Developing Informed Animal Models of Social Aging

Expert Meeting

May 8-9, 2017

Keck Center of the National Academies
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Meeting Summary

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Executive Summary

High-quality social relationships have long been considered powerful predictors of living a long and healthy life. Research with animal models allows us to examine these relationships in ways that we cannot in humans. This meeting, hosted by the National Institute on Aging (NIA) Division of Behavioral and Social Research (BSR) and the National Academies' Division of Behavioral and Social Sciences and Education, Board on Behavioral, Cognitive, and Sensory Science (BBCSS), offered an opportunity for researchers from both animal and human fields to exchange ideas and to think systematically about ways that animal models can be leveraged to understand social influences on aging in humans.

In the first session, presentations focused on lessons from comparative studies of animals and humans. Researchers examining social processes with animal models—including rats, different species of macaques, and dogs—and with human populations discussed how social relationships among individuals can affect health and well-being. Presenters discussed biological and social mechanisms that generate emotions and how these processes impact social relationships.

Presentations in the second session focused on insights into human social relationships that can be gained from studies of animals. In humans and other animals, social relationships seem to be beneficial, and social exclusion seems to have negative effects. Although early-life adversity can have life-long consequences, there is also evidence that the negative effects of such trauma can be overcome during the lifespan. In later life, many social relationships change, and an individual's response to these changes can have an impact on overall health.

The third session focused on gaps in human studies that could be addressed through animal studies. Such examples included mechanistic studies of how social relationships can both be a source of stress and lead to overall well-being, the possible health benefits of providing care to others, and the central role of dyadic social relationships in humans.

A series of moderated discussions followed the scientific presentations. The first explored possible mechanisms underlying the associations between social relationships, health, and behavior. While there are data relating genetic factors to early- and late-life social and health-related outcomes, the factors that influence mid-life health remain relatively unexplored. It is also not clear what the causal relationship between social connectivity and overall health is, or how an individual's needs might change over the course of a lifespan.

The second moderated discussion focused on ways to leverage animal studies to gain insights into the association between social connections and health. Given the shorter lifespans of many animals, animal models offer an opportunity to study changes in social relationships across a broader span of the life course than is possible in humans. Studies in animals, grounded in evolutionary theory, may also offer a window through which to explore human behavior. Animal studies also offer the opportunity to manipulate social relationships in ways that are not possible in humans.

The third moderated discussion focused on how studying micro-level social processes can provide insight into relationships, health, and psychological well-being. The discussants agreed that collecting micro-level data is difficult in humans and other animals, and that analyzing such data presents a challenge. However, there was also consensus that these data are important and that research in this area could benefit from the development of new studies and data analytic tools.

The second day of the meeting turned to new approaches and methods that might be used to address outstanding questions in the field. Attendees agreed that collaboration between animal and human researchers could lead to the development of new tools to address challenges surrounding the identification of objective measures of emotion, perhaps by incorporating evolutionary approaches into the analysis of human behavior. Attendees discussed the value of behavioral, self-report, and biomarker assessments of emotion in human studies and the challenge in relating self-report data from humans to animal studies.

In breakout sessions, three subgroups of attendees were asked to propose a study using an animal model to advance the understanding of the psychological and social factors that influence health and well-being in mid- and older life. One group proposed a study in which older humans and animals are given nominal control over the allocation of food during certain periods. The aim of the study would be to determine whether assuming control over the allocation of this resource—albeit temporarily—bestows upon the subject a higher social standing or other benefits. The second group proposed a study of social structure that would attempt to differentiate between those animals who spend time alone by choice and those who are alone due to social exclusion to understand the health impacts of both conditions. The third group proposed a study that investigated the role of early-life adversity on long-term health outcomes. This study would examine both animal and human subjects and measures of social connectivity and overall well-being.

The attendees believed that it would be possible to design interesting studies of social processes in aging that would be relevant across multiple species. They also concurred that better communication among researchers working in human and nonhuman systems will help to advance understanding of the role of social interaction in human aging.

Meeting Summary

Introduction

High-quality social relationships have long been considered powerful predictors of living a long and healthy life. However, it has been difficult to unambiguously demonstrate that social relationships have a causal effect on health and longevity. Understanding the causal versus correlative roles of social relationships for health, and identifying mechanisms of proposed beneficial effects is essential for evaluating their validity and identifying appropriate interventions. It is also important—especially in human studies—to appreciate the degree of individual variation in response to a given intervention.

Studies of animals suggest very deep evolutionary roots to human social behavior. In animals, it is possible to examine these sorts of mechanisms in ways that cannot be done in humans. To build on these studies, the National Institute on Aging (NIA) Division of Behavioral and Social Research (BSR) and the National Academies' Division of Behavioral and Social Sciences and Education, Board on Behavioral, Cognitive, and Sensory Science (BBCSS), sponsored a meeting on May 8-9, 2017, to provide researchers from both animal and human fields with the opportunity to think systematically about ways that animal models can be leveraged to understand human aging processes.

Dr. Barbara Wanchisen, BBCSS Director, opened the meeting by welcoming attendees and thanking them for volunteering their services on study committees to provide independent, objective advice to federal agencies, Congress, foundations, and others. Dr. Melissa Gerald, BSR Program Director, explained that the goal of the meeting is two-fold: to set research priorities regarding the role that animal models could play in bridging critical gaps in our understanding of the psychological, behavioral, and social factors in mid-life and older age that may be difficult to directly address in humans and to promote discussion and an exchange of ideas between researchers in animal and human behavior and foster a greater understanding of how each research community thinks about these questions.

This meeting report captures the key themes of the presentations and discussions that occurred during the 2-day meeting. The full agenda is provided in Appendix 1, and the participants list is provided in Appendix 2.

Lessons from Comparative Studies

Lessons from Comparative and Translational Affective Science

Eliza Bliss-Moreau, University of California, Davis

Dr. Bliss-Moreau studies the biological and social mechanisms that generate emotions. Specifically, she uses rhesus macaque models to study variations in affective processes—the feelings and responses, positive or negative, that are related to emotions—to understand what produces variations in these processes and why these variations are adaptive. For some of her studies, she and her colleagues examine homologs across species; these include comparisons of

visual attention, behavioral reactivity, cardiac psychophysiology, resting state functional neuroimaging, and vocal acoustics. She also examines proxy measures of emotions, including indices of social behavior and connections within social networks.

Dr. Bliss-Moreau stressed the importance of using large, representative samples to ensure the generalizability of observations to address issues that are relevant to larger populations. She noted that one limitation to studies in humans is that humans are exceptionally good at making inferences about mental state—even if it is not relevant. In other words, humans tend to see emotions in everything. Using self-report measures of emotions in humans thus has the potential to introduce bias in the interpretation of results.

We cannot ask animals how they feel; therefore, studying affective processes in animals requires a different approach. One such approach is based in a constructivist model, which holds that emotions emerge from more basic or fundamental parts, including internal physical states and external stimuli, and the coordination and integration of those parts lead to the emergence of emotion.

Dr. Bliss-Moreau found that macaques that received neurotoxic damage to their amygdala at age 2 weeks showed diminished reactivity when exposed to either positive or negative content on a video screen. Interestingly, while the degree of their overall response is blunted, their responses nevertheless seem to be calibrated to the degree of the stimulus. Historically, the amygdala has been associated with the response to threats, but these data suggest that it may influence neural processing of positive data as well.

Another method Dr. Bliss-Moreau uses is a living lifespan laboratory, in which individual animals can be intensively tracked for their entire lives. In this environment, it is possible to investigate the impact of specific neural structures on the affective processing of group-living animals and to evaluate how brain networks interact with social networks.

Using animal models, it is possible to conduct intensive translational psychological testing, conduct ongoing evaluations of social structures, manipulate biological and social factors, and study the same individual from womb to tomb.

