Genetics, Behavior and Aging

Summary of BSR Exploratory Workshop~~,~~
March 29, 2002

The Behavioral and Social Research (BSR) program at the National Institute on Aging is highly dedicated to developing research at the intersection of genetics, aging and the behavioral and social sciences. Currently, BSR supports a modest, but growing genetic portfolio. It includes a wide range of research perspectives and approaches (e.g. behavior genetics, biodemography) for investigating genetic influences on aging. Model organism, animal, and human studies comprise this portfolio. The levels of analysis span from studies of individuated loci to estimating the aggregate effects of genes, to evolutionary studies of processes that shape population gene pools.

A number of recent program activities devoted to building BSRs portfolio in genetics and behavioral research have been undertaken. Dr. Jennifer Harris is on special assignment at the BSR program to help develop these directions, and BSR plans to allocate special grant funds to this area. Other plans include follow-up to the NIA-sponsored National Research Council volume (2001) Cells and Surveys, which explored the feasibility and research opportunities of collecting biological indicators in social science and survey research.

On March 29, 2002 BSR held an exploratory workshop entitled 'Genetics, Behavior and Aging'. The purpose of this workshop was to review current research in behavior genetics and aging, to discuss important areas for future research development as applied to the study of aging, and to generate new ideas regarding optimal strategies and the most fruitful avenues for new initiatives. The workshop congregated researchers with expertise in an array of fields, including psychology, evolutionary theory, statistical methodology, economics, and animal systems, bringing together diverse perspectives to explore prevailing research questions. The presentations are the basis of papers that will be published in a special edition of the Journal of Behavior Genetics, of which Dr. Harris is guest editor. Summarized below are several themes that emerged during the meeting, both in presentations by participating researchers and subsequent discussions.

Gene-environment interaction

Although virtually all behavior is thought to result from complex interactions of genetic predispositions and environmental factors, documenting these interactions has proven difficult in human studies. In the atmosphere of newfound excitement regarding the sequencing of the human genome, researchers must not forget the importance of the environment. Social influence and personal experiences impact gene expression. As Scott Hofer (Pennsylvania State University) pointed out, the vast majority of existent human research has been carried out in two camps: researchers who study the environment, and by ignoring genetic predispositions, essentially average across genotypes, and those who study genetic influences, essentially averaging across environments. This makes it extremely difficult to apply population-based estimates to enhance understanding of the individual. Greater emphasis is needed on studying the dynamic processes by which genetic predispositions interact with environmental factors to influence developmental outcomes. Studies should be designed with the intent of testing for gene-environment interaction, rather than looking for interaction after the fact.

The inclusion of environmental information is critical in both classic quantitative genetic twin studies and molecular genetic studies.

Measuring the environment is not a straightforward task. Ted Wachs (Purdue University) and Keith Whitfield (Pennsylvania State University) elegantly reminded us of the importance of environmental context and the difficulty of measuring the environment. Concepts such as "shared" and "nonshared" environment, typically used in behavior genetics, are ambiguous and confusing to researchers outside of the field, as most any aspect of the environment can be shared or nonshared depending on the situation. Furthermore, they do not begin to capture the dynamic nature of environmental influences. The environment is multi-level, multi-dimensional, and hierarchical, with bi-directional linkages between these many levels. "Environmental epistasis", where multiple environmental factors interact, is likely as common as genetic epistasis is believed to be. We need a systems context of development to understand these multiple interacting influences. Furthermore, there are both subjective and objective aspects of the environment. Additionally, the environment operates in historical and individual time. Researchers also need to pay attention to the "fit" between individual's environmental demands and their competence level. Cultural and ethnic environmental influences are often ignored in the homogenous, largely Caucasian twin samples that currently exist. The Carolina African American Study of Aging (K. Whitfield) provides an important example of efforts to expand current twin studies to allow for study of these influences. Incorporating environmental risk factors into studies on aging requires many special considerations: How do we assess environment across the lifespan? Are there some aspects of the environment that are fundamental and invariant, while others change across time? Or are the dimensions of the environment invariant, while the salience of different dimensions changes? Often family environment is the target of study, but in aging research, the important environmental factors are likely to be both cumulative and short-term social and physical environments. Incorporating specific, carefully measured environmental information into longitudinal, genetically informative designs must be a priority for research on aging that parallels the new emphasis on including measured genotypes into research analyses.

An additional complication lies in the fact that environments are not independent of individuals' genotypes. Individuals actively select their environments, and react differently to the environments they encounter, and genetic predispositions play a role in these processes. This leads to gene-environment correlation. As Mike Neale (Virginia Commonwealth University), pointed out, teasing apart gene-environment interaction from gene-environment correlation is a difficult process, requiring special models which have yet to be fully developed.

