Hormones and Behavior 61 (2012) 259–265

Contents lists available at SciVerse ScienceDirect

Hormones and Behavior

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

Review

Vasopressin, oxytocin, and social odor recognition

Douglas W. Wacker [1], Mike Ludwig *

Centre for Integrative Physiology, University of Edinburgh, Edinburgh EH8 9XD, UK

ARTICLE INFO

Article history:
Received 22 June 2011
Revised 12 August 2011
Accepted 17 August 2011
Available online 30 August 2011

Keywords:
Vasopressin
Oxytocin
Olfaction
Pheromone
Social recognition
Somato-dendritic
Main olfactory bulb
Accessory olfactory bulb
Anterior olfactory nucleus

ABSTRACT

Central vasopressin and oxytocin, and their homologues, modulate a multitude of social behaviors in a variety of animal taxa. All social behavior requires some level of social (re)cognition, and these neuropeptides exert powerful effects on an animal's ability to recognize and appropriately respond to a conspecific. Social cognition for many mammals, including rodents, begins at the main and accessory olfactory systems. We recently identified vasopressin expressing neurons in the main and accessory olfactory bulb and in the anterior olfactory nucleus, a region of olfactory cortex that transmits and processes information in the main olfactory system. We review this and other work demonstrating that both vasopressin and oxytocin modulate conspecific social recognition at the level of the olfactory system. We also outline recent work on the somato-dendritic release of vasopressin and oxytocin, and propose a model by which the somato-dendritic priming of these neuropeptides in main olfactory regions may facilitate the formation of short-term social odor memories. This article is part of a Special Issue entitled Oxytocin, Vasopressin, and Social Behavior.

Contents

Introduction . . . 259
Social recognition . . . 260
Vasopressin and oxytocin: mechanisms of action . . . 260
Social odor processing . . . 261
Vasopressin and oxytocin in the olfactory system . . . 261
Vasopressin, oxytocin and social odor memory: a model . . . 262
Relevance to human studies . . . 263
References . . . 264

Introduction

In addition to their well established systemic physiological effects, vasopressin and oxytocin are potent modulators of social behavior in a variety of vertebrate taxa, including fish (Godwin, 2010), amphibians (Rose and Moore, 2002), birds (Goodson and Thompson, 2010), and mammals, including humans (Guastella et al., 2011; Insel, 2010; Young et al., 2011). These neuropeptides exert their effects on a range of behaviors that are incredibly diverse and run the gamut of what we consider social behavior. For example, aggression (Bosch et al., 2005; Veenema et al., 2010), affiliative behavior (Goodson et al., 2009), vocal behavior (Kime et al., 2010), sexual behavior and pair-bonding (Gil et al., 2010; Winslow et al., 1993), parental behavior and establishment of the mother–offspring bond (Bosch and Neumann, 2010), and social stress (Litvin et al., 2011) are all modulated by vasopressin, oxytocin, or their non-mammalian homologues.

Constructing a generalized model that accounts for the overall effects of central vasopressin and oxytocin on social behavior would be difficult, as these neuropeptides often have species- and/or context-dependent effects, and their actions vary across different brain regions (Goodson and Thompson, 2010; Insel et al., 1994; Kabelik et al., 2009). One potentially fruitful approach is to cluster particular sociobehavioral phenotypes (e.g. behavioral syndromes or coping styles) and examine how vasopressin and oxytocin signaling parameters might predictably correlate (Koolhaas et al., 2010; Sih et al.,

* Corresponding author. Fax: +44 131 650 2872.
E-mail address: mike.ludwig@ed.ac.uk (M. Ludwig).
[1] Current address: Department of Molecular and Integrative Physiology, University of Michigan, Ann Arbor, MI 48109, USA.

0018-506X/$ – see front matter © 2011 Elsevier Inc. All rights reserved.
doi:10.1016/j.yhbeh.2011.08.014

2004). Another approach is to find some common attribute or component of all social behavior and begin there. All social behavior involves some form of social cognition and/or recognition, on which vasopressin and oxytocin exert powerful effects. For example, failure to respond appropriately to what should be a familiar social stimulus may involve a disruption of social recognition or a problem with higher level processing, such as the proper integration of multiple contextual cues. Therefore, it is important to separate social recognition from subsequent responses when considering complex social behavior.

Social recognition

Social cognition involves the sensing, incorporation, integration, recognition, and processing of information about conspecifics, and allows an animal to react appropriately to social stimuli across a variety of contexts (Adolphs, 2001). For social recognition to occur, an animal must simply recognize another animal as something it has encountered before. This involves an initial sensing of the subject, whether by sight, smell, touch, hearing, etc., the formation and potential long-term consolidation of a memory, and the eventual remembrance of the subject in a subsequent encounter. Upon this recognition, an appropriate response may be enhanced or decreased olfactory investigation, aggression, or affiliation, initiation of a fight or flight response, etc., depending on the focal animal's previous experience with the subject. For example, female sheep can recognize their own offspring, allowing them, but not strange lambs access to their milk (Kendrick et al., 1992). Rats can differentiate colony members from strange intruders. Aggression within an established rat colony is often quite low, while aggression of colony members towards male intruders can be very high (Barnett, 1958; Blanchard et al., 1988). Continual interaction is not required for this difference, as removal and subsequent replacement of a colony member does not elicit such aggression (Alberts and Galef, 1973). This strongly suggests a role for social recognition in these context-dependent interactions. Olfaction plays an important role in social recognition in sheep and rodents (Levy et al., 1995; Noack et al., 2010), and vasopressin and oxytocin play a role in this olfaction-based recognition (Dluzen et al., 1998a; Kendrick et al., 1997; Larrazolo-Lopez et al., 2008; Tobin et al., 2010).

