Vole Meeting 2009

Atlanta, Georgia

Center for
BEHAVIORAL
NEUROSCIENCE

Abstract Booklet

SCHEDULE

8:00a - 9:00a	Continental breakfast and check-in
9:00a - 10:00a	Historical Perspective: A Brief History of Vole Research *Lowell Getz, C. Sue Carter*
10:00a - 10:30a	Short Talks (2) *Betty McGuire, Zoe Donaldson*
10:30a - 10:50a	Coffee Break
10:50a - 11:50a	Short Talks (4) *Karen Bales, Deborah Triant, Allison Anacker, Adam Perry*
11:50a - 12:00p	Group Photo
12:00p - 1:00p	Lunch (will be provided)
1:00p - 2:30p	Featured Lectures (3) *Nancy Solomon, Zuoxin Wang, Larry Young*
2:30p - 2:50p	Break
2:50p - 3:35p	Short Talks (3) *UnJa Hayes, Ashlee Vaughn, Katie Northcutt*
3:35p - 3:55p	Funding Opportunities (2) *Janine Simmons (NIMH), Dianne Witt (NSF)*
3:55p - 4:10p	Break
4:10p - 5:10p	Short Talks (4) *Maryam Bamshad, Kyle Gobrogge, Annaliese Beery, Karen Mabry*
5:10p - 6:30p	Advances in Resources and Technologies (4) *Todd Ahern, Alex Ophir, Angela Grippo, Lisa McGraw*
6:30p - 8:30p	Poster Session and Hors d'oeuvres

Dinner and social events will be on your own after 8:30 pm.

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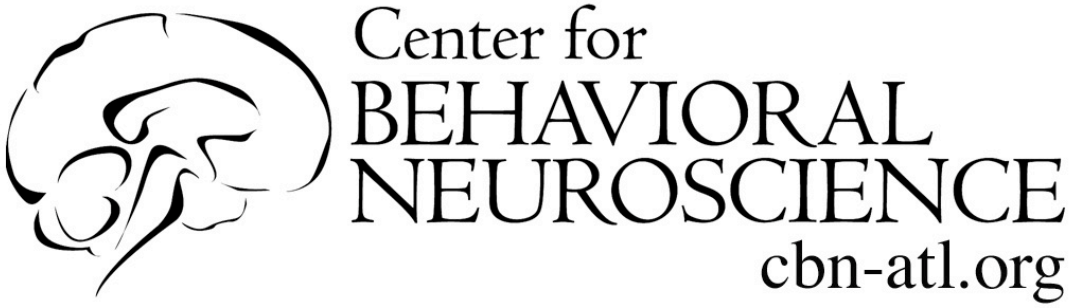
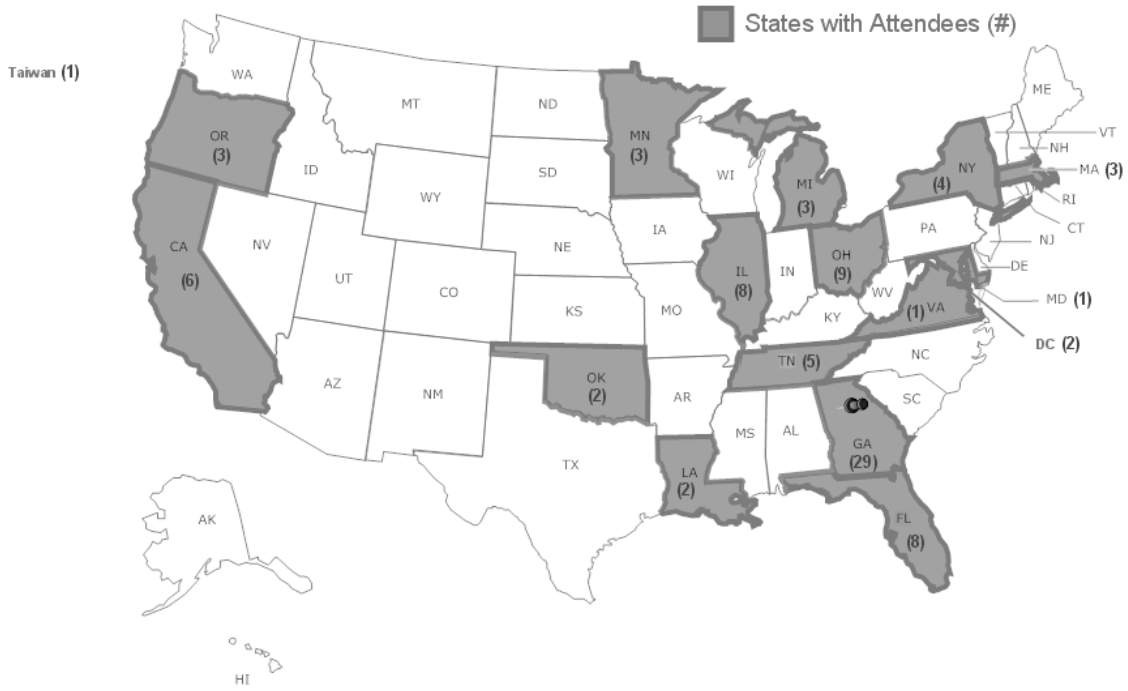
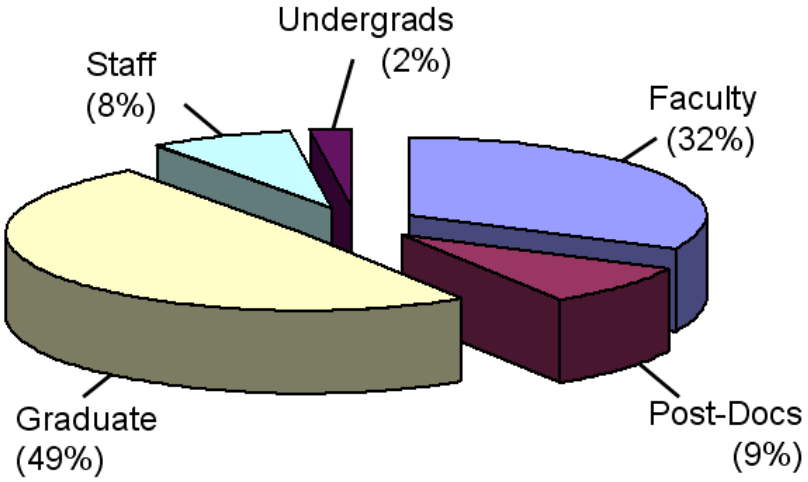


ATTENDANCE

92 Attendees





HISTORICAL PERSPECTIVES

From corn shocks to monogamy.

LL Getz
University of Illinois, Illinois

I went with my dad to the field to load up corn shocks to feed to our cattle. When he picked up the last bundle of corn, voles would scurry to nearby shocks. I chased after the voles in unsuccessful attempts to kill them. Thirty-seven years later, I began studying prairie voles found them to display behavioral monogamy. Recognition of such behavior was a simple event, requiring no intuitive foresight or unusual perception.

During those intervening 37 years, however, there were five events had any one of which not happened, I would not have studied voles and would not have identified monogamous behavior. These involved: a high school teacher becoming pregnant; a chance encounter, with a 10-15 second window; my father being diagnosed with terminal lung cancer, with a two week window; my advisor keeping some old unused multiple-capture live traps for twenty years; an almost bungled faculty position offer, with a two day window. Because all these events did happen, I began studying demography of the prairie vole in 1972.

During the first six years of the study, observations that a large proportion of the captures of adult prairie voles involved a male-female multiple capture, suggested pair formation. Radio-tracking confirmed cohabitation of male-female pairs. I then began a series of laboratory observations to test for monogamy. Not being a behaviorist, I repetitively called upon Sue Carter for advice regarding experimental designs and controls. She eventually asked me for breeding stock so she could see what I trying to test. Sue soon began looking into the hormonal implications of the monogamous behavior, which led to use of prairie voles as the animal model for examining genetic and neurobiological mechanisms involved in social behavior in vertebrates, including humans.

Monogamy and the Prairie Vole: The Early Days.

CS Carter
University of Illinois at Chicago, Illinois

Before coming to the University of Illinois I knew little about the prairie, and even less about prairie voles. As a child in the Ozarks, I did sometimes notice drowned voles in a lake near my home, and our cat would occasionally deposit one on our doorstep. However, live voles were not part of my world until I met Lowell Getz.

My first call from Lowell came in the fall of 1978. I was an assistant professor at the University of Illinois, and he was one of my colleagues in the Department of Ecology, Ethology & Evolution. Lowell studied voles for most of his life. In the process, he amassed a detailed understanding of prairie vole natural history. Several years before we met, Lowell had received a research grant from the National Institutes of Health. This support enabled him to examine a variety of factors associated with population cycles in voles, but it was when he tried to renew this grant that Lowell turned to me for help.

Laboratory research was necessary because something unusual had emerged from Lowell's field observations. Live-trap data suggested that male and female prairie voles were living in pairs and usually remained together as long as both members were alive. Even pairs that were reproductively inactive stayed together, proving that something besides reproduction was keeping male and female together. These socially monogamous mammals exhibited pair bonds marked by prolonged physical contact and aggression toward strangers. Prairie voles even avoided incest and used each other to buffer against stress. The parallels with human behavior were too obvious to miss and too intriguing to ignore.

Meadow voles, a related species, sometimes shared the fields with prairie voles, and were also captured in Lowell's studies. But unlike prairie voles, meadow voles were solitary and rarely found with a vole companion. Although voles were abundant in nature and widely studied by ecologists, little was known at that time about their reproductive biology or endocrinology. Lowell brought both prairie voles and meadow voles into the laboratory and put males and females of each species in large Plexiglas-bottomed tables filled with straw. Viewed from below, the voles established life-styles that resembled their routines on the prairie, further confirming Lowell's assertion that prairie voles (but not meadow voles) preferred living in monogamous pairs.

In spite of converging data, our work on pair bonding was slowed for about a decade by one incorrect assumption. I assumed (like many other biologists) that monogamy was mainly about fitness. Given a choice, female or male prairie voles should show a mating preference for the familiar partner. The only problem was that when given a choice in our laboratory studies, prairie voles did NOT consistently select a familiar partner. However, if we looked at another measure of preference – nonsexual social contact - then prairie voles did show reliable and consistent preferences for their partner. Prairie voles were “socially monogamous." The difference between sexual and social monogamy remained controversial until DNA fingerprints

became readily available. As predicted by our laboratory results, even in prairie voles many litters were fathered by more than one male. Although some individuals were sexually monogamous, others were not. This finding further emphasized the importance of sociality, suggesting that there is more to monogamy than sex.