Lessons from Non-WEIRD Populations: Aging among Contemporary Preindustrial Humans

Michael Gurven, University of California, Santa Barbara

Dr. Gurven studies populations that lie outside "Western-Educated Industrialized Rich Democratic" societies—that is, non-WEIRD populations. These nonmarket, preindustrial populations live much like humans have for most of our history. Specifically, he has studied the Tsimane, an indigenous people of lowland Bolivia who subsist on hunting, fishing, and farming, for 18 years. This society is attractive to researchers for several reasons. With 15,000 members, it is a relatively large population, permitting a reasonable sample size of older adults. They also have a high burden of pathogens, likely due to their close interactions with each other and the tropical environment; they exhibit "natural" levels of fertility without contraception; they have

minimal access to modern health care; and they inhabit small, kin-based villages. Studying them offers clues about what aging processes might have looked like prior to industrialization.

Human life stages evolved in the context of a hunter/gatherer lifestyle, which is based on a cooperative social structure. In this context, humans are net consumers of resources into their late teens, net producers in middle age, and net consumers in later years. For this social structure to be stable over the life course and within a population, the overall organization of the society must balance the flow of resources within and among generations. Presumably, this structure is supported by social elements such as social support, caring for others, and exchange of food, information, and other resources.

The Tsimane have the lowest reported levels of coronary artery disease, as measured by CT-based coronary artery calcification, of any population recorded to date. These findings are presumably a consequence of this population's very low low-density lipoprotein (LDL), low blood pressure, low blood glucose, minimal obesity and smoking, and high levels of physical activity. This finding was seen despite relatively high levels of systemic inflammation, due to their exposure to pathogens and relatively well-functioning immune systems—in other words, their inflammatory state was a natural response to their infectious environment. The absence of heart disease in this population suggests that more rigorous lifestyle modification alone could likely greatly reduce the incidence of heart disease in the US.

In this population, depression is not uncommon. Depressed mood is greatest among older adults, especially those with physical disabilities, with poorer perceived health, and who feel that they receive more food than they give away. The need to be viewed as productive and useful to others is a strong source of well-being in this population. Intriguingly, depression is more prevalent in villages that are close to towns than in those farther away, which suggests that some individuals' moods may suffer if they believe that they are not "measuring up" to the changing standards in more acculturated areas.

Many Tsimane show a highly externalized locus of control, that is, they do not believe they have control over their fates. Gossip was also observed to have a negative effect on individuals' moods, and is often voiced as a source of sickness by participants during health checkups. Shared decision-making in the Tsimane is often rife with tension, as is the maintenance of a large social network. A perceived loss of influence is associated with higher rate of respiratory infection, suggesting a connection between social status and health. Together, these findings suggest that, while human sociality has allowed us to thrive in diverse environments, these benefits do not come without costs.

A Role for Pet Dogs and Citizen Science in Aging Research?

Brian Hare, Duke University

A central challenge in studying the evolution of human cognition is identifying unique features of our intelligence and explaining the processes by which they arose. To better understand the abilities that allow humans to be social, Dr. Hare and colleagues study domestic dogs in the lab and through experimental data collected by citizen scientists via the website:

www.dognition.com. Domestic dogs are unusually skilled at reading human social and communicative behavior. These social skills have a heritable component that initially evolved during domestication. Studying cognitive function in dogs can lead to insights into the evolutionary processes that lead to human-like forms of cooperation and communication.

Dogs exhibit high levels of individual variation in their attempts to solve problems. For example, when food is placed in a clear box that cannot be opened by the dog, some animals try repeatedly to open the box on their own while others almost immediately turn to their human handlers for assistance. This is just one of several "personality types" that dogs exhibit. These "personality types" predispose individual dogs to certain tasks. For example, dogs that do well in detecting explosives in war zones have different behavioral profiles than dogs that perform well as assistance animals.

Domestic dogs and humans evolved social skills together. This has likely resulted in cognitive convergence in which human-like social skills have evolved in dogs, making dogs an attractive subject for research into human cognition. Scientists have observed a decline in cognitive ability in dogs as they age. This effect is seen in cross-sectional (but not yet longitudinal) data, and there is evidence that this decline is related to breed. Dogs may therefore be useful models to study human aging.

Using Comparative Neuroethology to Understand the Influence of Affect on Behavior

Stephanie Preston, University of Michigan

Dr. Preston and colleagues adopt a neuroethological approach to study the molecular basis of various behaviors in both humans and other animals. This interdisciplinary branch of behavioral neuroscience aims to understand how the central nervous system translates biologically relevant stimuli into natural behavior.

Studies of kangaroo rats have shown that removal of their hidden food stores leads to an increase in stress and food hoarding. Hoarding in rats is known to be mediated by the dopaminergic system. For humans, acquiring and discarding objects is routine, but in some people, disorders in this balance lead to clinical hoarding. Using functional magnetic resonance imaging (fMRI) to examine study subjects as they participated in a task that required acquisition and discarding of objects, Dr. Preston and colleagues found that the same brain regions activated in rats during hoarding behaviors were activated in humans, suggesting that these homologous behaviors share a common neural basis.

To study the biological basis of empathy, volunteers with lesions in various parts of their brains were asked to identify the emotions shown in a series of photographs of faces. People with damage to their somatosensory cortex, the part of the brain that represents one's own body, were impaired in accurately representing the emotional states of others. This suggests that people may decode emotions in others through the understanding of their experiences of those emotions. In other studies, Dr. Preston and colleagues have shown that patients who appear happy are more likely to receive assistance than patients who appear sad, who would presumably be in greater need of help.

Using a rat model of caregiving, Dr. Preston and colleagues explored the gap between the feeling of empathy and the act of behaving altruistically toward others. After giving birth, rats are very motivated to retrieve pups and return them to the nest—even pups that are not related to them. This behavior may be partially motivated by an empathic response to distress in the pups. Dr. Preston's research showed that many of the neural pathways activated in rats during this caregiving behavior are also involved in humans who show an inclination toward altruism.

Psychology has developed theories to explain aspects of human behavior such as altruism that appear to serve no obvious evolutionary purpose. However, these models may not be able to answer all the questions associated with selfless actions. It may be necessary to turn to molecular factors to understand the biological basis—and perhaps the true value—of our social relationships.

Social Inequalities in Health in Nonhuman Primates: Translation to Human Health Across the Lifespan

Carol Shively, Wake Forest School of Medicine

No matter what measures are used, people of higher socioeconomic status (SES) live longer, healthier lives. However, detailed study of this phenomenon is difficult because SES is a product of many variables, including economic and social factors, conditions in the immediate environment, and health behaviors, that are themselves interrelated.

To untangle these complex influences, Dr. Shively and colleagues have turned to animal models. Virtually all mammals that live in groups larger than a nuclear family organize themselves into a social hierarchy, with some animals at the top and other animals at the bottom. High-status animals typically have priority access to food, water, safe places to sleep, and mates. In times of plenty, this arrangement may be of little consequence to lower-status animals; during times of hardship, social status can be an important determinant in health or survival. Dominant animals inhabit a stable social environment, while subordinate animals live a more precarious existence. Subordinate female monkeys exhibit numerous signs of stress: they are the targets of more aggression, are groomed less, spend more time alone, and they have elevated cortisol levels, higher heart rate in response to stress, and poor ovarian function.

Dr. Shively studied social groups of monkeys who had been fed a western diet—a diet high in protein and fat—for 2 years. Animals fed the western diet accumulated more visceral fat than animals fed a standard diet. Interestingly, animals on the western diet who were stressed because of social subordination had double the risk of diet-induced coronary atherosclerosis. Indeed, these coronary lesions could be detected years before they would lead to overt cardiovascular disease (CVD).