Recognition memory is often split into two components, a long-term recollection of salient information about a recognized stimulus thought to involve hippocampal storage, and a shorter term familiarity with a recently encountered stimulus, thought to involve extra-hippocampal processing (Yonelinas et al., 2010). The ongoing recognition of a lamb by its mother and the recognition of fellow colony members by an adult rat are both associated with this long-term recognition. However, shorter term recognition is also important to these behaviors. The mother–lamb bond forms very quickly after birth (<2 h) and can initially be disrupted by separating the pair (Kendrick et al., 1997). Short term social recognition in adult rats has been assessed utilizing multiple testing paradigms including the social recognition test, habituation/dishabituation test, and social discrimination test (reviewed in Ferguson et al., 2002). In the social discrimination test, recognition is demonstrated when a focal animal spends more time investigating a novel versus familiar conspecific, usually a juvenile or ovariectomized female (Engelmann et al., 1995, 2011). Interestingly, male rats only retain the memory of briefly encountered social stimuli for about 45 min, and females for around 2 h, suggesting that longer-term consolidation does not occur in this test (Bluthe and Dantzer, 1990; Engelmann et al., 1998). It is unclear whether this short term recognition requires true individual recognition; rather it may simply involve the ability to differentiate familiar versus unfamiliar conspecifics, i.e. class recognition, based on some combination of currently undescribed attributes (Johnston, 1993).

Although the remainder of this paper will deal primarily with vasopressin/oxytocin modulation of short term social recognition, oxytocin clearly plays a role in longer term social odor memory storage in sheep, and both neuropeptides may be involved in longer-term social recognition and related behaviors in rodents (Kendrick et al., 1997; Wersinger et al., 2008; Yu et al., 1996a). There is evidence that vasopressin plays a more prominent role in short-term social recognition in male rodents, with oxytocin being more important in females (Bluthe and Dantzer, 1990; Engelmann et al., 1998; Ferguson et al., 2001; Tobin et al., 2010). More work in female rodents, especially in female rats, is required to more fully understand these differences.

Social recognition is modulated via different mechanisms than the recognition of inanimate objects, i.e. object recognition (Bielsky et al., 2004; Tobin et al., 2010). There is also evidence that conspecific social cues are processed differently than heterospecific (e.g. predator) social cues (Kang et al., 2009; Samuelsen and Meredith, 2009, 2011; Wacker et al., 2010). Vasopressin and oxytocin act on a variety of brain regions to both facilitate conspecific social recognition and to modulate subsequent behavioral responses (Bielsky et al., 2005; Tobin et al., 2010; Wersinger et al., 2008). Both neuropeptides modulate olfactory regions to alter social odor memory (Dluzen et al., 2000; Kendrick et al., 1997; Tobin et al., 2010). To appreciate how neural vasopressin and oxytocin may facilitate the formation of short-term social odor memories and thus, modulate social behavior, it is first crucial to understand the varied mechanisms of action of these peptides in the brain.

Vasopressin and oxytocin: mechanisms of action

Vasopressin and oxytocin can be released both axonally and somato-dendritically, and release via these two mechanisms can be differentially regulated (Landgraf and Neumann, 2004; Ludwig and Leng, 2006). Most work dealing with somato-dendritic release of these neuropeptides has been done in the hypothalamic supraoptic nucleus, mostly due to the ease by which the two release pools can be isolated experimentally in this region (Ludwig and Leng, 2006). That being said, there is ample evidence that somato-dendritic release of neuropeptides is widespread in the brain (Castel et al., 1996; Drake et al., 1994; Landry et al., 2003). Neurohypophyseal (axonal) release of oxytocin and vasopressin from the supraoptic nucleus is inducible by depolarization, but somato-dendritic release in response to depolarization is not observed without a prior mobilization of intracellular calcium (Ludwig et al., 2002, 2005). Increased cytosolic calcium, which can be induced by intracellular calcium mobilizers such as thapsigargin or cyclopiazonic acid, leads to the recruitment of large dense core vesicles into a readily-releasable pool close to the cell membrane (Tobin et al., 2004). Upon subsequent depolarization, these vesicles are released and increases in central, somato-dendritic oxytocin or vasopressin are observed. The initial increase in intracellular calcium, which does not itself require depolarization, “primes” neurons for subsequent somato-dendritic neuropeptide release in response to future depolarization (Ludwig et al., 2002, 2005). Such priming events potentially allow for experience-dependent somato-dendritic release as long as large dense cored vesicle recruitment persists (about 90 min for hypothalamic oxytocin or vasopressin), at which time these neuropeptides can modulate the firing properties of nearby neurons (Ludwig et al., 2002; Ludwig and Leng, 2006).

Central vasopressin and oxytocin act on metabotropic receptors to modulate neuronal function. Neural effects are mediated by three G protein-coupled receptors, the vasopressin 1a (V1a), the vasopressin 1b (V1b), and the oxytocin receptor (Barberis et al., 1998). Structurally, vasopressin and oxytocin are very similar; differing by only two amino acids in most Eutherian mammals, and crosstalk at the receptor level may be physiologically relevant (Barberis et al., 1992; Gimpl and Fahrenholz, 2001; Schorscher-Petcu et al., 2010). Signaling at all three receptors activates phospholipase Cβ and mobilizes calcium from intracellular stores (Dayanithi et al., 1996; Lambert et al., 1994; Sabatier et al., 1998). Some vasopressin neurons can also elicit cAMP-signaling cascades via V1 receptors (Sabatier et al., 1998; Wrobel et al., 2011). This signaling can sometimes be independent of PLC activation and may not involve mobilization of intracellular