilized to design targeted behavioral interventions involving compensatory strategies for daily issues related to memory deficits.

Cognitive Deficits in Mild Cognitive Impairment: Executive Functions

Executive functions are a group of highly interrelated functions that include planning, initiation, and regulation of behavior, working memory, response inhibition, and task switching.[32,34] The lack of standardized operational definition has had adverse consequences for both research and clinical practice.[35]

Impairment in frontally mediated behaviors is widely prevalent in MCI and may be found prior to any decline in daily functioning.[36] The huge differences in prevalence figures for executive MCI (3-30%) is due to the differences in recruitment criteria and assessment methods.[37,38]

The significance and nosological status of executive dysfunction in MCI is open to debate.[39] In recent years, there have been several perspectives on the conceptualization of executive dysfunction in aging/MCI. Details of these concepts are out of the scope of this review. However, it is important to be aware of different perspectives. Different theories postulate that the executive function deficits can be considered as one of the following:

- Variant of normal ageing—Change in the frontostriatal network supporting executive functions may occur as a part of healthy aging[40,41]
- Distinct subtype of MCI—Attention/executive MCI subtypes is regarded as a distinct predementia subtype[42,43]
- Early symptom or prodromal stage—Executive MCI may represent an earlier phase of Alzheimer's dementia separate from amnestic MCI and may remain unnoticed as both attention and executive deficits contribute to the observed memory deficit[44]
- Indicator for type of subsequent dementia—Subjects with multiple-domain MCI with executive dysfunction leading dementia are less likely to have an Alzheimer's-type dementia and are more likely to have cerebrovascular disease, stroke, vascular dementia, and other dementias.[45-48] EF is a weak cognitive marker of cerebrovascular disease in MCI, whereas episodic memory is more robustly associated to MCI-AD
- Prognostic marker — The prognostic predictability of executive dysfunction is controversial. Executive dysfunction may have adverse impact on the activities of daily living and enhance the risk of conversion from MCI to AD.[49] Further, conversion from MCI to AD after 2 years is better predicted by baseline test of executive function and functional capacity than biomarkers like MRI or CSF examination.[50]

Nature of deficit

The question of the exact nature of executive function deficit in MCI remains to be clarified. In contrast to the well-established finding of memory deficits in MCI, the executive function tests have revealed no-deficits on some studies to global impairments of EFs in others.[51,52] Zheng *et al*., found that both overall EF and all of the core EF components in the Miyake model of EF (working memory, task switching, and response inhibition) were significantly impaired in amnestic MCI patients, regardless of whether they had shown obvious clinical

executive dysfunction.[34] This is perhaps the only study that has evaluated the overall executive functioning of such patients.

A study designed exclusively to find out the selectivity of executive function deficits in MCI patients revealed impairment in planning/problem-solving and working memory, but not in judgment, among the MCI patients.[53] This was true even among those with a pure amnestic-MCI, which showed least deficits.

Other studies have also found impaired cognitive planning in MCI (on trail-making, verbal fluency tests, Porteus maze test), but no deficits in pre-potent response inhibition (no-go accuracy, two aspects of the Stroop effect, and negative priming).[54] However, *Traykov et al*., in 2007 reported deficits in response inhibition and task switching as well as cognitive rigidity in MCI, as evidenced by perseverations on Modified Card Sorting Test and lower performance on the Stroop test.[55] Similarly, Perry *et al*., reported specific problems with response inhibition and attention switching in a group of patients who were only impaired on episodic memory tests.[56]

Deficits in problem solving/planning and working memory are found in all MCI groups, even in single-domain amnestic MCI with more severe deficits in multiple-domain MCI subjects.[53] Similarly, EF deficits were found in pure amnestic MCI patients by Kramer *et al*., wherein they found that the MCI group performed less well than the normal control group, but better than the AD group on fluency of design and category fluency, modified trail tasks, and the Stroop interference condition.[28]

MCI individuals with executive dysfunction also have poorer verbal memory performance, suggesting complex interrelationship between memory and executive function.[57]

Subjects with amnestic MCI also have complex visuospatial executive dysfunction that can be explained by deficits in the formulation of initial strategy during early visual learning and online maintenance of task rules.[58]

