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Press Room, Oct. 17–21: (312) 791-6619

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NEW BRAIN RESEARCH EXPLORES INTERSECTION OF MALE BIOLOGY AND BEHAVIOR

Scientists investigate implications of both genes and environmental experience

CHICAGO — Scientists presented research on the spectrum of male behavior, physiology, and susceptibility to disease. In particular, new findings provide a better understanding of the full range of male behavior, from fatherhood, nurturing, and fairness on the one hand, to aggression, selfishness, and dominance on the other.

New findings presented at Neuroscience 2009, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health, offer new insights into male behavior. They support the idea that many gender differences lie in the brain and are influenced by both genes and environment.

Specifically, research released today shows that:

- Testosterone not only reduces generosity but also increases the likelihood that men will punish others for being selfish (Karen Redwine, abstract 371.1, see attached summary).
- The "winner effect" — the increased ability to win new fights after previous victories — may be due to changes in the brain caused by the victories, according to a new animal study. Previous research could not explain why some species exhibit the winner effect and others do not (Matthew Fuxjager, abstract 377.7, see attached summary).
- Animal research shows that how a father cares for his young is shaped by the care he received as an infant and, conversely, animals raised by inadequate fathers grew up to be inadequate fathers themselves. These findings suggest that the paternal care received during development may shape the amount and quality of paternal behavior (Erin Gleason, abstract 571.18, see attached summary).

Other recent research findings being discussed at the meeting show that:

- Both X and Y genes have intrinsic sex-specific effects on the brain, influencing brain function, behavior, and susceptibility to disease (Arthur Arnold, PhD, see attached speaker's summary).
- Father-deprived animals were more likely to suffer from abnormal decision-making, emotion, and reward functions, as well as impulsivity and aggression (Anna Katharina Braun, PhD, abstract 120.4, see attached speaker's summary).

"Differences in genes, gender, and environment make the brain of each animal unique, including humans," said press conference moderator Margaret M. McCarthy, PhD, from the University of Maryland School of Medicine, an expert in the development of sex differences in the brain. "Insight into the male brain is vital to improve our understanding of emotions, relationships and behavior, as well as those diseases and disorders that predominately affect men and boys."

This research was supported by national funding agencies, such as the National Institutes of Health and the National Science Foundation, as well as private and philanthropic organizations.

Related Presentation:

Special Lecture: **Biological Origins of Sex Differences in Brain Function and Disease**
Sunday, Oct. 18, 11:30 a.m.–12:40 p.m., Hall B1

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Abstract 371.1 Summary

Lead author: Karen Redwine (760) 805-2678
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Testosterone Makes Men "Stingy"

Hormone reduced generosity in human economics study

Testosterone makes men less generous, according to new human research presented at Neuroscience 2009, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health. The findings may help explain the broad spectrum of human social behaviors, from selfish to selfless.

The researchers, led by Karen Redwine at Claremont Graduate University in California, compared the behavior of individual men before and after they received testosterone. They had the men play the Ultimatum game, an experimental economics task. The men were given $10 and told to split it with a stranger. If the stranger accepted the offer, both parties got to keep the cash, but if the offer was rejected, both parties earned nothing.

Testosterone decreased the generosity of participants' offers by 27 percent. However, testosterone also increased the drive to punish others for making stingy offers.

"Our findings show, in the most direct way, that testosterone makes men selfish. But, testosterone also causes men to punish others for being selfish — a desire to enforce implicit sharing rules. The latter result gets men out of the doghouse — they are selfish, but they seek to maintain order in society by bearing the cost of punishing the stingy," Redwine said.

Research was supported by the MacArthur Foundation and the John Templeton Foundation.

Scientific Presentation: Monday, Oct. 19, 8–9 a.m., South Hall A

371.1, Stingy Alpha Males: Testosterone Administration Decreases Generosity in the Ultimatum Game

K. E. REDWINE, P. J. ZAK, R. KURZBAN, S. AHMADI, R. SWERDLOFF, J. PARK, L. EFREMIDZE, K. MORGAN, W. MATZNER; Whittier Col., Whittier, CA; Econ., Claremont Grad Univ., Claremont, CA; Psychology, Univ. of Pennsylvania, Philadelphia, PA; Endrocrinol., UCLA, Los Angeles, CA; Econ. & Business, Whitworth Univ., Spokane, WA

TECHNICAL ABSTRACT: How do human beings decide when to be selfish or selfless? In this study, we gave testosterone to men to establish its impact on prosocial behaviors in a double-blind within-subjects design. We also confirmed participants' testosterone levels before and after treatment through blood draws. Using the Ultimatum Game from behavioral economics, we find that "alpha males," compared to themselves on placebo, are 27 percent less generous towards strangers with money they controlled. We also found that alpha males had a 5 percent higher threshold for punishing others for a lack of generosity. Both of these effects scale with the man's level of total-, free-, and dihydro-testosterone. Our results continue to hold after controlling for altruism. We conclude that testosterone causes men to behave in a largely antisocial manner.

