Available online at www.sciencedirect.com

ScienceDirect

www.elsevier.com/locate/brainres

Editorial

Evolutionary perspectives on the role of oxytocin in human social behavior, social cognition and psychopathology

The articles in this Special Edition summarize the latest research on oxytocin (OT), and often arginine vasopressin (AVP), in human parental behavior, other social behaviors, social cognition, social information processing in the brain, as well as developmental disorders and psychopathology. These articles aspire to not only review progress in these areas but to identify the limitations of what have been done and also to articulate high priority directions for future research. The relevance of the emerging evidence for understanding the psychobiology of mental illness is emphasized. To set the stage, here we discuss how OT in the central nervous system (CNS) might have mediated the critical advances in social behavior during the evolution of placental mammals.

Selection for avid and sustained maternal behavior was critical for the successful evolution of placental mammals. OT was selected from phylogenetically earlier nonapeptides to enable the unique features of placental mammalian reproduction: birth of neonates after in utero fetal development (parturition); delivery into the mouths of suckling infants of high quality nutrition produced within the mother's body by the larger process of lactation (milk ejection); and activation of maternal nurturing of newborns. In all mammalian species tested to date, OT appears to facilitate the postpartum initiation of maternal behavior (Pedersen, 2013). In sub-primate mammals, this involves, in concert with and dependent upon the reproductive hormone conditions that promote the onset of parturition, OT-initiated motivation to exhibit hard-wired, species-specific sets of offspring-directed care-taking behaviors. To restate this point in a more general way that is a central theme of this Special Issue: with the evolution of placental mammals, OT was selected to activate brain systems promoting maternal behavior, a sustained and prosocial motivational state. Other social attachments and social behaviors that were selected later during mammalian evolution appear to be at least partially based on OT (and AVP) neural systems that first emerged during the evolution of maternal behavior. Supporting this contention are the OT and AVP dependence of pair-bond formation in the monogamous prairie vole (Young and Wang, 2004) and marmosets (Smith et al., 2010), studies indicating OT regulation of social interactions in rhesus macaques (Chang et al., 2012; Parr et al., 2013; Ebitz et al., 2013; Winslow et al., 2003) and the rapidly accumulating number of reports of OT influences (mostly positive) on human trust, cooperation and social cognition (e.g., see Meyer-Lindenberg et al., 2011).

During early placental mammalian evolution, OT was also coopted to produce affective changes vital to the success of maternal behavior, e.g., reduced fear/anxiety (see Febo and Ferris; MacDonald and Feifel, both this volume; Neumann et al., 2000; Figueira et al., 2008), which enabled suppression of newborn-directed aggression during parturition (McCarthy, 1990; McCarthy et al., 1986) and regulation of intruder-directed aggression during lactation (Bosch et al., 2005; Consiglio and Lucion, 1996; Consiglio et al., 2005; Giovenardi et al., 1998; Lubin et al., 2003) AVP (also selected from earlier nonapeptides during the evolution of mammals) appears to play an important role in activating and sustaining maternal behavior (Bosch and Neumann, 2008; Pedersen et al., 1994) and regulating affective changes and increases in intruder aggression associated with the onset of maternal behavior (see Febo and Ferris, this volume). These points are relevant to another theme that is central to this Special Issue: from early on in placental mammalian evolution, OT and AVP were selected for important roles in emotion regulation necessary for successful social behavior.

The evolution of avid and sustained maternal behavior as well as other unique aspects of placental mammalian reproduction effectively eliminated long-standing barriers to development of larger and more complex brains and, eventually, higher intelligence. In utero development and maternal protection during maturation as well as a uniquely rich and reliable source of nutrition, i.e., milk, substantially increased the percentage of offspring that survived to reproduce. Therefore, numbers of offspring required for reproductive fitness decreased allowing each offspring to be larger and endowed with a bigger brain. In addition, maternal protection during the lactation period allowed further brain growth and development to occur before offspring had to fend for themselves. This also created a malleable period during which epigenetic influences from the mother, siblings and the environment influenced brain development in survival-enhancing ways (McGowan and Szyf, 2010; Champagne, 2012). Selection for mental abilities that increased the

effectiveness of maternal behavior, and later paternal behavior, in enhancing the survival of offspring to reproductive age may have also spurred on the evolution of more complex brains and greater intelligence.