Stress is, in and of itself, a risk factor for poorer health in humans. The prevalence of a poor-quality diet can also raise the risk of CVD. Unfortunately, individuals of lower SES are more likely to be stressed and to eat a poor-quality diet. It is possible that a Western diet could amplify the stress responses that are associated with low SES, and that efforts to improve diet

quality in lower SES individuals could mitigate some of the health effects of stress. To test these questions, Dr. Shively and colleagues are comparing the effects in monkeys of a Western diet, in which protein and fat are derived mainly from animal sources, with a Mediterranean diet, in which protein and fat are derived mainly from plant sources rich in vegetables. Otherwise the two diets are matched on percent of calories derived from fat, protein, and carbohydrates, and on cholesterol content.

Over a 2-year period, the monkeys' social interactions, behavioral measures of stress, and physiological traits such as circulating lipids and inflammation will be measured. At the conclusion of the study, their coronary arteries will be examined to quantify atherosclerosis. This study highlights many of the strengths of animal models for studying the biological effects of social interactions: they offer extensive control of external variables, the ability to systematically assess the social effects on biology across the lifespan, and endpoints that are not possible to examine in humans.

Roundtable Discussion: Lessons from Comparative Studies

Moderator: Susan Alberts, Duke University

Dr. Alberts asked about a seeming contradiction between the findings presented in Dr. Gurven's and Dr. Shively's presentations: both the Tsimane people and the subordinate monkeys appear to have a relative lack of control over their social environments; yet, the Tsimane show much lower incidence of CVD, while the incidence for monkeys is far higher. Dr. Gurven hypothesized that the western diet consumed by the monkeys could be a key factor in worsening the pathological impact of stress in the monkeys; the Tsimane have much less fat in their diets. He also noted that many of the Tsimane seem to accept their lack of control over the environment, and so pathological manifestations may be absent in this population; indeed, Tsimane have low levels of cortisol. He suggested that this lack of control may simply manifest differently in this culture.

In a similar vein, Dr. Alberts asked whether there was a clear social hierarchy in the Tsimane. Dr. Gurven replied that, although there are clear differences in social status among tribe members, these differences do not seem as large in absolute terms as those seen in macaque populations or in modern technological society. Additionally, many Tsimane have large families that they can readily rely on for social support, which may help ameliorate the effects of stress.

Dr. John Haaga noted that, in studies of baboons, it is the "number two" animal in the social hierarchy who has the best health. This is presumably because he or she benefits from a relatively high social position without having to defend it. Dr. Alberts said that one key to this finding might be the nature of the competition among members of the hierarchy. For example, even when food is plentiful, there is still a dominant/submissive relationship between the monkeys. Dr. Shively noted that most of the reinforcement of social status in cynomolgus monkeys occurs through intimidation and social exclusion, not overt aggression.

Attendees agreed that although social networks can sometimes be a source of tension, having *no* social connections can be detrimental to health as well. What appears to be essential is that

individuals pursue and maintain social relationships that are personally rewarding. Furthermore, what represents "ideal" for a given individual may even vary across their lifespan.

Learning about Human Sociality from Animal Models

Models, Boojums, or Something in Between?

Alexander Ophir, Cornell University

Animal research is valuable for investigating a wide range of human biological processes and behaviors. At the genetic and physiological levels, humans are remarkably similar to other animals. However, when turning to animals for insights into humans, it is important to remember the distinction between an "example" and a "model." "Examples" constitute the real thing that is being studied, such as muscle tissue, while "models" are approximations of the thing that is being studied, such as an animal model of diabetes that relies on drugs to destroy pancreatic beta cells. Models are analogous, but not identical to, the object they represent. An over-reliance on animal models of human disease without consideration for the animals' natural history, evolutionary past, and ecological constraints could cause the study to be irrelevant to the human condition.

Finding good animal models for understanding social behavior is particularly challenging, because the underlying mechanisms may be conserved across species but used in very different ways. Understanding these similarities and differences is key to identifying what "good models"—especially given the difficulty of finding true "examples" of human social behavior in nonhuman animals.

The socially monogamous prairie vole has been used as a model species to explore a wide-ranging set of behavioral and biomedical research questions. Because of their propensity to form monogamous pair bonds and to provide biparental care to offspring, the prairie vole offers a model to study the role of parental care in social development. By exploiting natural variation in social organization and social behavior, this creates an opportunity for the perinatal social environment to influence interactions between genes, the brain, and behavior. There is evidence for plasticity in vasopressin and oxytocin receptors in several brain areas associated with social behavior and memory. Dr. Ophir and colleagues have shown that male prairie voles that experience social isolation—either raised fatherless before weaning or housed singly instead of as part of a pair after weaning—have diminished social discrimination abilities. For example, single males can distinguish between other males but are unable to distinguish between females.

Humans undergo profound transformations across the lifespan. The transition from being single to becoming a paired member of a mating bond (or the reverse), the transition to parenthood, and the loss of a child mark major milestones in any species. A set of cognitive and behavioral changes is frequently associated with these transitions. A better understanding of the way that transitions such as these naturally unfold, and what mechanisms are involved, could lead to insights into the variation found in cognitive, social, and physical health in later life.

The Benefits of Interpersonal Relationships and Consequences of Social Exclusion

Lauren Brent, University of Exeter

The Brent laboratory examines the benefits of interpersonal relationships and the consequences of social exclusion. The number and quality of a social animal's relationships are related to various measures of well-being, as well as overall health, fecundity, senescence, and survival. The benefits of studying social relationships in nonhuman animals include the ability to collect longitudinal data beyond what could be obtained in human studies; the absence of medical or cultural factors that might confound interpretation of the data; and the ability to measure social relationships directly in real time. If social behavior is found to have a common evolutionary basis across many species, these animal studies could yield important insights into the roots of human social interaction.

Dr. Brent and colleagues have been studying the social relationships of a colony of free-ranging rhesus macaques on Cayo Santiago Island in Puerto Rico. Rhesus are good models for human social behavior because they live in large, mixed-sex, and mixed-relatedness groups. And although rhesus have strict dominance hierarchies, individuals form social bonds with some group members but not others, and they can recognize third-party relationships and show a rudimentary understanding of the intentions of others. Finally, rhesus have a similar genetic profile to humans, and the same neural pathways are involved in the extraction of social information and reward and punishment in both species.

To quantify the nature of the rhesus macaque social network, Dr. Brent and colleagues have studied various types of social interactions such as grooming, aggression, and resting in proximity to others. They found that social integration—measured based on time spent being groomed by another monkey and time spent with others—was positively correlated with the number of surviving offspring, suggesting a benefit to having socially connected parents. There was also an effect of number of adult female relatives—a proxy for social integration—on survival of female monkeys during early adulthood and middle age, but there was no such effect in older females.

Dr. Brent and colleagues have also studied killer whales to understand the phenomenon of reproductive senescence. Humans, short-finned pilot whales, and killer whales are the only species in which females undergo reproductive senescence—menopause—in mid-lifespan. In a population of 78 killer whales in the Salish Sea, post-reproductive female killer whales are more likely to lead collective movement of their groups. Leadership by these females seems to be especially prominent in years when food is scarce. This finding suggests that one evolutionary benefit of menopause is that it provides an opportunity for older females to transfer knowledge to younger whales, thereby contributing to the health of the overall group.

These studies provide evidence for an interaction between interpersonal relationships and fecundity, reproductive senescence, and survival. What remains unknown for these associations is the nature of the causal relationship between the social connection and the outcome or the mechanisms through which these relationships are mediated.

Exploring How Sociality, Communication, and Cognition Link to Fecundity and Mortality via Health Across the Lifespan in Primates

James Higham, New York University

Dr. Higham studies how social behavior, cognition, and communication, along with their biological underpinnings, interact to influence fecundity and mortality, primarily through the study of the same rhesus population studied by Dr. Brent.

During periods of social stability, levels of glucocorticoids and androgens are uncorrelated with social status of macaques. However, during periods of social instability, these hormone levels and social status are inversely correlated, with lower ranking monkeys showing higher hormone levels. This suggests increased stress and aggression during these times.