Even subjects with amnestic MCI, irrespective of any clinically apparent executive dysfunction, have significant and comparable impairment in executive function tasks (the stop-signal task, the keep-track task, 2-back task, and the more-odd shifting task), suggesting that all the chief components of executive function (working memory, task switching, and response inhibition) suffer similar impairment.[52]

A day-to-day application of executive functions in MCI patients was tested by Griffith *et al*., who evaluated the financial abilities of such patients using the Financial Capacity Instrument.[59] Relative to controls, the MCI group demonstrated impairments in episodic memory, executive function, semantic knowledge, written arithmetic, and spatial attention, which were revealed by impairments in the domains of conceptual knowledge, financial transactions, and in overall financial capacity. At the same time, control and MCI groups performed significantly better than patients with AD on most financial capacity and cognitive measures.

Other Cognitive Impairments

In addition, the memory deficits subjects with MCI show deficits in abstract thinking.[60]

Further subjects with MCI also exhibit deficits in visual personal familiarity and recognition of facial emotional expression.[61,62] They also have impairment in accessing contextual knowledge that aids in delineation of general concepts or identification of an object or a person.[61] Such deficits lead to impaired social cognition and may adversely impact the patients' efficacy in handling complex situations and tasks.

Pathology and pathophysiology of mild cognitive impairment

In spite of the ever-growing efforts laid on identifying the candidates of MCI and its progression to AD, much less is known about its pathology and pathophysiology. In a recent study by Yan *et al*., the results from mGCA showed decreased effective connectivity among the middle temporal gyrus, hippocampus (HC), and fusiform gyrus, as well as between the precuneus/posterior cingulate cortex (PreCN/PCC) and HC in patients with amnestic MCI.[63] In a study by Liu *et al*., the participants with MCI (persisting MCI) showed accelerated sulcal widening, especially in the superior frontal and superior temporal sulci.[64] The sulcal morphology of subjects who reverted clinically from MCI to NC was more consistent with stable NC than with persisting MCI.

Nho *et al*., observed strong associations between ADNI-Mem and atrophy of medial and lateral temporal lobe. Reduced ADNI-Exec scores were associated with advanced GM and cortical atrophy across broadly distributed regions, especially in the bilateral parietal and temporal lobes.[65] On evaluation of ADNI-Exec adjusted for ADNI-Mem associations between GM density and cortical thickness, specifically in the bilateral parietal, temporal, and frontal lobes were found. These associations emerged strongest in patients with MCI and AD during within-group analyses.

Recent evidence indicates that neurofibrillary tangles (NFT) density is also greater in MCI than in normal cognitive aging, although no differences in the density of amyloid plaques were observed.[66] The distribution of NFTs is primarily limited to the HC and entorhinal cortex in the early stages of these cases and gradually becomes more widespread with disease progression.[67,68] Furthermore, NFT density in the medial temporal lobe is strongly correlated with memory dysfunction.[66] A recent study report comprising of individuals who were followed longitudinally until death found a significantly higher tangle counts in the nucleus basalis of Meynert in subjects who had converted from cognitively normal to MCI than in cognitively NC.[69]

Subjects with executive dysfunction MCI have thinning in bilateral dorsolateral prefrontal and posterior cingulate cortices.[57] Furthermore, they have more white matter radial and mean diffusivity in regions underlying medial orbitofrontal, rostral middle frontal, caudal anterior cingulate, posterior cingulate, and retrosplenial and entorhinal cortices. The inhibition/switching performance are associated with

white matter radial and mean diffusivity underlying superior frontal, rostral middle frontal, lateral/medial orbitofrontal, and retrosplenial cortices, while caudal middle frontal cortical thickness was associated with attention and divided attention.[37]

Ancelin *et al*., indicated that the use of anti-cholinergic drugs can also lead to a clinical picture similar to MCI, with poor performance on attention, reaction time, narrative recall, delayed non-verbal memory, visuospatial construction, and language tasks.[70] Although these subjects are not at increased risk for dementia, still caution is advised before using anticholinergic drugs in elderly people and before prescribing acetyl cholinesterase in subjects with MCI who are already receiving anticholinergic agents.

