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Study protocol: Language profile in mild cognitive impairment: A prospective study

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Abstract

Background: The present study will be a longitudinal investigation of language abilities in individuals with mild cognitive impairment (MCI). The research question will include whether there will be an evidence for language impairment in individuals with MCI, and if so, what aspects of language will be the most affected and whether language abilities will be significantly changed over a 12-month period.

Methods: We will diagnose 30 individuals with mild cognitive impairment (MCI), Alzheimer's disease (AD), and controlled participants using Montreal Cognitive Assessment-Basic (MoCA-B), as a cognitive test, and by asking expert opinions and conducting interviews. Participants will be selected from memory clinics and nursing homes in Tehran during 2018-2019. A comprehensive language test (Barnes Language Assessment (BLA)) will be performed to obtain baseline performance in the elderly. These tests will be repeated after 3, 6, and 12 months. Repeated measures analysis of variance (ANOVA) will be used to determine whether there will be a significant change in participants' language abilities over a 12-month period. In the case of deficient language performance, a discriminant function analysis will be used to identify the language task type that will be highly sensitive to change.

Results and Conclusion: The present study will provide evidence for the nature of language change and will be done in a-year course on individuals with MCI and AD and on healthy elders. Also, in this study, the relative sensitivity of various language components to MCI will be determined, and the relationship between language performance and performance on (MoCA-B) neuropsychological test will be examined.

Keywords: Mild cognitive impairment (MCI), Alzheimer's disease, Language profile, Early language impairment

Conflicts of Interest: *None declared*
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Introduction

Aging is associated with changes in cognition and dementia-producing diseases. Despite the fact that normal aging does not significantly affect people's ability to take care of themselves, Alzheimer's disease has profound financial, social, and emotional effects on patients and governments (1, 2). Therefore, it is of paramount importance to find faster, easier, and less invasive tools for diagnosing individuals at MCI stages of AD because pharmacological options and life-style changes can be used to prevent or slow down the evolution of dementia (1). The rate of dementia develops with age, and it has thus become a vital health problem worldwide (3).

The increase in the aging of the population creates problems in the demographic structure of developing countries such as Iran (4). Overall, 10% to 20% of people over the

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↑What is "already known" in this topic:
Aging was increased from 3.9% during 2007-2012 to 8.26% in 2012 in Iran, making it a country with an aging population. Therefore, both MCI and AD are common consequence of this phenomenon.

→What this article adds:
In this prospective study, the most prominent means of communication between MSI patients (eg, language skills) will be studied, and also the sensitivity of language skills to the progression of MSI will be studied.

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age of 65 are affected by MCI, and 12% of them have early AD. The risk of dementia increases with age. Therefore, an early diagnosis of this disease and changing into subtypes of dementia disorders are extremely important.

MCI is an intermediate stage between healthy aging and AD, and its common symptoms are amnesia and difficulty in remembering a conversation. These symptoms may remain unchanged for years, change into AD, or improve in some cases (5, 6). In the present study, the definition of MCI is based on DSM-V criteria. According to this definition, MCI is associated with a decline in a variation of cognitive domains, including attention, executive function, learning and memory, language, motor and cognitive skills, and social understanding. Based on this definition, these cognitive deficits cannot be explained by other psychiatric and mental disorders, such as major depression, Alzheimer's disease, and Huntington's disease (HD) (7).

Language processing is impaired at the early stages of Alzheimer's disease. Some common aspects of impaired language include verbal fluency (8), naming (especially animal naming) (9, 10), semantic knowledge (11, 12), and discourse processing (13). Numerous researchers have studied AD or MCI with memory problems and ignored or excluded other disorders such as language disorders. A few studies have been conducted on other cases, especially on linguistic issues (14). A subgroup of patients with MCI could be those who have memory problems, while there are other groups with other cognitive abilities in addition to impaired memory (6).

