Review

The prairie vole: an emerging model organism for understanding the social brain

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Unlike most mammalian species, the prairie vole is highly affiliative, forms enduring social bonds between mates and displays biparental behavior. Over two decades of research on this species has enhanced our understanding of the neurobiological basis not only of monogamy, social attachment and nurturing behaviors but also other aspects of social cognition. Because social cognitive deficits are hallmarks of many psychiatric disorders, discoveries made in prairie voles can direct novel treatment strategies for disorders such as autism spectrum disorder and schizophrenia. With the ongoing development of molecular, genetic and genomic tools for this species, prairie voles will likely maintain their current trajectory becoming an unprecedented model organism for basic and translational research focusing on the biology of the social brain.

The need for a mammalian model of social behavior

Impairments in the ability to engage in healthy social interactions and to form stable social attachments are common characteristics of several mental health disorders, including depression, addiction, schizophrenia and autism spectrum disorders (ASDs). Identifying the neurobiological and genetic mechanisms contributing to normative social cognitive function is essential for understanding these disorders as well as for identifying potential targets for pharmacological interventions. Because the ability to form stable social attachments is rare in animals, particularly among those species typically studied in the laboratory, studies of the biological bases of complex social behaviors that recapitulate the richness of human social relationships have been limited. Thus, there is a dire need to identify model organisms ideally suited for investigating complex social behavior at a mechanistic level. Indeed, the US Department of Human Services Interagency Autism Coordinating Committee has recommended a 5-year budget of $75,000,000 to support research to standardize and validate at least 20 model systems that replicate features of ASDs and will allow identification of specific molecular targets or neural circuits amenable to existing or new interventions.

Few neuroscientists will argue the extraordinary value of the translational opportunities afforded by studies of biological phenomena in traditional mammalian laboratory animal models such as mouse (*Mus musculus*) and rat (*Rattus norvegius*). Several factors have ensured the dominance of these rodent models in biomedical research, including the ease of maintaining laboratory populations and the abundance of pharmacological, molecular and genomic resources available for these species. Their phylogenetic positioning relative to humans sets mice and rats apart from other model organisms (i.e. *Drosophila melanogaster* and *Caenorhabditis elegans*), particularly with regard to understanding the complexity of gene–brain–behavior relationships. However, the translational utility of a model organism is only as valuable as the traits it expresses, and although almost all eukaryotic animal models exhibit some form of social behavior, few recapitulate the richness of social behavior of humans, including our capacity to form lasting social attachments.

Here, we introduce a model organism, the prairie vole (*Microtus ochrogaster*), which is highly suited for the study of social behavior. We first provide an overview of the social behaviors displayed by this species and then highlight some of the areas in which prairie vole research has enlightened our understanding of the neurobiology and genetics of social bonding, parental care, the effects of early life experience on adult behaviors and the consequences of social loss or isolation. Finally, we reflect on how these studies have already impacted our understanding of social cognition in our own species.

The prairie vole model

The socially monogamous prairie vole has emerged as an excellent model species for examining the neurobiology of

Glossary

Alloparenting: parenting performed by individuals that are not the biological parents.
Pair bond: a long-term selective social attachment between a mating pair that is typically associated with a shared territory and nest, but does not imply sexual fidelity.
Partner preference: a laboratory measure of an individual's preference to associate with a partner versus a novel or opposite sex conspecific. Individuals that have formed a partner preference spend more time in close proximity to their partner than to a novel stimulus animal; however, the presence of a partner preference does not imply the establishment of a pair bond.
Philopatry: living groups consisting of multiple generations of related individuals.
Social monogamy: a long-term association between a male and a female that cooperate in producing and rearing offspring. Social monogamy, unlike genetic monogamy, does not imply sexual fidelity.

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Box 1. Gene–brain–behavior relationships in an ecologically relevant context

