Clinical Features of Mild Cognitive Impairment and Dementia in a Community: An update of the Osaki-Tajiri Project

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The borderline condition between normal aging and dementia is a major issue of concern for health policy planning because of an early intervention for possible prevention of dementia. Since 1988, the author has been involved in a community-based program on stroke, dementia, and bed-confinement prevention in Tajiri, northern Japan (the Osaki-Tajiri Project). As a part of the project, a cross-sectional study of aged patients with mild cognitive impairment in Tajiri was undertaken to investigate the clinical features of the condition, in addition to a longitudinal study to research its progression to dementia with possible risk factors. Impairment of the basic functions of attention and executive function was noted, as opposed to impairment in the cognitive domain itself. Magnetic resonance imaging (MRI) findings showed a pattern close to that of healthy persons in their 80s, rather than that of patients with cognitive deficit. The results of the longitudinal study showed more progression to dementia when the Clinical Dementia Rating (CDR) was 0.5 in domains other than memory. No effects of lifestyle, internal diseases or psychosocial intervention were confirmed. In progression to Alzheimer’s disease, generally low cognitive function and general atrophy were involved, whereas frontal lobe function, atrophy of the frontal and temporal lobes, white matter changes and cerebral infarction were related to progression to vascular dementia. For health policy planning for dementia prevention, we consider that excessive dependence on primary prevention should be avoided; rather, secondary prevention, using the CDR, psychological testing and MRI are desirable.

Keywords: executive function; mild cognitive impairment; CDR 0.5; progression to dementia; secondary prevention system.


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A part of this study was presented at the 2nd Japan-Taiwan Symposium on Dementias (JTSD-2), which was held on October 13, 2007, in Osaka, Japan.
derline condition are as follows. Dementia is defined as a condition in which a person cannot lead a normal social life due to cognitive deficit, whereas a borderline condition is defined as a low-level cognitive deficit causing no problems in terms of leading a social life. This is a logical idea based on the definition of dementia, which is defined as a functional disorder of multiple cognitive domains as the necessary condition and impairment of social activities as the sufficient condition. Cognitive function is evaluated by observation of daily life and neuropsychological tests, whereas social activities are assessed mainly by observation of daily life.

Flicker et al. (1991) first used the term mild cognitive impairment (MCI) for the borderline condition. Originally, MCI referred to severity classified as level 3 on the basis of the clinical observation scale called the Global Deterioration Scale (Reisberg et al. 1988). Later, Petersen et al. (1997) re-proposed the idea for MCI. Recently, the term MCI has been widely used as either a cross-sectional term to show older people whose condition is between that of healthy people and dementia patients or as a longitudinal term for a predementia stage that predicts further decline to dementia. However, MCI originated as a concept based on a longitudinal paradigm and was used to try to determine how early it was possible to identify those patients who would progress to cognitive deficit, especially Alzheimer’s disease (AD). When Petersen et al. (1997) suggested the use of the term MCI, it was defined as describing people who met the following five criteria, based on a longitudinal paradigm of early detection of the group of patients who develop AD, who display the following: (i) subjective memory complaints; (ii) a decrease in objective memory test results; (iii) generally normal cognitive function; (iv) normal daily life activity; and (v) no dementia.

Conversely, Dubois and Albert (2004) argued that MCI status would exist as the mildest condition of individual neurological disorders and there would be no one disease concept of MCI that would progress to AD, vascular dementia (VaD) or dementia with Lewy bodies (DLB). I agree with this theory. Neurodegenerative diseases, such as AD, are defined on the basis of a clinico-pathological theory. During the development of neurofibrillary tangles in the brain or senile plaques, a range of symptoms can be observed, including normal clinical symptoms (Morris et al. 1996), cognitive impairment that is not so severe as to cause problems in daily life (MCI status) or changes in a person’s ability to participate in daily life (dementia level). That is, MCI is not an independently established disease that may progress to cognitive deficit. There are diseases, such as AD, VaD and DLB, which have MCI status. This follows the same logic as the suggestion that there are various neurological diseases that can act as underlying causes for dementia.

In this review, I present a summary of neuropsychological and neuroepidemiological data of the Osaki-Tajiri Project (see below), to demonstrate the clinical features of MCI older adults and their progression to dementia in a community. I herein use the term MCI as a broad meaning corresponding to that of the Clinical Dementia Rating (CDR) 0.5. I would like to present a comprehensive prevention system for dementia in a community.

Osaki-Tajiri Project

Since 1988, the author has been involved in a community-based program on stroke, dementia, and bed-confinement prevention in Tajiri, Miyagi Prefecture, northern Japan (the Osaki-Tajiri Project). Fig. 1 illustrates the location of Tajiri. The total population in 1998 when the cross-sectional study was performed was 13,715 with the aging ratio being 23.4%.

