

Making Connections

MDMA Research on the Mechanisms of Affiliation and Trust

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One of the most important theoretical problems in social science is understanding what makes people feel solidarity, affection, and trust. Creating these connections among communities is the most important humanitarian and political problem facing humankind. Although we still know little about how people form social bonds, recent discoveries are providing valuable guideposts to lead us toward the answers. Social scientists are beginning to understand the kinds of interaction that create these feelings, while neuroscientists are beginning to understand the chemical processes and brain areas involved. But social scientists and neuroscientists rarely team up to work in this area, and existing research methods have serious limitations. We are taking an innovative, integrated approach to understanding sociability using a new research tool: MDMA.

MDMA is unique in evoking powerful feelings of trust, openness, affection, and identification; no other drug has comparable effects. Consequently, we have launched a program of research using MDMA to understand the natural behavioral, neurochemical, and neuro-anatomical pathways through which people form everyday social bonds. Because MDMA makes people feel close to each other, it must act on the mechanisms in the brain that normally respond to the social experiences that bring people together. By studying the neural mechanisms by which MDMA generates affection and affiliation, we aim to illuminate the kinds of social experiences that naturally activate these mechanisms. Overall, our goal is to understand how social interaction affects the neurobiological processes that in turn create affection, trust, and commitment—leading to behavior which in turns elicits these sentiments in others. Understanding these processes may eventually illuminate the mechanisms of love and close relationships, teamwork, ethnocentrism and xenophobia, intra-group cooperation and extra-group aggression, as well as provide insight into autism, psychopathy, personality disorders, and social anxiety disorder.

We have an excellent and well-integrated team with unique facilities at UCLA for this research. One member of our team is a psychological anthropologist, Alan Page

Fiske, whose ethnological research examines how people around the world create and sustain social bonds. Fiske is Director of the FPR-UCLA Center for Culture, Brain, and Development; he was also the co-founder and Director of the UCLA Center for Behavior, Evolution, and Culture. Another member of our team is a behavioral neuroscientist, David Jentsch. His specialty is neuropsychopharmacologic research in vervet monkeys and rodents, including examinations of the behavioral effects of MDMA. Another team member is a psychologist/primatologist, Lynn Fairbanks, who studies the genetics and neurochemistry of social behavior. In her research, she has developed a number of observational protocols for assessing vervet personality, particularly sociability. Fairbanks is the Director of the UCLA Vervet Research Colony (VRC), one of

the few research facilities in the world where primates are socially housed. Matthew Jorgensen, a psychologist who coordinates all research activities at the VRC, has 14 years of experience in behavioral research with nonhuman primates. Another team member, Wael Salameh, is an endocrinologist who studies behavioral genetics, especially the impact of X gene overdosage on the altered sociality of XXY patients. Salameh is an expert on hormone assays and molecular biology methods. Three members of this group are collaborating to teach the first UCLA graduate course on the Neurobiology of Sociality. Our team also has close colleagues ready to collaborate in brain imaging, cognitive

neuroscience, social psychology, and social anthropology.

Our primary and ultimate goal is to understand the neurobiology of human trust, identification, solidarity, affection, love, and forgiveness. We want to determine whether MDMA affects social motives and emotions through the action of oxytocin, vasopressin, dopamine, and cortisol—chemicals which are known to be involved in maternal care and pair-bonding. We also aim to locate the regions in the brain where MDMA acts, along with the genes that it activates and the receptors involved. The first stages of our research focus on animals because many kinds of neurophysiological research are only feasible in animals. What exactly does that mean? Also, are animals killed in this study? I think a brief discussion of the study

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Mother vervet grooming her daughter

ethics is necessary, since animal research is fairly controversial in our membership. Moreover, mammals share many basic neurophysiological mechanisms, despite differences in the behavioral expression of these mechanisms. Working with rats and vervets, we are currently studying how MDMA affects social interaction while the drug is in the brain and afterwards. Specifically, we are looking at whether MDMA increases attraction, reduces social anxiety, or both. Later we want to identify the neurohormones that are crucial for communication between neurons in the areas of the brain that MDMA activates and that mediate sociability. Almost nothing is known about the effects of MDMA on animal social behavior, so our pioneering studies will provide an essential foundation for our own and others' subsequent research.

The next stage of our research—for which we seek funding—will use MDMA to study the neurobiology of group formation, trust, and affection in vervet monkeys. The vervet is an Old World monkey that is an ideal model for research in this area. Vervets live in stable matrilineal societies. Females remain in their natal group with their mothers and female kin, while males leave at puberty and seek admission into neighboring groups. Social relationships within groups are generally affiliative and cooperative, while relationships between groups are hostile. Group members join together to defend their territorial borders against incursions from outsiders. In order to transfer between groups, males must overcome the natural hostility of the new group members to outsiders, and must also compete with other males for dominance. In the wild

and in the UCLA Vervet Research Colony (VRC), this is the most challenging experience of an adult male's life and the time of greatest conflict.