Although prairie voles are considered socially monogamous, genetic monogamy in which a male–female pair cohabitate and share exclusive parentage of offspring is often not the norm. Initial observations of the socially monogamous mating system of prairie voles stemmed from field observations in which male–female pairs were repeatedly captured together within the same home ranges [52–55] and subsequent laboratory studies determined that when female prairie voles lose a mate, they often fail to take on a new partner [56]. However, in addition to male–female pairs, prairie vole populations often consist of single females (presumably survivors of male–female pairs) and communal groups with philopatric offspring. In addition, although most male prairie voles display a ''resident'' strategy where they form a pair bond with a female, defend a territory and assist females in the rearing of offspring, many males (~35–45%) assume a ''wandering'' tactic where they acquire large home ranges that overlap territories of one or more ''resident'' pairs [57,58]. ''Wanderer'' males typically only sire offspring via extra-pair fertilizations and provide no care for their young. Thus, despite the notoriety that prairie voles receive for their monogamous behavior, genetic determination of paternity in natural and semi-natural populations has revealed that between 23% and 56% of litters are sired by multiple males [59,60]. Furthermore, even among prairie vole populations, there are significant geographic differences in social behavior. For example, prairie voles from Kansas are less social and display lower levels of physical contact between adult males and females, less spontaneous alloparental and parental behavior, and are more aggressive than Illinois prairie voles [61,62]. However, Kansas voles are more socially and genetically monogamous than voles in an Indiana population [63] and some of these population differences are associated with differences in estrogen receptor expression in the brain [64].

The tremendous variation in social behaviors both within and between natural prairie vole populations exemplifies both the need and utility of studying the genetics and neural circuitry of social behaviors in an ecologically relevant context. For example, to determine how the reproductive tactics of ''resident'' males versus ''wandering'' males relates to V1aR expression patterns in the lateral septum and ventral pallidum, Ophir et al. (2008) used radio telemetry to track spatial use of sexually naïve adult prairie voles within semi-natural, outdoor enclosures [3]. After approximately 3 weeks, they assessed the paternity of litters and then examined the distribution of V1aR in adult male forebrains. Most males (74%) were classified as a member of a bonded pair, whereas the remaining males assumed the ''wandering'' tactic. Surprisingly, although AVPR1A in the ventral pallidum and lateral septum have been shown to be involved in the regulation of partner preference formation and paternal care, levels of V1aR in these regions did not correspond to male mating tactic, male mating success, nor the male's propensity to engage in extra-pair copulations. Instead, V1aR density in the posterior cingulated/retrosplenial cortex, a region of the brain involved in spatial learning and memory, predicted reproductive success in ''wanderers''. Males with lower densities of V1aR in this brain region assumed larger home territories, sired more offspring and were more likely to engage in extra-pair copulations. These studies emphasize the importance and exciting opportunities of coupling laboratory and field studies to more thoroughly understand the mechanistic basis of complex social behaviors.

complex social behaviors, including social bonding. Prairie voles differ considerably from more traditional laboratory models because they are exceptionally social and often form long-term, socially monogamous relationships with their mates. Both parents contribute nearly equally to nurturing young, and in natural environments alloparental care is commonly observed [1] (Box 1; Figure 1a). By contrast, other related vole species such as the meadow vole (*M. pennsylvanicus*) and the montane vole (*M. montanus*) are relatively asocial and do not readily form social bonds, providing a useful point of comparison for identifying neurobiological and genetic systems leading to diversity in social behaviors [2]. In addition, laboratory-reared prairie vole colonies are systematically outbred, often only a few generations from the field, allowing for the study of individual variation in neurochemistry and sociobehavioral traits (Figure 1b). This inter- and intra-species diversity in brain and behavior set prairie voles apart from mice and rats, making this species an ideal model organism for studying the biological mechanisms underlying natural variation social behaviors relevant to our own species.

Prairie voles are hamster-sized Microtine rodents (typically 30–60 g) that are geographically distributed throughout grasslands in central North America. Prairie voles and related vole species are easily maintained and housed in standard rodent vivariums and are also routinely studied in their natural and semi-natural habitats [3,4] (Box 1). Both laboratory-reared and recently captured wild voles are amenable to pharmacological and genetic manipulations and classic behavioral paradigms used in mice and rats. The prototypical behavioral assay used in prairie voles is the 'partner preference test' (PPT), which is used to quantify social attachments between mates [5]. In this test, the experimental animal and a "partner" are allowed to cohabitate for a set period of time, during which mating might or might not be permitted. Following cohabitation, the "partner" animal and an unrelated, novel "stranger" animal are tethered to opposite ends of a three-chambered arena. The test animal can freely explore the arena for 3 h and is said to have formed a "partner preference" if it has spent at least twice the amount of time in contact with its "partner" versus the "stranger". In prairie voles, mating facilitates the formation of a partner preference, but longer cohabitations without mating also lead to a partner preference [5]. Non-monogamous vole species, such as montane or meadow voles, typically do not form partner preferences even after extended periods of cohabitation. Sophisticated and extremely accurate automated technologies are now routinely used for high-throughput analysis of the PPT in real time allowing up to 36 tests to be performed within a 24-h period without the need for human scoring [6] (Figure 1c). As described in the following section, the PPT used in conjunction with pharmacological and genetic manipulations has been instrumental in identifying neural and genetic mechanisms underlying social attachment in voles.

