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Advances in Neuroendocrine Mechanisms

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Steroid hormones are key modulators of the inter- and intra-cellular communications network used by the central nervous system. These hormones, although simple in structure, have the capacity to influence virtually all neural functions in a myriad of ways: from the programming, organization and maintenance of neurons and their connections during development, the activity and function of neurons in adulthood, to the death of neurons during aging and neuropathology. To stimulate scientific interactions between US and South American neuroendocrinologists interested in steroid hormone influences on a variety of physiological and behavioral events, including development, reproduction and energy homeostasis, the First US-South American Workshop in Neuroendocrinology was held in Viña del Mar, Chile from August 7–10, 2011. The site is known for its natural beauty and its historic importance in neuroscience [1] and provided an interesting backdrop for this important interchange. In a small and informal setting, this meeting fostered in-depth discussion of new ideas and interactions between young and established investigators using a wide array of model systems, strategies and technologies, from molecular to behavioral. It also provided a unique opportunity for 16 competitively chosen young investigators to present their research in oral or poster presentations and discuss their findings with established investigators in the field. This Special Issue of *Hormone and Metabolic Research* comprises the reviews and original articles that arose from this workshop. All have significant input from our promising young investigators who were in attendance.

The meeting began with a keynote address by Jeffrey Blaustein (University of Massachusetts, Amherst) who explored the role of neuronal steroid hormone receptors as integrators of the internal and external environment [2]. The address provided a broad overview for this meeting and summarized key concepts that led to major advances in our understanding of how steroid hormone receptors are regulated in brain and influence behavior. He provided an overview of the neuroendocrine field, starting with the 1960s discovery of their regulation by steroid hormones, to the current day understanding of their regulation by neurotransmitters, membrane-initiated second messenger signaling pathways, and somatosensory inputs. Furthermore, he discussed how external factors, like stress, could

have long-term effects on brain remodeling and steroid receptor regulation. Following his presentation, Victor Ramirez (University of Illinois, Urbana-Champaign) and Valeria Rettori (CEFYO-CONICET-UBA, Buenos Aires, Argentina) provided a brief account of the rich interaction between the Americas over many decades. In particular, there was a tribute to the pioneers in the field, the late Samuel M. McCann, Charles H. Sawyer, and Bernardo Houssay whose scientific contributions had a tremendous impact across the continents. The discussion set the tone for the scientific sessions, which showcased presentations by young investigators alongside those of established investigators. Several of these young investigators are the lead authors of the reviews in this volume, which summarize the presentations within each of the sessions.

Steroid sensitive neural circuits are implicated, not only in the control of reproductive hormone secretion and behaviors, but also in nonreproductive functions such as energy balance, stress and anxiety, emotion, aggression, cognition, metabolism, feeding, etc. The circuitry undergoes programming during development in a sex dependent manner that is dependent on genomic factors. In addition, environmental factors, both in utero and post-natal, also influence these functions throughout the lifespan. This issue attempts to encapsulate the current cutting-edge research on these various aspects that are related to steroid hormones. The reviews underscore some of these common themes. The first review discusses the current state of understanding of the molecular mechanisms of steroid hormone action [3]. Nugent et al. [4] integrates hormonal programming and function, from development through aging, on various tissue types including neurons, glia, and blood vessels. This review also discusses exciting genomic and epigenomic mechanisms that may work to alter the expression of critical hormone receptor genes. A discussion of steroid hormone action is never complete without a discussion of its role in regulating gonadotropin-releasing hormone (GnRH) and reproduction across species. Christiansen et al. [5] discuss several aspects of the regulation of GnRH by addressing a number of critical questions such as strategies involved in GnRH regulation and the internal and external conditions that modulate function and behavior. The review by Ismail et al. [6] demonstrates that a proper regulation of the stress axis relies on the complex interplay between genetic and environmental factors. Such influences could also affect the physiology and health of the offspring, including its role in metabolism as highlighted in the article by Boersma et al. [7]. The steroidal influences in not only metabolism, but neuropsychiatric health as well, rely on the interphase of the reproductive and stress axes as pointed out in the review by Fernandez-Guasti et al. [8]. How sex differences, programmed during development, and activated and subsequently modulated by gonadal steroids influence the outcome of risks to various psychiatric disorders are also discussed.

Many challenges for this burgeoning field exist for the future. In the coming decade, important advances must be made in the field of neuroendocrinology using innovative technologies spanning the fields of molecular, computational, and systems biology to examine critical questions in the field. Such an integration of approaches is not that distant as exemplified by Sergio Ojeda (The Oregon Health Science University) in his presidential keynote address. His research on the basic mechanisms involved in GnRH regulation of puberty using novel systems biology approaches of high throughput screening has identified a highly organized hierarchical network of genes. Such powerful techniques have transformed our traditional views on regulation of puberty and the function of the brain. We are now witnessing the use of such novel approaches in the contributions of the young investigators in this volume. While the technologies available are certainly powerful, we cannot lose sight of the fact that traditional techniques will also find their place in the iterative process to define the function of the newly identified gene networks. We also cannot lose sight of the centralizty of neuroendocrinology modulation of most biological systems.

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