Lower morning to evening cortisol ratio is associated with cognitive impairment in men but not women: An analysis of 733 older subjects of the cross-sectional KORA-Age study.

A dysregulated hypothalamic-pituitary-adrenocortical axis (HPA) is thought to play a role in the pathophysiology of cognitive impairment. Surprisingly, little agreement exists on the association of cortisol and cognitive impairment. Thus, we sought to examine the association between cognitive function and salivary cortisol levels in a representative sample of older men and women. A cross-sectional analysis was conducted among 733 study participants (65-90 years old, mean age=74.9) of the population-based KORA (Cooperative Health Research in the Region of Augsburg)-Age study. Associations were examined between cognitive function (determined by telephone interview for cognitive status-modified, TICS-m) and salivary cortisol measured upon waking (M1), 30 min after awakening (M2), and in the late evening (E). In a dose response manner, lower morning (M1 and M2), and increased evening levels were observed in participants with probable dementia (4.5%, N=33) and slightly increased in those with mild cognitive impairment (MCI) (13.8%, N=101) compared to healthy individuals. Higher morning to evening ratios were associated with reduced odds of cognitive impairment, even after adjustments for important confounders (M1/E ratio: OR=1.50,
95% CI=1.08-2.07, M2/E ratio: 1.41, 1.01-1.95, per 1 standard deviation (SD) increase). However, the significant association of an increased risk for cognitive impairment was observed among men (M1/E: OR=1.94, 95% CI=1.24-3.02; M2/E=1.74, 1.12-2.71) but not women (M1/E: OR=1.11, 0.69-1.78; M2/E=1.09, 0.67-1.77). Our findings suggest that dysregulated HPA axis reactivity, evidenced by blunted diurnal cortisol responses, are associated with impaired cognitive function in an aged population.