When paradigms for testing social preferences became established, we began a serious search for the neurobiology of pair bonding. Research in rats and sheep, conducted around the time we began our work with voles, revealed that peptide hormones, and specifically oxytocin and vasopressin, could regulate maternal bonding. Parallels between maternal behavior and pair bonding drew us to examine the hypothesis that these same peptides might be critical to social bond formation in prairie voles. There is now no doubt that oxytocin and vasopressin can facilitate social behavior and that together these peptides (and other neurochemicals) form a cocktail that is essential for monogamy and other forms of selective sociality. Studies in voles, done in many laboratories, have begun to define the neural circuits and molecular biology of mammalian sociality. The behavioral biology of pair bonding has attracted new generations of scientists, doing work that is helping us understand various forms of mental illness. We now know that the endocrine basis of social behavior is different in males and females. In addition, the biology of social behavior is intimately interwoven with the capacity to regulate reactivity to stress. In turn, these insights are now shedding light on sexually-dimorphic disorders such as autism, schizophrenia, anxiety, and depression. Even very human concepts such as “love” and “jealousy” are seen in a different light thanks to the humble prairie vole.

The biology of prairie vole social monogamy and the neuroendocrine glue holding it together became the focus of research in my laboratory for more than three decades. For this I am grateful to many colleagues, but especially Lowell Getz. It was Lowell’s insights into prairie vole biology and dedication as a scientist that set the stage for those who would follow.

SHORT TALKS (Morning)

Comparative Analyses of Suckling Behavior in Prairie, Pine, and Meadow voles.

B McGuire, WE Bemis
Cornell University, New York

Studies on the evolution of parental care in arvicoline rodents showed that presence of paternal care and a suite of six characters of pup behavior, maternal features, and maternal care sharply differentiate the prairie + pine vole clade from the clade including meadow voles. New, detailed observations of suckling behavior in prairie, pine (woodland), and meadow voles allow us to elucidate the six characters related to pup behavior and maternal care during suckling and weaning. For each species, we observed 10-14 pairs with their litters in seminatural environments. Each pup within a litter was dyed on day 3 postpartum and observed for 20 minutes every other day from day 3 through day 19. During these focal observations, we scored the frequency and duration with which each pup was attached to a nipple. Additionally, we scanned each litter every 20 minutes for 2 hours on each day of observation and recorded the nipple to which each pup was attached. Finally, we weighed each pup on days 3, 9, 20, and 30. Species differences were marked. Prairie and pine vole pups shared several behavioral features, such as attachment to particular nipples for long durations. In contrast, meadow vole pups frequently switched nipples. Whereas prairie and pine vole pups displayed our previously reported preference for hindmost nipples, meadow vole pups showed no obvious preference for any nipple pair. All measures of suckling behavior declined more rapidly in meadow voles than in prairie and pine voles. Finally, our data on pup weights document a developmental trend in which litter effects become progressively less important and the behaviors of individual pups more important with age. These new observations on suckling behavior provide further evidence of the uniqueness of the prairie + pine vole clade.

Production of transgenic prairie voles using lentiviral vectors.

ZR Donaldson, SH Yang, AWS Chan, LJ Young
Emory University, Georgia

The study of non-traditional model organisms has yielded tremendous insights regarding behavioral and physiological traits not displayed by more widely used animal models, such as rats and mice. For instance, studies on monogamous prairie voles have been instrumental towards our understanding of social bonding. However, laboratory studies of non-traditional organisms, such as prairie voles, have been limited by a lack of genetic tools, such as those that have been optimized for mice and drosophila. One particularly powerful genetic tool is the ability to modify an organism's genome to determine the function of various genes and regulatory elements. In order to extend germline transgenic technologies into non-traditional animal models, we have made a GFP-expressing prairie vole line. Injection of a GFP-containing lentiviral vector into the perivitelline space of 23 embryos yielded three live offspring (13%), one of which (33%) contain germline integration of a GFP transgene driven by the ubiquitin promoter. In comparison, transfer of 23 uninjected embryos yielded 6 live offspring (26%). GFP in the transgenic line is expressed across multiple tissues and is heritable and stable across at least two generations. This technology has the potential to allow investigation of specific gene candidates in prairie voles and provides a general protocol to pursue germline transgenic manipulation of many different rodent species. For instance, we are currently generating “knockdown” voles in which genomically-integrated siRNAs target degradation of a specific gene in order to directly assess the role that gene plays in behavior.

Costs of Male Parenting in Prairie Voles.

*J Campbell, KD Laugero, JD Cohen, JA van Westerhuyzen, CM Hostetler, KL Bales**
**Speaker*
UC-Davis, California

The present study examines the long-term effects that pairing and parenting have on the male prairie vole. We hypothesized that there would be a significant weight loss over the course of pairing and parenting, presumably from the increases in energy expenditures that accompany these changes in social status. In a longitudinal study, we followed 10 male prairie voles through being housed with their brother; paired with a female; and caring for three litters. We found a significant drop in both bodyweight and plasma leptin levels (leptin is a hormone produced by fat cells). We found that there was a maximum weight loss near the weaning of the first litter, and before the birth of the second litter. Corticosterone (another hormone associated with energy metabolism) did not change significantly across time points, and activity levels also did not vary significantly over the course of the study. Males spent less time eating when placed with a female and throughout caring for pups. However, behavioral measures showed that the greatest decreases in feeding duration occurred in newly paired, and expectant fathers before the birth of their first litter. In addition, newly paired males showed a significant increase in preference for a 2% sucrose solution during a three-hour test, indicating a metabolic need for more calories. A cross-sectional study, in which we examined losses in fat, confirmed the same results. These results show that it is not only parental care that confers a cost to male voles, but also pair bonding and cohabitation.

Molecular evolution in the genus Microtus.

DA Triant, JA DeWoody
Louisiana State University, Louisiana

Microtus is one of the most taxonomically diverse mammalian genera. Although the genus is thought to have originated less than two million years ago, it has since diversified to over 60 extant species. If these numbers are taken at face value, then an average of 30 microtine speciation events have occurred every million years. This is an extremely rapid speciation rate given that vertebrates typically undergo a speciation event every 2-3 million years. One explanation for the rapid rate of cladogenesis in Microtus could be the karyotypic differentiation exhibited across the genus. Diploid numbers range from 17 to 64, which is among the highest rates of karyotypic evolution among mammals. To determine whether nucleotide substitution rates are also elevated in voles, we sequenced the entire mitochondrial genome in the Eurasian sibling vole (Microtus rossiaemeridionalis) and performed pairwise sequence comparisons with the mitochondrial genomes of other mammalian genera. We found that Microtus mitochondrial genomes are evolving more rapidly than any other mammalian lineage sampled, as gauged by the rate of nucleotide substitution across the mitochondrial genome. Additionally, we isolated and characterized fragments of mitochondrial DNA that have been transferred to the nucleus in Microtus. We have previously found that mitochondrial transfers are widespread in arvicoline rodents and they appear to be more pervasive within Microtus than in either Mus or Rattus. The integration of mitochondrial DNA into the nuclear genome is thought to be facilitated by chromosome repair mechanisms. Thus, given the abundance of karyotypic rearrangements that have occurred throughout the evolutionary history of Microtus, the fact that the genus has had extensive nuclear integrations is not entirely surprising. Rates of molecular and karyotypic evolution vary dramatically among mammals and Microtus may serve as a model to help us understand the evolutionary dynamics of the mitochondrial and nuclear genomes.

The Prairie Vole: A Novel Model for the Effect of Social Affilations on Alcohol Drinking.

Anacker, AMJ, Kaur, S, Loftis, JM, Ryabinin, AE
Oregon Health and Science University, Oregon

Alcohol use and social relationships have complex effects on each other, which have been difficult to model in a laboratory animal, given that traditional laboratory rodents do not show strong affiliative behaviors, and do not show high levels of alcohol drinking. However, in the prairie vole, a species known for its strong social bonds, there is also a high preference for alcohol in an oral self-administration paradigm. Interestingly, some neuropeptides important for pair bond formation (arginine vasopressin, corticotropin-releasing factor, and urocortin) are also known to regulate ethanol consumption. Thus, the prairie vole may be an invaluable species for modeling the complex and important interactions of social relationships and alcohol drinking. We have begun to study the effects of psychosocial stress on alcohol drinking using a social isolation paradigm. Adult prairie voles are first housed for five days with one same-sex sibling, then either separated into individual cages or kept as a pair, where paired animals are separated by a wire mesh through which they can interact, but cannot cross over to the other side, so that individual drinking can be monitored. Each animal has 24-hr access to both water and ethanol, and consumption of each is measured daily. Using this procedure, we observed a decreased preference for alcohol in the isolated voles, compared to the paired animals. One interpretation is that the effects of alcohol are less rewarding for socially isolated individuals. Additionally, we have observed a strong correlation of alcohol intake between the two members of a pair housed together, but not in separated siblings. Given these results, the prairie vole may be a useful model for social drinking behavior.

Sex and the Single Vole: The Role of ER_ in Reproductive Behavior.

AN Perry, CS Carter, BS Cushing
University of Illinois at Chicago, Illinois

In the majority of mammalian species, the goal of male reproductive behavior is to maximize reproductive encounters and avoid social obligations that might limit subsequent copulation, such as providing parental care. Therefore, in order to generate a male that displays high levels of prosocial behavior, the brain must be re-patterned to restrain typical masculine behavior and facilitate prosocial behavior, while at the same time maintaining normal male copulatory behavior. Estrogen receptor (ER) _ is expressed in many regions of the social brain and contributes to all aspects of male reproductive behavior. For species in which males show high levels of prosocial behavior, there appears to be a selective reduction in ER_ expression in the medial amygdala (MePD), whereas ER_ expression in the medial preoptic area (MPOA), which is more intimately connected to male copulatory behavior, is unaltered. Experimentally increasing ER_ expression specifically in the MePD of socially monogamous male prairie voles reduces alloparental care and increases social preferences for novel females, both shifts in behavior are consistent with the pattern displayed by polygynous males. Social isolation of male prairie voles in adulthood also leads to increased ER_ expression in the MePD and enhances the temporal pattern of male copulatory behavior. Isolation has the opposite effect on the expression of tyrosine hydroxylase (TH) in the MePD; therefore, changes in dopamine signaling may also contribute to the alterations in reproductive behavior. Thus, ER_ and TH expression in the MePD appear to be extremely sensitive to the composition of the social environment and may function to optimize the expression of male reproductive behavior, specifically by determining the relative balance between copulatory and prosocial behavior.

FEATURED LECTURES

Integrating laboratory and field studies improves our understanding of genetic influences on complex social behaviors.