Neural circuitry of social bonding

Much of our understanding of the neuronal systems involved in social bonding has stemmed from pharmacological and comparative neuroanatomical studies between monogamous and non-monogamous vole species [7,8]. These studies have demonstrated that arginine vasopressin (AVP), oxytocin (OT) and dopamine (DA), along with their respective receptors, act within specific brain circuitry to facilitate social attachment in a gender-specific manner [9]. Although there are few species differences in the distribution of AVP and OT in the brain [10,11], there are striking species differences in the location and

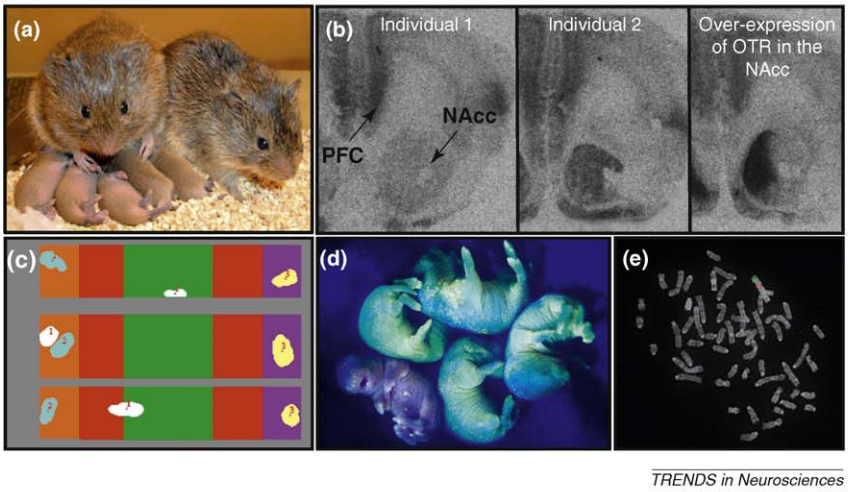

Figure 1. The prairie vole as a model organism. **(a)** This hamster-sized rodent forms selective social bonds with its partner and displays biparental behavior both in nature and in the laboratory (photograph provided by T. Ahern). There is considerable individual variation in social behavior, which is reflected by variation in neuropeptide receptor distributions in the brain. For example, the two autoradiograms on the left of panel **(b)** illustrate the individual variation in OTR binding densities in the NAcc of female prairie voles, variation which has been linked to variation in alloparental behavior. Artificially increasing OTR binding using viral vector-mediated gene transfer (right autoradiogram) facilitates partner preference formation in females (adapted with permission from Ref. [16]). Thus, prairie voles are useful models for dissecting the neurobiological basis for diversity in behavior. **(c)** Partner preference formation can be accurately quantified in a high-throughput manner using automated behavioral analysis systems (adapted with permission from Ref. [65]). **(d)** Lentiviral transgenesis can now be used to manipulate the genome of prairie voles as demonstrated by the green prairie vole pups that are transgenic for expression of a green fluorescent protein (photograph provided by Z. Donaldson). This technique, when applied to behaviorally relevant genes, will facilitate research into understanding the relationship between genes and behavior. **(e)** Genomic resources are rapidly becoming available for the prairie vole, including cytogenetic maps, single nucleotide polymorphisms (SNP) panels, bacterial artificial chromosome (BAC) libraries, and the full genome is slated to be sequenced by the National Human Genome Research Institute (NHGRI). Shown is fluorescent *in situ* hybridization (FISH) localizing two prairie vole BAC clones with known homology to the mouse genome to the prairie vole X chromosome.

density of their respective receptors [7,8]. As the neural circuitry of pair bonding has been reviewed extensively elsewhere [12,13], here we provide just a brief overview of the neuronal systems that influence social bonding, including new data where appropriate.