Neuroimaging Studies in MCI

Several studies in recent years have also focused on neuroimaging findings in different neuroimaging modalities by using different computational techniques in subjects with MCI. These are too extensive to be subsumed in a single segment and, in fact, merit a separate review, similar to the review by Schuff and Zhu.[71] We have presented some pertinent research work and opinions on this domain.

Several studies have demonstrated structural changes in the brain on MRI imaging in MCI. These include reduction in volumes of HC and entorhinal cortex with reductions lying between NC and AD.[72-75] Reduction in the volume of the CA1 and subiculum subregions of the HC is a good predictor of MCI progressing to AD.[76]

In addition, the rate of reduction in the volume of HC and entorhinal cortex is more rapid in MCI than in NC.[77,78]

Follow-up studies using voxel-based morphometry (VBM) measurement on serial MRI scans in subjects with MCI have revealed that loss of grey matter volumes is seen in anterior HC, amygdale, and entorhinal cortex early in the course of disease and progresses to the entire HC, temporoparietal, amygdala, and even frontal lobe regions as the subjects convert to frank AD.[79,80]

Fan *et al*., studied the pattern of atrophy across different regions of the brain in subjects with MCI and AD using a non-linear multivariate analysis technique called high-dimensional pattern classification.[81] About an overwhelming two-thirds of the subjects showed extensive brain atrophy across several regions of the brain, while about one-third had findings similar to healthy controls. The ones who had extensive brain involvement similar to AD also showed a more rapid decline in mini–mental state examination in follow-up over a year, thereby yielding a useful marker for assessing prognosis in MCI.

A comprehensive study on MCI by Mridula *et al*., showed that nearly 70% had abnormalities on magnetic resonance imaging (MRI) with vascular lesions in more than one-third, diffuse atrophy in about one-fifth, and medial temporal lobe atrophy in one-sixth of the subjects.[82]

Some researchers have also attempted to study the subtypes of MCI on neuroimaging. A study by Griffith *et al*., focused on volumetric assessments on MRI in amnestic MCI subjects and found that reduced volumes of HC, angular gyrus, and precuneus were correlated with impaired performances on neuropsychological tests.[83]

However, structural changes on MRI are not specific to MCI and may occur in other neurodegenerative diseases and chronic vascular compromise.[84,85]

Hence, some researchers advocate use of non-invasive multimodal MRI techniques for structural, functional, metabolic, and hemodynamic assessment of the brain as a surrogate biomarker to assess MCI and risk for MCI and AD in cognitively intact individuals; the heterogeneity and non-specificity of findings limits such clinical application currently.[86]

While, traditionally, studies have focused on grey matter deficits, white matter alterations have also emerged as focus of interest with the emergence of diffusion tensor imaging (DTI) with significant findings demonstrated in regions such as the HC, thalamus, posterior cingulum bundle, regions in posterior white matter, para HC, and temporal, frontal, and parietal lobes.[87-91]

The neuroimaging findings on DTI have been found to also correlate with lobar specific cognitive functions changes like episodic memory and executive functions.[92]

Goldstein *et al*., investigated the association of integrity of white matter in medial temporal lobe on DTI and memory.[93] They found that, although loss of integrity of white matter in medial temporal lobe has been associated with impaired performance, the discrimination did not categorical indicate toward unconscious use of alternative encoding strategies such as image visualization of verbal information material and verbal encoding of designs.

In a remarkable study, DTI of cingulum fiber bundle was found to increase the diagnostic specificity of MCI to 75% from the 63% accuracy conferred by reduced hippocampal volume alone on structural MRI.[91]

[18F]-2-fluoro-2-deoxy-Dglucose-positron emission tomography (PET) studies regarding cerebral metabolic rate of glucose consumption (CMR glu) have found substantial CMRglu reduction in MCI in the HC limbic system, medial thalamus, and posterior cingulated, corresponding to the reduction in volumes seen on structural MRI.[94,95]

Single-photon emission computed tomography (SPECT) studies on cerebral blood flow (CBF) in MCI have revealed diminished CBF in the parietal cortex, PCC, and precuneus in MCI with high rates of CBF decline in the HC and para HC gyrus on serial SPECT studies MCI, especially in those progressing to frank AD.[96-98]

Outcome of MCI

It is a well-known fact that not all MCI patients progress to florid AD. The religious orders study, for example, performed postmortem biopsies and found that, of the 134 patients

diagnosed with MCI, 54.4% had pathologically diagnosed AD, 19.4% had mixed pathologies, and 39.1% had gross macroscopic infarcts.[99]

Of the 179 persons diagnosed with probable AD, nearly half (45.8%) had mixed pathologies, most commonly AD with macroscopic infarcts, neocortical Lewy body disease, or a combination of the two.

