MIND, BRAIN, AND EDUCATION

What Are Little Learners Made of? Sugar and Spice and All Things Nice, and Leptin and TNFα and Melatonin

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Two articles in this special section introduce a set of hormones which have been shown, in basic research, to play a role in cognition and learning, but which have not as of yet reached the public eye and educators' and policy-makers' attention. A prior special section of this journal focused on stress hormones, and in particular the stress-sensitive hormone cortisol, and its potential role in learning (Blair, 2010; Bugental, Schwartz, & Lynch, 2010; Lisonbee, Pendry, Mize, & Gwynn, 2010; Rappolt-Schlichtmann & Watamura, 2010). While important, and a key focus of my own research (Adam, 2012), cortisol is only one of many circulating hormones that are influenced by children's experience and behavior, and cross the blood–brain barrier to reach centers of the brain involved in regulation of mood, attention, alertness, and executive functioning and memory processes. Successful calibration and regulation of each of these aspects of neurobiology are increasingly being recognized as central to school readiness and successful learning (Blair, Granger, & Peters Razza, 2005).

My title, a small twist on a 200-year-old nursery rhyme, is intended to imply that little learners are made of many things, and among them a much wider range of biological, and in particular hormonal factors than have previously been implicated. Child neurobiology, including aspects of neurobiology central to learning, is constantly being informed and sculpted by experience and by children's engagement with their environments (Fischer, 2009; Nelson, 2000). One pathway by which experience is conveyed is by way of circulating hormones, which are in turn informed by our experiences of our environments and by our current and past health behaviors. The role of spice is perhaps debatable, but, as the current set of articles explores, levels of obesity-related hormones such as leptin and tumor necrosis factor (TNFα) and circadian hormones involved in the regulation of sleep and wakefulness, such as melatonin, may well play an important and understudied role in children's school readiness and learning.

The innovative study by LeBourgeois, Wright, LeBourgeois, and Jenni (this issue) examines sleep patterns (both objectively and diary reported) and melatonin levels in a small sample of young children in over the course of 6 days in their home settings. Repeated measurement of salivary melatonin over the evening hours allows them to identify each child's "dim light melatonin onset (DLMO)," an evening increase in levels of the hormone melatonin that is an indicator of each child's circadian rhythm. Knowing a child's DLMO provides insight into the time of night at which the child is likely to fall asleep with the greatest ease, because he/she is biologically at his/her lowest level of alertness. The study finds that parents who put their children to bed too close in time after their DLMO are likely to encounter greater levels of bedtime resistance from their children. Although it was not tested in the current study, the authors suggest that selecting a bedtime that aligns with the child's individual biology (e.g., delaying bedtimes slightly for children with later DLMOs) may result in smoother bedtime transitions and, provided total sleep times are adequate, better overall quality of sleep. The authors also suggest that smoother bedtime transitions and good quality sleep could in turn pay large dividends in terms of improved mood, behavior, cognitive functioning and learning.

An important point to be taken from the LeBourgeois et al.'s article is that influence of children's biology on their behavior and their readiness to learn is not deterministic—rather,

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differences in biology interact with environmental constraints and behavioral choices (in this case parent-imposed bedtimes). A suggested implication of this article is that better knowledge of children's biology (in this case, their biologically driven circadian preferences) could serve to guide parents (and educators and policy makers) in making choices that have positive implications for children's readiness to learn and their educational outcomes. When applied at the level of the individual child, this implies a kind of "biologically informed personalized parenting" akin to movements such as personalized medicine which tailor treatments to the unique biological state of the individual. Before parents rush to request evening melatonin measurements for their young children, however, more research is needed. The obvious next step in this line of research, as noted by the authors, is to test whether altered bedtime choices, guided by measurement of child melatonin, do in fact result in reductions of bedtime resistance, longer and better sleep, and improvements in cognition and learning.