Abstract 377.7 Summary

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Winning Fights Changes the Brain

Mice that win more bouts after early victories show changes in androgen receptor

The "winner effect" — the increased ability to win new fights after previous victories — may be due to changes in the brain, according to new animal research. The study was presented at Neuroscience 2009, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health.

Matthew Fuxjager and his colleagues at the University of Wisconsin, Madison, found that in mouse species that experience the winner effect, winning aggressive encounters changed the amount of androgen hormone receptors in brain areas that control social behavior. California mice, which experience the winner effect, showed the androgen receptor changes, but white-footed mice, which do not experience the winner effect, did not.

Many animal species, possibly even humans, show the winner effect, but some species do not, and researchers have not known why until now.

"To our knowledge, our data for the first time suggest the possibility that species variation in the winner effect is caused in part by brain-level differences," said Fuxjager, who led the study. "This implies that the brain's capacity to change to enhance future victories is an evolved trait that might help an individual survive and reproduce in its surrounding environment," Fuxjager said.

Research was supported by the National Science Foundation.

Scientific Presentation: Monday, Oct. 19, 10–11 a.m., South Hall A

377.7, A Neural basis for Interspecific Variation in the Winner Effect: Winning Experience Differentially Alters Brain Androgen Receptor Immunoreactivity in Two Species of Rodents

M. J. FUXJAGER[1], R. M. FORBES-LORMAN[2], C. AUGER[2], A. P. AUGER[2], C. A. MARLER[2]; [1]Zoology, Univ. of Wisconsin Madison|910007542|0, Madison, WI; [2]Psychology, Univ. of Wisconsin-Madison, Madison, WI

TECHNICAL ABSTRACT: The winner effect is defined as an increased ability to win aggressive encounters following previous victories. Although the winner effect is observed in numerous taxa, its magnitude and robustness can vary among even closely related species. To date, it is unclear whether species-level differences are due to neurobiological differences or other physiological differences that are associated with winning and aggressive behavior. In this study, we examined whether there is a neural basis for observed differences in the winner effect between California mice (*Peromyscus californicus*) and white-footed mice (*Peromyscus leucopus*), as the former demonstrates a clear, robust winner effect and the latter does not. As such, in each species, we first measured whether individuals acquire a winner effect following past winning experience. We then collected the brains of these individuals and assessed whether winning experiences alter androgen receptor immunoreactivity (AR-ir) in select brain regions. We found that California mice demonstrate a full and robust winner effect after acquiring past wins, whereas white-footed mice do not. We also found that California mice with past winning experiences show elevated AR-ir in specific nodes of the social behavior network (i.e. bed nucleus of the stria terminalis), as well as the reward pathway (i.e. nucleus accumbens). In contrast, white-footed mice with the same amount of winning experience showed neither a full winner effect, nor changes in AR-ir in any of the investigated brain regions. Our results suggest the changes in AR-ir at the level of the brain might underlie the winner effect. Moreover, these changes can in fact be species-specific, which likely contributes to the observed interspecific variation in the winner effect.

Abstract 571.18 Summary

Lead author: Erin Gleason (845) 702-5446
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Fathers Shape Sons' Paternal Behavior

Mouse study suggests non-genetic transfer of paternal behaviors

How a father cares for his young is shaped by the care he received as an infant, according to new animal research presented at Neuroscience 2009, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health. The findings highlight the importance of early-life experiences in shaping adult behaviors.

"A strong body of evidence shows that behavioral environment during development is a key factor in shaping maternal behavior, but very little is known about whether similar mechanisms exist for males. Our results suggest this may, in fact, be the case," said Erin Gleason at the University of Wisconsin, Madison, who led the study in the laboratory of Catherine Marler, PhD.

Gleason and her colleagues studied California mice, one of the few mammalian species to exhibit paternal behaviors. In these mice, castration reduces fathering behaviors. The researchers observed the paternal behaviors of adult male mice raised by castrated fathers. They found that intact mice raised by deficient fathers grew up to be deficient fathers themselves.

"Our results suggest that early behavioral environment, and in particular the paternal care received during development, may shape the amount and quality of paternal behaviors expressed by mammalian fathers, perhaps including humans," Gleason said.

Research was supported by the Animal Behavior Society and the National Science Foundation.

Scientific Presentation: Tuesday, Oct. 20, 9–10 a.m., South Hall A

571.18**,** Epigenetic Transmission of Paternal Behavior in the Monogamous and Biparental California Mouse, Peromyscus Californicus

E. D. GLEASON[1], C. A. MARLER[2]; [1]Psychology, Univ. of Wisconsin-Madison, Madison, WI; [2]Univ. Wisconsin, Madison, WI

TECHNICAL ABSTRACT: In the monogamous and biparental California mouse (*Peromyscus californicus*), paternal care is critical for maximal offspring survival. Moreover, animals form pair bonds and do not engage in extrapair matings. We hypothesized that similar to female house mice and rats, paternal behavior could be passed on to future generations via epigenetic mechanisms. Previous studies have shown that testosterone supports paternal behavior in California mice, and castration reduces the amount of huddling and grooming (HG) that a male contributes to offspring. We castrated a group of male California mice, and allowed them to raise young without any further intervention. Sons of these castrated males (F1 males) were then paired with females in adulthood, observed during courtship interactions, and subsequently with their own offspring. Preliminary review of the data indicates that sons of low HG fathers also huddle and groom their young at lower levels than the sons of sham-operated fathers. In addition, sons of castrates also appear to respond to a paternal behavior challenge by spending less time with the pups, and leaving the nest more frequently. These data support the hypothesis that paternal behavior, like maternal behavior, can be transferred to future generations via epigenetic mechanisms, and suggests that in a biparental species both parents may be contributing to offspring behavioral development.

