Oxytocin, Vasopressin, and Related Peptides in the Regulation of Behavior

The mammalian neurohypophyseal peptide hormones oxytocin and vasopressin act to mediate human social behavior – they affect trust and social relationships and have an influence on avoidance responses. Describing the evolutionary roots of the effects that these neuropeptides have on behavior, this book examines remarkable parallel findings in both humans and non-human animals.

The chapters are structured around three key issues: the molecular and neurohormonal mechanisms of peptides; phylogenetic considerations of their role in vertebrates; and their related effects on human behavior, social cognition, and clinical applications involving psychiatric disorders such as autism. A final chapter summarizes current research perspectives and reflects on the outlook for future developments.

Providing a comparative overview and featuring contributions from leading researchers, this is a valuable resource for graduate students, researchers, and clinicians in this rapidly developing field.

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Preface

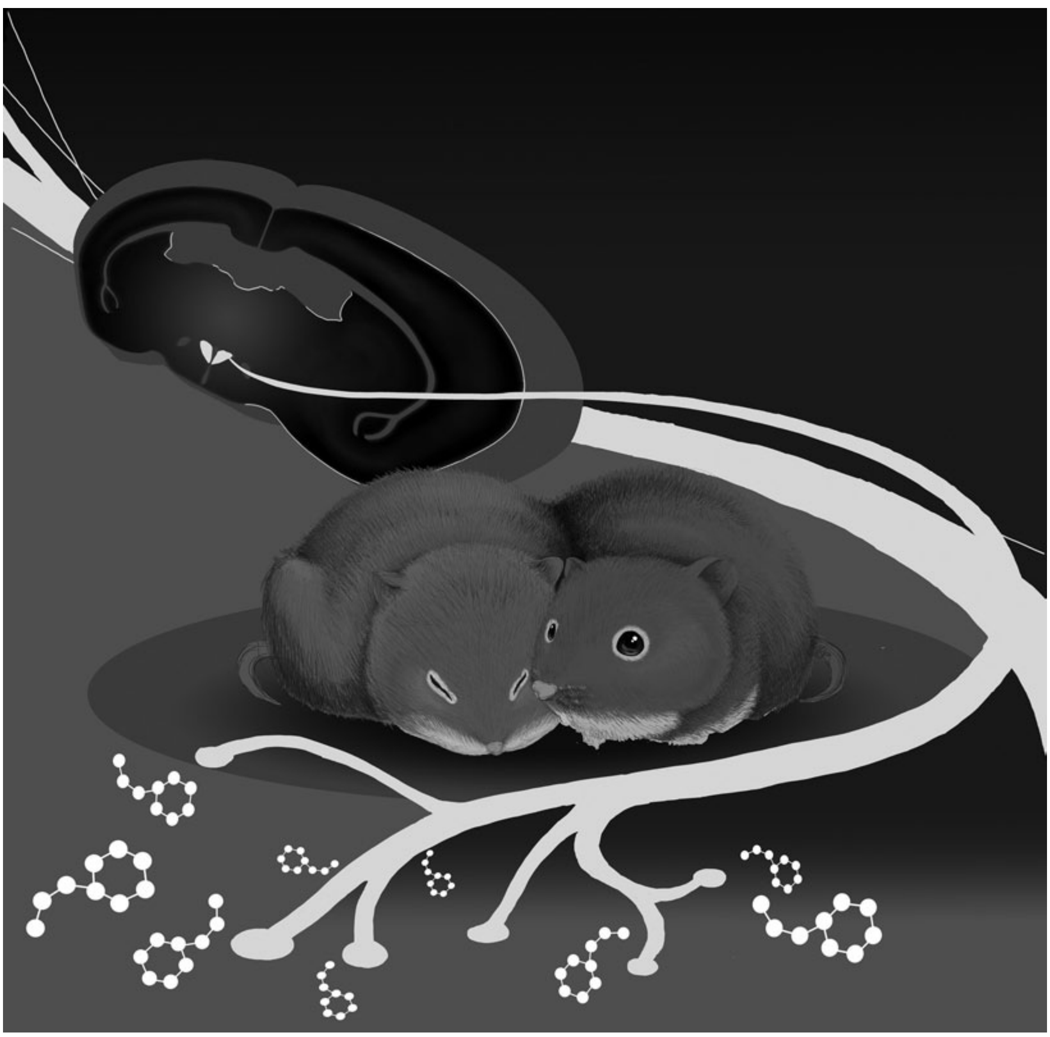

Figure 1 Courtesy of Anna Phan and Christopher Gabor.

