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Introduction to the Special Section on "Hormones and Cognition: Perspectives, Controversies, and Challenges for Future Research"

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The research of the past two decades has firmly established that hormones modulate numerous aspects of cognitive function, including memory, attention, decision-making, and sensory processing. That such a wide variety of hormones influence cognition mediated by multiple nonhypothalamic brain regions illustrates the critical importance of hormones to neural and cognitive function. The diversity of hormonal effects on cognition is evident in the collection of reviews and original research articles assembled for this special section. Together, these articles provide an overview of recent research on varied topics in hormones and cognition, address controversial issues in the field, and discuss challenges that must be overcome in future research to gain a better understanding of the mechanisms through which hormones modulate cognitive function.

Keywords: behavioral neuroendocrinology, rapid hormone effects, sex steroids, stress hormones, cognitive function

During the past two decades, it has become evident that hormones can profoundly affect numerous aspects of cognition by modulating regions of the brain that mediate cognitive function. Among the most influential data establishing the significance of hormonal regulation of brain regions critical for cognitive function was published by Bruce McEwen and colleagues in the early 1990s. In a series of seminal articles (Gould, Woolley, Frankfurt, & McEwen, 1990; Woolley, Gould, Frankfurt, & McEwen, 1990; Woolley & McEwen, 1992, 1993), they reported that the density of dendritic spines on hippocampal CA1 pyramidal neurons increased 30% when levels of the sex steroid hormone 17β-estradiol (E_2) were endogenously or exogenously elevated in female rats. The fact that these morphological alterations could occur within just 24 hours of exposure to high E_2 levels demonstrated that the hippocampus is exceptionally sensitive to sex steroid hormones, and suggested that memory might be modulated by these hormones. The years since have seen an explosion of research into the many aspects of cognitive function affected by hormones in numerous regions of the brain. This work has demonstrated that hormones are critically important modulators of the neurobiological mechanisms that underlie much of cognitive processing.

The goal of this special section was to assemble reviews and empirical articles that address contemporary topics in hormones and cognition. Articles were submitted in response to a Call for Papers published by *Behavioral Neuroscience*, and each was subjected to anonymous peer-review. Because the articles were generally unsolicited, they do not address all facets of hormones and cognition research; the primary classes of steroid hormones discussed are sex steroid hormones and stress hormones, with little mention of hormones such as growth, gastrointestinal, and pancreatic hormones. However, the articles detail research conducted in a variety of species (birds, rodents, humans) using multiple techniques to study disparate questions related to the general subject of hormones and cognition. As such, the articles provide a glimpse into the diversity of the field, and address issues that are critical to driving the field forward.

The articles are grouped into three categories: rapid hormone effects, sex steroids, and stress hormones and endocrine disruption. In the lead article, McEwen and colleagues (McEwen, Akama, Spencer-Segal, Milner, & Waters, 2012) review evidence for a relatively new concept that hormones can act in a rapid transcriptionally independent manner to influence cognitive function. This notion is supported by two subsequent reviews on the rapid effects of the potent estrogen 17β-estradiol (E_2) on auditory processing in birds (Yoder & Vicario, 2012) and memory in rodents (Frick, 2012). The next group of seven articles discusses the effects of sex steroid hormones on cognitive function from motherhood to menopause. Workman and colleagues (Workman, Barha, & Galea, 2012) review the effects of hormone exposure during pregnancy and the postpartum period on memory and mood, followed by an empirical article by Henry and Sherwin (Henry & Sherwin, 2012) on this topic. Subsequent articles examine the effects of early androgen exposure on spatial and mechanical cognition in humans, (Berenbaum, Korman Bryk, & Beltz, 2012), interactions among hormones affecting social recognition in rodents (Gabor, Phan, Clipperton-Allen, Kavaliers, & Choleris, 2012), and interactions between E_2 and serotonin affecting auditory processing in white-throated sparrows (Matragrano et al., 2012). This group of articles