Several surveys have been performed as part of the project. Part of findings on the prevalence study in 1998 and the incidence study in 2003 were herein reviewed. Fig. 2 illustrates the selection protocol of subjects: 1,654 residents agreed to participate in the prevalence study and 625 were randomly selected for the cross-sectional study. For the longitudinal study, 258 adults were involved.

Cross-Sectional Study

Table 1 summarizes the clinical features of...
Fig. 1. Location of Tajiri.

Fig. 2. Selection protocol of subjects.

| Table 1. Clinical features of MCI with reference to normal aging and dementia. |
|-----------------|-----------------|-----------------|
|                 | Normal aging    | MCI             | Dementia        |
| CDR             | 0               | 0.5             | 1+              |
| Cognitive function | Normal         | Slightly impaired | Impaired        |
| Memory          | Normal          | Slightly impaired | Impaired        |
| Attention       | Normal          | Impaired         | Impaired        |
| Daily life      | Normal          | Slightly impaired | Impaired        |
| MRI findings    | Normal          | Like healthy 80's | Atrophy         |

MCI, mild cognitive impairment; CDR, Clinical Dementia rating; MRI, magnetic resonance imaging.
MCI with reference to normal aging and dementia. Detailed information was described below.

**Cognitive deficit**

With regard to cognitive deficits, MCI is considered to be a condition that falls on the borderline between healthy people and patients with dementia (Meguro et al. 2002). In aged MCI outpatients, clear differences are observed in test results between patients who are almost healthy and those who almost qualify as having dementia. However, one of the features of neuropsychopedemiology undertaken in the Tajiri project is the cognitive deficit test for aged people who were selected from aged people in the community with a small bias.

Using the Alzheimer Disease Assessment Scale (ADAS)-Cog word list learning test to confirm language memory (Hashimoto et al. 2004), MCI patients showed good results in a recognition test, but the level of free recall was low. In addition, words that were never recalled in three tests (never-recall words) were confirmed in MCI patients. Because education must have an impact on the language task, the learning effect was evaluated using nonsense figures (Rey figure) (Kasai et al. 2006). As a result, a learning effect was confirmed in healthy people, whereas no such effect was observed in MCI patients. In addition, an assessment of free writing results in the Mini Mental State Examination (MMSE) from standpoints of wrong shapes and the use of words, such as wrong declensional Kana ending (Akanuma et al. 2004), a decreased attention in writing was suggested (Glosser et al. 1999). In addition, distinctive ability was assessed using the Benton visual form discrimination test with small burden on memory (Sato et al. 2001). The assessment results confirmed a significant difference in total points, even in the group who showed normal results in the test of delayed recall of three words.

A common feature of the aforementioned test results was the disorder of attention that is considered to be the basis of cognitive domains, such as memory, language and visual–spatial cognitive function. Attention may be classified as sustained attention, divided attention or shifting. It has been reported that divided attention and shifting would be damaged in early stages of AD (Perry and Hodges 1999). It is supposed that a base of cognitive deficit may be developed even in patients with broad MCI.

**Problems in daily life**

As mentioned above, MCI is defined as a condition that produces no problems in daily life, although patients may have cognitive dysfunction. However, broad MCI includes cases with mild disorders in daily life, although these patients do not have severe problems, as seen for patients with dementia. Although no difference was found between healthy people and MCI patients with regard to memory complaints, a feature of MCI patients was distinctively expressed awareness of problems in daily life. The CDR examines the ability of patients to participate in activities relating to the domains of “Home and Hobbies” and “Community Affairs” (Meguro 2004).

In household tasks of daily life, sequencing (e.g. washing, hanging out to dry, folding laundry for storage), parallel activity (e.g. cooking while using a washing machine) and planning (e.g. shopping after setting the menu and then starting to cook) are required. These processes are referred to neuropsychologically as executive functions. The ability to operate home appliances, such as a television remote control and electrical switches, is considered to be instrumental ADL. People with broad MCI may show mild disorder in both functions. Another feature of MCI patients is moderately passive participation and lowered interest in their favorite activities. In addition, careful attention should be paid to cases of broad MCI to prevent non-compliance with medication regimens. Some patients have a reduced ability to manage schedules and therefore may sometimes visit a physician on the wrong day, or are reluctant to participate in voluntary tasks as, for example, a member of an aged group. Another feature of patients with broad MCI is decreased activity due to lowered desire to participate in local activities etc (Meguro et al. 2004).
Magnetic resonance imaging findings

Independent of the CDR assessment, the MRI findings of atrophy were assessed by neurologists visually on a four-point scale as follows (Ishii et al. 2006): 0, no atrophy; 1, an intermediate level of atrophy; 2, obvious atrophy; and 3, significant atrophy. Findings having scores of 2 or 3, which were considered clinically obvious atrophy, were assessed as positive. As a result, it was confirmed that the AD group showed atrophy of the medial temporal lobe and that the findings of MCI patients were close to those of healthy people aged in their 80s. Obvious differences in atrophy in the medial temporal lobe between healthy people aged in their 80s and AD patients are clinically important.

