（第３号様式）

学　位　論　文　要　旨

氏　　名　　郭　海燕

論　文　名　　老年者における夜間血圧の異常は軽度認知機能障害と関連する

学位論文要旨

Introduction

Dementia is a major health burden for many countries where life expectancy is continuously growing and the proportion of elderly is rapidly growing. Mild cognitive impairment (MCI) is a transition phase between normal cognitive function and dementia.　Early detection of amnestic MCI (aMCI), a preceding phase of Alzhiemer's diseases of which frequency was estimated to be 6 to 10% in community elderly, is essential in the secondary prevention of dementia. Increasing blood pressure (BP) variability has been reported to be a risk for cardiovascular events. Since aMCI and cardiovascular diseases shares several traditional risk factors, such as arterial stiffness, hypertension and diabetes mellitus, it is hypothesized that BP variability could also be a risk for aMCI. However, few studies have investigated the possible association between BP variability and cognitive decline. Here we aimed to clarify the association between circadian BP variation and aMCI in community dwelling middle-aged to elderly persons.

Subjects and Methods

Study subjects consisted of 144 community residents (68±7 years) without definitive dementia or symptomatic cerebrovascular disease. Subjects were consecutively participants in the medical check-up program at Ehime University Hospital Anti-aging Center. Among the participants, persons who underwent aMCI screening and ambulatory BP monitoring were enrolled in this analysis. aMCI was assessed by the MCI screen, a computer-based staff administered test. Ambulatory BP was monitored using an automatic cuff-oscillometric device which was pre-set to measure BP every 15 min during daytime and 30 min at nighttime. Subjects were classified into 4 group according to the percentage decline in nocturnal BP; extreme dipper, ≥20%; dipper, 10-19%; non-dipper, none to 9% and riser, any increase in nocturnal systolic BP. Brachial-to-ankle pulse wave velocity (baPWV) was measured as an index of arteriosclerosis. Apolipoprotein E4 genotype was analyzed using DNA extracted from peripheral blood. All study participants gave singed informed consent.

Result

Frequency of extreme dipper, dipper, non-dipper and riser was 17.4, 36.8, 34.7, and 11.1% respectively. There were no significant differences in age (p=0.151), sex (p=0.740), and body mass index (BMI) (p=0.949) among the four nocturnal BP groups. Occasional systolic BP (SBP) was significantly higher in riser and non-dipper than dipper and extreme-dipper (151±25, 139±20, 133±17, 131±20 mmHg respectively, p=0.005) whereas no significant difference was observed in

ambulatory measured 24-hourmean SBP (p=0.236). Mean SBP during awaking period also did not differ among the four groups (p=0.655); nocturnal BP pattern was therefore determined by the differences in nighttime SBP. Other clinical difference among the four groups was faster baPWV in riser and non-dipper (1866±400, 1716±315, 1576±249, 1536±357 cm/sec, p=0.001).

Thirty-eight persons (26.3%) were diagnosed as having aMCI. aMCI subjects were significantly older (aMCI 74±6, normal cognitive function 67±6 years old, p<0.001), and more often had the apolipoprotein E4 genotype (36.8, 18.9%, p=0.025). aMCI subjects also showed significantly higher ambulatory measured (135±15, 128±14 mmHg, p=0.019), but not clinic measured SBP (139±19, 136±20 mmHg, p=0.358). Significant correlation was also observed between aMCI and baPWV (1808±380, 1595±285 cm/sec. p=0.001). There were J-shape relationship between the nocturnal BP pattern and frequency of aMCI; aMCI was more often in extreme dipper (32.0%), non-dipper (29.4%), and riser (50.0%), than dipper (13.2%, p=0.018). Multiple logistic regression analysis adjusted for possible covariates including the apolipoprotein ε4 genotype identified unusual nocturnal BP pattern, i.e. extreme-dipper non-dipper, and riser, as an independent determinant for aMCI (odds ratio=3.06 (95% C.I. 1.06-9.93), p=0.039).

Discussion

In the present study, we found that there were J-shaped relationship between nocturnal BP change and frequency of MCI in a general population sample with no definitive dementia. Our observation is in agreement with a concept that early dementia is preceded by BP instability. Underlying mechanisms relating abnormal BP profile and MCI is uncertain. Several previous studies reported significant associations between nocturnal BP patterns and cerebral white matter lesions, as well as asymptomatic lacunar infarction. Silent cerebral infarction was suggested to be a predictor of future development of MCI. Given these findings together with our present data, asymptomatic cerebrovascular damage might be a possible mechanism explainable for the relationship between unusual nocturnal BP pattern and MCI. The frequency of MCI was highest among risers. Risers were slightly older and had higher baPWV. Since, arterial stiffness has been suggested to contribute to the progression of cognitive impairment, advanced arteriosclerosis and concomitant cerebral arterial remodeling may also be a factor for the frequent MCI among risers. The present study subjects were free from symptomatic cerebral diseases. aMCI eventually progress into Alzheimer-type dementia, abnormal nocturnal BP profile may therefore predict future development of Alzheimer-type dementia, but not other type of dementia. Unusual nocturnal BP profile may provide a clue to elucidate at-risk persons for aMCI.

キーワード（3～5）	ambulatory blood pressure monitoring, mild cognitive impairment, nocturnal blood pressure