

Longitudinal associations between diurnal cortisol variation and later-life cognitive impairment

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Study objective and summary result

This study examined whether hypothalamus-pituitary-adrenal axis (HPAA) dysfunction is prospectively associated with global cognitive impairment in old age. Loss of diurnal HPAA variation was prospectively associated with worsened cognitive function in later life.

What is known and what this paper adds

Various studies have suggested that HPAA dysfunction is relevant to the development and progression of cognitive impairment, but the nature of this relationship is unclear. This investigation provides further evidence that HPAA dysfunction is a predictor of global cognitive impairment in later life.

Participants and setting

The investigators analyzed data from 2 longitudinal studies: the Whitehall II study, which follows middle-aged individuals employed in the British civil service, and the MRC National Survey for Health and Development (NSHD), which follows individuals born in Britain during a single week in March 1946. The Whitehall II data were collected in 2002–2004 ($n = 6,967$), 2007–2009 ($n = 6,761$), and 2012–2013 ($n = 6,318$), and the NSHD data were collected in 2006–2010 ($n = 2,229$).

Design, size, and duration

Global cognition were harmonized from the Mini-Mental State Examination (MMSE) in the Whitehall II study and the Addenbrooke's Cognitive Examination, Third Version, in the NSHD. Saliva samples were collected from the participants at various points in the day. Salivary cortisol levels were measured with an immunoassay, and cortisol AM:PM ratios were calculated to quantify diurnal HPAA variation.

Primary outcome measures

The primary outcomes were associations between cortisol AM:PM ratios and global cognition scores.

Table Relationships between 1-SD increases in cortisol am:pm ratios and cognitive outcomes

Model	Change in MMSE errors (95% CI)	Change in verbal fluency score (95% CI)
Univariate	-0.03 (-0.02 to -0.04)	0.06 SD (0.04 SD to 0.08 SD) increase
Fully adjusted	-0.02 (0.00 to -0.03)	0.03 SD (0.01 SD to 0.05 SD) increase

Main results and the role of chance

Increased cortisol AM:PM ratios were prospectively associated with better cognitive function outcomes measured years after saliva collection ($p < 0.01$).

Bias, confounding, and other reasons for caution

There were missing cortisol data for participants from both studies, although multiple imputation analyses resulted in the same conclusions. While the authors harmonized both the Whitehall II and NSHD study data, the 2 studies used different protocols.

Generalizability to other populations

The present study's reliance on data from a predominantly white British Caucasian population may limit generalizability to other ethnic groups.

Study funding/potential competing interests

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A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The corresponding author(s) of the full-length article and the journal editors edited and approved the final version.

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