NG Solomon, B Keane, P Harding
Miami University, Ohio

Integrative studies of genetics, neurobiology and behavior demonstrate that single genes play a substantial role in modulating complex social behavior. The neuropeptide arginine vasopressin has been shown to be a key component in the regulation of a variety of social behaviors in male mammals, including male social attachment to females, through its action on the vasopressin 1a receptor (V1aR). However, most studies of the effects of the gene encoding the V1aR (avpr1a) on social behavior have been conducted in laboratory settings. These studies provide insight into mechanisms of action and suggest potential human applications of these findings, but understanding the extent to which the V1aR mediates variation in social behavior in nature requires investigating the consequences of avpr1a polymorphism in a natural setting. While length polymorphism in avpr1a predicts individual differences among male prairie voles in some social behaviors under laboratory conditions only a single short-term study has attempted to find a relationship between avpr1a allele length and measures of monogamy among prairie voles in ecologically relevant conditions. We examined the relationship between avpr1a length and monogamy among male prairie voles from semi-natural populations during a time span representing their natural lifespan. Population density was also manipulated to investigate whether measures of social and genetic monogamy were influenced by this demographic factor. There was a significant effect of density but not avpr1a allele length on some indices of social monogamy among males. Interestingly, we found that males with shorter avpr1a alleles had significantly more mates and more offspring than males with longer avpr1a alleles. Our experiment has shown that results from field studies can substantially increase our understanding of the effects of genes and environment on social behavior since effects seen in the laboratory may not reflect behavior in nature.

Nucleus accumbens dopamine mediates social and drug reward interaction in monogamous male prairie voles.

ZX Wang, Y Liu, BJ Aragona, KA Young
Florida State University, Florida

Prairie voles (Microtus ochrogaster) display mating-induced partner preference (PP) and this behavior is mediated by several neurotransmitters including dopamine (DA). Recently, we have shown that amphetamine (AMPH) is rewarding to prairie voles as it induced conditioned place preferences (CPP). In the present study in male prairie voles, we used PP and CPP paradigms to reveal behavioral interactions between social bonding and AMPH reward. Males that were pair bonded for two weeks needed a higher dose of AMPH to induce CPP as compared to their sexually naïve counterparts. In addition, saline-treated control males displayed mating-induced PP but this behavior was diminished in males that had received prior exposure to AMPH. We then examined the role of central DA in AMPH inhibition of pair bonding. We found that AMPH-treated males had an increase in the density of DA D1, but not D2, receptor mRNA in the nucleus accumbens (NAcc) as compared to saline-treated controls. As our previous studies demonstrated D1 receptor inhibition of PP, we treated male voles with a D1 receptor antagonist or saline during AMPH conditioning. Blockade of D1 receptors in the NAcc restored PP in males that had AMPH experience. Together, our data demonstrate that social bonding enhances resistance to AMPH whereas exposure to AMPH inhibits social bonding. In addition, an up-regulation of NAcc D1 receptors by AMPH is responsible for impaired social bonding in male prairie voles.

Translational Implications of Prairie Vole Research.

LJ Young, HE Ross, ME Modi
Emory University, Georgia

Prairie voles are an emerging model organism that has already proven useful for understanding the genetic and neurobiological mechanism underlying complex social behavior. But to what extent are the principles discovered in prairie voles applicable to the human condition? I will highlight findings in both vole and human research that suggest that discoveries made in the prairie vole system have important implications for translational research. Work from several labs has highlighted the roles of oxytocin and vasopressin in regulating social bonding in prairie voles. Infusing these neuropeptides into the prairie vole brain accelerates partner preference formation. Variation in the distribution of oxytocin and vasopressin receptors in the brain is thought to contribute to both species differences and individual variation in affiliative behavior. Increasing peptide receptor expression in the nucleus accumbens and ventral pallidum using viral vector gene transfer enhances partner preference formation. In humans, oxytocin also influences social cognition. Specifically, intranasal oxytocin enhances interpersonal trust and memory for faces, increases the ability to infer emotions of others from facial cues, and increases eye-to-eye contact. Multiple studies have linked mutations in genes encoding for the oxytocin system with populations of individuals with autism. There is preliminary evidence that oxytocin may increase some aspects of social cognition in subjects with autism spectrum disorder. In prairie voles, polymorphisms in the 5' flanking region of the vasopressin receptor 1a gene (*avpr1a*) have been associated with variation in *avpr1a* expression in brain, and variation in social behavior in the laboratory. Similar polymorphisms in the human *APVR1A* have now been reported to be associated with autism, altruistic behavior, and brain activation patterns during a face processing task. A recent study found that polymorphisms in this region of the *AVPR1A* are also associated with measures of pair bonding in humans. Because of the apparent conserved nature of the mechanisms regulating social cognition in voles and man, we propose that partner preference formation in voles may be a useful behavioral assay for identifying pharmacological targets that may be useful for treating social cognitive deficits in psychiatric disorders such as autism and schizophrenia. With this in mind, we tested the hypothesis that D-cycloserine, a cognitive enhancer used in clinical trials, would enhance partner preference formation in prairie voles. Indeed, D-cycloserine administered peripherally, or directly into the nucleus accumbens and amygdala, accelerate partner preference formation. We are testing the hypothesis that D-cycloserine will act synergistically with oxytocin to enhance social cognition and accelerate partner preference formation. If correct, we propose this combination should be considered as a potential therapeutic for enhancing social cognition in autism.

SHORT TALKS (Early Afternoon)

Role of pelvic signaling during delivery in postpartum maternal care.

UL Hayes, A Ortiz, C Gill, S Balaban, JZ Smith, SI Powers, M Perry-Jenkins
University of Massachusetts, Massachusetts

Female prairie voles show a dramatic shift in their reactions to pups at parturition. As virgins, female prairie voles are infanticidal (i.e., attack young). They continue to attack pups during pregnancy but become maternal upon delivery of their pups. The quick onset of maternal behaviors at delivery suggests that events closely associated with parturition trigger the change in maternal responsiveness. One possible event is pelvic afferent signaling resulting from distention of the birth canal during delivery. Our research has shown that pelvic afferent signaling at delivery is important for the induction of maternal behavior in infanticidal females. Procedures that block sensory outflow from the cervix (i.e., artificial delivery and pelvic neurectomy) preclude the induction of maternal behaviors. Based on these findings, our current clinical research examines the influence of pelvic signaling during delivery on maternal depression, a predictor of the quality of maternal care in women.

With the growing popularity of cesarean deliveries, concern that the absence of a vaginal delivery would promote mental distress spurred many clinical studies that examined the relationship between cesarean delivery and postpartum depression. Previous clinical studies reported that cesarean delivery posed no risk for developing postpartum depression. However, these studies examining the link between delivery and mental health did not correct for the use of epidural anesthesia, another popular obstetric treatment that blocks pelvic signaling. In our study, we compared women who delivered via cesarean and/or received epidural anesthesia (Intervention) with women who delivered vaginally without an epidural (No Intervention). We found that women in the Intervention group reported more depressive symptoms 12-months after delivery than those in the No Intervention group (HLM: _=3.541, SE=1.54, P<0.05). With the routine use of obstetric intervention during delivery, blocked pelvic signaling may contribute to the high prevalence of depression found in women after delivery.

Sperm investment in meadow voles.

AA Vaughn, J delBarco-Trillo, MH Ferkin
University of Memphis, Tennessee

One strategy male voles use to assess the risk and intensity of sperm competition involves responding to the presence of scent marks of conspecific males found near a sexually receptive female. Previously, we have shown that males will increase their sperm investment if they copulate in the presence of the odors of another male conspecific. The aim of the present study was to test the hypothesis that males assess differences in the relative quality of competing males and adjust their sperm investment accordingly. We did so by allowing males to copulate when they were exposed to the scent mark of a 24-h food-deprived male (low-quality male) or the scent mark of a male that was not food deprived (high-quality male). The data indicate that male meadow voles did not increase their sperm investment during copulation when exposed to the scent mark of a food-deprived male but did so when they were exposed to the scent mark of a male that was not food deprived. The results support the hypothesis that male voles are able to adjust sperm investment when they encounter the scent marks of males that differ in quality.

Dopaminergic cells in the male prairie vole extended olfactory amygdala are possible nodes in the unique neurochemical networks mediating monogamy.

KV Northcutt, JS Lonstein
Michigan State University, Michigan

Prairie voles display many indices of monogamy, including the formation of life-long pairbonds after mating and biparental care towards pups. Recently, our lab discovered a very large number of dopaminergic cells in the male prairie vole posterodorsal medial amygdala (MeApd) and principal nucleus of the bed nucleus of the stria terminalis (pBST). Interestingly, none or very few tyrosine hydroxylase-immunoreactive (TH-ir) cells were found in the MeApd and pBST of either sex of three non-monogamous rodents that we examined, including the closely related meadow vole. Furthermore, there was a sex difference in prairie voles, with females having far fewer TH-ir cells than males. This sex difference was due to adult circulating gonadal hormones, as castrating males or giving testosterone to females eliminated it.

We hypothesize that these cells may be particularly involved in the monogamous behaviors displayed by male prairie voles. To begin investigating this possibility, Fos expression was examined in TH-ir cells of the MeApd and pBST in male prairie voles after they interacted for 30 min with a sexually receptive female, pups, a familiar female sibling, or nothing. Fos expression was significantly elevated in TH-ir cells in males that mated to ejaculation, but not in males interacting with pups or a sibling. Similar effects were found for Egr-1 expression in TH-ir cells. Immediate-early gene expression in TH-ir cells of ejaculating males was less than 10%, so we are currently examining if Fos expression in these TH-ir cells is even greater after males interact with a sexually receptive female for 6 or 24 h, durations that facilitate partner preference formation. We believe that dopaminergic cells in the male prairie vole MeApd and pBST, and the regions they innervate, may be part of a network influencing mating interactions and pair-bond formation in prairie voles.

FUNDING OPPORTUNITIES

NIMH Funding Priorities.

JM Simmons
National Institute of Mental Health, Washington, DC

The National Institute of Mental Health provides support for research programs in the areas of basic neuroscience, basic behavioral science, and research training through the Division of Neuroscience and Basic Behavioral Science (DNBBS). Within DNBBS, areas of high priority include studies on the fundamental mechanisms of complex social behavior. Proposals and grants within this area, including those using the vole model, are handled within the Affect, Social Behavior, and Social Cognition Program. As the Chief of this program, Janine Simmons will discuss NIMH funding priorities as they relate to vole research and research training, within the context of the NIMH Strategic Plan (http://www.nimh.nih.gov/about/strategic-planning-reports/nimh-strategic-plan-2008.pdf).

NSF Funding Opportunities.

