

Blocking progression from intervenable mild cognitive impairment to irreversible dementia, what can we do?

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SUMMARY With the rapid growth of the elderly population, dementia has become a global challenge that governments must address. Given the incurable nature of dementia, rehabilitation interventions starting in the mild cognitive impairment (MCI) stage may offer a solution. For a rehabilitation intervention to be implemented as early as possible, existing problems of identification of MCI and development of MCI-specific forms of rehabilitation must be addressed. Use of computer technologies such as virtual reality and artificial intelligence might be helpful in overcoming these problems. Multi-disciplinary integrated approaches to rehabilitation should be the direction that dementia-related rehabilitation takes in the future. In addition to early rehabilitation, prevention of cognitive decline through the development of public community-based services for the elderly might be a more reasonable approach.

Keywords dementia, mild cognitive impairment, virtual reality, rehabilitation, elderly care facilities

1. Background

Dementia is a pathophysiological state characterized by a decline in cognitive domains including memory, attention, movement, language, communication, and executive function. It is usually caused by a spectrum of diseases, such as Alzheimer's disease (AD), vascular dementia, dementia with Lewy bodies, and Parkinson's disease-related dementia. Dementia markedly impacts activities of daily living (ADL) and quality of life (QOL), with dementia-related death being frequently reported (1). Todd *et al.* reported that the median survival time from dementia onset ranges from 3.3 to 11.7 years, with most studies indicating 7-11.7 years (2). This implies that patients with dementia must live for an extended period in a state requiring care, significantly increasing the burden on their families and society. Dementia has become a global public health concern with aging of the population. Dementia typically progresses through seven stages (Figure 1). Once patients reach the dementia stage, existing treatments have minimal impact on their functional activities and QOL (3). Mild cognitive impairment (MCI) is the initial stage before mild dementia, where cognitive impairment is mild and does not affect the ability for self-care. The annual

conversion rate of MCI to dementia is reportedly 10-15%, approximately four times that for individuals with normal cognition. Over 80% of individuals develop dementia after six years (4). Nonetheless, intervention in the MCI stage might be beneficial, particularly with early rehabilitation (5,6). In this regard, the MCI stage might be the only stage when intervention could prove useful. Thus, timely identification of MCI and subsequent effective interventions might be the only useful approach for dementia so far.

2. Identification of MCI

Identifying cognitive impairment, and MCI in particular, is a challenge. Over 50% of individuals with dementia are left undiagnosed or diagnosed late in primary care settings (7). Several factors contribute to this issue:

i) Most widely-used neuropsychological tools for dementia, such as the Montreal Cognitive Assessment (MoCA) and Mini-Mental State Examination (MMSE), are investigator-reported scales. Although some objective tasks are included, some items remain subjective (8). Importantly, the thresholds for MCI are questionable. A recent study reported that the conversion rate from MCI to AD increased to 84% when the MCI threshold was set