In many rodent species (e.g., rats, mice), the strong, OT-dependent maternal motivation that is activated at parturition is directed towards newborns in general. Mothers in these species do not bond to individual offspring (Pedersen, 2013). OT appears to have been centrally involved in the next evolutionary leap in prosocial behavior in mammals; formation of selective attachments to specific individuals. The formation of selective bonds requires the ability to learn the identity of important conspecifics (e.g., offspring, mothers, mating partners). In sub-primate mammals, individual identification is based largely on learning the unique olfactory cues of others. Oxytocin was coopted during the evolution of selective social bond formation to facilitate acquisition of the memory of odor cues of other individuals. For example, OT release in the olfactory bulbs is necessary for ewes to encode the memory of the specific odors of their newborn lambs in the immediate postpartum period (Kendrick et al., 1997). The capacity to form selective, olfactory-based bonds may have emerged from the ability earlier in evolution to form transient memories of the odors of novel conspecifics. For example, rats and mice are able to remember the unique odor of a novel individual for approximately 1–2 h. Experiments with OT gene knockout mice or central administration of OT antagonists have demonstrated that formation of transient social memory is entirely OT dependent (Ferguson et al., 2000; Takayanagi et al., 2005). These findings indicate that OT has played a significant role in social cognition since early in mammalian evolution. Evidence for extensive involvement of OT in human social cognition is another major theme developed in many of the articles in this Special Issue.

During the evolution of primates, maternal and other social behaviors have become less dependent on specific sex hormones and olfactory cues. The neurobiological control of social interactions has evolved from hard-wired behavioral programs reflexively triggered by specific sensory cues to more flexible and complex processing and integrating of cues from multiple sensory modalities. These evolutionary changes in the psychobiology of social relationships in primates have certainly been facilitated by, and perhaps contributed to the selection for, expansion of non-olfactory regions of the cortex and advances in intelligence. OT still clearly plays a crucial role in primate maternal behaviors. Intracerebroventricular (ICV) infusion of OT in nulliparous rhesus macaques increases their interests in infants measured by looking, touching, maintaining proximity, and lip-smacking (Holman and Goy, 1995). Furthermore, peripheral administration of OT antagonist delivered to the limbic regions of the CNS substantially reduces nulliparous female macaque's interest in infant and sexual behavior (Boccia et al., 2007). Using non-human primates also permits unique investigations into the role of OT in mediating more complex social behaviors and social cognition than maternal behaviors and pair-bonding. Converging evidence from the studies examining the role OT in complex social cognition in non-human primates as well as in humans (Bartz et al., 2011) suggests that the effects of OT are critically gated by social contexts and intrinsic social orientations. For example, ICV administration of OT in male squirrel monkeys increases associative behaviors in low status males but increases sexual assertiveness in higher status males, upon exposures to female monkeys (Winslow and Insel, 1991). Furthermore, increasing OT levels in the CNS via OT inhalation in rhesus macaques promotes either other-regarding or self-regarding behaviors depending on social decision contexts (i.e., what the available options are concerning self and others) (Chang et al., 2012), while controlling for the state of social vigilance toward specific social stimuli (Parr et al., 2013; Ebitz et al., 2013). Taken together, these findings endorse the idea that OT interacts closely with the neural systems involved in social perception and decision-making. Chang and Platt (this issue) review selected studies of OT and social behavior in non-human primates, focusing on the interplay between social motivation and social vigilance for promoting social behaviors. The emergence of OT research in non-human primates (see Chang and Platt; Evans et al., this volume) provides a platform for investigating the neurobiology of central OT for shaping complex social cognition. Importantly, a non-human primate model can further help test the efficacy and safety of long-term OT-based therapies in the same subjects by systematically monitoring neurophysiological and other physiological and behavioral changes (see Chang and Platt, this volume).

In this volume, Febo and Ferris summarize their pioneering functional magnetic resonance imaging (fMRI) studies in awake rats, including nursing mothers, and Swain et al. provide a review including the latest fMRI studies of brain activation in human parents elicited by visual and auditory stimuli from infants. Both show the remarkably complex neural processing associated with parental behavior toward the lower end and the peak of mammalian evolution. Many brain areas activated by nursing stimuli in rat mothers and infant visual and auditory stimuli in human parents are analogous, specifically areas involved in sensory processing, mobilization of hard-wired, instinctive nurturing behaviors (referred to as reflexive/instrumental caring responses by Swain et al.), and emotion regulation. Febo and Ferris surmise from evidence that many of these brain areas contain high concentrations of OT receptors in rats and are activated by ICV administration of OT as well as that central OT release during parturition may produce the coordinated activation of these many brain areas during the onset of rat maternal behavior, a conclusion that is supported by extensive studies in sheep (Kendrick, 2000). In humans, Swain et al. point out that these areas are most prominently activated by stimuli from very young infants whose behavior is limited to communicating basic needs (e.g., hunger, cold, discomfort). However, the more interactive stimuli from older human infants activate higher cortical regions and cortico-limbic connections implicated in mentalization, empathy and Theory of Mind which may enable human parents to provide more attuned and sensitive responses to their infants' social cues that are critical for the development of secure attachment in their offspring. However, little is known about relationships between central OT systems and the brain activation pattern in human parents, in part because of the lack of reliable methods to locate OT receptors in the human and non-human primate