DM Witt
National Science Foundation, Virginia

The National Science Foundation (NSF) provides funding opportunities for basic neuroscience throughout the foundation, with the bulk of this type of research reviewed in the Directorate for Biological Sciences, within the Division of Integrative Organismal Systems (http://www.nsf.gov/bio/ios/about.jsp). Proposals using the vole model are reviewed by the Neural Systems Cluster (Modulation panel) which focuses on the robust emergent properties of the nervous system that underlie adaptive behavior, learning, and the ability to engage in complex social interactions, covering cellular communication within the nervous system and interactions with other physiological systems and the environment. The Behavioral Systems Cluster (Animal Behavior Panel) also focuses on the development, function, mechanisms, and evolutionary history of behavior, with emphasis on a vertically integrated understanding of the behavioral phenotype in nature. I will identify funding sources for vole researchers and describe current funding priorities, as they align with NSF's strategic goals.

SHORT TALKS (Late Afternoon)

Why are some males parental? Insights from a male prairie vole.

M Bamshad
Lehman CUNY, New York

Infant nurturance results from a positive emotional state that drives the animal to approach an infant and engage with it socially. Research in female mammals has shown that changes in neuroendocrine factors during pregnancy stimulate the appetitive positive affect system in the brain. Hence the parturient female finds infant stimuli rewarding and directs her attention and resources towards infant care and survival. Prairie voles are unusual mammals because of their mating system and social behavior. The male prairie vole enhances his reproductive fitness by remaining with the female after mating and nurturing his offspring rather than increasing his progeny by leaving the natal nest to seek other mates. Research in my laboratory is focused on understanding the biology of paternal behavior in prairie voles. Previously, we showed that the intensity with which male prairie voles engage in paternal care changes during the reproductive period. Currently, we are investigating the mechanisms that influence the male's brain to make infants the objects of his attention and increase his ability to care for them.

Anterior hypothalamic vasopressin regulates selective aggression in the socially monogamous male prairie vole.

KL Gobrogge, Y Liu, LJ Young, ZX Wang
Florida State University, Florida

After mating, male prairie voles (Microtus ochrogaster) display aggression toward novel females but not toward their female partner. This selective aggression is important for the maintenance of pair bonds in this socially monogamous species. Here we show that selective aggression in pair bonded male prairie voles is associated with increased release of vasopressin (AVP) in the anterior hypothalamus (AH). Furthermore, activation of AVP-V1a receptors (V1aR) in the AH induces selective aggression in sexually naive males while blockade of those receptors diminishes selective aggression in pair bonded males. Pair bonded males have higher densities of V1aR binding in the AH, and over expressing V1aR in the AH facilitates selective aggression in sexually naive males. Together, these data reveal a novel socioneurobiological mechanism residing in the AH programming ethologically valid aggressive responses in male prairie voles through specific AVP signaling properties.

Same-sex partner preferences in meadow voles: what can non-monogamous rodents teach us about social behavior?

AK Beery, I Zucker
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The neurobiology of social bonding has been greatly elucidated through studies of maternal attachments and reproductive pair-bonds. However not all social bonds are with offspring or sexual partners. Meadow voles (Microtus pennsylvanicus) provide a model for the study of non-reproductive social behavior. In summer months, meadow voles are aggressive towards same-sex conspecifics, but in winter months they huddle in groups. Seasonal shifts in behavior can be triggered by altering day length in the laboratory, and are concomitant with changes in oxytocin receptor densities in several brain regions. I will present results from two recent experiments: one documents variation in oxytocin receptor density with day length and estradiol treatment; the second demonstrates the effects of oxytocin infusion on same-sex partner preference formation. Together these experiments suggest that non-sexual social behavior is both similar to and different from sexual bond formation in its neuroanatomical substrates.

Geographic variation in the social and genetic mating systems of the prairie vole.

KE Mabry, CA Streatfeild, B Keane, NG Solomon
Miami University, Ohio

Very few mammalian species (<3-5%) exhibit either social or genetic monogamy. The prairie vole (Microtus ochrogaster) is frequently cited as an example of mammalian monogamy. The characterization of prairie voles as monogamous is based primarily on laboratory studies and a long-term field study of social behavior in Illinois (IL). Relatively little is known about the social mating system of free-living prairie voles outside IL, but some evidence suggests that voles are less socially monogamous in Kansas (KS) than in IL. Thus, the social mating system may be flexible across the range, perhaps in response to variation in environmental conditions. We used live-trapping, radio-telemetry, and genetic parentage assignment to describe the social and genetic mating systems in two free-living populations of prairie voles: KS and Indiana (IN). IN males had larger home ranges than females, but there were no between-sex differences in home range size in KS. These space-use patterns suggest that prairie voles may be more socially monogamous in KS than in IN. In both KS and IN, there was a lower frequency of male-female pair social units than previously reported for IL. Results from genetic parentage analysis were consistent with observations of social mating systems: IN voles were genetically less monogamous than KS voles. In IN, we observed a higher frequency of multiply-sired litters, and both males and females produced offspring with multiple partners more often in IN than KS. Our results suggest that both the social and genetic mating systems of the prairie vole vary across the species' range, and are more complex than previously appreciated.

ADVANCES IN RESOURCES & TECHNOLOGIES

Automated methods for the analysis of partner preference in prairie vole (Microtus ochrogaster).

TH Ahern, ME Modi, JP Burkett, LJ Young
Emory University, Georgia

Prairie voles are socially monogamous rodents that form selective, enduring attachments, or pair bonds, between mates. Most studies of vole social bonding require the use of the partner preference (PP) test. The PP test is a powerful behavioral assay and has helped identify numerous neurochemicals that regulate social bond formation, including oxytocin, vasopressin, and dopamine. Traditionally, manual scoring of videotaped tests has been necessary to accurately quantify behavioral metrics such as time in close proximity or huddling with the partner or stranger. To assess the possibility of using automated systems for high through put behavioral analysis of PP test, we have compared several different scoring techniques, including three computerized systems: Noldus Ethovision 3.0 and Clever Sys Inc. SocialScan 2.0, which process video, and Vole Tracker, an infrared beam-break system. Ethovision and Vole Tracker both quantify time in "social proximity," whereas SocialScan measures time in "immobile social contact" as a proxy for "huddling." Initial verifications demonstrated that automated methods correlated highly with real-time and 16X manual scoring of "huddling" ($R > 0.90$). SocialScan's measure of "immobile social contact," however, achieved a significantly better accuracy ($R = 0.99$; $P < 0.001$). We then compared Ethovision's "social proximity" and SocialScan's "immobile social contact" in their ability to detect group PPs in both males and females after 24-hours and 1-week of cohabitation; both scored the same video footage. SocialScan detected a significant PP in both males and females at both time points ($P < 0.05$ for all). Ethovision's results were similar, but it failed to detect a PP in males after one week of cohabitation ($P = 0.109$). Thus, automated scoring of PP test provide accurate data approximating manual scoring, but systems that quantify "immobile social contact" are more sensitive for identifying partner preferences.

Telemetry in the field: Space use, paternity and mechanisms of monogamy.

AG Ophir, JO Wolff, SM Phelps
Oklahoma State University, Oklahoma

Studying the socially monogamous prairie vole has potential to provide insight into mating strategies and human social attachment by understanding the mechanisms that underlie prairie vole monogamy. Research using this model has revealed that, among males, the action of arginine vasopressin on its receptor, V1aR, induces social attachment and pairbond formation. Much of this work, however, has been performed under laboratory conditions and ignores the natural variation in prairie vole behavior. While most males establish long lasting pairbonds with females, defend territories and provide care to offspring, approximately one quarter of males remain single and adopt a non-monogamous pattern of behavior in which males have much larger non-defended territories and attempt to mate multiply with several different females. We integrate tools from behavioral ecology, molecular biology and behavioral neuroscience to provide a deeper understanding of the mechanisms that influence the suite of behaviors collectively described as monogamy. For example, space use reflects the intensity and frequency of social interactions between conspecifics and indicates which males are living with females and which are not. Paternity assessment indicates which males successfully mated and which did not. By describing the patterns of space use, paternity and V1aR expression in a sample of prairie voles allowed to behave freely in outdoor enclosures, we provide a more complete description of the mechanisms that underlie prairie vole monogamy in nature. These data reveal that prairie vole monogamy is complex, and mediated by several social and molecular interactions. Integrating tools from disparate but complementary disciplines will lead to important discoveries and novel insights.

Social behavior, mood, and cardiovascular disease: a focus on the integration of behavior and cardiac function using radiotelemetry technology.

AJ Grippo
Northern Illinois University, Illinois

There is a documented association between depression and cardiovascular disease in humans, however the mechanisms underlying this link are not well understood. Reactions to the social context may play a role in underlying depressive behaviors and physiological responses indicative of cardiovascular dysregulation. Socially monogamous prairie voles (Microtus ochrogaster) provide a useful translational model for examining the role of the social environment in mediating the association of mood and cardiovascular disorders. Radiotelemetry technology is currently available for continuous electrocardiographic recordings, and can be employed in small rodents to provide insight into autonomic and cardiac function. This presentation will focus on the integration of behavior and cardiac function in the prairie vole, which can guide experimental research and contribute to our understanding of neurobiological mechanisms involved in the association of depression and cardiovascular disease.

Mammalian sociogenomics: developing transgenic and genomic resources in the prairie vole (Microtus ochrogaster).

LA McGraw, , JK Davis, P De Jong, KM Rudd, CL Martin, TC Glenn, NISC, LJ Young, JW Thomas
Emory University, Georgia

The prairie vole (Microtus ochrogaster) is an emerging model organism for elucidating the genetic and neurobiological mechanisms governing complex social behavior in vertebrates. Unlike the majority of mammalian species, including laboratory mice and rats, prairie voles are highly affiliative, socially monogamous, form enduring social bonds and display extensive biparental care of offspring. However, to date, deciphering the mechanisms underlying social behavior in this species has been limited to the study of a handful of candidate genes and hampered by a paucity of molecular genetic and genomic tools. To further enhance the utility of this model organism for understanding social behaviors and mental health, we have constructed a 10X coverage prairie vole BAC library (http://bacpac.chori.org/library.php?id=481). The BAC library has already been utilized to isolate and begin to fully sequence 19 genes that are of high interest to the vole research community. In addition, construction of a first-generation linkage map of the prairie vole genome comprising ~300-500 informative SNP and microsatellite markers is underway. To date, we have identified ~750 SNPs from 175 discrete regions of the genome. To complement and inform the genetic linkage map, we are also developing a FISH cytogenetic map by using a panel of approximately 80 vole BACs that have end-sequences that share homology with mouse and are evenly distributed across the genome. The availability of these genomic resources to the vole research community will aid in fostering a new trajectory towards understanding the links between the genome, the brain and the expression of social behaviors.

POSTERS

Poster: 1

The opiate system modulates pair bond formation in female prairie voles.