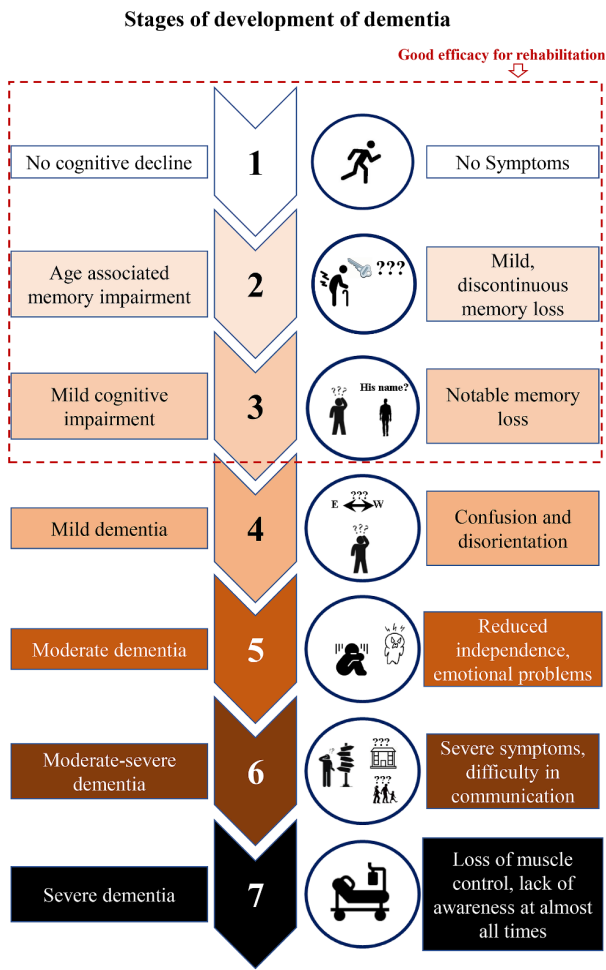


Figure 1. Stages of dementia.

to 22.85 (vs. the recommended 16). Since the threshold to identify MCI is crucial, a better threshold for MCI was proposed for clinical settings according to the subtypes of dementia (9).

ii) Compliance with dementia-related tests is questionable, as patients' individual status and environment may greatly influence diagnosis. For example, the elderly commonly have age-related hearing loss (ARHL). Whether the poor performance in these tests is due to ARHL is still uncertain (as an example, they cannot properly hear the investigator's questions) (10).

iii) Biomarkers like amyloid-beta (Aβ) and tau protein have been found to predict the progression from MCI to AD, but the actual diagnostic value of those biomarkers still requires further verification. A study reported that the combination of Aβ1-42 and Tau had a high sensitivity of 95% and a specificity of 83% in predicting the progression of MCI to AD (6).

iv) Functional neuroimaging, such as positron emission tomography and functional magnetic resonance imaging (fMRI), might be helpful in identifying MCI. For example, a previous study by the current authors identified an MCI-related pattern of brain changes (11).

However, such methods need to be verified further with robust evidence. Moreover, the prohibitive expense of these examinations might preclude their verification in a large-scale clinical trial, as well as their clinical use.

Thanks to advances in computer technologies in medicine, evaluation of an individual's behaviors has become possible, including evaluating cognitive changes in real time and remotely (12). Virtual reality (VR) equipment can be used to develop many objective tasks. Wearable sensor-based equipment can be used to check a patient's trajectory in real time. Apps for a smart device can be developed to assess cognitive functions. All of the acquired data can be transmitted wirelessly and compiled on a server in the cloud, and then the technologies of artificial intelligence (AI) and machine learning can be used to analyze these data, hopefully constituting an AI-based approach to diagnosing MCI.

3. Rehabilitation interventions for MCI

Compared to patients who have been labeled as "handicapped" or "disabled", patients with MCI commonly exhibit a mild decline in cognitive functions and ADL that might be amenable to intervention and reversible with rehabilitation (13,14). Cognitive training has been found to be effective in modulating cortical and subcortical neural functions, maintaining a resilient and healthy cognitive state, preventing cognitive decline, and delaying the progression of cognitive impairment in patients with MCI (15). Therefore, rehabilitation for MCI patients should be initiated rapidly after the diagnosis is confirmed. Several principles should be considered in clinical settings for MCI rehabilitation:

i) The principle of humanity, which means that forms of rehabilitation should be devised to minimize the burden of intervention. They should be friendly, inclusive, and sustainable. Psychological and emotional support is also indispensable.

ii) The principle of goal-directed rehabilitation. Setting a reasonable rehabilitation goal is important. Rehabilitation goals should be set in conjunction with the patient's expectations along with the patient's physical condition. Patients with MCI, and even patients with mild-to-moderate dementia, may help to set the rehabilitation goal (16).

iii) The principle of personalization. This is crucial to the patient's adherence to the rehabilitation plan. Lissek and Suchan reported on Maximizing Cognition (MAXCOG), a home-based four-session individualized face-to-face cognitive rehabilitation intervention (15). This personalized rehabilitation plan achieved satisfactory efficiency in patients with MCI and early dementia (15).

