Psychoneuroendocrinology (2014) 41, 33—45

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/psyneuen

Within-adolescent coupled changes in cortisol with DHEA and testosterone in response to three stressors during adolescence

Kristine Marceau [a,b,c,*], Elizabeth A. Shirtcliff [d], Paul D. Hastings [e], Bonnie Klimes-Dougan [f], Carolyn Zahn-Waxler [g], Lorah D. Dorn [a], Elizabeth J. Susman [a]

[a] The Pennsylvania State University, United States
[b] Division of Behavior Genetics, Rhode Island Hospital Department of Psychiatry, United States
[c] Brown University Center for Alcohol and Addiction Studies, United States
[d] University of New Orleans, United States
[e] University of California-Davis, United States
[f] University of Minnesota, United States
[g] University of Wisconsin, United States

Received 13 September 2013; received in revised form 3 December 2013; accepted 4 December 2013

KEYWORDS
Cortisol;
Testosterone;
DHEA;
Social stress;
Venipuncture;
Within-person coupling;
Adolescence

Summary It is hypothesized that hypothalamic-pituitary-adrenal and hypothalamic-pituitary-gonadal axes function together to maintain adaptive functioning during stressful situations differently in adolescence than the characteristic inverse relations found in adulthood. We examined within-person correlated changes (coupling) in cortisol, DHEA and testosterone in response to parent-adolescent conflict discussion, social performance, and venipuncture paradigms. Data are derived from two samples of boys and girls from the Northeastern US (213 adolescents aged 11—16, $M = 13.7$, $SD = 1.5$ years; 108 adolescents aged 9—14, $M = 11.99$, $SD = 1.55$) using different biological sampling vehicles (saliva and blood). Results consistently show that across samples, vehicles, and contexts, cortisol and DHEA and cortisol and testosterone are positively coupled in response to environmental stimuli. Findings underscore the importance of considering the effects of multiple hormones together in order to further our understanding of the biological underpinnings of behavior, especially during adolescence, as adolescence is a developmental transition period that may be qualitatively different from adulthood in terms of hormone functioning.

* Corresponding author at: Center for Alcohol and Addiction Studies, Brown University, 121 S Main St. Room 413, Providence, RI 02903, United States. Tel.: +1 414 940 7380.
E-mail addresses: Kristine_Marceau@Brown.edu, kristine.marceau@gmail.com (K. Marceau).

0306-4530/$ — see front matter
http://dx.doi.org/10.1016/j.psyneuen.2013.12.002

1. Introduction

Changes in output hormones of the hypothalamic-pituitary-adrenal (HPA) axis (i.e., cortisol, dehydroepiandrosterone [DHEA]) have long been studied as predictors of psychopathology during adolescence, and an emerging literature considers hypothalamic-pituitary-gonadal (HPG) axes (i.e., testosterone) changes likewise as predictors of psychopathology symptoms, especially during adolescence. Cortisol, DHEA, and testosterone all demonstrate stress-reactive properties to various types of stressors during adolescence. However, dual-axis approaches highlight that the effects of each hormone are unlikely to influence biological processes and later behavior individually (Mastorakos et al., 2006; Rivier et al., 1986; Viau, 2002). A major gap in the literature is the lack of a basic understanding of how hormones of the HPA and HPG axis operate together across development. The present study addresses this gap by examining how cortisol, DHEA, and testosterone are associated in response to three laboratory-based stressors commonly used to assess hormone—behavior associations during adolescence.

In adults, activation in the HPA axis suppresses the activity of the HPG axis (Romeo, 2005; Stratakis and Chrousos, 1995; Terberg et al., 2009). However, adolescence is both stressful and a period of intense physical growth and development, so suppression of the HPA axis by the HPG axis or vice versa, could be developmentally inappropriate and even harmful since both systems undergo major reproductive and physical developmental changes during adolescence. Preliminary evidence reveals that a positive association between HPA and HPG hormone activity may be present in adolescents (Susman et al., 1987; Marceau et al., 2012; Matchock et al., 2007; Popma et al., 2007), potentially due to increased levels of activity in both axes during puberty (Gunnar et al., 2009; Romeo, 2005). Indeed, a small but growing group of studies in adolescents show positive associations between testosterone, DHEA, and cortisol responses to environmental stimuli (i.e., MRI: Eatough et al., 2009; exercise: Kraemer et al., 2001; venipuncture: Marceau et al., 2012). Theoretically, the ways in which these three hormones respond to stressors together (i.e., coupled responses), or separately (i.e., uncoupled) may index the hormonal milieu, or endogenous hormonal environment, and better characterize endocrine functioning. Hereafter, associations in how disparate hormones respond together is defined as coupling.