<u>Speaker's Summary</u>

Lead author: Anna Katharina Braun, PhD (49-39) 1675-5001
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Scientific Presentation: **Dad Matters, Too! Paternal Deprivation Delays/Suppresses Dendritic and Synaptic Development in the Orbitofrontal and Somatosensory Cortex** (120.4)
Sunday, Oct.18, 8:45–9 a.m.

Research indicates that paternal care is essential for the development of limbic brain regions, *i.e.*, a brain system, which mediates emotional behaviors as well as learning and memory formation. Comparing the brains of male degus (Octodon degus, or "trumpet tailed" rat, a biparental rodent) raised by both parents with those that had been raised by a single mother revealed that paternal deprivation results in delayed or suppressed cortical dendritic and synaptic growth and reorganization.

Modern societies are increasingly concerned that fatherless children are at dramatically greater risk of drug and alcohol abuse, poor educational performance, and criminality. Since the establishment of functional neuronal networks in the brain of animals, including humans, is essentially sculpted by childhood experience (emotional and cognitive), the impaired behavioral development observed in fatherless children may be caused by the lack of paternal input, resulting in delayed brain development and even permanently retarded brain function.

In order to test this hypothesis, the researchers raised newborn degus either in single-mother families or in families, where both parents took care of their pups. In support of our hypothesis, we found significantly reduced densities of excitatory spine synapses in the orbitofrontal (limbic) and somatosensory (*i.e.*, touch, pain) cortex. In addition, the length and ramification of neuronal dendrites (i.e. the neuron´s "antenna" bearing synapses to receive signals from other neurons), a measure of neuronal network complexity, was reduced in fatherless animals. Whereas biparentally raised animals have reached adult spine density values already at the age of three weeks, synaptic development in the fatherless animals is delayed, but seems "to catch up" later until reaching similar adult values compared to biparentally raised animals. However, dendritic extension and the total number of synapses per neuron was still lower in adult father-deprived animals.

These results suggest that paternal deprivation delays and partly suppresses the development of neuronal networks within orbitofrontal circuits. Thus, the father-deprived animals may suffer from hypofunctionality of this associative limbic cortical region, whose functions such as decision making, emotion and reward as well as impulsivity/impulse control and aggression may be impaired. Our study also shows that neurons in limbic cortex are continuously developing at least until puberty, which opens up an extended developmental time window, during which the detrimental brain effects of paternal deprivation may be ameliorated or compensated, e.g. by providing care by other emotionally significant family members (grandparents, new father etc), professional caretakers or peer groups.

Speaker's Summary

Speaker: Arthur Arnold, PhD (310) 825-2169
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Los Angeles, Calif.

Special Lecture: **Biological Origins of Sex Differences in Brain Function and Disease**
Sunday, Oct. 18, 11:30 a.m.–12:40 p.m., Hall B1

Sex differences in disease are often explained by hormones, but not always. New evidence shows that sexual imbalance of genes on the X and Y chromosomes can directly influence traits including the susceptibility to disease.
Many diseases and syndromes (multiple sclerosis, depression, ADHD — attention deficit hyperactivity disorder), occur more in one sex than the other. If we can understand the factors that protect one sex from a disease, we may be able to find treatments that enhance that factor to reduce disease in both sexes. That's one reason for studying the biological origins of sex differences in physiology.

The Sry gene on the Y chromosome causes males to have testes instead of ovaries. Sry makes the difference between an animal that is exposed to hormones coming from the testes instead from the ovary. The difference in action of these hormones probably produce most sex differences in physiology and disease.

But hormones don't explain all sex differences. XX and XY cells are inherently unequal in the level of expression of some X and Y genes, just because of the different numbers of X and Y chromosomes in each male or female cell. We have recently studied whether these X and Y genes contribute to sex differences in traits.

To study the effects of XX and XY genetic constitution separated from the effects of hormones, we use mice in which the Sry gene has been moved from the Y chromosome to another chromosome (autosome). That means that having a Y chromosome no longer determine if the mouse has testes. The mouse model, called the "four core genotypes" makes mice with testes that are either XX or XY, and mice with ovaries that are either XX or XY.

XX and XY mice with the same type of hormones show differences in numerous traits. XX mice are more susceptible to induced conditions similar to multiple sclerosis and lupus, and they have much more body fat. They have greater response to nociceptive stimuli, and show differences in brain chemistry.

Our goal is to identify the X or Y genes that make males and females different, and to understand how these genes operate. We hope to provide information that will improve the understanding of the factors controlling disease.