Multi-disciplinary integrated approaches to rehabilitation should be the future direction for dementia-related rehabilitation. Older patients often suffer from multiple frailty-related conditions (17).

Accordingly, a comprehensive rehabilitation plan is indispensable. For instance, physical exercise is commonly combined with psychological rehabilitation and nutritional interventions for patients with MCI, which helps to improve the patient's overall status. Buele *et al.* reported that dual intervention (sequentially conducting motor and cognitive training in sessions of 40 min per day, twice a week for 6 weeks) improved cognitive function in patients with MCI, and their MoCA-S scores increased from 22.36 to 25.29 (18). The efficacy of combining other technologies and cognitive rehabilitation to treat MCI was widely reported, including computer technologies and non-invasive brain stimulation (NIBS) (19). The combination of NIBS and computer-assisted cognitive rehabilitation should be useful in preventing cognitive decline in healthy older adults (20). VR is a booming technology, and its value in cognitive rehabilitation has been reported (21). Recently, Porras-Garcia *et al.* reviewed immersive VR training for patients with cognitive impairment and depression (3). They noted that use of VR training can help patients overcome the negative emotions. Improvement in the domains of attention and memory can be achieved by stimulating neurotransmitters, including the cholinergic and dopaminergic systems. The advantages of this VR-based rehabilitation lie in the full compliance of patients. First, the VR technology allows a therapist to design a full-fledged, fun rehabilitation program based on the patient's condition and requirements and to maximize the patient's motivation to participate. Second, home-based telerehabilitation could be developed, and it might be easily accepted by the elderly. Third, VR-based rehabilitation may be subtly designed to focus on training in ADL and compensatory cognitive-behavioral memory (3). Thus, VR-based tools could be used in cognitive rehabilitation.

4. Problems in elderly care facilities

Elderly care facilities, such as nursing homes (NHs), are set up to provide 24-hour professional nursing care for older people who cannot be cared for at home but who do not require hospitalization. The original intent behind a NH is to reduce the burden on families and improve the QOL of these older people. However, older people in NHs are more likely to develop cognitive problems. A meta-analysis of 53 studies covering 17 countries reported that the overall prevalence of MCI in older people in NHs was significantly higher than that in the general community (21.2% vs. 17.3%) (22). Reasons for that might be a lack of care, a worse mood due to being alone, and being in an unfamiliar environment. However, given the increasing older population, such community-based nursing and group rehabilitation might be the trends of the future. Thus, more humane and friendly elderly care facilities need to be established. To that end, here are several suggestions based on the

status quo of NHs and the current authors' experience:

i) Establishment of a family-style NH. This novel NH provides fast, effective, flexible care. More importantly, it allows patients to be in a family-like environment, including friendly people, familiar furniture, interesting programs, and positive social interactions. In addition, the NH should be conveniently located to meet with family members. Such an NH would help to improve the well-being of residents, help to maintain their mental health longer, and also help to prevent further decline. Indeed, such small-scale, family-style care facilities have been increasingly established in developed countries such as Sweden, the Netherlands, and the United States (23).

ii) Professionalization of nursing staff and criteria for care. First, the quality of care depends on the nurse-patient relationship and the caregiver's ability to communicate and interact with older people, which helps to create needs-oriented care and a respectful and reliable relationship between the caregiver and the elderly patient. Second, criteria for care need to be established and rigorously followed. In this regard, appropriate training and education of the staff of NH is indispensable.

5. Conclusion

With the rapid growth of the elderly population, the problem of dementia has become a tough nut to crack but will have to be faced by governments worldwide. Due to the incurable nature of dementia thus far, rehabilitation interventions starting in the MCI stage might be a solution. Beyond these, prevention of cognitive decline might be more reasonable. Development of public community-based services for the elderly might be a useful solution, since a study reported that a 10% enhancement in the coverage of community-based services might lead to a 1.4% reduction in the probability of residence in an NH (24). Indeed, now is the right time to seriously think about how to fight dementia.

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