Awareness of the nature of linguistic performance is very important as it is closely related to the rapid progression of the disease and the overall decline of the brain. Therefore, researchers have studied language complaints as the early signs of MCI and AD (15-17). The early language damage of MCI is created from failure at the pragmatic and semantic level of language process (18). Learning the nature of language performance is highly important as it is associatedd with a faster progression of the disease (19) and brain deterioration (20). Lexical semantic treatment indicates positive therapeutic effects in early AD (20). Therefore, it is essential to describe language deficits in studies on people with MCI to reveal the difficulty in verbal fluency, especially in categorizing, confrontation naming, and language comprehension. However, their abilities to make grammatical judgment seem to be fully or partly intact (22, 23). Discourse analysis man be a sensitive component for investigating language performance impairment at early stages of the brain illness. In this regard, different results have reported impairments in semantic function such as lexical decision making, semantic categorization, and semantic coding. A variety of results have reported the receptive and expressive speech processing in individuals with MCI and syntactic ability (5). In general, language impairment in individuals with MCI is typically associated with semantic processing, but syntactic processing partially remains unaffected (23). However, a few studies have been conducted on the early language changes in individuals with MCI. Despite the fact that other researchers have reported changes in language abilities in individuals with MCI, no longitudinal study has been done on the changes in language skills and knowledge.

The present study will aim to investigate whether clinicians will be able to diagnose people with MCI according to language function analysis.

Methods

The study will be non-experimental, prospective, and longitudinal with case-control design.

Participants

The ethics of the present study will be evaluated by the Research Council, School of Rehabilitation and the Ethics Committee of Tehran University of Medical Sciences (TUMS). All participants will sign consent forms. The statistical population will consist of 3 groups: those with MCI, AD, and a control group, with each group consisting of 30 participants. Participants will be selected from those who have already registered in our databases.

The participants will be enrolled according to the exclusion and inclusion criteria. In this phase, we will accept all types of MCI (aMCI and NA-MCI). At this stage, we will accept all types of MSI patients, as different MSI types have memory conflicts and we do not know which linguistic function is affected (6).

Inclusion and exclusion criteria

Control participants will be enrolled according to the following criteria: normal cognitive ability based on neuropsychology tests; absence of neurologic diseases based on the neurologist's approval; aged 45 years and over; non-alcoholic drinkers; non-consumption of psychiatric drugs; antiseizure medications; non-consumption of hypnotic pills; normal hearing; normal or corrected vision; and absence of head trauma. Inclusion criteria for those with MCI and AD will be confirmed according to cognitive tests (MoCA and a new version of MoCA in the present study, MoCA-B), self-report, face-to-face interviews, filling out demographic information, and expert's views (7). Other inclusion criteria will be similar to those set for the control group.

Assessment

All MCI and AD participants over 45 years will be selected from memory clinics and special hospitals. Both groups will undergo formal and informal tests. First, they will be diagnosed with MCI and self-report, MoCA-B test, face-to-face interview, and based on an expert's opinion.

The persons with Alzheimer's disease who have been referred to the memory clinic will be evaluated by the neuropsychological test – MoCA-B- and finally by an expert cognitive neurologist.

In addition, the Persian version of the BLA test, as a comprehensive test of language skills for the elderly, will be used for all 3 groups. To achieve the aims of the present study, all tests will be done on all study participants at intervals of 6 and 12 months. Indirect observations will also be recorded in addition to the above-mentioned tests. We will repeat the test 3 times in 3 long periods (at the onset, 6 and 12 months after the study). We will use a series of BLA with 2 different random orders to avoid the practice effects

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and its low performance (15). We will use it at 3-month intervals in the present study (26).

Description of tests

The Montreal Cognitive Assessment (MoCA) is a fast screening questionnaire for diagnosing MCI (27).

MoCA has been validated in a group of educated elderly (the total mean education year will be 13) to diagnose MCI. This test helps to distinguish MCI group from healthy controls. Although most of the MoCA's items are highly dependent on the level of education and are not suitable for illiterate clients, the new MoCA test is more suitable for those with low literacy and illiteracy. MoCA-B assesses the same cognitive domains as in the original MoCA: orientation, executive function, language, conceptual thinking, calculation memory, visuo-perception (instead of visuo-constructional skills), and attention and concentration. It takes 15 minutes to administer MoCA-B and the total score is 30 (28).

The BLA assessment is designed to evaluate the possibility of speech and language impairment in the elderly (8, 26).

This assessment lasts for about an hour. The components of this test are as follow: word-picture matching, oral reading, semantic verbal fluency (animal pictures), digit-span, following commands, phonological verbal fluency, picture naming, written spelling to dictation, word definition, TROG (Test for the Reception of Grammar), sentence writing, storytelling (immediately), and picture description (verbal).

Primary outcome measures

Alzheimer's disease begins about 20 years earlier than its diagnosis. Language disorders can happen at the primary stages of this sickness and develop over time (16, 17). In the present study, we will follow language function over time and diagnose any language component decline (29). Also, we will measure cognitive functions and language skills by MoCA-B and BLA, respectively (Persian version).