The study of LeBourgeois et al. is based on a small sample of healthy, normally functioning, normally sleeping children, all of whom take regular naps. My own research in a large, nationally representative sample has shown that the timing of child and adolescent sleep is related to a broad range of environmental factors, including demographic factors such as socioeconomic status and race/ethnicity, family functioning variables such as warmth and conflict, and child activity choices such as television viewing (Adam, Snell, & Pendry, 2007). These factors influence parent and child bedtime choices, and may also play a role in altering or entraining child biological rhythms over time. Placing the current approach, measurement of child biological rhythms via melatonin levels, in a broader social and ecological context by examining multiple possible determinants of child biological rhythms and parent bedtime choices in larger, more diverse samples, would further extend the promise of this novel line of work.

The article by Miller et al. (this issue) examines another set of hormones that has been understudied in relation to educational outcomes—obesity-related hormones. They include in this list hormones relevant to the control of appetite and satiety, such as leptin, glucagon-like peptide-1 (GLP-1), and ghrelin, which are related to body mass index (BMI) and obesity. They also include markers of inflammation, including interleukin-6 (IL-6) and TNFα, which are regulated by fat tissue. They note that these obesity-related biomarkers have in turn also been related to behavioral and cognitive states relevant to school readiness and learning, including mood states, motivation, executive functioning, and memory processes. Most of the existing research on obesity-related hormones has been conducted in animal models or adults; Miller et al.'s article is the first to examine associations between obesity-related hormones and aspects of school readiness in young children. The authors providing a compelling argument for the possible importance of obesity-related hormones for school readiness, and present a conceptual model that links contextual stress, such as poverty, to school readiness, by way of alterations in BMI and the proposed set of obesity-related hormones.

The results presented, based on a small pilot sample, are only partially in accord with the authors' proposed model. As expected, the measured obesity hormones were strongly interrelated, and the satiety hormone leptin was associated with improved emotion regulation. Contrary to expectations, however, the proinflammatory cytokine TNFα was associated with better rather than worse emotion regulation. In addition, of the measured obesity-related hormones, leptin was the only one found to be related to BMI at this young age. Future research, with a larger sample and a longitudinal design, would help to clarify whether the expected associations emerge over time with age and with a longer history of overweight or obesity. Future research should also reveal whether the proposed impacts on learning associated with obesity-related hormones are sizeable enough to warrant attention by parents, educators, and policy makers. Certainly, there are many health reasons to target overweight and obesity in children as an important arena for intervention; demonstrating substantial impacts on school readiness and performance would serve to further reinforce this issue as a policy imperative.

Interesting potential connections exist between the two articles in this special issue. Past research has shown that inadequate sleep has profound effects not only on mood, cognition, and learning; it also affects inflammation, metabolic hormones such as leptin and ghrelin (Spiegel, Tasali, Penev, & Cauter, 2004), and the development of increased BMI over time in children (Snell, Adam, & Duncan, 2007). Thus, the types of sleep disruptions highlighted in LeBourgeois et al.'s article could affect school readiness and learning, at least in part, by way of their impact on the obesity-related hormones highlighted by Miller et al. and the findings reported by Miller et al., could, at least in part, be accounted for by variations in child sleep.

Scientists tend to specialize in particular biological systems with their particular sets of hormones (e.g., stress, obesity and metabolism, sleep and circadian biology), but increasingly, measurement of multiple biological systems and the interactions among them reveal finely woven and dynamic webs of mutual regulation across systems. For example, the prior special section emphasized direct effects of stress hormones on learning by way of their effects on brain regions involved in executive functioning (Blair, 2010). However, stress hormones, such as glucocorticoids, have been shown to have important influences and mutually regulatory interactions with sleep processes and with the circadian and metabolic hormones and markers of inflammation that are the focus of the current special section (Spiegel et al., 2004; Zeiders, Doane, & Adam, 2011). The fact that that multiple hormone systems of potential relevance for learning are mutually regulatory, each influencing the other in the moment and over time, is important in understanding pathways to dysregulated biology and learning, and also for planning interventions to improve biological functioning and learning. One implication is that dysregulation in one environmentally sensitive biological system, such as stress biology or sleep biology or metabolism, can have a cascade of downstream effects across multiple other aspects of children's biological, behavioral, emotional, and cognitive functioning. However, the fact that multiple hormones, and the social and behavioral ecologies which they respond to, form a mutually regulatory system is also hopeful, in that it implies that an effective intervention to improve functioning in any aspect of this system may in turn cause a positive cascade of improved functioning across other components of the system. It also implies that interventions affecting multiple aspects of children's behavior and biology (e.g., targeting stress, sleep, and weight), may be particularly effective.