In macaques, females generally spend their entire life in matrilineal kin groups, whereas males typically leave their natal groups some time during adolescence. This phenomenon—termed "dispersal"—is associated with changes in gene expression. Genes related to the immune response are more highly expressed in pre-dispersal males than post-dispersal males. This shows that analysis of gene expression may provide a finer definition of an individual's social status than hormone levels.

Studies in humans have shown that early-life adversity can alter the nature of the response to stress later in life. Dr. Higham and colleagues examined the levels of cortisol and alpha-amylase—a biomarker that reflects the sympathetic nervous system—in macaques and found that animals who had experienced early-life adversity had higher basal levels of cortisol in relation to alpha-amylase and did not show an increase in cortisol levels in response to stress, as seen in animals who had not experienced early-life adversity. This asymmetry between the major components of the psychobiology of stress is associated with atypical behavior in youth and suggests that early experiences can have significant effects on an animal's response to threats over its lifespan.

To measure attentional biases to threats, Dr. Higham and colleagues simultaneously showed young monkeys a picture of the same unfamiliar male making a threatening facial expression and a neutral expression. Animals with negative early-life experiences consistently spent more time looking at the threatening face compared to those without early-life adversity; this asymmetry was correlated with their hormonal response to stress. This observation suggests that physiological stress markers reflect real-world reactions to stress. Early-life experiences therefore seem to influence the stress response at both the biological and behavioral levels.

Dr. Higham also discussed crested macaques, and the need to consider animal models in which the social style and social relationships differ. In contrast to rhesus macaques, which have a highly despotic and nepotistic social style, crested macaques have extremely tolerant and egalitarian social relationships, representing an interesting comparison.

What Can You Learn about Aging from Wild Primates?

Susan Alberts, Duke University

Dr. Alberts studies a population of wild savannah baboons, an emerging model of aging, in the Amboseli ecosystem of East Africa. This population has been closely studied for over 40 years. Longitudinal studies of this population have yielded a great amount of insight about patterns of age-related changes across the lifespan. Like those of humans, baboons' aging patterns differ based on sex, with females living longer than males. Females have one offspring approximately every 2 years and rarely experience reproductive senescence. Body mass index peaks in middle age and declines in old age. Males, more so than females, show an increased rate of illness as they age.

Relatively few studies have found that or even sought to determine whether social relationships in animals affect survival. However, Dr. Alberts and colleagues found that affiliation levels, both with other females and with males, predicted female survival in their study population. Affiliation levels, in turn, depended on several other factors. Female social status predicted affiliation levels with adult males, with higher ranking females showing more affiliation with males. In contrast, social status had no effect on affiliation levels with females, but whether a female's mother and adult daughters were still alive did; once mothers and daughters die, they are apparently difficult for females to replace as social partners. Interestingly, female social status did not contribute directly to survival, but because it affected affiliation levels with males, Alberts and colleagues concluded that social status has indirect effects on female survival.

Females who experienced higher levels of early-life adversity had considerably shorter lifespans than those who experienced little or no diversity. Further, experiencing high levels of adversity was related to low levels of affiliation with other females in adulthood, but high-adversity females did not show reduced affiliation with males. Thus, relationships with male and female partners play distinct roles in the lives of female baboons, with early-life adversity impeding female-female relationships while having little impact on female-male relationships.

The social effects that we see in baboons and other non-human animals occur without the confounding influence of varying health habits that occur in humans, such as smoking, drinking, diet, and exercise. These findings indicate close associations between early adversity and survival even in the absence of these confounding variables. In baboons, social status facilitates access to social resources; a similar process may play out in human social relationships.

Roundtable Discussion: Learning about Human Sociality from Animal Models

Moderator: Robert Levenson, University of California, Berkeley

In response to a question about why humans benefit more from social connections than nonhuman species, Dr. Brent said that this might be because most wild animals deal with existential threats while most human populations have the relative luxury of confronting primarily social issues. Many of the brain regions activated in response to social shunning are

the same as those associated with physical pain, suggesting that the impact of the social world may be quite important.

Much of the discussion of the variables in these presentations has categorized things in a binary way—high *versus* low, haves *versus* have-nots. It is possible that these analyses miss important nuances because they fail to capture degrees of stimuli.

Responses to stress vary across species; for example, in anticipation of conflict, bonobos show a large increase in cortisol (a stress hormone), while chimpanzees show a large increase in testosterone (an aggression hormone). In humans, a stress response may be beneficial if it leads people to seek support from others. This underscores the importance of understanding a given response in the appropriate social context.

Dr. Preston pointed out that, in humans, glucocorticoid response does not correlate with self-report as feeling stressed. This raises the question of how to reconcile the discordance between biomarkers and self-reported emotions, and how "stress" should be defined in humans and other intelligent animals.

Gaps in Human Studies That Could Be Addressed with Animal Studies

How Can Social Relationships Promote Health in Challenging Environments?

Thomas Bradbury, University of California, Los Angeles

Dr. Bradbury and colleagues study the factors that predict success in married couples. People living in low-SES neighborhoods who described themselves as being "satisfied" or "moderately satisfied" with their relationships had significantly lower rates of metabolic syndrome than those who described themselves as "dissatisfied" or were single or divorced. This observation connects self-reported psychological well-being with pathological disease.

People who had conversations with their partners about their health reported higher levels of emotional support, which was associated with positive health changes in their lifestyles. Additionally, engaging in more "healthful" behaviors significantly reduces the risk of poor health. Income is also clearly related to health: low-income individuals are more likely to be diagnosed with two or more chronic health conditions. Dr. Bradbury and colleagues hypothesized that life disadvantage and stress compromise health, and that these factors lead to unhealthful behaviors.

The notion that social relationships can be a source of stress and a source of strength presents an opportunity. If stress resulting from scarcity reduces cognitive capacity, then social relationships could potentially offset this deleterious effect, which presents an opportunity to intervene and address stress in vulnerable individuals. This question could be addressed through studies that manipulate stress levels and social relationships directly in animals.

The Role of Support-Giving in Human Health and Well-Being

Naomi Eisenberger, University of California, Los Angeles

Social relationships are strongly linked to health and well-being. Across many different studies and populations, individuals who have higher levels of social integration have a significantly lower mortality rate. Typically, when considering ways that social ties keep people healthy, we focus on the benefits of receiving social support from others. However, it is possible that some of the benefit from social connectivity is a result of giving social support to others.

In a study of more than 800 adults, those who reported providing more support to others showed a reduced risk of mortality, better mental health, and lower blood pressure. This was particularly true for older adults.

How might support-giving improve health in the giver? Studies in mice have shown that regions including the ventral striatum and the septal area contribute to maternal behavior. Moreover, regions like the septal area have been shown to reduce threat-responding to facilitate caregiving during stress. The septal area is involved in reducing fear-responding impulses through inhibitory connections with the amygdala. To test whether providing support activates the same region in the human brain, Dr. Eisenberger and colleagues used MRI scans to study the brains of 20 women as they held the arms of their romantic partners who stood just outside the scanner and received unpleasant electric shocks. For the support-giver, holding her partner's arm while he experienced physical pain led to significantly more activity in the ventral striatum and the septal area. Increased activity in these regions was correlated with a lower threat response in the amygdala.

In a separate study, Dr. Eisenberger and colleagues found that individuals who had higher self-reported support-giving tendencies had lower neural reactivity to an evaluative stress task. This suggests that providing comfort to others is associated with reduced threat reactivity. Finally, in an experimental study, individuals who provided support to others (vs. a control task) prior to completing a stress task showed reduced sympathetic-nervous system activity during the stress task. This fits with other work showing that acting in prosocial ways is associated with reduced expression of pro-inflammatory genes.