Other measurements

We will record daily activity, pharmacotherapy, health condition, additional treatment, and other conditions.

Data analysis

The collected data will be analysed using statistical methods and according to objectives of the study. Moreover, we will use ordinal logistic regression and multinomial methods. Statistical analysis will include the following cases:

- Descriptive data such as mean, median, and standard deviation
- A comparison of mean scores of language skills among the 3 groups using repeated measures analysis of variance (ANOVA)
- Determining the effects of language skills among the 3 groups using generalized estimating equations (GEE)
- Determining the levels of different language skills using latent class models (LCM).

Discussion

Despite the fact that MCI is a very important stage before AD, no comprehensive study has been conducted on language skills in individuals with MCI and how they change over time. The present study will aim to record language abilities in individuals with MCI at intervals of 6 and 12 months to diagnose possible changes.

Globally, 6.1% of MCI cases exist among people aged 60 and over and the annual prevalence of MCI is 13.2/1000 (30). By the passage of time, stable or regenerated natural conditions can be seen for the MCI cases, but delays in diagnosis can result in an advanced dementia within 5 years for about 50% of patients (31).

It is predicted that Alzheimer's disease (AD) at all ages will occur among over 13 million people in the US by 2050, with the incurred treatment cost of about 1.2 trillion dollars. Aging military veterans have been showing a rapid increased risk for the incidence of AD, which may be due to traumatic brain injury, posttraumatic stress disorder, and service-based injuries. There is an increasing population of elderly people with health problems and long-term disabilities and this factor increases the costs of health care for AD and dementia. Such problems are accompanied by much younger burgeoning military veterans with long history of disability and high-risk AD and other types of dementia, highlighting the necessity of accelerating national and international investigations on the breakthrough discoveries capable of altering the path of AD and dementia (1).

In 2015, in the United States, the global cost of dementia was reported to be 818 billion dollars, indicating an increase up to 35% estimated at 2010.

The same is true for informal care and direct social care, and medical care includes a small amount of these costs. It was estimated that the value of these services in the United States in 2018 was about 1 trillion dollars (2).

Deficit of language skills can generally be described and observed from the early stages of the disease (32).

Difficulties in performing language tasks have long been reported in people with AD who are tested for semantic knowledge, such as verbal fluency, naming, object recognition, and some other relevant tasks. These symptoms show early and progressive impairment in semantic memory in the disease (33).

Language skills deficits in persons with MCI have been investigated during the past 10 years and revealed some language difficulties in 2 major groups: (1) phonetics and phonology, (2) lexicon, semantics, and pragmatics (15).

In other words, these impairments can be categorized according to verbal fluency, especially in categorization (10), confrontation naming (8, 9), and ability to judge grammatically, and picture naming (11). On the other hand, different studies have reported difficulties in semantic functions, such as lexical decision, semantic categorization, and semantic encoding (6, 13, and 14). According to previous studies, language impairment in individuals with MCI was mostly at the semantic level of processing, and despite the obtained inconclusive results, syntactic processing remained partially unaffected (23).

The tests with limited periods were more sensitive to individuals with MCI (eg, verbal fluency in patients with

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mild amnestic cognitive impairment). However, impairment in executive functions rather than in language (6) may contribute to language performance deficits.

Based on research reports, language deficits in people with AD can be seen at the early stages of disease, but a few linguistic methods have been introduced in this regard. Furthermore, language difficulties can be seen at a stage before AD, which is called MCI. Future studies can investigate some language impairments in people with MCI to prevent the progress or to design some suitable interventions. The present study is significantly important because it can be used in health care centers for early detection of MCI and for finding the best intervention to prevent its progress.

Research advantages

The present study will focus on language abilities in individuals with MCI and how they may change in a 12-month period. The obtained results will have clinical value for speech therapists, neurologists, and other health professionals who are involved in treating the elderly.

Conclusion

According to the literature, language disorders, apart from memory deficits, can be a sign of mild cognitive impairment. In fact, results of this study may indicate that deterioration in language skills can be an early sign of MCI.

Scientific limitation

There is sparse information in the literature on the diagnosis and differentiation of MCI, AD, and controls. There is little information about the differential diagnosis and differentiation of Alzheimer's patients, mild pathologic patients, and healthy people. However, despite current scientific limitations, such as frequent requests from patients and the limitations of specialized linguistic tests, this study can be a useful step forward in this regard.

Conflict of Interests

The authors declare that they have no competing interests.

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