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ends with a review by Sherwin (Sherwin, 2012) and empirical article by Chisholm and Juraska (Chisholm & Juraska, 2012) that discuss how the age-related loss of sex steroid hormones affect cognitive function in females. The next group of five articles focuses on stress hormones and endocrine disruption. Two empirical articles segue from sex steroids to stress hormones by considering how motherhood affects the mnemonic response to acute stress (Maeng & Shors, 2012) and whether E_2 and chronic stress interact to affect spatial memory and hippocampal morphology (Conrad, McLaughlin, Huynh, El-Ashmawy, & Sparks, 2012). Two subsequent studies conducted in humans describe how stress hormones can influence cognitive bias toward negative information in young women (Kreher, Powers, & Granger, 2012) and threat-related decision making among police officers (Akinola & Mendes, 2012). Finally, the special section concludes with empirical data from Eilam-Stock and colleagues (Eilam-Stock, Serrano, Frankfurt, & Luine, 2012) demonstrating that the endocrine disruptor Bisphenol-A impairs memory and decreases hippocampal and prefrontal dendritic spine density in male rats.

This special section is subtitled, "Perspectives, Controversies, and Challenges for Future Research" with the intent of providing an update on the current state of, and future directions for, the field of hormones and cognition. Various perspectives are offered by all of the articles, but are most prominent in the reviews that discuss rapid hormone actions on neural and cognitive function (Frick, 2012; McEwen et al., 2012; Yoder & Vicario, 2012), cognitively relevant interactions among steroid hormones (Gabor et al., 2012), and the enduring influence of hormonally significant events like pregnancy, motherhood, and menopause on cognition (Sherwin, 2012; Workman et al., 2012). The articles also address numerous controversies, most notably the decade-long debate about hormone replacement therapy as a treatment for age-related cognitive decline in menopausal and postmenopausal women (Chisholm & Juraska, 2012; Sherwin, 2012). Other controversial issues of importance to the field also receive attention, including the origins of sex differences in cognitive abilities (Berenbaum et al., 2012), the extent to which brain-derived hormones contribute to cognitive functioning (Yoder & Vicario, 2012), the effects of social stressors on cognitive functioning (Akinola & Mendes, 2012), and the cognitive impact of exposure to the endocrine disruptor Bisphenol-A (Eilam-Stock et al., 2012).

The challenges for future research are plentiful. Although the extraordinary complexity of the nervous system provides an unending source of questions to be answered, most neuroendocrinologists would argue that studying hormones is exceptionally complicated. As one anonymous reviewer of my own article remarked, "Hormones are messy", and I must wholeheartedly agree. A primary factor in this "messiness" is that steroid hormones share a common biochemical progenitor, cholesterol, and thus, share numerous structural similarities. Furthermore, within a class of steroid hormones (e.g., sex steroid hormones), the metabolites of biologically significant steroids are significant in-and-of themselves. For example, progesterone is metabolized into androgens, which are then converted into estrogens. Thus, determining whether the effects of progesterone are the result of progesterone binding directly to its own receptors, or rather of the downstream actions of androgens, estrogens, or neurosteroid progestin metabolites can be particularly challenging. Behavioral neuroendocrinologists who seek to understand how hormones affect cognitive function must grapple with many important questions including (but not limited to) the following:

- How does my hormone of interest affect my behavior of interest, and does it do so of its own accord rather than via metabolism to another steroid?
- How does this hormone affect the brain regions and circuits that mediate the behavior of interest?
- Which receptors mediate the hormone's effects on the brain and behavior, and do these receptors act through traditional gene transcription mechanisms or more rapid transcriptionally independent events?
- What are the roles of brain-synthesized hormones in modulating the behavior of interest?
- How do activational (prepubertal) and organizational (postpubertal) hormone exposures affect the expression of the behavior of interest?
- Does the hormone affect behavioral expression similarly in males and females?
- Does the age-related loss of sex-steroid hormones impact the hormonal regulation of the behavior of interest?
- Under what environmental and biological conditions does the hormone affect this behavior?
- What other hormones affect the behavior of interest and how might these hormones interact to produce particular behavioral outcomes?
- Are the modulatory effects of the hormone of interest evolutionarily conserved across species?

Answering these questions will not be easy, but doing so is imperative to gain a complete understanding of the neurobiological mechanisms underlying cognitive function. Recent research on hormones and cognition has revolutionized not only behavioral neuroendocrinology, but also many fields of neuroscience. However, we have surely exposed only the tip of the iceberg thus far, and each new discovery will open many exciting avenues of research. With this special section, I have aimed to provide readers with an overview of the many ways in which hormones can regulate cognitive function, and hope the articles will inspire readers to investigate hormonal modulation of their own favorite cognitive processes.

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