There are multiple mechanisms by which hormone responses may be coupled. Biologically, cortisol and DHEA are likely positively coupled in response to stressors because both hormones are released from the adrenal gland as part of the HPA stress response (Sapolsky, 1992, 2003), and cortisol and DHEA responses to social stress has been demonstrated to be correlated in men and women (Lennartsson et al., 2012). Evidence of the suppression of the HPG axis by the HPA axis through inverse relations between cortisol and testosterone suggests that testosterone and cortisol would be inversely coupled in adults. However, positive associations between cortisol and testosterone and cortisol and DHEA in adolescents suggest that we may find positive coupling in adolescents, potentially due to increased activation of both axes generally due to puberty (Marceau et al., 2013). From an environmental perspective, while different types of environmental stimuli precipitate a release in testosterone and in cortisol, there is some evidence of individual differences in the extent to which the same environmental cue precipitates the recruitment of multiple hormones (e.g., Eatough et al., 2009; Kraemer et al., 2001; Marceau et al., 2012). Considered simultaneously, the three hormones examined here could comprise a more comprehensive biomarker during adolescence than examining one hormone at a time (see Marceau et al., in press).

1.1. Hormonal milieu

Multiple hormones may impact biological underpinnings of behavior such that together they maintain allostasis, or the body's ability to adapt and regulate to changing environmental challenges (Sterling and Eyer, 1988). Given the observed negative associations between hormones of the HPA and HPG axes in adults (Viau, 2002), it is reasonable to hypothesize that the HPA and HPG axes are implicated in counter-regulation mechanisms maintaining allostasis, just as multiple neuroendocrine systems have been implicated in counter-regulation mechanisms in drug addiction (e.g., Koob and Le Moal, 2001). Thus, examining multiple hormones acting in concert may be more fruitful than examining single hormones: the influence of multiple hormones on behavior may be a better index of the complex system represented by these hormones.

There is a brief history of considering how hormones of the HPA and HPG axes are together associated with behavior. Much of the literature examining associations of multiple hormones on behavior has used cortisol—DHEA (e.g., Goodyer et al., 1998, 2003; Izawa et al., 2008, 2012; Young et al., 2002) and testosterone—cortisol ratios (e.g., Van Honk et al., 2010, Montoya et al., 2012; Terberg et al., 2009). According to the cortisol—DHEA ratio hypothesis, DHEA balances cortisol and buffers the body from harmful effects of prolonged exposure to cortisol (e.g., Herbert, 1997, 1998; Kimonides et al., 1998; Mao and Barger, 1998), so a high cortisol-to-DHEA ratio indicates an imbalance that, for example, may predispose individuals to psychopathology or diverse behavior problems (Goodyer et al., 1998, 2003).

According to the testosterone—cortisol ratio hypothesis, high testosterone in the presence of low cortisol is associated with aggression and externalizing problems in adults through up-regulation of gene expression in several brain regions including the amygdala (Van Honk et al., 2010; Montoya et al., 2012). Similarly, higher levels of testosterone predicted overt aggression in boys and men who had low cortisol levels, but not in boys who had high cortisol levels (Dabbs et al., 1991; Popma et al., 2007; Mehta and Josephs, 2010; see Montoya et al., 2012). Studies testing the testosterone—cortisol ratio have included mainly adults and suggest that elevated testosterone levels in the context of impaired adrenal responses may be characteristic of the "fight" response. Notably, these studies examine levels of each hormone, rather than responses of multiple hormones to specific stressors. One study found that increased testosterone-to-cortisol responsivity (in response to a countdown/unannounced loud noise task and the Trier Social Stress Test assessing uncontrollability and social evaluative threat) ratios were associated with psychopathy among adults (Glenn et al., 2011) but these findings have not been replicated in youth.