



Capitol Sleep Medicine Newsletter

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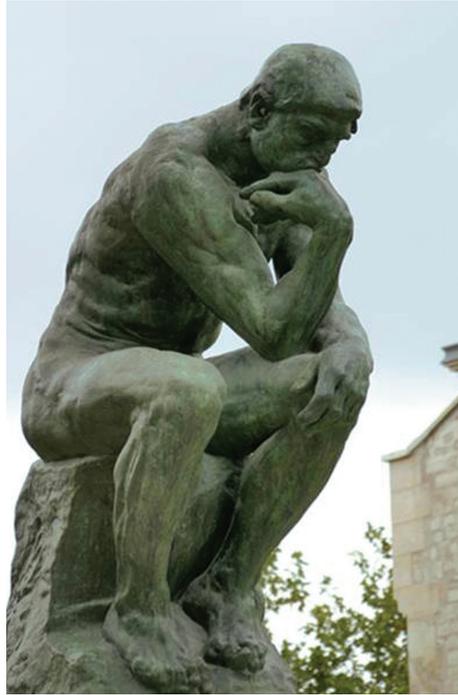
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Drugs and Dreams in Alzheimer's Disease

Alzheimer's dementia is a leading cause of dementia, or memory loss in the United States. REM sleep is crucial for the consolidation of new memories and dreams may be abnormal in patients with Alzheimer's disease.

It has been well documented that in normal subjects memory improvement for various cognitive functions frequently correlates with an increase in REM sleep.¹ For example, studies have shown an association of memory and REM sleep for learning trampolining,² intensive learning of a foreign language,³ Morse code learning,⁴ visual field inversion⁵ and visual discrimination tasks.⁶ Each of these studies demonstrated an increase in REM sleep following successful learning.

REM sleep is driven from the brainstem by the neurotransmitter acetylcholine. The primary medications used to treat Alzheimer's disease are in the family of acetylcholine esterase antagonists. These medications inhibit the metabolism of acetylcholine, thereby increasing it. Acetylcholine is also one of the main neurotransmitters used by the frontal lobes during wakefulness. A meta-analysis of 13 randomized, double blind, placebo controlled trials in patients with mild, moderate or severe dementia due to Alzheimer's disease demonstrated that the acetylcholine esterase antagonist medications donepezil, galantamine and rivastigmine at recommended doses all produced improvements in cognitive function.⁷ Interestingly, these medications also cause a significant increase in REM sleep.⁸ Is there a relationship between the ability of these medications to increase REM sleep and their improvement on memory? Donepezil may significantly increase REM sleep over baseline for up to 6 months of treatment. In this patient group REM sleep frontal and centroparietal alpha power significantly correlated with the cognitive improvement rate on the Alzheimer Disease Assessment Scale.⁹ Another study was performed using just 5mg of donepezil daily that demonstrated a significant positive correlation between cognitive improvement and the increase in the percentage of REM sleep.¹⁰



It has been suggested that the waking visual hallucinations seen by patients with Alzheimer's disease may represent a waking release of REM sleep dreaming intruding into what would otherwise be normal wakefulness. REM sleep phenomena such as vivid dreams and acting out dreams (REM sleep behavior disorder) are more frequent in patients with Alzheimer's disease who have frequent waking hallucinations compared to those who do not (26.9% vs. 9.3%). This suggests that disordered REM sleep may be at least partially responsible in influencing the occurrence of waking visual hallucinations in patients with Alzheimer's disease.¹¹ Further, medications such as donepezil may also increase the frequency of nightmares, but this effect can be diminished when the medication is dosed in the morning as opposed to taking it just before bedtime.¹²

Do acetylcholinesterase inhibitors such as donepezil slow down the progression of Alzheimer's dementia? A randomized, double-blind, placebo-controlled study in 67 patients with mild to moderate Alzheimer's disease using magnetic resonance imaging to assess hippocampal neurodegeneration was performed where patients received 24 weeks of treatment with donepezil (5 mg/day for the first 28 days and 10 mg/day thereafter) or placebo. The donepezil-treated patients had a significantly smaller decrease in hippocampal volume, compared with the placebo-treated patients. The authors concluded that donepezil may have a potentially protective effect in Alzheimer's disease.¹³

Sleep, per chance to dream, perchance to remember...

¹ Walter, T (2007) Chapter 2, The History of Sleep and Memory Until Just Recently. In *REM Illumination Memory Consolidation* (pp. 15-23), Grove City, OH: Lotus Magnus.
² *Perceptual and Motor Skills*, 1988, 67, 635-645.
³ *International Journal of Psychophysiology*, 1989, 8, 43-47.
⁴ *Physiology and Behaviour*, 1989, 46, 639-642.
⁵ *Canadian Journal of Psychology*, 1991, 45, 125-139.
⁶ *Nature Neuroscience*, 2000, 3, 1335-1339.

⁷ *Cochrane Database Syst Rev*, 2006 Jan 25;(1):CD005593.
⁸ *Drugs Aging*, 2006;23(6):503-11.
⁹ *Sleep*, 2006 Feb 1;29(2):199-205.
¹⁰ *Psychiatry Clin Neurosci*, 2004 Dec;58(6):660-5.
¹¹ *Neurol Sci*, 2007 Apr;28(2):96-9.
¹² *Nervenarzt*, 2005 Sep;76(9):1127-8, 1129.
¹³ *Am J Psychiatry*, 2003 Nov;160(11):2003-11.

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