JP Burkett, LL Spiegel, LJ Young
Emory University, Georgia

Socially monogamous prairie voles (Microtus ochrogaster) form enduring pair bonds between mates, and have become an informative animal model for exploring the neurobiology of social attachment. The opiate system has long been implicated in the regulation of infant-mother attachment, but its role in adult pair bonding has not been explored. Mu-opioid receptors in the nucleus accumbens (NAcc) mediate the reinforcing properties of natural rewarding stimuli, and the NAcc also plays a critical role in partner preference formation. We hypothesize that endogenous opioids play a role in partner preference formation in prairie voles via activation of these _-opioid receptors in the NAcc. To test this hypothesis, we first administered the non-selective opioid antagonist naltrexone (NTX, IP, 7.5 mg/kg Q6H) or vehicle to adult female prairie voles during an 18-hour mating period with a male partner. Subjects treated with NTX mated significantly less during cohabitation ($p < 0.01$) and significantly preferred a stranger over their partner in a partner preference test ($p < 0.01$). We then explored the role of _-opioid receptors in the NAcc by site-specific administration of the _-opioid selective antagonist CTAP (3 _g/side) or vehicle to the NAcc and caudate-putamen (CP) at 12-hour intervals during a 24-hour mating period. Control females displayed a significant partner preference ($p = 0.01$), while voles receiving CTAP to the NAcc or CP displayed no preference. Furthermore, the antagonist did not affect mating behavior during cohabitation. While localization of the effect is not established by these results, the data strongly implicate the opiate system in pair bond formation in female prairie voles, and suggest that _-opioid receptors in the NAcc may mediate these effects.

Poster: 2

Influence of avpr1a microsatellite length on space use by male prairie voles under semi-natural conditions.

FR Castelli, B Keane, NG Solomon
Miami University, Ohio

The neuropeptide arginine vasopressin has been shown to play a key role in the regulation of male social attachment to females through its action on the vasopressin 1a receptor (V1aR). Length polymorphisms in microsatellite DNA within the regulatory region of the gene that codes for V1aR (avpr1a) are correlated with neural expression and differences in male behavior. Evidence from laboratory studies suggests that male prairie voles (Microtus ochrogaster) with longer avpr1a microsatellites are more socially monogamous than males with shorter avpr1a microsatellites. However, behavior of animals under laboratory conditions may not reflect behavior in nature. In this study, prairie voles were selectively bred to accentuate differences in avpr1a microsatellite length in males and to reduce the chance that other genetic factors linked with avpr1a affected behavior. Adult voles of equal sex ratio were released into semi-natural enclosures. Half of the founder males in each enclosure had alleles with long avpr1a microsatellites and half had alleles with short avpr1a microsatellites. Previous research suggests that Illinois voles are more socially monogamous than Kansas voles so we examined voles from both populations. All founders were radio-tracked for five consecutive days, 8-10 weeks after release into enclosures. Home range size and overlap with females were calculated using 50% and 95% kernel estimators. We predicted that males with two long avpr1a microsatellites would have smaller home ranges, have home ranges that overlap fewer female home ranges, and a greater home range overlap with a single female than males with two short avpr1a microsatellites. However, neither avpr1a microsatellite length nor population of origin significantly influenced these measures under the conditions of this study. These results are consistent with those from other field studies, suggesting that avpr1a microsatellite length does not influence the patterns of space use of male prairie voles, one indicator of social monogamy.

Poster: 3

Parasite infection does not affect social or genetic mating of prairie voles.

AS Chesh, KE Mabry, B Keane, NG Solomon
Miami University, Ohio

The parasite-mediated sexual selection hypothesis predicts that given a choice between males of differing parasite load, females will preferentially mate with less-parasitized males. In many socially monogamous species, females produce offspring sired by males other than their social partner (with whom they live). In these cases, the parasite-mediated sexual selection hypothesis predicts that a female will live (or nest) with a male with fewer parasites to decrease parasite transmission to herself and her offspring. Likewise, the extra-pair mates of females should also have fewer parasites. We tested these predictions for the effects of both ecto- and endoparasites on social monogamy and reproductive success in a natural population of prairie voles (Microtus ochrogaster) near Lawrence, Kansas. Live-trapping data collected during eight weeks was used to classify adults as either nest residents or wanderers and determine the composition of social units. We collected tissue samples from field-caught voles and performed genetic parentage analysis using microsatellite loci. Parasite loads were determined by combing all adults for ectoparasites and by quantifying the number of endoparasite eggs in the feces of adult males. Neither the prevalence of ectoparasites nor the intensity of endoparasites had any significant relationship to the number of pups sired or mates obtained by adult male prairie voles. There was no significant difference in endoparasite intensity between socially monogamous resident males and males without a social partner (residents and wanderers). However, body mass and body condition had a positive relationship with both the number of pups sired and the number mates obtained by adult male prairie voles. These results suggest that neither ecto- nor endoparasites affect the social and genetic mating systems of prairie voles in Kansas and other male characteristics, such as total body mass or body condition, may be more important in this natural population.

Poster: 4

Family background and gestational conditions affect social bonding in prairie voles.

JT Curtis
Oklahoma State University Center for Health Sciences, Oklahoma

Pre- and peri-natal influences have been shown to impact adult behavior in prairie voles. To date most studies have focused on the effects of perinatal manipulations, while little attention has been focused on more natural variations in the peri-natal environment. Here we present the results of a retrospective study examining social behavior in light of ancestry and in utero conditions. We found that behaviors of adult voles in social situations differed depending on the breeder pair from which they descended. Further, birth litter composition could alter behavior both of the subject and of animals with whom it interacts. For example, females avoided males from all-male litters. Thus, it may be necessary to include ancestry and birth litter composition as covariates.

Poster: 5

CNS Estrogen Receptor Beta expression in the prairie vole (Microtus ochrogaster).

SD Zito, JL Eaton, BS Cushing
The University of Akron, Ohio

There are two primary nuclear estrogen receptors (ER) subtypes, alpha and beta. While there is a large body of data on the role of ERalpha in regulating social behavior and in expression within the CNS there is significantly less known about ERbeta. This is due in part to the fact that the existence of ERalpha has been known for much longer and in part to the difficulty in visualizing ERbeta. Primary antibodies developed for labeling ERbeta have had limited success in rats and mice and none have worked in prairie voles (Microtus ochrogaster). Here for the first time we characterize the expression of ERbeta immunoreactivity, using immunocytochemistry, in the brains of prairie voles. ERbeta immunoreactivity was compared in juveniles, 21-days of age, and in adult males and females. Results form adults indicate that ERbeta may not be as widely distributed as reported in rats and mice and unlikely ERalpha, ERbeta expression is not sexually dimorphic.. While low levels were observed in several other regions ERbeta immunoreactivity was primarily observed in several in the pre-optic area and in the hypothalamus, especially the paraventricular and supraoptic nuclei. The visualization of ERbeta in prairie voles is important as the socially monogamous prairie vole functions as a human relevant model system for studying the expression of social behavior and social deficit disorders and ER is know to major a role in the expression of social behavior. Future studies will now be able to determine the effect of treatments on the expression and/or develop of ERbeta in this highly social species.

Poster: 6

Exposure to Female's Somatosensory Cues after Mating Enhances Male Prairie Vole's Ability to Care for Infants.

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Lehman College-CUNY, New York

ABSTRACT
Monogamous male mammals show parental care. However, it is unclear how they become motivated to care for infants. Using prairie voles as a model of monogamous species, we tested the hypothesis that somatosensory cues from a female after mating influence male's tendency to seek physical contact with infants. Sexually-naïve males either remained unmated or were allowed to mate. Subjects were placed in an oversized cage divided into two compartments with a perforated clear plastic barrier. Males remained in physical contact with their mate (MATEDCON), received their mate's distal cues (MATEDCUES) or received no cues from their mate (MATED). A separate group of unmated males received distal cues from an unfamiliar pregnant female (CUES). At mid-gestation, the bedding and females were removed and two 3-6 day-old infants were placed across the barrier. Male behavior was recorded for 5 minutes with the barrier in place and for an additional 10 minutes after the barrier was removed. A higher percentage of MATEDCON males showed "Kyphosis" (crouching over infants), and they did so more frequently than MATED and CUES males. Also, the MATEDCON males spent more time on kyphosis than the MATED males. The MATEDCON males were more frequently in contact with infants and spent less time on non-social activities than MATED and CUES males. A higher percentage of MATEDCON and MATEDCUES males interacted with both infants compared to CUES males, and did so more frequently. The latency to approach infants was significantly shorter in MATEDCON and MATEDCUES males compared to CUES males. No differences were found in duration of licking and frequency of retrieving infants. Data suggest that exposure to female distal cues after mating is sufficient to increase male's parental attentiveness, but female's tactile cues affect male's tendency to remain in physical contact with infants.

Poster: 7

Self-Grooming Response of Meadow Voles to the Odor of Opposite-Sex Conspecifics in Relation to the Dietary Protein Content of Both Sexes.

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Many animals self-groom when they encounter the scent marks of opposite-sex conspecifics. Self-grooming transmits odiferous substances that contain information about the groomer's condition, which is affected by its nutritional state. We tested the hypothesis that the amount of time that individuals self-groom to opposite-sex conspecifics is affected by the amount of protein in their diet and that of the scent donor. We did so by feeding meadow voles (Microtus pennsylvanicus) a diet containing 9%, 13%, or 22% dietary protein for 30 days and observing their self-grooming behavior when they were exposed to bedding scented by an opposite-sex conspecific (odor donor) fed one of the three diets, or fresh cotton bedding (control). The hypothesis was partially supported. We found that the protein content of the diet of male and female groomers did not affect the amount of time they self-groomed. However, the protein content of the diet of male odor donors affected the amount of time that female voles spent self-grooming. Female voles self-groomed more in response to male odor donors fed a 22% protein-content diet than to those produced by male odor donors fed either a 9% or a 13% protein-content diet. Interestingly, the amount of time males self-groomed was not affected by the protein content of the diet of the female odor donor. These results may, in part, be explained by the natural history of free-living meadow voles, sex differences in costs associated with mate attraction and reproduction, and the direct or indirect benefits that females receive from males fed a diet high in protein content.

Poster: 8

Alcohol consumption in periadolescent prairie voles.