These studies show that providing social support to others may be beneficial not only for the receiver but also for the giver. However, animal models are needed to determine the extent to which caregiving contributes to physical and cognitive health. Furthermore, the question of causation remains unresolved: are individuals who are less likely to respond negatively to stress more likely to engage in social behavior, or does caregiving reduce stress by inducing changes in the brain? Finally, it is not known whether these neural processes are different in males and females. Animal models could be a valuable resource to study these questions.

Dyadic Interaction in Intimate Relationships: Emotions, Aging, and Health

Robert Levenson, University of California, Berkeley

Dr. Levenson studies the ways that emotions are generated, regulated, and recognized by partners in committed relationships through the study of dyadic interactions. Over the course of a relationship, both normal aging and the common diseases of late life create changes in emotional functioning that alter the nature of interactions within couples. Use of a semi-naturalistic approach to studying the emotional qualities of dyadic interaction across the lifespan has illustrated age-related changes in emotional functioning as well as links between dyadic interactions and health.

The dyadic interaction studies involve observing 15-minute conversations between couples that touch on day-to-day interactions, including positive and negative activities. Outcome measures include physiologic factors, behavior, and self-reported experience of feelings. Dr. Levenson and colleagues have found that high levels of anger (but not fear or sadness) in relationships are associated with increasing cardiovascular symptoms over time. They concluded that angry marriages may present a significant hazard to cardiovascular health. They also found that greater affiliation—synchronized changes in heart rates or movement—were associated with better long-term relationship satisfaction. These emotional attachments were associated with stronger emotional connections and better health over time.

Across these and other studies. Dr. Levenson has found a strong association between relationship satisfaction and health and well-being. These findings, however, are very general and do not provide causal or directional information. By extending these studies into animals, it may be possible to assess the mechanisms that underlie these outcomes, as well as factors that can accentuate or ameliorate the effects of adversity on interpersonal dynamics and whether there are critical periods during which relationships are particularly vulnerable. A long-term goal is to determine whether couples can learn to change their behavior toward one another, with the goal of increasing overall well-being and promoting better health.

Preliminary studies to investigate these questions have been conducted in male/female pairs of coppery titi monkeys, using proximity to one another and physical contact as approximations of "marital satisfaction." This model can be a valuable tool in promoting understanding of the physiological benefits of healthy relationships.

Roundtable Discussion: Gaps in Human Studies That Could Be Addressed with Animal Studies

Moderator: Susan Alberts, Duke University

Dr. Alberts wondered how the Tsimane might react to the kinds of stress in relationships that Dr. Levenson described. Dr. Gurven replied that the nature of "marriage" is different in the Tsimane culture—families are much larger and more connected so the dissolution of a marriage is a more consequential event. Additionally, within this population there is less casual intimate contact, perhaps resulting in fewer opportunities to stray from the marital bond. This

observation reinforces the concept that social relationships should be interpreted in their own context.

Dr. Higham noted that it is important to separate the social system from the mating system, particularly in animal studies. Dr. Eisenberger echoed this concern and wondered, as human coupling behavior has diverged from mating behavior, to what extent do these factors influence the analysis of human relationships? Dr. Alberts wondered whether, as is the case in baboons, social relationships might supplant marriage partners, which is seen in some widows who outlive their husbands and go on to establish robust networks of friends. Across animal species, there are many different variations of male/female pair bonds and their durability. Dr. Hare noted that the domestication of dogs has led to the loss of parent/offspring bonding in that species.

Moderated Discussion: Mechanisms Underlying Associations Between Health and Behavioral Factors and Social Phenomena

Moderator: Robert Levenson, University of California, Berkeley

This discussion addressed the question: Where are the current knowledge boundaries, and what are the most urgent questions related to the following:

- The mechanisms underlying associations between health and variation in the quality and quantity of close social relationships, as well as the stability of close social bonds and social groups;
- The mechanisms underlying differential health impacts of exposure to adverse experiences at different time points across the life course; and
- The direct and indirect benefits of social capital conferred to individuals, and how social capital contributes to health and well-being at older ages?

Dr. Nielsen of the NIA prefaced the discussion by saying that the Institute was interested in hearing from the discussants ideas about activities and types of research studies that the NIA could support to address identified gaps in knowledge.

Dr. Brent wondered whether there is relationship between social connectivity and changes in health and reproduction in humans, and if so, whether it is causal. There are relatively little animal data to support a causal relationship between these two characteristics. Dr. Gurven noted that, because of the way that resources— such as social capital—are transferred in humans, their uneven allocation could make resource-rich individuals more attractive as social partners.

Dr. Eisenberger explained that in the absence of a good working model of stress in the brain it is difficult to understand how social connections might work to reduce stress and promote overall mental health.

Dr. Preston stated that there is relatively good information about the influence of genetic factors that act early and late in life on social and health-related outcomes, but relatively little

data on factors that are important in mid-life. Interventions in mid-life could potentially address genetic predispositions or negative early-life influences. Dr. Higham noted that interventions in veterans with post-traumatic stress disorder have been shown to measurably improve their quality of life.

Attendees considered at length what the overall goal of any proposed research effort should be. This discussion raised questions about different ways to define and measure well-being. Dr. Nielsen noted that the mission of the NIA is to support research on aging and the health and well-being of older people, and that NIA has made substantial investments in the development and use of measures of subjective well-being. To the extent that social connections can improve well-being, psychological function, and physical health, studies to address this would fit within the mission.

Different key questions stood out to different researchers. Dr. Gerald offered, as an example, whether social connections improved cognitive performance. Dr. Nielsen asked what about social connections made them beneficial. Dr. Shively noted that the benefit of the social connection was related to the quality of the partner. Dr. Alberts wondered about the mechanisms by which the social environment leads to improvements in physical health. Dr. Levenson observed that, while biomarkers exist for many physical diseases, researchers do not yet have good biomarkers for things like "happiness," making questions about emotional outcomes difficult to answer, especially in animal models. Dr. Preston thought that studies in animals could provide insights into biomarkers of behavior and behavior changes that could be correlated to physical changes, such as cortisol levels.

Dr. Bliss-Moreau cautioned that humans tend to project their own life experiences on other species. However, achieving "happiness" as a life goal may not be universal even among humans. In America, being successful and happy is widely seen as a worthy goal; other cultures may prize different outcomes, such as stability. More work is needed to understand the relationship between emotions and culture.

Dr. Nielsen said that before designing an intervention, researchers need to know what behavioral or social mechanisms or processes to target and consider ways to do so effectively—both in terms of the nature of the intervention and its timing. NIA is interested in interventions that can help people maintain a positive trajectory toward healthy aging.

Moderated Discussion: Leveraging Longitudinal Studies of Wild or Captive Animal Populations to Gain Mechanistic Insight into Associations Between Health and Behavioral or Social Phenomena.

Moderator: Susan Alberts, Duke University

This discussion explored promising approaches for using animal models to address the following topics:

- The importance of close and stable social bonds and social groups for health and well-being at older ages.
- The differential impact of exposure to adverse experiences at different time points across the life course on later life health.
- Direct and indirect effects of social capital on aging-relevant health outcomes.

Dr. Eisenberger noted that studies of dogs have shown that specific stimuli from mothers can produce attendant responses in her pups. It is thought that this phenomenon is mediated at least in part through olfactory function, which is often a proxy for physical closeness.

Dr. Brent asked whether long-term studies in monkeys might examine how social connections evolve over time and how old connections may be supplanted by new ones. These relationships could be observed in both wild and captive monkeys, although captive monkeys would provide greater opportunity to experimentally manipulate their social conditions.

Dr. Ophir explained that social development continues across the lifespan, offering an opportunity to intervene at multiple times in an animal's life. Many significant events occur over the course of a lifespan—parenthood, marriage, divorce, death of a parent, death of a spouse—that change behavior and likely change gene expression, among other outcomes.