In female voles, OT plays a critical role in regulating the formation of a partner preference by activating OT receptors (OTRs) in the nucleus accumbens (NAcc) and prefrontal cortex [10,14]. Sociosexual interactions trigger the release of OT into the NAcc from neuronal fibers that probably originate from magnocellular neurons in the hypothalamus that also project to the pituitary [10]. Infusion of OT into the brain during cohabitation with a male accelerates the development of a partner preference, whereas blocking OTRs in the NAcc during mating prevents this behavior [14,15]. There is remarkable individual variation in OTR density in the NAcc which could contribute to natural variation in the propensity to form a pair bond (Figure 1b). For example, overexpressing OTRs within the NAcc of prairie voles using viral vector-mediated gene transfer accelerates the formation of a partner preference in female prairie voles (Figure 1b) [16]. Females in non-monogamous vole species as well as mice display very low or no OTR binding in the NAcc, whereas the monogamous common marmoset (*Callithrix jacchus*) has high densities of OTRs in this region much like the prairie vole [17].

In male prairie voles, AVP plays a critical role in the regulation of partner preferences, although it is probable that OT also plays a role [18,19]. Specifically, blocking vasopressin V1a (AVP1A) receptors in the ventral pallidum or lateral septum with antagonists prevents partner preference formation following mating [20,21]. Although there are few species differences in the distribution of the AVP peptide, as is the case for OTRs, there are significant individual and species differences in AVPR1A distribution in the brain that can contribute to variation in social behavior. For example, socially monogamous male prairie voles have high densities of AVPR1A binding in the ventral pallidum, a major output of the NAcc, whereas non-monogamous vole species do not [2]. Interestingly, other monogamous species, including common marmosets and the California mouse (*Peromyscus californicus*) also have similarly high levels of V1aR in this ventral forebrain region compared with related non-monogamous species [17,22]. Overexpressing the gene encoding the prairie vole AVPR1A, *Avpr1a*, in the ventral pallidum of male meadow voles using viral vector-mediated gene transfer results in the ability of this promiscuous species to display partner preferences [23]. These studies in female and male prairie voles suggest that variation in OT and AVP receptor regulation can contribute to diversity in social behavior, a concept that might be highly relevant to disorders characterized by impairments in social cognition.

In addition to the AVP and OT systems, the neurotransmitter dopamine DA, acting within the NAcc, plays a critical role in social bond formation in both male and female prairie voles [24,25]. D2-type DA receptor activation facilitates partner preferences, whereas D1-type DA receptor activation prevents partner preference formation [26]. Thus, the D1 and D2 dopamine receptors have antagonistic influences on initial pair bond formation. However, once a pair bond has been established and maintained for 2 weeks, males show a significant increase in the density of D1, but not D2, receptors in the NAcc [26]. This increase in D1 receptors following the initial pair bond formation can serve to prevent subsequent pair bond formation as a consequence of extra-pair copulations. Interestingly, non-monogamous meadow voles have high levels

