

Abstract

Background: In recent years, increasing research and clinical attention has been paid to the mild end of the cognitive spectrum that spans normal aging to Alzheimer's disease (AD). There is a probable transitional stage between normal aging and the development of clinically probable early AD. Various terms, such as mild cognitive impairment, questionable dementia and preclinical dementia, have been used to describe such a transitional stage. There have been many studies that aim to differentiate the neuropsychological aspects that are found in normally aging elderly people from those that are found in elderly people with mild Alzheimer's disease. However, the extent to which everyday life functions are affected in this transitional stage remains unclear. This study compared the profiles of cognitive impairment, behavioral symptoms, and functional disability in Chinese subjects with "questionable dementia" and those of subjects with normal aging and mild AD. The neuropsychological and behavioral correlates of functional disability were also investigated.

Methods: The neuropsychological, behavioral, and functional profiles of 241 subjects were evaluated. Fifty-two cognitively normal elderly controls (Clinical Dementia Rating [CDR] 0), 113 subjects with questionable dementia (CDR 0.5), and 76 subjects with mild AD (CDR 1) were recruited. The subjects with questionable dementia (CDR 0.5) were categorized into two groups: a CDR 0.5/MCI group with predominantly isolated memory impairment and a CDR 0.5/incipient dementia group with impairment in multiple CDR domains. The four diagnostic groups were matched for age and education.

Results: The two CDR 0.5 groups displayed intermediate performance in the neuropsychological tests between the CDR 0 and CDR 1 groups. The CDR 0.5/incipient dementia group had a lower performance in the neuropsychological tests, such as CMMSE, ADAS-Cog, delayed recall test, category verbal fluency test

(CVFT), reverse visual span test, and functional assessment (Disability Assessment for Dementia scores), than the CDR 0.5/MCI group. The CDR 0.5/incipient dementia group performed intermediately between the CDR 0 and CDR 1 groups in the functional assessments of instrumental activities of daily living (ADL), but there was no significant difference in the functional performance of the CDR 0 and CDR 0.5/MCI groups. Apathy, depression, and irritability were more prevalent in the CDR 1 group than in the other comparison groups, and apathy was also more common in the CDR 0.5/incipient dementia group than in the CDR 0 group. Psychotic symptoms were uncommon in the study sample. Regression analyses revealed that the ADAS-Cog total scores, CVFT scores, and the presence of apathy and irritability were all significant predictors of performance of the instrumental ADL. The CVFT scores and reverse visual span test scores were significant predictors of the performance of the basic ADL.

Conclusion: Subjects with a CDR of 0.5 (questionable dementia) constitute a heterogeneous group with varying degrees of cognitive impairment and functional disability. Although the neuropsychological and functional impairment was subtle, the subjects in this study with questionable dementia could be differentiated from the cognitively normal controls and from the subjects with mild Alzheimer's disease. Global cognitive ability, executive dysfunction, and frontally mediated behavior were important predictors of functional disability. The early identification of the high-risk groups for early intervention may help to reduce disability or delay the progression to dementia. This study allows a better understanding of the cognitive decline and functional changes that are involved in the dementia process.