Dr. Bradbury mentioned data showing that, among people prone to alcoholism, interpersonal relationships can lessen the likelihood of alcohol abuse even in individuals at high risk. The theory behind this observation is that the potential substance abuser feels responsible to other people for his or her behavior. This is a consequence both of feeling as though someone is "watching" one's behavior and a feeling that one is important to another and therefore has an obligation to meet certain standards of behavior. This point highlights mutual benefit of receiving and giving care explored in Dr. Eisenberger's presentation.

Dr. Higham noted that, within only 2 to 3 million years, humans have changed their sexual pairing patterns, mating systems, fathers' role in child care, menopause, and grandmothering, in addition to changing various social norms. Researchers do not know what drove these changes, but if we could better understand their origins we could probably better understand our current situation. Dr. Brent said that the resident killer whales have evolved menopause during the past 30,000 years—a rather recent development. Because there is a great evolutionary cost to the social group of supporting a nonreproducing older female, this implies a strong evolutionary benefit in this population to prolonged nurturing female life after reproductive age.

Dr. Hare noted that evolutionary theory could also be used to make predictions. For example, if we can identify the brain regions of humans and monkey species that differ, we can begin to identify which regions might correspond to which cognitive functions. This builds on the idea that many social constructs that humans and monkeys share have an evolutionary basis; it seems reasonable to think that the ones that differ between the two species have an evolutionary basis as well.

Moderated Discussion: Micro-Level Social Processes and Insights into Inter-Individual Interactions, Social Relationships, and Health- and Psychological-Related Vulnerabilities across the Life Course

Moderator: Robert Levenson, University of California, Berkeley

Micro-level social processes serve as reliable cues about individual differences in personality and status. They are also the mechanisms through which social relationships are established, maintained, and disrupted. Observing these processes in animals could yield novel insights into the features of social relationships that influence health or that signal individual strengths or vulnerabilities to conspecifics.

In this discussion, attendees were asked to reflect on the following:

- The role of social processes in preserving mental, cognitive, and physical functioning as we age;
- The role of time-specific and trait-like associations between social variables in shaping individual health trajectories and health transitions;
- The social and behavioral processes by which social asymmetries and social relationships are formed, maintained, and change over the life course; and
- How to disentangle the complex association between marriage and health and between social inequalities and health.

Considering the challenges of quantifying behavior, social connectedness, and well-being, Dr. Levenson asked whether it was possible to know what a person was feeling by his or her facial expression. Mentioning his own work, he asked about the appropriate time period over which to study these phenomena. Dr. Alberts agreed that this problem is challenging. Her studies of baboons analyze fecal samples, providing only average levels of metabolites over a 12-hour period. Dr. Higham noted that researchers are limited by their tools; as they develop new tools, they can ask different questions. Dr. Bliss-Moreau noted that similar problems existed 15 years ago in the field of neuroimaging, until new tools were developed that propelled the field forward. One way to address the relative deficiency of tools to quantify social and emotional variables would be to support the development of new tools.

Dr. Brent said that it can be difficult to conduct micro-level studies on the rhesus macaque population she observes, because she spends only 10 minutes observing each individual in the sample. Her research team is considering using bio-logging—attaching a collar to a subset of rhesus macaques—to collect data on location, movement, social interactions, heart and breathing rate, and other data. Dr. Bliss-Moreau said that researchers spend a lot of time training monkeys to perform specific tasks that, in and of themselves, are not important but that foster social interaction, which is important for her studies.

Dr. Bradbury noted that during the 1970s, researchers would study human families by following and filming them throughout their day. While rich in detail, these studies were very expensive and logistically difficult. Dr. Levenson said that, even in families, the dyad may be the most

important relationship, especially because much emotional processing does not involve spoken language but is mediated through facial expressions, posture and body language, and relationships between individuals in space.

Drs. Gurven and Eisenberger observed that new technologies have the potential to collect data noninvasively, such as through facial mapping. However, it will still be important to ground these data with interviews and other direct observations. Dr. Preston cautioned against charging ahead with automated data collection lest researchers amass large amounts of data that are not useful in answering relevant research questions.

Overview of Day Two and Identification of Possible Breakout Session Topics

Susan Alberts, Duke University

During breakout sessions on Day 2, each group will design a prospective study that addresses a key knowledge gap identified during the discussions on Day 1. The NIA is particularly interested in collaborative human and animal studies of social causation as they relate to health-related outcomes in later life. Each group will be asked to propose an intervention study in humans and animals that is designed to change health behavior in a positive way.

Roundtable Discussion: Methods Toolbox

Moderator: Robert Levenson, University of California, Berkeley

In this discussion, invited experts revisited the methods they introduced in their presentations on Day 1 and discussed the methodological strategies that might be employed to overcome barriers to addressing questions related to the psychological, behavioral, and social processes that shape health and well-being of humans in mid-life and older ages.

A challenge in human behavioral research is distinguishing between public and private phenomena, or between self-report and reality. Sometimes people report one emotion in the moment and later describe their emotion quite differently. Attendees debated what “true” emotion really is—is it what the person describes at the moment; what the person describes later, after reflecting on the experience; or what the biomarkers indicates? Dr. Bliss-Moreau suggested that all of these observations represent data points in our understanding of emotion.

Dr. Shively said that her group’s model of depression in subordinate monkeys took nearly 25 years of observation to emerge, illustrating the difficulty of linking biology to behavior. Dr. Higham noted that, in monkeys, it is possible to analyze the relationship between vocalizations and behavior. Dr. Nielsen said that this approach is being used in human studies that link behavior and biology by sampling real-world experiences of well-being and other phenomena, and combining these assessments with biomeasures and survey interviews.

Much of the behavioral data that is collected records average values over time. What may be more important collection of in-the-moment data that can provide insights into reactions to specific stimuli.

Dr. Gurven noted that, although it can be difficult to extrapolate from animal data to human data, cross-species comparisons will be necessary to move both fields forward. Dr. Higham said that some methodologies work best in animals and others work best in humans; it will be important to find common ground to be to apply insights from one field to the other. For example, Dr. Bradbury noted that most human interactions occur in dyads, whereas nonhuman animal interactions tend to occur in larger social groups. Dr. Ophir added that, while there is strength in comparing nearly identical situations in animals and humans, there is also value in using animal data to develop hypotheses that can be tested in humans (or vice versa).

Dr. Levenson noted that animal behavior researchers generally incorporate evolutionary theory into their models, but many human behavior researchers do not. Dr. Hare replied that much of social and developmental psychology incorporates evolutionary theory even if it is not explicitly labeled as such.

Dr. Levenson said that different circumstances might call for different measures—observations or self-reports. Dr. Alberts added that many emotions are not observable but may produce measurable biological reactions. Dr. Preston stressed the importance of collecting as much data of as many different kinds as possible for a given phenomenon.

Drs. Hare and Levenson discussed the role of expectations in well-being. If an individual expects to be dominant, is that individual less happy if he or she is displaced than if he or she had never been dominant to begin with? If a person is in a good relationship, does that make the person less or more unhappy during difficult times?

Dr. Preston returned to the importance of culture in setting expectations about achievement and well-being. As an example, Dr. Gurven cited societies in which marriages of two strangers are arranged by their families; these couples do not report being significantly less satisfied than couples who chose to marry.

Breakout Sessions: Design a Prospective Study Employing Animal Models to Further Understanding About the Psychological, Behavioral, and Social Processes That Shape Health and Well-Being of Humans in Mid-Life and Older Age

Participants were divided into smaller groups to design a prospective study that addresses a key knowledge gap discussed during the meeting.

Report from Breakout Group I

Robert Levenson, University of California, Berkeley

Group I proposed a study to examine whether control over resources can increase positive social interaction, leading to better overall health and well-being. In both humans and monkeys, positive social interactions tend to decline with age, and these changes correlate with negative influences on health and well-being. This study would test the hypothesis that

increasing control over food resources would increase social and physical contact in both humans and monkeys, resulting in improved health and well-being among individuals who exert control.

