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• 計畫英文名稱	Sleep Physiology and Circadian Gene Expression in Mild Cognitive Impairment		
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• 中文關鍵字	阿茲海默症; 輕微認知功能障礙; 睡眠; 快速動眼期		
• 英文關鍵字	Alzheimer's diease; Mild cognitive impairment; sleep; iNOS; PER1; REM sleep		
• 中文摘要	本研究探討正常認知功能老人、輕微認知功能障礙、阿茲海默症病人於睡眠中快速動眼期、非快速動眼期與清醒期時基因表達知不同。吾人發現快速動眼期時與記憶相關的基因 iNOS 表達在阿茲海默症病人組中顯著上升，而與約日（circadian）調節相關的基因 PER1 則再三組中無顯著差異。		
• 英文摘要	Sleep disturbance and circadian disarrangement are both common manifestations of behavioral and psychological symptoms of dementia. Sleep disturbance could be an indicator for poor outcome of dementia. Sun-downing phenomenon of circadian disarrangement causes a heavy burden for care-givers of dementia patients. Sleep is important in many neurocognitive functions. Memory consolidation processes during sleep is crucial for some visual-spatial memory and specific task-learning, especially in rapid eye movement (REM) stage. The initiation of REM sleep is mainly acetylcholine-dependent and inducible nitric oxide synthase (iNOS) is involved in maintenance of REM sleep. Cholinesterase inhibitors which can increase intracerebral acetylcholine levels have become the standard therapy of Alzheimer's disease (AD) to improve cognitive function. Since up-regulation of iNOS could be linked to memory consolidation by maintenance of REM sleep, over-expression of iNOS might be an important mechanism for compensation of deterioration of cognitive function. On the other hand, sleep is one of the most important presentations of circadian rhythm, which is controlled by at last 9 genes, including period 1 (PER1). There are transcriptional feed-back loops of these circadian genes for regulation of circadian rhythm. Period 1 (PER1) expression is not only controlled by the circadian feed-back loops but also		

regulated by light. Light could entrain the circadian rhythm by up-regulating the PER1 expression without getting involved the transcriptional feed-back loop and then alter the circadian rhythm dominantly. Silencing PER1 shortens the circadian period and even markedly disturbs the circadian rhythm. In this preliminary study we surveyed the iNOS and PER1 mRNA expression in peripheral blood during REM, non-REM and wake stages respectively among the patients with AD, mild cognitive impairment (MCI) and controls under polysomnography (PSG) examination. We found iNOS expression significantly increased during REM sleep in AD patients, but not in MCI, in comparison to controls. There are no significant differences of PER1 expression between these three groups but an increase of PER1 expression in wake stage was observed among all participants. The possible cause of increase of iNOS expression in REM sleep in AD patients might be a compensation for the lower acetylcholine levels in brains of AD patients. However, the real role of nocturnal expression of iNOS in AD remains further investigation.