

High Saliva Cortisol May Flag Cognitive Trouble

Megan Brooks | August 19, 2015

Measuring cortisol in saliva may help identify healthy older people with cognitive impairment, a new study hints.

The study team observed that higher evening cortisol levels in saliva were associated with lower total brain volume and poorer global cognitive function in older dementia-free community-dwelling elderly individuals. On the other hand, higher morning saliva cortisol levels seemed to correlate with greater white matter volume and some aspects of cognitive function.

Teasing out the differential effects may have clinical implications down the road, note Lenore J. Launer, PhD, from the National Institute on Aging, Bethesda, Maryland, and colleagues.

Their study is published online August 19 in *Neurology*.

"Studies have shown that depression increases the risk for dementia, but we don't know much about how this relationship occurs," Dr Launer explains in a statement from the American Academy of Neurology. "High levels of the stress hormone cortisol have been found in people with depression, and the theory is that cortisol has a toxic effect on the hippocampus area of the brain, which plays an important role in memory."

The researchers studied 4244 adults (mean age, 76 years) without dementia from the Age, Gene/Environment Susceptibility (AGES)—Reykjavik Study, who underwent brain MRI and a battery of cognitive tests and provided saliva samples once in the morning and in the evening.

The mean morning cortisol level was 20 nmol/L and the median (10th to 90th percentile) evening cortisol level was 2.3 nmol/L.

Higher evening cortisol levels correlated with smaller total brain volume, the authors report (highest vs lowest tertile, -16.0 mL [95% confidence interval (CI), -19.7 to -12.2 mL], adjusted for age, sex, education, intracranial volume, smoking, steroid use, white matter lesions, and brain infarcts).

After further adjustment for body mass index, systolic and diastolic blood pressure, diabetes, physical activity, alcohol use, and depressive symptoms, the association attenuated but remained statistically significant (highest vs lowest tertile: -13.8 mL; 95% CI, -17.5 to -10.1 mL).

"The smaller volumes were observed in all brain regions but were significantly smaller in gray matter than in white matter regions," the authors report. Higher evening cortisol was also associated with poorer cognitive functioning "across all domains."

Higher morning cortisol levels were not associated with total brain volume but were associated with "slightly" larger white matter volume (but not gray matter volume) and with better processing speed and executive functioning (but not memory).

"Since this study just looked at a snapshot in time, we don't know which came first: the high levels of cortisol or the loss of brain volume," Dr Launer said. "It's possible that the loss of brain volume that can occur with aging leads to a lesser ability of the brain to stop the effects of cortisol, which in turn leads to further loss of brain cells.

Understanding these relationships may help us develop strategies to reduce the effects of cortisol on the brain and thinking skills," Dr Launer added.

"This is area of investigation," Dr Launer commented to *Medscape Medical News*. "There are many feedback mechanisms involving different regions of the brain and receptors in the brain that regulate the levels of cortisol. Gray matter and white matter differ in rates of atrophy and density of receptors and possibly this is reflected in the gray/white matter differences."

"This study has no immediate clinical message," Dr Launer added. "However, in any case, stress should be managed to the extent possible. There is a whole field of study and practical ways that stress can be reduced."

Reached for comment, Marwan Sabbagh, MD, director, Banner Sun Health Research Institute, Sun City, Arizona, and American Academy of Neurology member, told *Medscape Medical News*, "People have been trying to link stress responses, and by extension cortisol, to cognition, and this study is the first one I think that really neatly and cleanly ties elevations in cortisol levels with adverse effects on brain structure, brain volumes, and cognition."

"We don't know why. This is not a mechanistic correlation; this is simply an observation showing that one may impact the other," Dr Sabbagh cautioned. "How elevation of cortisol, which is a surrogate marker of stress, adversely affects the brain, through what mechanism, is something that will eventually be teased out."

It's definitely a worthwhile area of research, he said. "There is no doubt about it. All across the board, we are looking for what are the negative contributors to cognitive function over time and how are they causing damage to the brain," Dr Sabbagh said.

The study was supported by the National Institutes of Health, National Institute on Aging, Icelandic Heart Association, and Icelandic Parliament. The authors and Dr Sabbagh have disclosed no relevant financial relationships.

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