



# Mild Cognitive Impairment: Memory, Cortisol and Hippocampal Volumetrics

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## BACKGROUND

•Studies of Alzheimer Disease (AD) patients have found that dysregulated cortisol levels are associated with cognitive dysfunction (de Leon et al., 1988) and reduced hippocampal volumes (e.g., O'Brien et al., 1996; de Leon et al., 1988).

•Importantly, in many studies of cortisol it appears to be a *flattening* of the cycle (i.e., increases in the evening cortisol levels and/or decreases in morning levels), not necessarily an overall increase in cortisol levels that is indicative of dysregulation.

•The amnesic subtype of mild cognitive impairment (MCIa) has been suggested as a precursor to AD, with patients exhibiting early signs of memory loss and hippocampal degeneration.

•In the current study, we examined relationships among memory, cortisol levels and hippocampal volumes in a group of older adults, some of whom met criteria for MCI.

## AIMS

1) To learn whether individuals with MCIa would exhibit an abnormal diurnal cortisol response compared to age- and education-matched controls. We predicted that MCIa participants would demonstrate a flattening of the diurnal salivary cortisol curve.

2) To investigate the relationship between cognitive function (regardless of group classification) and an abnormal cortisol response. We predicted that lower memory scores would be associated with a flattened diurnal cortisol curve.

3) To examine the relationship between hippocampal volumes (regardless of group classification) and cortisol abnormality. We hypothesized that an abnormal (flattened) cortisol curve would be associated with smaller hippocampal volumes.

## PARTICIPANTS

### Demographics/Cognitive Function

Variable	MCIa (N = 13)	Control (N = 13)	Significance
Age	69.3 (9.7)	72.0 (7.4)	ns
Men: Women	6: 7	8: 5	ns
Years of Ed.	14.8 (2.2)	16.2 (2.9)	ns
WASI 2-Test IQ	110.4 (15.9)	117.4 (8.3)	ns
MMSE	28.7 (1.6)	28.9 (1.2)	ns
HVLT comp-z	-2.2 (0.8)	-0.6 (0.8)	p < 0.001

## PROCEDURES

•**Neuropsychological testing:** Classification of MCI was based on a consensus conference that took into account function in daily activities, intellectual estimates, and performance on neuropsychological measures (e.g., tests of declarative memory). A composite z-score (delayed recall and total recall) for the HVLT was calculated for use in analyses.

•**Cortisol** was collected via saliva at home 5x/day over three days. Average salivary cortisol levels were calculated over two days (excluding the initial buffer day). Cortisol slope was calculated by subtracting cortisol levels at time five (before bed) from those at time one (awakening).

•**Hippocampal** and whole brain volumes were measured in a subgroup of participants (N = 12) by raters blind to diagnosis. Hippocampal volumes were normalized to whole brain volumes to account for differences in overall brain size.

## RESULTS

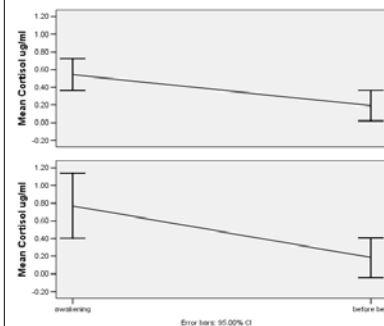


Figure 1. Relationship between group status and cortisol slope.

Aim 1: Difference scores for the MCI participants ( $M = 0.55$ ,  $SD = 0.30$ ) were significantly lower than those for the controls ( $M = 0.85$ ,  $SD = 0.33$ ),  $t(23) = 2.38$ ,  $p = .03$ ; Cohen's  $d = 0.99$ . Thus, MCI participants had flatter slopes.

## RESULTS (cont.)

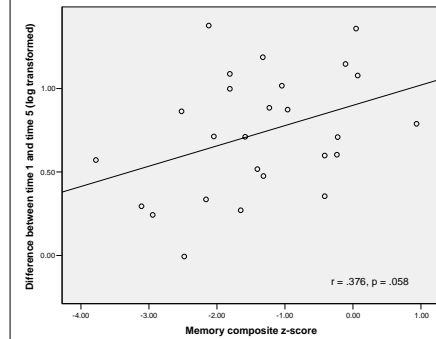


Figure 2. Relationship between memory performance and the change in cortisol levels from time one to time five (N = 26).

Aim 2: Flattening of the diurnal slope was related to worse memory performance.

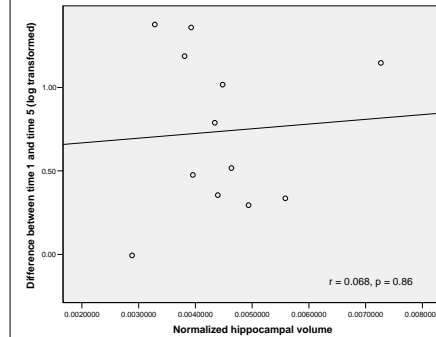


Figure 3: Relationship between normalized hippocampal volume and change in cortisol levels from time one to time five.

Aim 3: There was no evidence of a relationship between hippocampal volume and flattened cortisol curves.

## CONCLUSIONS

•Relative to 'healthy' age matched adults, MCI patients experienced a flattening of the diurnal cortisol curve. This cortisol pattern related to poor memory scores but not hippocampal volume.

•The measurement of cortisol secretion, in combination with other variables such as hippocampal volume, might prove to be helpful in early detection of AD.

•Future research should incorporate longitudinal designs, investigation of cortisol's impact on other brain regions (including the frontal cortex) and examination of the relationships among physiological or psychological stressors (e.g., surgery), cortisol levels and progression from MCI to AD.