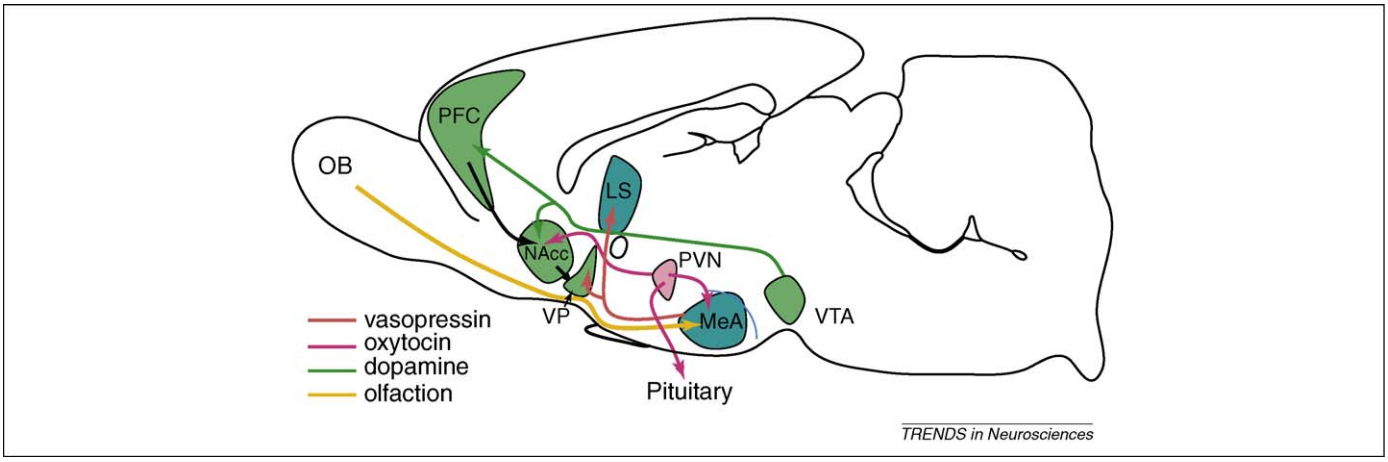

Figure 2. A schematic illustrating the proposed neural circuitry of social bonding in prairie voles. OT neurons in the paraventricular nucleus of the hypothalamus (PVN) project to the NAcc as well as to the posterior pituitary [10]. Sociosexual interactions in female prairie voles stimulate the release of both OT and dopamine into the NAcc. In males, vasopressin neurons in the extended amygdala project to the ventral pallidum (VP) and the lateral septum (LS). Concurrently, olfactory signatures of the sexual partner are processed through the amygdala. It is hypothesized that the simultaneous activation of the neuropeptide and dopamine receptor systems in these regions leads to a conditioned partner preference by linking the rewarding nature of the sociosexual interaction and the olfactory signatures of the partner. Inter- and intra-species variation in OTRs and AVPR1A in these regions contribute to diversity in social behaviors in voles (modified with permission from Ref. [66]).

of D1 receptors in place in the NAcc even prior to mating. When antagonists are used to block these receptors, males show greater affiliate behavior towards a female after a short cohabitation period but do not form a partner preference [26]. These data suggest that although these receptors are associated with species differences in social behaviors, they are not solely responsible.

Studies of AVP, OT and DA systems demonstrate the critical role of the reward and reinforcement circuitry of the brain in social bond formation, which has lead to a neural circuitry model of social bonding (Figure 2). Within the reward system, simultaneous activation of OTRs or AVPR1A receptors and DA receptors can result in the establishment of an association between the social olfactory cues of the partner and the rewarding or reinforcing aspects of copulation, reminiscent of classical conditioning. Because the reinforcing nature of drug abuse and social bonding are mediated by a common neural system, DA within the NAcc, prairie voles serve as a valuable model for understanding the interaction between social relationships and addiction [27].

Neurogenetics of social bonding

Although many of the neural components underlying social bonding are beginning to be identified, little is known of the genetic regulation of these systems. Insights into the genetic mechanisms producing diversity in sociobehavioral traits have emerged from studies attempting to identify the molecular mechanisms giving rise to species differences and individual variation in AVPR1A distribution in the vole brain [28]. First identified in comparative genomic studies between prairie and montane voles, a polymorphic microsatellite element located near proximal regulatory regions of *Avpr1a* may contribute to the variation in AVPR1A distribution in the brain [29,30]. Early studies suggested that variation in the *length* of this microsatellite might explain both species differences in social organization among voles, and individual variation in social attachment in prairie voles. For example, montane and meadow voles have considerably shorter microsatellite elements than prairie voles [30], and male prairie voles with relatively short microsatellites had lower levels of AVPR1A binding in the olfactory bulb and lateral septum, and were less likely to display a partner preference than males with longer microsatellites [31]. However, it is now known that length *per se* does not predict social organization of other Microtus species [29,32], and *sequence variation* within the microsatellite might have a greater influence on expression than length itself [3]. The precise mechanisms by which the microsatellite element contributes to variation in receptor distribution and behavior is still poorly understood; however, as discussed below, there is now growing evidence that similar microsatellite variability in the human *AVPR1A* contributes to variation in human social cognition and behavior [28].

The neural regulation of parental care

Just as the prairie vole's propensity to form pair bonds has allowed for investigation of the mechanisms underlying social bonds between mates, the biparental nature and remarkable individual variation in parental care displayed by prairie voles provides an excellent opportunity to investigate the neural mechanism underlying parental nurturing behavior. Studies of both alloparental behavior and paternal behavior have revealed that common pathways underlie pair bonding and parental nurturing behavior. This suggests that social bonding in monogamous species could have evolved through subtle tweaking of ancient neural circuits regulating parental behaviors.