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Deficits in social behavior, such as decreased affiliation, can often result from excessive alcohol consumption. At present, there is no suitable rodent model available for studying the impact of social problems on alcohol intake. The prairie vole (Microtus ochrogaster), a monogamous rodent species, displays affiliative behavior and is a novel model for research into alcoholism. We investigated alcohol drinking in periadolescent prairie voles in this study. Male and female prairie voles, approximately 4 weeks of age, were removed from their home cages and either single-housed or pair-housed as same-sex pairs in custom-made cages, containing a wire-mesh divider. Alcohol consumption was determined using the standard 24 h access two-bottle choice paradigm. The concentration of ethanol was increased gradually: 4 days of water, 4 days of 3 % ethanol, 4 days of 6 % ethanol, 4 days of 10 % ethanol and 4 days of 20 % ethanol. After the fourth day of 20 % ethanol, after a short break, preference to 0.04 % saccharine and 0.0018 % quinine was examined. Immunohistochemistry was then performed for neuropeptides that are important in social affiliation and/or alcohol consumption: urocortin, arginine vasopressin (AVP), oxytocin and CRF in voles designated as low (< 16 g/kg ethanol intake) or high (> 16 g/kg intake) drinkers and compared to naïve controls. Results showed that social isolation decreased preference to, as well as intake of, 3 % and 6 % ethanol. However, social isolation had no effect on preference to saccharine or quinine. Alcohol drinking affected AVP levels in the supraoptic nucleus and oxytocin levels in the paraventricular nucleus. All other brain regions and neuropeptides examined showed no significant effects. Social isolation results in reduced alcohol consumption in periadolescent prairie voles. Periadolescent prairie voles are, therefore, a good model for investigating the relationship between social behavior and alcohol intake.

Poster: 9

Does avpr1a allele length affect parental care in male prairie voles?

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In many socially monogamous species, pair-bonded males often contribute substantially to the care of the pair's offspring. Previous laboratory studies have implicated polymorphism in the length of microsatellite DNA in the regulatory region of the gene that codes for the vasopressin 1a receptor (avpr1a) in influencing male parental behavior. Specifically, males with longer avpr1a alleles display a greater rate of pup grooming and a shorter latency to investigate an unfamiliar pup than males with shorter avpr1a alleles. To replicate and expand upon this study, we are conducting an ongoing laboratory study to further investigate the relationship between avpr1a allele length and paternal behavior in male prairie voles, using males that were selectively bred to possess avpr1a alleles substantially longer or shorter than the population average. Maximizing differences in the length of avpr1a alleles among the males in our trials should provide a rigorous test of the hypothesis that male prairie voles with longer avpr1a microsatellite alleles show greater paternal care relative to males with shorter alleles. In addition, our breeding plan was designed to uncouple the effects of avpr1a microsatellite length from other genetic factors by generating males that had either two short or long avpr1a microsatellite alleles, but otherwise similar genetic backgrounds. If avpr1a allele length affects parental behavior, we predicted that males with longer alleles would display a greater frequency of pup grooming, spend more time in the nest with pups, and retrieve their own pup more quickly when it is removed from the nest, relative to males with shorter avpr1a alleles. We also expected these effects to be greater than in the previous study by Hammock and Young. At this time, our preliminary results suggest that avpr1a microsatellite length does not influence male parental behavior in prairie voles under the conditions of our experiment.

Poster: 10

Amphetamine experience alters pair bonding behavior and neurotransmitter receptor density in the brain of male prairie voles.

Y Liu, KA Young, BJ Aragona, Z Wang
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Prairie voles (Microtus ochrogaster) display mating-induced pair bonding, and this behavior is mediated by several neurotransmitters including dopamine (DA), vasopressin (AVP), and oxytocin (OT). Recently, we have shown that amphetamine (AMPH) is rewarding to prairie voles as it induced conditioned place preference. In the present study, we demonstrated that AMPH experience inhibited pair bonding in male prairie voles, as 24 hrs of mating induced pair bonding in intact males but not in males that received AMPH treatment. In addition, we found that AMPH treatment altered the density of the receptors for DA, AVP, and OT in selected brain regions. Specifically, AMPH treatment increased DA D1- and D2-type receptor mRNAs in the nucleus accumbens, but decreased the level of AVP V1a receptor binding in the medial prefrontal cortex and central nucleus of the amygdala. AMPH treatment also decreased OT receptor binding in xxx. As central DA, AVP, and OT are involved in the regulation of pair bonding, our data indicate that region-specific changes in the receptor densities following AMPH treatment may be responsible for the AMPH inhibition on pair bonding.

Poster: 11

A field test of kin based mate choice in prairie voles (Microtus ochrogaster).

KE Lucia, B Keane
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The ability of an individual to distinguish a relative (e.g., a sibling from a previous litter that dispersed earlier) from non-related individuals could have long term consequences on the reproductive success of that individual, should the individual choose to mate with an unknown sibling and those litters experience some form of inbreeding depression. We manipulated potential mates by placing sexually mature prairie voles (Microtus ochrogaster) into 0.1 ha rodent enclosures with known siblings (littermates), unknown siblings (siblings from a different litter), and unrelated conspecifics. Analyses of multiple capture data indicate that males and females are more likely to be captured in the same trap than male-male and female-female pairings. Unrelated male-female pairings did not occur significantly more than expected by chance; however, of the multiple captures between related individuals, male-female littermates were captured together significantly more frequently than male-female unknown siblings. Spatial organization and nearest opposite sex neighbor calculations revealed patterns similar to the multiple capture data. Genetic analyses of embryos from pregnant females are planned to determine if females were mating in a pattern similar to that observed from the social data.

Poster: 12

The effects of environmental endocrine disruptors on reproductive behavior of the Prairie vole, Microtus ochrogaster.

BT Martinez, A Dunlap, R Kiesling, C Lehman
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Artificial chemicals added to managed ecosystems such as biofuel plantations can disrupt the functioning of endocrine systems, with potential effects on resident wildlife populations. Consequences have been severe in aquatic vertebrates, but effects in terrestrial vertebrates are largely unknown. This project will examine the effects on terrestrial populations using prairie voles (Microtus ochrogaster) as a representative species. Specifically, the project will test whether four common endocrine disrupting compounds (EDCs) significantly affect the reproductive behavior of the monogamous prairie vole. The project will be a replicated laboratory design with three treatments: (1) Pristine, no EDC in the diet; (2) Ambient, diet has concentrations of EDC matched to expected levels in the environment; (3) Elevated, diet has concentrations of EDC matched to higher levels in the environment. The four compounds to be tested are 4-nonylphenol, 17a-ethynylestradiol, 17b-estradiol, and dioctyl phthalate. To simulate animals in the wild, voles will be exposed to EDCs throughout their lifetimes, from gestation forward. Behavioral observations will be collected on exposed voles when they are breeding and later when they are caring for offspring. The strength and nature of the pair bond will be observed in an experimental setting and actual paternity determined. Behavioral characteristics will be used to assess possible changes in population dynamics and potential value of management methods to control these substances in the environment. Because endocrine pathways are broadly conserved across mammalian species, results will be relevant to other terrestrial species, including humans.

Poster: 13

Effect of Kava on Social and Affect Behaviors of Prairie Voles, Microtus ochrogaster.

K Measor, K Herrera, MJ Balick, M Bamshad
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The roots of the Kava (Piper methysticum) plant have been used for centuries by Western Pacific Islanders to make an intoxicating beverage. The properties of this beverage and it chemical constituents have been shown to have anti-anxiety effects in humans, mice and chicks. Based on ethnobotanical studies of the traditional use of kava, it is also hypothesized that kava reduces aggression and fosters social bonding among those drinking it. To test this hypothesis, we are using prairie voles because this animal displays social and affect behaviors that are similar to humans. Two methods of Kava administration were utilized in this study. The first method consisted of using commercially-available powdered Kava root to make a solution similar to what would be traditionally imbibed by humans. This solution was given to a group of sexually naïve females for a period of approximately 48 hours in place of their regular water source. The second method of administration used commercially-available kava extract that was serially diluted and injected intraperitoneally into a separate group of females. After administration of Kava, the voles were first tested for aggression/affiliation behavioral changes by placing the experimental animal into a neutral cage with a unfamiliar female stimulus vole. The behavior of the animals were recorded and scored for any aggressive or affiliative behaviors. After a rest period the experimental vole were also tested on the elevated plus maze to determine any anxiolitic effects of the Kava administration. Initial results have indicated that the Kava may have lowered anxiety in the experimental animals; however experimental voles did not demonstrate more affiliative behavior as predicted. These subjects actually spent significantly less time in direct contact with the stimulus animals as compared to their control counterparts, suggesting an alternative effect that Kava may be having on social behaviors.

Poster: 14

Prairie Voles as a Model for the Development of Novel Theraputics to Enhance Social Cognition: The effects of D-cycloserine.

ME Modi, LJ Young
Emory University, Georgia

Social bonding in the highly affiliative, socially monogamous prairie vole is a complex cognitive process involving social motivation, integration of social information, and social learning and memory. We propose that an assay of social bonding may be an effective approach to identify novel pharmacotherapies for the treatment of the social deficits associated with neuropsychiatric disorders, such as autism. In the laboratory, social bonding is assessed by measuring partner preference formation. Previous studies in prairie voles have implicated an interaction between the oxytocin (OT), dopamine (DA) and glutamate (Glu) receptor systems in nucleus accumbens (NA) in the formation of partner preferences. In this study we directly examine the role of the Glu receptor system in social bonding using two clinically relevant compounds that target ionotropic Glu receptors, D-cycloserine (DCS) and Ampakine CX614. The Glu receptor system functions in the cellular encoding of learning and memory and has been utilized in the clinical setting to enhance cognitive processes. We hypothesize that by enhancing Glu neurotransmission with these compounds, partner preference formation will be accelerated during cohabitation.

DCS accelerated partner preference formation in female prairie, suggesting that this drug enhances social cognition. We hypothesize that by enhancing glutamatergic transmission in the nucleus accumbens, we are expediating the process of social learning, potentially through interactions with the oxytocin system. Future studies will test the hypothesis that combined oxytocin agonist and DCS will act synergistically to accelerate social bond formation in female prairie voles. If this hypothesis is correct, we predict that a similar combined therapy may be useful in ameliorating the social cognitive deficits in autism.

Poster: 15

What yo' mama nev'a told ya' about oxytocin circuitry.