In humans, this would be tested by examining the social roles of older widows or widowers who move into assisted living facilities. In monkeys, this would be tested by examining the social implications of older monkeys moving into new colonies. In both cases, researchers would study the social impact of introducing an older individual into an existing social milieu.

The intervention in the study would be to allow the new community member to control the availability of food during social dining. In humans, the new person would be allowed to choose a menu and invite people to a dinner, inspired by an experiment conducted where low-ranking monkeys who were trained to control distribution of popcorn were not only buffered from harassment from higher-ranking animals, but some of these animals were even groomed more often. For the new resident, the meal would take place in a social setting in which both the subject and his or her guests were present.

Short-term outcome measures would include social and physical contact during the following month. In humans, this would include social contact, touch, and reconciliation after negative social interactions. For monkey interventions, this would include grooming, proximity, and reconciliation after physical altercations. Long-term outcomes would include overall health and well-being.

Dr. Nielsen asked whether, in addition to immediate effects, there might be longer-term carry-over effects. The key research question is what behavioral or social factor is manipulated by hosting the dinner. Dr. Levenson replied that possible outcomes could include social network size, feelings of competency (in humans), and providing “care” to others, but these were intermediate steps in reaching ultimate goals of health and well-being.

Dr. Bliss-Moreau expressed concerns about the practical issues of introducing new, older monkeys into an existing colony. Dr. Hare said that the study did not need to be limited to monkeys—researchers could study great apes, particularly bonobos, who have more permeable social group boundaries than monkeys. Dr. Bliss-Moreau said that the discussion reinforced the need for scientists working on different species to talk to each other.

Dr. Ophir raised concerns about the feasibility of manipulating human behavior. Dr. Nielsen suggested pilot studies to demonstrate that the proposed approach would yield the expected results. Dr. Gerald added that a fundamental question to be addressed is what are the social requirements and needs of aging people, noting that they may differ for individuals. Many may be healthy with limited social networks. For others, a few high-quality connections may be sufficient to ensure good health in later years.

Report from Breakout Group II

Stephanie Preston, University of Michigan

Group II considered the impact of early-life adversity on long-term outcomes. The group considered one hypothesis—that individuals who face early-life adversity have poorer sociability as adults. An alternate hypothesis is that once individuals have adapted to their early-life adversities, they may be positioned to succeed later in life, either in a dominant social niche or a "safe" social niche. What differentiates these two hypotheses is that, in the first, the primary driver of adult success is the early-life environment, while in the second, the primary driver is the adaptability in adult life to overcome early-life adversity. A third option is that, whatever one's early-life experiences, it is possible to find social niches in which to thrive.

One way to test these hypotheses would be to study the differences between *loner* monkeys, who prefer to be alone or engage with a small social circle, and those who are *lonely*, who would like to engage with a larger social circle but are unable to do so.

Social isolation is associated with a heightened inflammatory response, but the direction of causality is not known. To answer this question, researchers could track early-life conditions in monkeys and follow the animals into adulthood to measure differences in social behavior. In humans, it might be possible to capture data from developmental studies that track early life and socialization in a preschool setting and compare this information longitudinally with adults for whom retrospective data are available.

Possible outcome variables to capture in future studies could include cognitive bias, threat vigilance, and appraisal biases that predispose one to treat social or negative stimuli as threatening; social motivation; response to rejection; reproductive success; interoceptive awareness; and subjective experiences of loneliness and self-reported reasons for being alone.

In considering this research, the following questions are important: To what degree are individuals able to adapt to early-life adversity? Are there loners who adapt and go on to achieve reproductive success? How much of this adaptation is related to the concept of agency—did an individual choose to be alone or was it forced upon him or her? These questions reinforce the notion that, while the degree of social connectivity is a relatively straightforward thing to measure, understanding of these interactions must consider the very personal nature of relationships.

Future studies could address questions such as:

- Are some individuals more or less able to benefit from early adversity?
- Are there loners who have good reproductive success outcomes?
- Do outcomes vary depending on one's perception of the environment and whether one feels rejected or chooses to be a loner?
- To what degree is an individual aware of his or her social status?

In humans, a potential complicating factor is that different people have different preferences for social engagement, such that a relatively paltry set of social contacts for an extrovert might represent a generous set of contacts for an introvert. Such variability is likely to exist in nonhuman animals as well, and may complicate analysis of population-based studies. It is unlikely that a one-size-fits-all solution to the question of social engagement exists.

Report from Breakout Group III

Susan Alberts, Duke University

Group III proposed a multi-species, mixed-method study to shed light on the causal relationship between social behavior and health. This study would explore the ways in which early- and late-life experiences influence adult success. This study would involve the following observations of four species:

- In prairie voles, early adversity and adult social environments would be manipulated to measure proxy outcomes for health.
- In rhesus macaques, detailed social analyses of adult sociality would be related to proxy health outcomes obtained via blood draws and morphometric analyses.
- In baboons, a cradle-to-grave analyses would assess early adversity and adult sociality noninvasively.
- In the Tsimane, the effects of social perturbations on health would be measured.

Dr. Brent proposed performing an analysis in rhesus macaques akin to that done in the Tsimane people—recording detailed information about social interactions and social health of individual animals over a period of 4 to 5 years. Dr. Alberts added that these studies could be incorporated into cradle-to-grave analyses of early adversity and adult sociality.

Many nonhuman primate species have very different social structures than humans—females tend to live and die in the same social group while males tend to leave the group that they were born into and set out on their own to form new connections. However, different primates have different social structures. This could be an area in need of further study.

Dr. Levenson noted that two of the four proposed studies were observational studies—those in baboons and the Tsimane. The rhesus and vole studies offer the opportunity for an interventional study. He also asked why these species were chosen given that not all of them share the same social organization.

Dr. Nielsen suggested that the group add a study in which an assessment of early-life adversity in humans is correlated with later-life social connectivity. Data exist on outcomes of children who have been adopted, which could provide a resource for future study. Dr. Hare asked about the possibility of studying orphan apes in the wild. Dr. Shively said that losing one's parents is one of the most stressful things in life and therefore these animals might represent too extreme of an emotional response to produce meaningful data. Dr. Hare replied that some species of non-human primates seem to show no adversity in later life after the loss of parents, while others do, suggesting species-specific reactions to early-life adversity.

Synthesis and Next Steps

Robert Levenson, University of California, Berkeley
Susan Alberts, Duke University

This meeting highlighted the silos that sometimes separate nonhuman and human studies of social interaction. Moving forward, it would be helpful to develop ways to increase communication between investigators in these two fields. This could be accomplished through conferences and meetings or through mechanisms that promote cross- or multi-species collaborative studies to bridge the human and animal worlds.

The study of social processes in aging animals provides an excellent opportunity to identify measures and manipulations that can be used across various species to identify mechanisms of behavior and social interaction. In thinking about these studies, however, it will be important to appreciate the uniqueness of the individual within the population—whether in animals or humans, it is likely that the optimal set of social relations may not be the same for all individuals.

Research that aims to identify behavioral mechanisms that are common across species would benefit from a greater emphasis on measures that are based on objective observations of behavior and physiology. Self-report measures of individual, subjective experience in humans do not readily translate into studies of other species.

Finally, this workshop demonstrated that it is possible to design interesting and feasible interventions and model-testing studies of social processes in aging that involve multiple species. A challenge for researchers is to design studies of this sort that are informed by greater communication between researchers working in human and nonhuman systems to advance our understanding of the role of social interaction in human aging.