Both virgin and post-partum female prairie vole adults display nurturing behavior toward infants. However, there is remarkable individual variation in the maternal-like behavior displayed by virgins, referred to as alloparental behavior. Approximately 60% of adult females display spontaneous maternal nurturing toward novel pups, whereas 40% either ignore or attack pups [33–35]. This intra-species variation in nurturing behavior provides a unique opportunity to elucidate the neurological mechanisms underlying maternal care. For example, virgin female prairie voles that display maternal behavior have higher densities of OTRs in

the NAcc than non-maternal females [33,34]. Furthermore, an infusion OTR antagonist into the NAcc prevents the display of spontaneous maternal behavior [33]. Although high densities of OTRs within the NAcc are correlated with high levels of alloparental care in females, viral vector-mediated overexpression of OTRs within the NAcc of adult female prairie voles does not result in enhanced alloparental behavior, even though partner preference formation is accelerated in those same animals [35]. These results suggest that variation in OTR density during development or perhaps OTRs in additional brain regions contribute to the diversity in alloparental behavior.

Prairie voles are also an important model for understanding the genetic and neurobiological basis of paternal care. Early comparative studies discovered that in prairie voles, cohabitation with a female resulted in a decrease in AVP content in the lateral septum (probably reflecting a release of AVP from neuronal fibers in the region), which was coincident with an increase in paternal responsiveness. This phenomenon was not observed in meadow voles [36,37]. Infusion of AVP into the lateral septum increased paternal behaviors, whereas an AVPR1A antagonist decreased time spent tending the pups [38]. These studies suggest that, as in females, the neural mechanisms involved in pair bond formation also play an important role in the regulation of paternal care.

Early life experience and its effect on adult social behavior

There is now growing evidence that the quality of early life nurturing received can have life-long consequences on adult social behavioral tendencies. Prairie voles have proven particularly useful for investigating how early life experience can impact later life social behaviors. For example, a recent study directly manipulated the social environment in the laboratory to reflect various rearing conditions of voles from natural populations (Box 1). This was accomplished by raising prairie vole pups in either single mother or biparental units. The single mother-reared pups received less parental nurturing (e.g. licking and grooming) than biparentally reared pups. In addition, females raised in single mother units were less likely to display alloparental behavior, and both male and female offspring from this group required longer cohabitation periods than biparentally reared offspring to form partner preferences [39]. Varying the family structure also altered the number of OT neurons in the paraventricular nucleus of hypothalamus. This paradigm offers an excellent opportunity to understand how early life experience alters the neurochemistry underlying social cognition, as well as for potentially exploring gene by environment interactions, which has important implications for psychopathologies affecting social relationships. For example, women who have experienced abuse and neglect in childhood have reduced OT concentrations in their cerebrospinal fluid compared with controls [40].

Social loss, depression and heart disease

Just as early life experience can have profound effects on later life social behaviors, social experiences encountered during adult life can also have significant influences, not only on subsequent social behavior but also on mental and physical health. Because of their highly social nature, prairie voles have become an important model for studying the consequences of social loss or social isolation on mental and physical health. When prairie voles are chronically isolated, or separated from their pair bonded partner, they display behaviors similar to those found in depression. For example, female prairie voles that are socially isolated have reduced sucrose intake and higher plasma levels OT, AVP and corticosterone than socially housed females [41]. Cardiac disturbances including increased heart rate and reduced heart rate variability also follow social isolation [42]. Administration of OT during periods of social isolation can alleviate some of the behaviors relevant to depression including elevated basal heart rate [43]. Prairie voles have also been used as a model of social loss. Disruption of an established pair bond leads to high levels of passive behavior (immobility) in the forced swim test and the tail suspension tests, a behavioral response reminiscent of grieving and bereavement in humans. This response appears to be mediated by the corticotropin releasing factor (CRF) system receptor because it has been shown that a CRF antagonist blocked the development of social loss-induced depressive-like behavior [44]. Thus, in addition to understanding the mechanisms promoting social attachments, prairie voles are a valuable model for understanding the consequences of social loss and deprivation, which has important implications for understanding common human conditions such as depression and bereavement.

Contributions towards understanding of human social behaviors

A growing number of studies have revealed a remarkable conservation between the mechanisms underlying social behaviors in prairie voles and social cognition in humans, particularly with regard to the OT and AVP systems [28,45]. For example, intranasal OT administration has been shown to enhance interpersonal trust, increase eye-to-eye contact and even enhance the ability of a person to infer the emotions of another person based on facial expression [45]. These findings have enormous implications for developing treatment strategies to ameliorate the social deficits in disorders such as ASDs and schizophrenia. For example, OT infusions in high-functioning ASD subjects have been reported to enhance retention of social information [46], although much more research into this area is needed. In addition, at least three independent studies have now reported associations between polymorphisms in the human OT receptor gene (OXTR) and symptoms of ASDs [45].