It is hard to overestimate the intricacy with which the various biological systems discussed across these two papers are interwoven, with each other and which children's environments and behaviors. This makes the study of the role of ANY of these hormones complicated, but an important and worthy effort. It also suggests that, as this field develops, studies which incorporate measures of multiple hormone systems, and do so in careful consideration of the environmental and developmental contexts affecting children's biology and behavior, may come closest to revealing the complex ways in which hormones affect children's learning. We are still only beginning to understand "what learners are made of," but increasing attention to multiple aspects of biology, and how those are influenced by and influence children's daily experiences at home and at school, may be an important and understudied ingredient in children's neurobiological and behavioral readiness to learn.

REFERENCES

Adam, E. K. (2012). Emotion-cortisol transactions occur over multiple time scales in development: Implications for research on emotion and the development of emotional disorders. In T. A. Dennis, K. A. Buss, & P. D. Hastings (Eds.), *Physiological measures of emotion from a developmental perspective: State of the science. Monographs of the Society for Research in Child Development, 77(2)*, 17–27.

Adam, E. K., Snell, E. K., & Pendry, P. (2007). Sleep timing and quantity in ecological and family context: A nationally representative time-diary study. *Journal of Family Psychology*, *21*(1), 4–19.

Blair, C. (2010). Going down to the crossroads: Neuroendocrinology, developmental psychobiology, and prospects for research at the intersection of neuroscience and education. *Mind, Brain, and Education*, *4*, 182–187.

Blair, C., Granger, D. A., & Peters Razza, R. (2005). Cortisol reactivity is positively related to executive function in preschool children attending head start. *Child Development*, *76*, 554–567.

Bugental, D. B., Schwartz, A., & Lynch, C. (2010). Effects of an early family intervention on children's memory: The mediating effects of cortisol levels. *Mind, Brain, and Education*, *4*, 159–170.

Fischer, K. W. (2009). Mind, brain, and education: Building a scientific groundwork for learning and teaching1. *Mind, Brain, and Education*, *3*, 3–16.

Lisonbee, J. A., Pendry, P., Mize, J., & Gwynn, E. P. (2010). Hypothalamic–pituitary–adrenal and sympathetic nervous system activity and children's behavioral regulation. *Mind, Brain, and Education*, *4*, 171–181.

Nelson, C. (2000). The nerobiological bases of early intervention. In J. Shonkoff & S. Meisels (Eds.), *Handbook of early childhood intervention*. New York, NY: Cambridge University Press.

Rappolt-Schlichtmann, G., & Watamura, S. E. (2010). Inter- and transdisciplinary work: Connecting research on hormones with problems of educational practice. *Mind, Brain, and Education*, *4*, 156–158.

Snell, E. K., Adam, E. K., & Duncan, G. J. (2007). Sleep and the body mass index and overweight status of children and adolescents. *Child Development*, *78*, 309–323.

Spiegel, K., Tasali, E., Penev, P., & Cauter, E. V. (2004). Brief communication: Sleep curtailment in healthy young men is associated with decreased leptin levels, elevated ghrelin levels, and increased hunger and appetite. *Annals of Internal Medicine*, *141*, 846–850.

Zeiders, K., Doane, L. D., & Adam, E. K. (2011). Reciprocal relations between objectively measured sleep patterns and diurnal cortisol rhythms in late adolescents. *Journal of Adolescent Health*, *48*, 566–571.