Appendix 1: Agenda

Day 1: May 8, 2017

8:30 a.m. **Sign-in and Badge Pick-up**

9:00 **Welcome to the National Academies**
Barbara Wanchisen, Director, BBCSS

9:05 **Introductory Remarks from the National Institute on Aging**
Melissa Gerald, Division of Behavioral and Social Research

9:15 **Setting the Stage for the Meeting**
Robert Levenson, University of California, Berkeley
Susan Alberts, Duke University

9:25 **Lessons from Comparative Studies**
Eliza Bliss-Moreau, University of California, Davis
Michael Gurven, University of California, Santa Barbara
Brian Hare, Duke University
Stephanie Preston, University of Michigan
Carol Shively, Wake Forest School of Medicine
10-minute presentations from invited experts describing lessons they have learned from their comparative studies of social phenomena and what unique perspectives might be gained by applying a comparative approach to aging-related studies of behavioral, psychological, and social processes; relationship qualities; and interpersonal dynamics. Following each presentation, 5-minutes will be devoted to Q&A.

10:50 **Roundtable Discussion: Lessons from Comparative Studies**
Moderator: Susan Alberts

11:20 **Learning about Human Sociality from Animal Models**
Susan Alberts, Duke University
Lauren Brent, University of Exeter
James Higham, New York University
Alexander Ophir, Cornell University
10-minute presentations from invited experts who employ animal models to examine various aspects of sociality that may have implications for healthy aging. Presenters will discuss the potential value that animal models can offer to aging-related studies of behavioral, psychological, and social processes; relationship qualities; and interpersonal dynamics. Following each presentation, 5-minutes will be devoted to Q&A.

12:20 p.m. **BREAK TO PURCHASE LUNCH**

12:45 **Roundtable Discussion: Learning about Human Sociality from Animal Models**
Moderator: Robert Levenson

1:15 **Gaps in Human Studies That Could Be Addressed with Animal Studies**
Thomas Bradbury, University of California, Los Angeles
Naomi Eisenberger, University of California, Los Angeles
Robert Levenson, University of California, Berkeley
10-minute presentations from invited experts who examine different aspects of human social relationships. Presenters will discuss key knowledge gaps in their respective fields that can be potentially be overcome with the use of animal models. Following each presentation, 5-minutes will be devoted to Q&A.

2:00 **Roundtable Discussion: Gaps in Human Studies That Could Be Addressed with Animal Studies** *Moderator: Susan Alberts*

2:30 **Moderated Discussion: Mechanisms Underlying Associations between Health and Behavioral Factors and Social Phenomena**
Moderator: Robert Levenson
Where are the current knowledge boundaries and what are the most urgent questions related to:

- The mechanisms underlying associations between health and variation in the quality and quantity of close social relationships, as well as the stability of close social bonds and social groups;
- The mechanisms underlying differential health impacts of exposure to adverse experiences at different timepoints across the life course; and
- The direct and indirect benefits of social capital conferred to individuals, and how social capital contributes to health and well-being at older ages?

3:30 **BREAK**

3:45 **Moderated Discussion: Leveraging longitudinal studies of wild or captive animal populations to gain mechanistic insight into associations between health and behavioral or social phenomena**.
Moderator: Susan Alberts
Invited experts will participate in a moderated discussion of the most promising approaches for using animal models to address the following topics:

- The importance of close and stable social bonds and social groups for health and well-being at older ages;
- The differential impact of exposure to adverse experiences at different timepoints across the life course on later life health;
- Direct and indirect effects of social capital on aging-relevant health outcomes

4:45 **Moderated Discussion: Micro-level social processes and insights into inter-individual interactions, social relationships, and health- and psychological-related vulnerabilities across the life course**

Moderator: Robert Levenson

Micro-level social processes serve as reliable cues from which observers can make inferences about individual differences in personality and status. They are also the mechanisms through which social relationships are established, maintained, and disrupted. Participants will explore how studies of micro-level social and behavioral processes in captive and wild animals might yield novel insights into the features of inter-individual interactions and social relationships that confer health benefits or risks or that signal individual strengths or vulnerabilities to conspecifics.

- The role of social processes in preserving mental, cognitive, and physical functioning as we age;
- The role of time-specific and trait-like associations between social variables in shaping individual health trajectories and health transitions;
- The social and behavioral processes by which social asymmetries and social relationships are formed, maintained, and change over the life course; and
- How to disentangle the complex association between marriage and health and between social inequalities and health.

5:45 **Overview of Day Two and Identification of Possible Breakout Session Topics**

Susan Alberts

6:00 **Adjourn Day One**

Day 2: May 9, 2017

9:00 a.m. **Summary of Day One Sessions**

Brief reflections on the main takeaway points from Day One sessions. Invited experts will provide 5 minutes of reflection, followed by 5 minutes of group discussion.

Lessons from Comparative Studies—Mechanisms Underlying Associations between Health and Behavioral Factors and Social Phenomena

Eliza Bliss-Moreau, University of California, Davis

Learning about Human Sociality from Animal Models—Leveraging Longitudinal Studies of Wild or Captive Animal Populations

Lauren Brent, University of Exeter

Gaps in Human Studies That Could Be Addressed with Animal Studies—Micro-Level Social Processes

Naomi Eisenberger, University of California, Los Angeles

9:30 **Roundtable Discussion: Methods Toolbox**
Moderator: Robert Levenson
Invited experts will revisit the methods they introduced in their presentations on day one and engage in a discussion of methodological strategies that might be employed to overcome barriers to addressing questions related to the psychological, behavioral, and social processes that shape health and well-being of humans in mid-life and older ages.

10:15 **Setting the Stage for Breakout Session**
Susan Alberts, Duke University

10:25 **Breakout Session: Design a Prospective Study Employing Animal Models to Further Understanding About the Psychological, Behavioral, and Social Processes that Shape Health and Well-Being of Humans in Mid-Life and Older Age**
Participants will be divided into smaller groups to design a prospective study that addresses a key knowledge gap discussed during the meeting.

11:45 **BREAK TO PURCHASE LUNCH**

12:15 **Reports from Breakout Groups and Discussion of Proposed Studies**

1:15 **Synthesis and Next Steps**
Robert Levenson, University of California, Berkeley
Susan Alberts, Duke University

2:15 **Closing Remarks**
Melissa Gerald, National Institute on Aging

6:00 **Adjourn**

Appendix 2: List of Participants

Invited Speakers:
Susan Alberts, PhD, Duke University
Eliza Bliss-Moreau, PhD, University of California, Davis
Thomas Bradbury, PhD, University of California, Los Angeles
Lauren Brent, PhD, University of Exeter
Naomi Eisenberger, PhD, University of California, Los Angeles
Michael Gurven, PhD, University of California, Santa Barbara
Brian Hare, PhD, Duke University
James Higham, PhD, New York University
Robert Levenson, PhD, University of California, Berkeley
Alexander Ophir, PhD, Cornell University
Stephanie Preston, PhD, University of Michigan
Carol Shively, PhD, Wake Forest School of Medicine

National Institutes of Health
Prisca Fall, MA, Research Program Analyst, BSR, NIA
Kimberly Firth, PhD, Health Science Administrator, Scientific Review Branch, NIA
Melissa Gerald, PhD, Program Director, BSR, NIA
John G. Haaga, PhD, Director, BSR, NIA
Amelia Karraker, PhD, Health Scientist Administrator, BSR, NIA
Jonathan King, PhD, Program Director, BSR, NIA
Kimberly Jane Kramer, MA, Guide Liaison, Division of Extramural Activities, NIA
Laura Major, MPH, Research Program Analyst, BSR, NIA
Carmen Moten, PhD, Scientific Review Officer, Division of Extramural Activities, NIA
Evelyn Neil, Program Analyst, BSR, NIA
Lis Nielsen, PhD, Chief, Individual Behavioral Processes Branch, BSR, NIA
Georgeanne Patmios, MA, Acting Chief, Population and Social Processes Branch, BSR, NIA
Michael Spittel, PhD, Health Scientist Administrator, Office of Behavioral and Social Sciences Research
Courtney Paige Wallin, PhD, Office of Legislation, Policy, and International Activities, Office of the Director, NIA

Division of Behavioral, Cognitive, and Sensory Sciences, National Research Council
Barbara Wanchisen, PhD, Director
Tina Winters, Associate Program Officer