Longitudinal study

When the mildest symptoms of a specified disease (ex. DLB) may be assumed based on distinctive neurological symptoms, such as visual hallucinations and parkinsonism, individual criteria can be used to diagnose each disease. The problematic case is a patient who meets no clear diagnostic criteria and therefore follow-up observations are required. Specifically, these cases include patients with the mildest AD or those with vascular MCI; however, not all these cases necessarily progress to dementia. An investigation performed 5 years after the prevalence survey in 1998 showed that approximately 40% of MCI patients progressed to cognitive deficit. As a result of assessing which features observed in patients during the initial period were related to a tendency for the progression to dementia, it was determined that older patients and those patients with CDR 0.5 in domains such as “Memory,” “Home and Hobbies” and “Community Affairs” were more likely to progress to dementia. Subjects also underwent detailed assessment regarding their living habits (e.g. smoking, alcohol consumption, diet and social support), their history of systemic diseases (e.g. hypertension and diabetes) and the effects of psychosocial intervention. No significant effects of these parameters on the progression to cognitive deficit were found.

Next, logistic regression analysis was performed for AD and VaD to assess the possibility of predicting progression to dementia based on the results of neuropsychological tests and MRI findings during the initial period. No significant relationship was found between progression to dementia and white matter diseases or cerebrovascular disorder, although the MRI findings suggested a relationship between generally low cognitive function and overall atrophy in AD patients. However, in VaD patients, a significant relationship was confirmed between cognitive functions, especially frontal lobe functions (e.g. fluency), and atrophy of the frontal and temporal lobes, severe white matter diseases and cerebrovascular disorders.

Table 2 summarized the features of MCI older adults likely progress to dementia.

| Table 2. Features of MCI older adults likely progress to dementia. |
|---|---|---|
| **AD** | **VaD** |
| Age | older age |
| CDR | CDR domains of Home and Hobbies, Community Affairs rated as 0.5 as well as that of Memory |
| cognitive tests | generally low function together with memory impairment |
| MRI findings | frontal lobe dysfunction |
| generalized atrophy including hippocampus | cerebrovascular disease, white matter lesions |

MCI, mild cognitive impairment; AD, Alzheimer’s disease; VaD, vascular dementia; CDR, Clinical Dementia Rating; MRI, magnetic resonance imaging.
In progression to VaD, we found two patterns: (i) some patients met the NINDS-AIREN criteria as a result of developing cerebral infarction in the cortex; and (ii) CDR 0.5 patients with cerebrovascular disorder who met the diagnostic criteria of subcortical VaD and subsequently progressed to dementia as a result of the poor control of vascular risk factors. As mentioned above, neuropsychologically it may be considered that executive functions and Instrumental ADL would cause problems in daily life. It is supposed that executive dysfunction, in particular, may be caused by damage to the frontal subcortical network or the hippocampal parietal/frontal network (Meguro et al. 1999, 2000). Executive dysfunction may cause a disorder of social adjustability. Concretely, this is often suggested as problems relating to the performance of household work, in home life or decreased local activities. In particular, intervention against risk factors for vascular diseases is important. Specifically, there may be a vicious cycle in which aggravation of risk factors occurs as a result of difficulties visiting medical institutions or management of medication regimens, resulting in reoccurrence of the disease. Support, such as local intervention, to enable patients to cope is required.

Conclusions

Can we prevent dementia?

First, what type of support should be provided and to which groups needs to be discussed. Regular observation is required while always considering the possibility of specific neurological disorders and possible diagnosis criteria. For subcortical and other types of VaD, the management of risk factors, such as hypertension and diabetes, and support to enable patients to manage their medication is very important. Some patients with broad MCI may progress to clinical AD. A combination of observation of daily activities based on CDR, neuropsychological tests and MRI findings is effective in identifying the group of MCI patients most likely to progress to cognitive deficit.

Although the focus tends to be on primary prevention when considering dementia prevention, it is important to encourage a correct understanding of the disease without an excessive burden being placed on patients. This is because ‘self-responsibility of patients with dementia’ may be suggested when primary prevention is focused in connection with their daily habits. To examine the effect of lifestyle-related diseases, a long-term study is required that should start when subjects are in middle age. In addition, to assess the possibility that psychosocial intervention may delay the onset of cognitive deficit, careful consideration should be given to the design of future prospective studies. These should be discussed sufficiently, but it is important for local citizens to encourage the development of local societies to provide individuals with a venue for safe social interaction, even after they develop cognitive deficits, rather than recommending therapies for the prevention of cognitive deficit. To this end, a correct understanding of dementia and appropriate support systems are necessary.

References