As the first step in a series of studies using MDMA to explore the neurobiology of sociality and aggression in this context, we now propose to measure the acute and long-term effects of MDMA on the quality of social relationships following vervet male immigration. For years, Fairbanks and her collaborators have studied the processes of male immigration and social integration at the UCLA VRC. In the course of this research, Fairbanks and her collaborators have developed methods to measure subtle variations in social behavior, personality, and interaction. This expertise will enable us to accurately assess the social effects of MDMA on the vervet immigrants. In collaboration with our pharmacology colleague, William Melega, we will initially determine the doses of MDMA that, for vervets, correspond to prevalent human recreational doses. Then we will launch our study.

In the first study, four groups will be formed with four males and four females per group. In two of the groups, all of the males will be given MDMA at regular intervals, probably once a week, during the group formation process. In the other two groups, the male vervets will undergo the same procedures using a saline control solution. Within each group, males will vary in their prior familiarity with one another. Thus, each of the eight male subjects will have potential relationships with familiar males, unfamiliar males, and unfamiliar females. We have developed (and used in a number of other studies) standardized observational scoring methods for measuring social bonding, including rates of social approaches initiated and received, time spent in contact and proximity, greeting behavior, grooming, and indicators of anxiety in a social context. Conflict and aggression are measured by scoring dominance displays, threats, chases, and fights. This study will take two years, due to the limited number of vervets ready for group transfer each year, and the importance of following up each group for several months to determine the long-term social relationships that emerge. (However, when funding is assured for at least one year, we will get the project underway, since pilot data will enable us to plan future studies and prepare grant applications to NSF and NIH.)

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effect on relationships among familiar individuals. If this is the case, then we will begin to be able to differentiate between two important components of sociality: overcoming hostility versus facilitating attachment.

The proposed study is the necessary foundation for future studies with rodents and vervets, using agents to block the action of oxytocin, vasopressin, dopamine, serotonin and cortisol, to determine which specific neurochemical systems are involved. Eventually we will attempt to identify the genes whose expression affects sociability, using transgenic or knockout mice.

Mammals share many basic neurochemical processes, so it makes scientific sense to begin with rats and vervets. However, no other animal forms bonds as complex as the human relationships we ultimately aim to understand. Ultimately, we want to use our findings in this animal research to determine how humans form affectionate, trusting, compassionate, committed relationships. Building on our animal work, we plan to use functional mag-

netic resonance imaging (fMRI) to locate the regions of the human brain that are activated by MDMA. The first study will consist of fMRI scanning of people interacting with the experimenter through the subject's video goggles and headphone. We will compare brain activation without MDMA and with administration of three levels of MDMA. We will correlate brain activation with MDMA dose and with self-report of closeness, empathy, and trust toward the experimenter. Previous imaging studies of activation induced by MDMA have focused on psychological tests which, if anything, blunt the emotional experience. Our goal is to observe the changes in human brain activation facilitated by MDMA when subjects have the opportunity to feel close to others, including others they love.

However, we judge that to develop our research beyond the current rat studies, the study with greatest potential is the vervet study outlined above. We have to begin by

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showing that vervet response to MDMA resembles the human response. If we can get the funds to demonstrate that MDMA reduces hostility and/or enhances affiliativeness among vervets, we will have excellent prospects for obtaining large scale funding from NSF and NIH for research that will rapidly advance the understanding of the neurobiology of human connection. All of us have obtained substantial grants from these sources for other research, so we are optimistic that the data we collect in the vervet study will enable us to get major federal funding for the MDMA studies that will build on this innovative approach.

Our ultimate goal is to understand how these affiliative processes in the human brain are activated by social experience, and how these brain processes motivate and orient social action. The brain is a social organ, and we want to understand how it mediates social relationships, including how the brain is affected by social relations. We hope our brain research will lead us to a better understanding of what human actions enable people to open themselves to others, love, trust, and forgive.

Budget for Vervet Immigration MDMA Study

Year 1

Animal purchase: 8 male subjects @ \$1820 each
= \$14,560 (no charge for the loan of females to the study)

Animal per diem: 16 subjects (8 males + 8 females)
@ \$4/animal/day = \$23,360

Experienced behavioral observer
(100% salary + benefits) = \$41,000
Matt Jorgensen¹ (25% time) = \$15,000
First year total = \$93,920

Second year: the same as above

Total for complete study: \$187,840

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¹ Mott Jorgenson will be responsible for implementing the study design, animal selection, group formation, regulatory compliance, research data management and data analysis.