Further insights into the genetics of human social behaviors have stemmed from studies of the microsatellite polymorphism in the vole *Avpr1a*, as similar polymorphic microsatellites are found upstream of the human *AVPR1A*. Variation in these microsatellite elements in the human *AVPR1A* appear to contribute to variation in social cognition, altruistic behavior, brain activation patterns and *AVPR1A* mRNA levels in the hippocampus [28]. In addition, there have now been three independent reports of a genetic association between these polymorphisms in the human *AVPR1A* and symptoms of ASDs [47–49]. One of these studies found that *AVPR1A* polymorphisms

specifically, mediated socialization skills in subjects with ASDs [49]. Perhaps most remarkably, one of these polymorphic markers in the *AVPR1A*, which has been associated with altered brain activation patterns during a face processing task, has been associated with pair bonding behavior in humans, including measure of partner bonding, perceived marital problems, marital status, as well as spousal perception of marital quality [50]. These observations illustrate how taking advantage of the genetic diversity in laboratory populations of prairie voles can lead to exciting insights into how variation in gene regulation affects behavior in rodents as well as in humans.

Sociogenomics: the future of the prairie vole model

The continued trajectory of the prairie vole as a powerful model organism for understanding the social brain requires the development of genomic resources and transgenic technologies equivalent to those available in mice and rats. Progress to date toward this end is promising. Lentiviral-mediated transgenesis has been used to create green fluorescent protein transgenic voles as a proof of principle (Figure 1d) [51], and progress is being made combining this approach with shRNA technologies to silence gene expression. In addition, the prairie vole is now targeted for full-genome sequencing (http://www.genome.gov/10002154) and several genomic resources including a 10× coverage BAC library (http://bacpac.chori.org/library.php?id=481), a panel of over 700 single nucleotide polymorphisms (SNPs), a cytogenetic and genetic linkage map and a comprehensive catalog of prairie vole gene sequences are or will be available shortly (Figure 1e).

With the ongoing development of this comprehensive prairie vole genomic toolbox, exciting frontiers in understanding the relationship between the complexities of the genome and the complexities of the social brain are rapidly becoming possible. The availability of these tools and technologies will provide insights into the abundance, distribution and sequence characteristics of genes and gene families that differentiate social and asocial individuals and/or species. As prairie vole genome sequence becomes available, the ease of isolating and/or amplifying vole-specific gene sequences will allow for targeted tissue, brain region or neuron-specific overexpression or knock-down of genes relevant to social behavior using transgenic technology and will aid in the development of more sophisticated technologies to knock-out or replace genes of interest. In addition, these resources will expedite the development of other genomic tools such as tiling arrays, SNP chips or genome-wide methylation screens that comprehensively span both coding and non-coding elements. When combined with traditional neuroscience techniques, these resources and technologies will open exciting new avenues in prairie vole research and will allow for discovery-based genome research and the development of additional molecular and genetic tools to dissect the relationship between the genome and the social brain in ways that previously have only been possible in traditional model organisms.

Concluding remarks

Although it is unlikely that studies of social behavior in prairie voles will identify the exact etiologies of human psychiatric disorders, this model organism has exceptional potential to begin to guide us in understanding the genetic pathways and neurobiological systems that regulate aspects of sociality that are often impaired in these patients. For example, although prairie voles cannot model disrupted aspects of social cognition characteristic of individuals with ASDs, such as facial processing, empathy or calculating theory of mind, they do provide an unprecedented animal model for understanding the neural and genetic basis of social motivation and social processing. Even if these systems are not dysfunctional *per se* in psychiatric disorders, a more comprehensive understanding of them could represent an avenue for developing pharmacological targets to enhance social motivation and cognition in patients who suffer from these disorders.

The past two decades of prairie vole research have led to the development of a model organism that is unparalleled for understanding the social brain. The rapid development of transgenic technologies and genomic resources coupled with unique opportunities to integrate genetic, neurobiological and behavioral ecological approaches to understand social behavior in this species will ensure that prairie voles continue to develop as a premier model organism for identifying mechanisms regulating complex social behaviors, which will directly impact the understanding of our own sociality and inform future treatment of psychiatric disorders of the social domain.

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