HE Ross, LJ Young
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Oxytocin receptors (OTR) in the nucleus accumbens (NAcc) have been implicated in the regulation of spontaneous maternal care and social bonding in prairie voles. There is significant individual and species variation in the density of OTR in the NAcc, which may contribute to variation in social behaviors. Blocking OTR in the NAcc inhibits the ability to form a partner preference in this socially monogamous species. Using viral vector mediated gene transfer, we tested the hypothesis that variation in OTR density in the NAcc in the adult can contribute to variation in partner preference formation. Adult, sexually naïve female prairie voles were injected bilaterally into the NAcc with either an adeno-associated viral vector (AAV) containing the prairie vole OTR gene under the control of the CMV promoter (AAV-OTR), a control GFP expressing vector (AAV-GFP), or were sham operated. The voles were then tested for a partner preference following 18 hours of cohabitation with a sexually experienced male. AAV-OTR treated voles, but not control or sham animals, spent significantly more time with their mating partner compared to the stranger ($p < 0.05$). 80% of AAV-OTR injected voles developed a partner preference, compared to only 31% of AAV-GFP injected animals. There was, however, no difference in mating behavior between groups. The NAcc also contains numerous oxytocin-immunoreactive fibers of unknown origin. We used retrograde tracing combined with immunocytochemistry to determine which oxytocin neuronal populations project to the NAcc, and therefore regulate pair bond formation and alloparental care. Fluorogold (FG) was iontophoretically injected into the NAcc of female prairie voles. Retrogradely labeled oxytocin cells were localized in the paraventricular nucleus and the supraoptic nuclei of the hypothalamus. More importantly, these FG+ oxytocin cells were located in magnocellular regions. This anatomical study demonstrates for the first time that these regions are the source of the oxytocin projections to the NAcc, and therefore play a critical role in coordinating peripheral and central release to influence pair bond formation and alloparental behavior in the monogamous prairie vole.

Poster: 16

Effects of food restriction during lactation on maternal behavior in meadow voles, Microtus pennsylvanicus.

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For female mammals, a reduction in quantity of food during pregnancy and lactation may negatively affect maternal behavior, their ability to lactate, and the development of offspring. Food restricted dams may alter their maternal behavior by reducing the size of their litter and/or the amount of time they can spend nursing pups. We studied the effects of a calorie restriction of 30% on the behavior of lactating female meadow voles; lactation lasts 21 days in this meadow voles. Dams underwent a 30% calorie restriction during either days 1-7, days 8-14, or days 15-21 of lactation; a control group of dams did not undergo food restriction. We hypothesized that food restricted dams would show decreases in several measures of maternal behavior, including nursing the pups, grooming the pups, time spent with the pups and time spent maintaining the nest. Maternal behavior was observed twice a day at 0700 (onset of light cycle) and at 2100 (onset of the dark cycle). Our preliminary data suggest that food-restricted dams spent less time engaged in maternal behavior than did dams that were not food restricted. Dams that were food restricted from days 8-14 showed the most pronounced declines in maternal behavior relative to dams that were food restricted during days 1-7 and dams that were food restricted during days 15-21.

Poster: 17

Effects of Early Experience on Partner Preference are Sexually Dimorphic.

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We have previously shown that minor differences in early handling result in long-term, sexually dimorphic changes in social behavior in the prairie vole (Microtus ochrogaster). Reduced manipulation, achieved by transferring animals between cages by a cup (MAN0 treatment) instead of a gloved hand (MAN1 treatment), resulted in lower alloparenting in males, impaired pair-bonding in females, and higher anxiety in both sexes. In this prior study (Bales et al. 2007, Developmental Psychobiology) we used a six-hour cohabitation to investigate the effects of early handling on partner preference, and found that females were impaired whereas males were not. In the current study, we asked whether early handling could either facilitate pair-bonding following a very short cohabitation period (30 minutes) or impair it following a very long cohabitation period (24 hours). Preliminary data indicate that MAN0 manipulation impairs pair-bonding in both sexes, with sexually dimorphic time-courses. While MAN0 females showed differences from MAN1 females only after the six hour cohabitation, MAN0 males were both less social overall ($F1 = 6.17$, $p = 0.0191$) and displayed less of a preference for the partner ($F1 = 7.97$, $p = 0.0099$) following both the 24 hour and 30 min cohabitations (but not the six hour). These results suggest additional, impairing effects of MAN0 treatment that were not apparent in the first study.

Poster: 18

Selection dynamics and MHC variability in cyclic montane voles.

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Determining the dynamics of selection maintaining genetic diversity in natural populations is a major focus of evolutionary biology. The major histocompatibility complex (MHC) is an ideal tool to investigate key questions concerning temporally varying selective forces. It has clear consequences for both parasite defense and mate choice, two processes affected by population density. By investigating how MHC allelic diversity changes nonrandomly over time in hosts that undergo dramatic population cycles, and how MHC allelic patterns are influenced by the selection pressures arising from mate choice and pathogen resistance, a greater comprehension of the evolutionary process can be gained. I will accomplish this with a combination of observational field studies and experiments, using cyclic populations of montane voles and their parasites as a model system.

Poster: 19

Effects of parent-pup separation on parental responsiveness and emotionality in prairie voles.

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Parental separation alters emotionality and maternal responsiveness in rat offspring. Unlike rats, the monogamous and biparental social system of prairie voles (Microtus ochrogaster) offers a unique opportunity to determine whether (1) the parental care of males and pair-bonded females is affected by pup separation, and (2) receiving increased social contact (i.e. two parents and siblings) can counteract the effects of early parental separation. We hypothesized that the biparental system compensates for the effects of early pup/parental separation.

During postnatal day (PND) 1-10, pups were removed from their parents for 0 (C), 15 (SS), or 360 (LS) min and housed either individually (PI) or with siblings (PS). Unhandled controls experienced daily lid opening (CU). Behavioral testing included tests for parental responsiveness and emotionality on PND 11 for parents and PND 90-92 for pups. Emotionality tests included open field test (OF) and elevated plus maze test (EPM), or forced swim test (FST).

The separation paradigm affected both parents and offspring. Although dams crossed more than sires in OF, SS males showed more crossing into the center in OF than SS females, while the opposite pattern was found in LS, C and CU parents. A similar pattern was found for time spent crouching during the parental behavior test. Parents handled daily (C, SS and LS) also exhibited more immobility in FST than non-handled (CU) parents. For the offspring, males spent more time in open arms of EPM than females, regardless of treatment. While no differences were found among males, unseparated females (C and CU) were immobile longer in FST than females in the SS and LS groups. We found an effect of sex, handling, separation and its duration on parental responsiveness and emotionality in the monogamous, biparental voles.

Poster: 20

Repeated amphetamine exposure blocks social bonding in monogamous female prairie voles; the involvement of mesolimbic dopamine.

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Prairie voles are monogamous rodents that form mating-induced partner preferences, a behavior mediated in part by dopamine (DA) in the nucleus accumbens (NAcc). Recently, we have established the prairie vole as an animal model of drug reward, and demonstrated that amphetamine (AMPH) induced conditioned place preferences in this species (Aragona et al., 2007, Neurosci Lett, 418:190-194). The current experiments tested the hypothesis that AMPH and social reward interact in the female prairie vole and that this interaction is mediated by NAcc DA. In the first experiment, female prairie voles formed place preferences after receiving low (0.2mg/kg) but not high doses of AMPH, indicating that low-dose AMPH is rewarding in females. Next, estrogen primed female subjects that received repeated saline (control) or AMPH (0.2, 1.0 or 5.0mg/kg) injections (1 injection per day for 3 days), were allowed to mate with a male for 24 hours and were then tested for partner preferences. While females injected with saline or higher doses of AMPH (1.0 or 5.0mg/kg) displayed partner preferences after mating, females treated with 0.2mg/kg AMPH did not show mating-induced partner preferences. These results demonstrate a dose-specific effect of AMPH on the inhibition of partner preference formation in female prairie voles. A third experiment investigated the mechanisms underlying this behavioral interaction. Female prairie voles received estrogen treatment alone (control) or estrogen treatment plus repeated AMPH injections (0.2 or 1.0 mg/kg AMPH; 1 injection per day for 3 days). Using the Western blot technique, females treated with 0.2mg/kg, but not 1.0mg/kg AMPH were found to have significantly lower levels of DA D2 receptors in the NAcc than females treated with estrogen alone. As D2R activation facilitates partner preference formation, these data, taken together, suggest a potential mechanism by which AMPH interferes with social bonding in the female prairie vole.

Poster: 21

The selective effect of estrogen receptor alpha and beta on activity and social behavior in neonatal male prairie voles.

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Until recently, estrogen (E) was thought of as a hormone that had significant effect on the organization/regulation of female behavior, but had little effect on males. Although male "typical" behavior is often associated with androgen, specifically testosterone (T), there is a significant body of literature that indicates that many male behaviors are actually regulated by estrogen through the enzyme aromatase acting on T hormones. E plays a role in regulating male social behavior and has many organizational effects on the male brain during development acting through the well known estrogen receptor (ER) _ and recently found ER_. Preliminary evidence from our own lab suggests a new aspect to support this data. On days 8-14, male prairie vole pups were endogenously injected with one of four treatments. Treatment groups include: 1) An aromatase inhibitor 1,4,6-androstatriene-3,17-dione (ADT) 2) a vehicle control, sesame oil 3) an estrogen receptor _ agonist propyl-pyrazole-triol (PPT) in solution with ADT 4) an ER_ agonist, diarylproprionitrile (DPN) in solution with ADT. On day 15, the treated pups were placed in a 40cm by 40cm open field test arena to judge if they display any anxiety-like behaviors. Those in the control group and ADT group showed no significant change in overall activity measured by number of lines crossed in a twenty minute period. However, in groups where the animals were injected with ER_ agonist with ADT, numbers of lines crossed were significant over both control and ADT groups. Also, ER_ agonist treated animals showed an increase in time spent social sniffing over both control and ADT groups. Immuncytochemistry staining for c-fos also shows a significant increase in cells expressing the early indicator gene in the dorsal thalamic nucleus in both ER agonist groups over control and ADT groups.

Poster: 22

Effects of early separation on pair-bond formation and corticosterone responsiveness in prairie voles.

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Neonatal stress affects physiological and behavioral development. Early social isolation evokes stronger plasma corticosterone responses and more vocalizations in the pups of highly social prairie voles than montane voles (Shapiro and Insel, 1990). This finding suggests that separation is a highly stressful event for prairie voles. As adults, exposure to stressors alters pair-bond formation and cortisosterone levels in prairie voles (DeVries et al., 1995, 1996, 2002). We examined the effects of early social isolation on adult pair-bond formation and stress reactivity. We hypothesized that neonatal stress, like stressors in adulthood, disrupts pair-bond formation and adult corticosterone responsivity.

During postnatal day (PND) 1-10, pups were removed from their parents for 0 (C), 15 (SS), or 360 (LS) min and housed either individually (PI) or with siblings (PS). Unhandled controls experienced daily lid opening (CU). After PND150, half the animals in each litter were paired with an opposite-sex vole for 24 hours and tested for partner preference. Stress reactivity was measured in all animals at 0, 30, or 60 min after exposure to a forced swim.

