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Antecedent longitudinal changes in body mass index are associated with diurnal cortisol curve features: The multi-ethnic study of atherosclerosis

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ABSTRACT

Context. Prior studies have shown a cross-sectional association between body mass index (BMI) and salivary diurnal cortisol profile features (cortisol features); however, to our knowledge prior population-based studies have not examined the longitudinal association of body-mass index (BMI) with cortisol features.

Objective. To examine the association of (1) prior annual BMI percent change over 7 years with cortisol features, (2) baseline cortisol features with subsequent change in BMI over 6 years and (3) the association of change in cortisol features with change in BMI over 6 years.

Design. Longitudinal study.

Setting. Multi-Ethnic Study of Atherosclerosis (MESA) Stress I & II Studies (2004–2006 & 2010–2012).

Participants. 1685 ethnically diverse men and women attended either MESA Stress exam (mean age 65 ± 10 years at MESA Stress I; mean age 69 ± 9 years at MESA Stress II).

Outcome Measures. Log-transformed cortisol features including wake-up cortisol, cortisol awakening response, early decline slope (30 min to 2 h post-awakening), late decline slope (2 h post-awakening to bedtime), bedtime, and total area under the curve (AUC) cortisol.

Results. Over 7 years, following multivariable adjustment, (1) a 1% higher prior annual BMI % increase was associated with a 2.9% (95% CI: −5.0%, −0.8%) and 3.0% (95% CI: −4.7%, −1.4%) lower current wake-up and total AUC cortisol, respectively; (2) there was no significant association between baseline cortisol features and subsequent change in BMI and (3) among participants with BMI ≥ 30 kg/m^2, flattening of the late decline slope was

Abbreviations: 11β-HSD1, 11 beta-hydroxysteroid dehydrogenase type 1; AUC, area under the curve; BMI, body-mass index; CAR, cortisol awakening response; HRT, hormone replacement therapy; HPA, hypothalamic–pituitary-adrenal; MESA, Multi-Ethnic Study of Atherosclerosis; WC, waist circumference; WHR, waist-to-hip ratio.

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associated with increases in BMI (every 1-unit increase late decline slope were associated with a 12.9% increase (95%CI: −1%, 26.8%) in BMI, respectively).

Conclusions. We found a significant association between prior annual BMI % change and cortisol features, but no significant association between baseline cortisol features and subsequent change in BMI. In participants with obesity increases in BMI were associated with less pronounced declined. Collectively, our results suggest that greater adiposity may lead to a blunted diurnal cortisol profile.

1. Introduction

The prevalence of obesity has been rising over the last twenty years and currently affects over 1 in 3 Americans [1]. Given the epidemic proportions of obesity and its involvement in many of the leading causes of death [2], it is essential to identify novel contributors to the underlying physiology of obesity. The role of dysregulated cortisol in obesity is one such novel mechanism. The HPA axis is a major component of the neuroendocrine system that controls the response to stress and contributes to the regulation of energy storage and expenditure. The terminal response of the HPA axis is production of cortisol from the adrenal gland with a classic circadian rhythm (diurnal cortisol profile): cortisol rapidly rising after awakening, reaching a peak after 30–45 min and then gradually declining over the course of the day [3,4].

Perturbations of the diurnal cortisol profile are cross-sectionally associated with obesity and conditions linked to obesity including insulin resistance, type 2 diabetes, metabolic syndrome and cardiovascular disease [5–7], as well as cardiovascular and all-cause mortality [8]. Cross-sectional associations of the diurnal cortisol profile with measures of obesity include: (1) higher BMI, WHR and WC are associated with lower wakeup and morning cortisol [9–15]; (2) CAR is positively associated with WHR [16] and WC [17]; and (3) higher WHR is associated with lower diurnal cortisol variability [18,19], and lower total AUC cortisol [15]. In MESA Stress I, BMI and WC are negatively correlated with wake-up cortisol and CAR AUC and positively correlated with the early decline slope (indicating a flatter slope) [20]. Despite the extensive cross-sectional literature on the HPA axis and obesity, longitudinal associations of diurnal cortisol curve features (Fig. 1) with obesity are lacking, limiting understanding of the directionality and temporality of these associations [6]. Thus, we used data from MESA Exams 1–5 and both MESA Stress exams to assess the temporality of the association between cortisol features and BMI/WC. Specifically, we investigated 3 aims: (1) the association of prior annual BMI and WC percent change with cortisol features over 7 years; (2) the association of baseline cortisol feature at MESA Stress I with subsequent change in BMI and WC over 6 years; (3) the association of changes in cortisol features with simultaneous changes in BMI and WC over 6 years.

2. Methods

2.1. Study Population

MESA is a multi-center, longitudinal cohort study of the prevalence and correlates of subclinical cardiovascular disease and the factors influencing its progression [21]. Between July 2000 and August 2002, 6814 men and women, 45–84 years of age, without clinical cardiovascular disease who identified themselves as White, Black, Hispanic or Chinese, were recruited from six U.S. communities: Baltimore City and Baltimore County, Maryland; Chicago, Illinois; Forsyth County, North Carolina; Los Angeles County, California; and St. Paul, Minnesota. Details on the sampling frames and the cohort examination procedures have been published previously [21]. The MESA Stress I Study collected detailed measures of stress hormones, including salivary cortisol measures between 2004 and 2006 (during period of MESA Exam 3 and Exam 4) at the New York and Los Angeles MESA study sites. The MESA Stress II Study collected similar data, on a subsample of 1082 participants at the New York, Los Angeles and Baltimore MESA study sites between 2010 and 2012 during MESA Exam 5 (Supplementary Fig. A.1). Informed consent was obtained from each participant and the institutional review boards of all the participating institutions approved the study and consent procedures.

2.2. Hormonal Measures

In MESA Stress I, salivary cortisol measures were collected over 3 days with 6 time points measured per day. The first

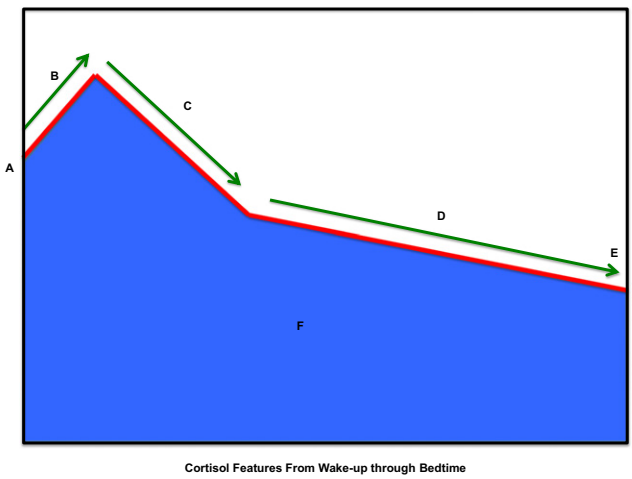

Fig. 1 – Diurnal cortisol profile: summary of diurnal cortisol features. Key: A. Wake-up cortisol (Time 0). B. Cortisol awakening response (0 min to 30 min). C. Early decline slope cortisol (30 min to 2 h). D. Late decline slope cortisol (2 h to bedtime). E. Bedtime cortisol. F. Total area under the curve (0 min to bedtime) cortisol.