Comparative approaches to oxytocin, vasopressin, and vertebrate behavior

This text is intended by the three of us to serve upper-level undergraduate students and beginning graduate students who are interested in how relatively well understood neurochemical systems regulate natural behaviors in animals, including humans. Some of the strongest causal links discovered, to date, between molecular biological phenomena and behavioral regulation have to do with hormones. This is especially true for hormones whose chemistry is relatively simple. Classically, those causal links have involved steroid hormones, produced in peripheral organs, telling the brain what is going on in the rest of the body, and thus allowing the brain to regulate behavior in a manner consonant with the state of the body. In this text, chapters explicate molecular/behavioral regulation in the opposite direction: hormones that are produced in the vertebrate brain, by specific groups of nerve cells in the basal forebrain, not only enter the circulation but also act as neuromodulators within the central nervous system. Oxytocin and arginine vasopressin, whose chemical structures in the vertebrates were elucidated during the 1950s and whose genes were cloned during the 1980s, each has only nine amino acids and each peptide has its structure constrained by a disulfide bridge. Differing from each other by only two animo acids, the two neuropeptides or "nonapeptides" have a fascinating role across the vertebrates.

As described, you will see in this text that oxytocin, vasopressin, and related neuropetides have a variety of behavioral actions in vertebrate animals ranging from fishes to humans. In the broadest sense the two hormones produced in the brain are "telling" the body what behavioral and physiological function these particular basal forebrain cell groups need to have accomplished. A series of foundational chapters lay the basis for understanding the regulation and expression of oxytocin and vasopressin systems. This is followed by a number of chapters that utilize a phylogenetic/comparative approach to describe the behavioral roles of oxytocin and vasopressin and related neuropetides across vertebrate species. Finally, a number of chapters consider the roles of oxytocin and vasopressin in the modulation of human behavior.

Evolutionary foundations and the roles of oxytocin/vasopressin-related neuropetides in invertebrates

Although this text is designed to provide a comparative behavioral approach to oxytocin and vasopressin and related peptides in the vertebrates, to more fully appreciate the roles of oxytocin and vasopressin it is useful to understand their evolutionary history and invertebrate foundations. Although oxytocin and vasopressin are only found in mammals, members of the two neuropeptide systems constitute one of the most ancient and evolutionarily conserved neuropetide systems. OT and AVP belong to a large superfamily found in a wide range of vertebrate and invertebrate (e.g., hydra, worms and some insect) species (for reviews see Archer, 1972; Donaldson and Young, 2008; Goodson 2008). In the jawed vertebrates oxytocin-like and vasopressin-like neuropetide lineages arose from a common ancestral gene by local duplication in a gawed vertebrate ancestor (Goodson, 1998). Invertebrates, with a few exceptions (e.g., cephalopods), have only one oxytocin/vasopressin gene family homolog (e.g., annetocin (annelid worms), conopressin (snails, sea hare, leeches), inotocin (some insects)) (Donaldson and Young, 2008). Interestingly, in the insects oxytocin/vasopressin-like peptides were found in flies, mosquitoes, some beetles but not in the more advanced eusocial honey bee (Stafflinger et al., 2008).

The molecular structure and behavioral actions mediated by these neuropeptides and their receptors in the invertebrates are in many respects comparable to those of vertebrates. For example, just as oxytocin and vasopressin are produced in the neurosecretory magnocellular neurons in the vertebrate hypothalamus so the oxytocin/vasopressin homolog, annetocin, is expressed in, and released from, the sensory neurosecretory "brain" counterpart of annelid worms. Indeed, the annelid neurons express the same micro-RNAs and transcription factors as do the neurosecretory magnocellular neurons of vertebrates (Tesmair-Raible et al., 2007). At a functional level oxytocin/vasopressin-like neuropetide involvement in osomoregulation and fluid balance is also evident across the animal phyla (Goodson, 1998). It is tempting to speculate that this early involvement in the regulation of responses to osmotic stress may lay the foundation for the evolution of neuropetide mechanisms that modulate interactions with the environment and stress responses.

Oxytocin and vasopressin's association with reproduction, parental and socio-sexual behaviors and responses are also evolutionarily conserved, even though the specific behaviors affected can be species and taxa specific. For example, several members of the oxytocin/vasopressin family evoke response related to reproduction in annelids and leeches (Fujino et al., 1999; Wagenaar et al., 2010). Similarly, conopressin, a molluscan (snail) homolog of oxytocin/vasopressin, modulates ejaculation in males and egg-laying in females. (Oumi et al., 1996). These early reproductive roles may have set the stage for the evolution of the involvement of these neuropetides in various socio-sexual functions described in this book for the vertebrates. Snails present another particularly fascinating example of the evolutionarily flexibility of the oxytocin/vasopressin system. The venom of cone snails contains an endogenous vasopressin analog, conporessin-T, that functions as a vasopressin antagonist. These venoms, which are injected through specialized mouth parts of the cone snail and are used to catch prey or for protection against predators, may in part exert their actions thorough modifications in the effects of vasopressin-like neuropetides (Dutertre et al., 2008). Finally, in the most advanced of the molluscs, the cephalopods (octopus, cuttlefish), there are two superfamilies of oxytocin/vasopressin-like peptides members (octopressin and cephaloctocin (Minakat, 2010)) that exert effects on cuttlefish learning and memory similar to those of OT/AVP in mammals (Bardou et al., 2010). As described, you will see in this text a range of behavioral roles of oxytocin and vasopressin the vertebrates that build upon these invertebrate foundations.

Comments to us by students and other readers will be welcome, because shortcomings of the current effort could be remedied in a second edition of this text.

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E. C., D. W. P. and M. K.
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