Across a 3-hour preference test, animals exposed to different separation conditions varied in their choice between the partner or neutral cage, but not the stranger cage. Overall, females and males significantly increased time spent in the partner cage each hour, though SS/PI females took one hour longer to prefer the partner to the neutral cage. LS/PS males increased partner cage time each hour, though C males did not increase partner time until the third hour. Females spent more time with their partners and had higher and more reactive corticosterone levels than males. In agreement that prairie voles are highly sensitive to social variables, preliminary data suggest that adult corticosterone levels correlate with degree of partner bonding more than with exposure to a forced swim test.

Poster: 23

Developmental effects of dopamine manipulations on anxiety, alloparenting, and partner preference in the prairie vole.

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Dysfunction of dopamine regulation is implicated in a number of human psychological disorders, including addiction and ADHD. Therefore it is critical to understand the normal functional role dopamine plays in behavior as well as the developmental sensitivity of this system to biological and clinical manipulations. We studied the effects of neonatal dopamine manipulations on adult prairie vole behavior, using selective agonists and antagonists for dopamine D1- and D2-like receptors. At 8 days old, pups were given a single injection of one of five treatments: eticlopride (D2 antagonist), quinpirole (D2 agonist), SCH23390 (D1 antagonist), SKF38393 (D1 agonist), or saline control. As adults, animals were given a number of behavioral tests including: elevated plus-maze, alloparenting, and partner preference. The overall ANOVA for time spent in the open arms of the plus maze was significant [$F(40,65)=1.67$, $p=0.03$], with treatment*sex interaction effects ($p=0.036$). Post-hoc comparisons revealed that females treated with eticlopride, the D2 antagonist, spent increased time in the open arms of the plus maze when compared to saline controls ($p>0.01$). In the alloparental care test, this same group of eticlopride-treated females displayed no infanticidal behavior, and this was significantly different from saline controls (__=5.85, $p=0.015$). In the partner preference test, the overall ANOVA for time spent with the partner was significant [$F(37,37)=1.86$, $p=0.03$], with a significant treatment effect ($p<0.01$). Post-hoc comparisons showed that animals treated with the D1 agonist SKF38393 fail to form a partner preference ($p=0.01$). These findings provide further support for a modulating role of dopamine on the development and expression of prairie vole social behavior. Funding for this project was provided by NSF 0437523; NIH R01 MH073022; McNair Scholars program; and Sigma Xi.

Poster: 24

Early life family structure influences monogamous behaviors and neuropeptides in adult prairie voles (Microtus ochrogaster).

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Early-life experience exerts a profound influence on neurophysiology and behavior in adulthood. Prairie voles are highly affiliative, socially monogamous, and biparental, thus providing an ideal model for the study of early social environment on development. In the wild, prairie vole pups are raised by single-mothers, two parents, or communal groups. We recreated some of this variation in the laboratory to examine the effects of biparental (BP) and single-mother (SM) care on the development of adult behavior and neuropeptide systems. Our first study quantified the effect of family structure on the amount of parenting received by pups, post-natal days 1-16. Our second analysis examined how rearing condition influences adult behavior, including open-field, elevated plus maze (EPM), spontaneous parenting, and partner preference. Our third analysis investigated the effects of rearing on several neuropeptide receptor systems. Significant differences were detected between the BP and SM conditions in the amount of time pups were alone on the nest ($F_{2,19}=16.56$, $P<0.001$) and licked and groomed ($F_{2,19}=6.67$, $P<0.01$). Behavioral assays of the adult offspring revealed increased exploratory activity for SM-reared offspring ($P<0.05$ for open field and EPM), as well as decreased anxiety in SM-reared females ($P<0.01$). Socially, SM-reared females demonstrated lower spontaneous maternal behavior and both SM-reared females and males exhibited delayed partner preference formation compared to BP-reared counterparts ($P<0.01$). Rearing condition also affected the brain in a region-specific manner. Contrary to our hypotheses, no group effects were seen in V1aR, OTR, CRF-R1, nor CRF-R2 in the nucleus accumbens ($F_{2,27}=0.319$, $P=0.729$), but there was a group effect on CRF-R2 in the dorsal raphe (DR; $F_{2,27}=6.95$, $P<0.01$; SM > BP, $P < 0.05$). There was also a significant increase in OT mRNA clusters in the paraventricular nucleus of the hypothalamus ($P<0.05$). The use of this paradigm in prairie voles is potentially useful for understanding how variation in early-life social experience alters the neural systems underlying adult social behaviors.

Poster: 25

Toward the development of an Oxytocin PET Ligand for imaging oxytocin receptors in living voles, primate and man.

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The development of a PET radioligand to enable pharmacological studies of oxytocin receptors (OTR) in living rodents, primates and humans would greatly enhance the ability to understand the neurobiological mechanisms underlying oxytocin's behavioral effects. The small molecule, 1-(1-(2-(2,2,2-trifluoroethoxy)-4-(1-methylsulfonyl-4-piperidinyloxy) phenylacetyl)-4-piperidinyl)-3,4-dihydro-2(1H)-quinolinone, has been shown to possess a high affinity for OTR in humans. We have developed a similar molecule, 1-(1-(2-(2-fluoroethoxy)-4-(1-methylsulfonyl-4-piperidinyloxy) phenylacetyl)-4-piperidinyl)-3,4-dihydro-2(1H)-quinolinone (Compound **1**), that is a potential target for *in vivo* PET studies. A competition curve was performed using I-125 OVTA as the radioligand and the cold compound **1** as the competitor. The autoradiography was performed on prairie vole brain sections. A series of dilutions ranging from 0 to 10^{-10} M of compound **1** were incubated along with 50 pM of the I-125 OVTA. Quantitative analysis revealed that the compound has a high affinity for the prairie vole OTR, with an EC50 of approximately 50 nM. A similar experiment was performed for vasopressin receptors using the V1aR radioligand, 125-linier V1a Antagonist. Compound **1** also displaced this ligand, indicating that it does bind to V1aR, however the affinity is much lower than for the OTR. These preliminary investigations suggest that compound **1** may be a viable candidate for *in vivo* PET imaging studies of the OTR. To test its viability, [^{18}F]**1** will be synthesized to perform peripheral injections into prairie voles to quantify its localization in the living brain using PET.

Poster: 26

Visible Implant Elastomers as a viable tagging option for voles.

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Ecological research such as the estimation of populations using mark/recapture techniques requires effective identification of individual animals. In mark/recapture studies tag loss is a problem, disallowing effective individual identification or requiring redundant tagging. Ear tag loss can be an especially large problem in red-backed voles (Myodes gapperi). Presented here is a "proof of concept" study using a novel, redundant marking technique: Visible Implant Elastomers (VIE).

In 2007 and 2008 all Myodes gapperi captured were tagged with both Monel ear tags and VIE in the field. In 2007 ear tags were lost in 37 of the 166 animals marked with ear tags and whose re-capture was confirmed with VIE. VIE markings were not visible in subsequent re-captures confirmed by ear tag in only 1 of 162 animals injected. Seven animals showed signs of ear tears consistent with tag loss in which no VIE was visible. These animals may have lost both tags, or may have torn the ear in another manner.

In 2008 230 animals were dual marked. Ear tags were confirmed lost in 96 instance. Vie tags were confirmed lost or no longer visible in 14 animals, with an additional 18 animals either loosing both tags, or sustaining an injury to the ear that resembled tag loss.

Tagging with Visible Implant Elastomers may be an effective and humane method of marking wild animals in whom other tags are not appropriate, or as a redundant tag to recapture when other identifiers are lost. Using different color injections, varying the injection site, and controlling for animal sex, the author was able to re-create recapture data for several individuals after the initial tag was lost. VIE tags were confirmed still visible over 100 days after initial injection, with one lasting a minimum of 400 days.

Poster: 27

Oxytocin injections in early life reversed negative behavioral effects of repeated early life manipulation.

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Early life experiences and neuropeptides, including oxytocin (OT) and vasopressin, have been implicated in the development and expression of social behaviors, especially in the socially monogamous prairie vole (Microtus ochrogaster). Previous research in this species revealed that repeated early handling/ manipulation of parents and offspring (MANr on postnatal day 1; PND1), in comparison to a single manipulation (MAN1), was associated in later life, especially in MALES, with increases in anxiety, a reduced tendency to show alloparental behavior and an increase in pup attacks. In the present study prairie vole parents and offspring were briefly handled 3 times on PND1 (MANr). On PND8 pups received either subcutaneous injections of OT or saline or no injections. On PND22 juveniles of both sexes were tested for alloparental behavior and on PND25 for behavior in an elevated-plus maze (EPM). MANr males treated with OT on PND8 approached pups more quickly, spent more time in close contact with infants, were less likely to attack pups and were more exploratory in the open arm of the EPM. Measured on PND25 OT-immunoreactivity was elevated in the PVN in OT-treated MANr males. These data confirm that repeated manipulations are associated with later increases in anxiety and disruptions of spontaneous parental care normally exhibited in juvenile males. Results also suggest that in male prairie voles exogenous OT can prevent the negative behavioral changes displayed in animals experiencing MANr, possibly through an upregulation of endogenous OT.

Poster: 28

The Effects of Estradiol Benzoate Treatment on Anxiety-Like Behavior and Oxytocin in Isolated Female Prairie Voles.

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The purpose of these experiments was to investigate the relationship between estrogen and the neuropeptide oxytocin (OT), in particular their relationship in mediating anxiety-like behavior. Data previously collected in the laboratory demonstrated that social isolation in females increases anxiety-like behavior and produces autonomic dysfunction. The goal of these preliminary studies was to determine the effects of estrogen in isolated females on anxiety-like behavior, central OT expression, and autonomic measures. In experiment 1, isolated intact female prairie voles were treated with EB (n=7, 2mg, dissolved in sesame oil (2mg/50ml), I.P.) or vehicle (n=8) once per day for 14 days. 24-hr after their final injection, animals were tested in the elevated plus maze. EB-treated females demonstrated increased anxiety-like behavior as indexed by less time being spent in the open arms of the maze, though these data did not reach significance (p=0.08). EB treatment significantly increased the amount of OT immunoreactivity in the PVN (p=0.008), suggesting that EB enhanced expression of OT. In experiment 2, female prairie voles were OVX and implanted with radiotelemetry devices to monitor heart rate. Following two weeks of isolation, animals were implanted with silastic capsules containing either EB (n=3) or nothing (n=3). Two weeks after EB capsules were implanted, the heart rate of these animals was monitored during a resident-intruder (R-I) test. Animals implanted with EB-containing capsules showed a significantly larger heart rate increase during the R-I test (p=0.03), indicating a robust effect of EB treatment on stress-responsivity. EB treatment, however, had no effect on baseline heart rate values. These studies suggest that estrogen enhances anxiety-like behavior, stress-responsivity, and OT expression in the PVN. The role of estrogen-induced increases in OT in anxiety-like behavior is not known and will be investigated in future experiments.

NOTES

NOTES

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