Thus, identification of the factors that facilitate this progression is of utmost importance for application of both pharmacological and non-pharmacological therapies. Recently, much stress has been laid on the identification of the factors that prevent and facilitate the progression of MCI to AD. Recognition of MCI as a transition phase between healthy ageing and dementia is important in the investigation of treatments aimed at secondary prevention of dementia.

People with MCI progressed to dementia in several studies at very different rates, with an average conversion rate of 10% per year. This suggests a linear progression of conversion to dementia over time.[1,5,100,101]

Petersen reported that, after approximately 6 years, 80% of the MCI cohort has progressed to dementia.[1]

Most of the current knowledge stems from clinical samples. This study utilized a representative general population for sampling and examined the evolution of MCI to dementia over an observation period of 6 years.

Ganguli *et al*., found that, as compared to clinical samples, community based samples were less likely to worsen (0-3% progressed to CDR rating >1 and ≤20% developed severe cognitive impairment and more likely to improve or reverted to normal (6-53%) or stay stable (29-92%) over a follow-up period of 1 year.[102]

Huey *et al*., state that single-domain executive MCI has a better outcome than amnestic MCI and that executive dysfunction in multiple-domain MCI does not independently increase the risk of progression to dementia.[47]

Subjects with MCI may also progress to non-AD outcomes such as vascular dementia, especially if they have subcortical microvascular disease, mild parkinsonian signs at baseline, non-amnestic MCI, multi-cognitive deficit MCI, vascular comorbidity, signs of vascular disease on brain imaging, mood disorders and behavioral symptoms.[103-105]

Subjects with MCI may also go on to develop other neurodegenerative disorders like lewy body disease.[106] Furthermore, nearly one-third of the subjects with MCI may have potentially treatable causes like hypothyroidism, normal pressure hydrocephalus, vitamin B12 deficiency, and subdural hematoma.

A meta analysis of 41 robust inception cohort studies by Mitchell *et al*., revealed that the average annual conversion rate to dementia is 5-10% and that most subjects do not progress to dementia even on a follow-up of up to 10 years.[107]

In the meta analysis, the annual rate of conversion to dementia, Alzheimer's dementia, and vascular dementia was 9.6%, 8.1%, and 1.9%, respectively, in specialist clinical settings and 4.9%, 6.8%, and 1.6% in community studies.

Several studies also report that as many as 33-55% actually improve and revert to normal cognition over time. Sachdev *et al*., investigated factors associated with reversion of MCI to normal cognition or the good prognostic factors.[108]

The data derived from prospective, population-based Sydney Memory and Ageing Study sample revealed that higher complex mental activity, greater openness to experience, better vision, better smelling ability, larger combined volume of the left HC and left amygdala, and a larger drop in diastolic blood pressure between baseline and follow-up was associated with reversion to normal cognition, while presence of multiple-domain MCI, a moderately or severely impaired cognitive domain or an informant-based memory complaint were poor prognostic markers for MCI. The association of fall in diastolic blood pressure is significant, as it suggests that a tighter control of vascular factors may be promising intervention for MCI. In addition, intervention programs incorporating cognitively enriching experiences may also be beneficial.

Conclusion

MCI is characterized by a variety of neuropsychological impairments including but not limited to memory function and executive functions. The classification of MCI has valid neurobiological underpinnings, but needs more discriminatory research regarding the exact nosological status and prognostic significance. The evidence base for the exact neuroanatomical basis of MCI comprises of neuropathological and neuroimaging investigations, but it is not robust yet. However, to address the controversy and debate regarding various aspects of MCI, better-designed systematic studies are required before the translation into clinical applications can be devised.

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