In addition to the use of new twin modeling methodologies, Carol Ryff (University of Wisconsin) reminded us of the importance of returning to the study of discordant monozygotic and dizygotic twin pairs; this methodology provides an important way to study environmental risk factors that contribute to differences in outcome, while providing a degree of control over genetic risk factors. They also allow a unique methodology for the study of resilience, in the context of individuals who are at genetic

risk but do not manifest problems, and in individuals who endure many environmental risk factors without manifesting problems. The characterization and study of protective environments, in addition to more traditionally studied risk environments, is an important and underdeveloped area of research. Understanding resilience in genetically informative designs has the potential to offer insight on social inequalities and health outcomes. For example, while several studies have found that education is protective with respect to a variety of disease outcomes, we do not know if education is equally as protective even in the face of genetic risk factors. Perhaps alternative or additional intervention is necessary among those genetically at risk, or perhaps education is especially protective among those who are at genetic risk (i.e., a buffering effect). Better understanding of resilience and gene-environment interaction could play an important role in conquering the health disparities that currently exist. Behavior genetic methodologies allow researchers to uniquely address questions of health disparities and social inequalities.

Animal research

The complexities inherent in studying gene-environment interaction in humans create a need for animal models of research to complement human studies. As Gerald McClearn (Pennsylvania State University) discussed, animals have shorter life spans and it is possible to collect tissues in animal studies. There is reason to believe that underlying genetic processes may be similar, allowing animal studies to yield insight into biochemical pathways involved in aging processes in humans. Although it is less likely that there will be direct parallels between environmental risk factors in animals and humans, animal models can provide illustrations of dynamic systems of interaction to provoke thought and study in human data. Examples of gene-environment interaction are currently more readily available in animal models. Richard Miller (University of Michigan) presented results in which they have identified genes in mice with effects that are limited to early or later stages of life, or to only one gender, demonstrating both age- and sex-specific effects, respectively. Daniel Promislow (University of Georgia) presented findings showing that, across species, selection for longevity inadvertently creates selection for decreased fecundity, suggesting that sexual conflict favors sex-specific genes. James Carey (University of California at Davis) discussed how in wasps, extended longevity is a precondition for the evolution of sociality, demonstrating how behavior can be tied to changes in longevity. These results from animal studies clearly demonstrate that behavior and predispositions are inextricably linked in dynamic developmental systems. Because animal systems can provide valuable insight into parallel systems in humans, interaction between animal and human researchers is critical.

Methodological considerations unique to aging

The study of aging provides a number of unique challenges for assessment. Can the same measurement model be applied to different age groups? Are the constructs that one is measuring really the same across development? Are there different social pressures on self-reporting behavior at different ages? Can a construct be assessed using the same measure across development? These challenges must be addressed in all aging research, including twin studies. To begin to explore these questions, Michael Stallings (University

of Colorado) studied Cloninger's construct of novelty-seeking in the AARP volunteer twin sample. They found that in 50-80 year olds, novelty-seeking did appear to be a static construct. Stallings also examined the question of whether we should be studying changes across age, as measured using a continuous variable, or in different cohorts. There was also discussion as to whether age may be the wrong variable all together to study, and whether increased efforts should be directed toward studying changes across developmental milestones. Following currently studied samples across development should prove helpful in answering many of these challenging questions regarding assessment across the lifespan.

Mortality also presents a special challenge in aging research. Often pairs are only used in genetic analyses when both twins are alive and able to respond; this can affect estimates of genetic and environmental influence. Nancy Pedersen (Karolinska Institutet) used multiple imputation models to impute missing data and death. These analyses suggests that the intrapair correlation often seen in twin studies is an artifact of survival; when corrected for by imputation for death, the data suggest that common environmental factors play a larger role than genetic factors.

New methods of analysis are currently being developed to model many of the complexities evident in developmental research. Steve Boker (University of Notre Dame) and Mike Neale (Virginia Commonwealth University) introduced their work on dynamical systems, or systems that exhibit time dependence in their states. These models can incorporate both linear and nonlinear elements, and have great potential for application to the study of aging. Jack McArdle (University of Virginia) expanded on the elegance of models now available for twin data. These models can incorporate external variables (both measured genotypes and environmental factors). They allow one to look for different growth patterns in different groups, and they can use change variables as the outcome. He emphasized a need for confirmatory, theoretically driven models. Finally, he discussed the need for better characterization of the assumptions and limits of current models, including the need for models that more readily allow for the incorporation of extended family members.

Finally, Andrew Heath (Washington University School of Medicine) reminded us that questions remain regarding the most appropriate point to start studying the aging process. As James Carey importantly pointed out, there is no study where behavior has been studied and recorded over the entire lifespan. In order to understand the life course, we must have the foresight to develop and follow-up studies of all developmental stages. Additionally, we must include measures at the baseline stages of prospective studies that will be relevant to long-term understanding of the aging process.

Gender differences

There are well-established gender differences in relation to aging. Women tend to live longer and are at a higher risk of dementia, but the reasons for this are unknown. It is possible that differential dementia is simply an artifact of differential mortality. Using Swedish aging data, Margaret Gatz (University of Southern California) presented data

demonstrating that when age is controlled for, there is no difference in incidence, age of onset or type of dementia between the sexes. However, there was suggestion of differences in influences on dementia, with males showing a greater influence of common environmental factors, and females showing greater evidence of genetic factors, with the possibility of some dominance. There was also some suggestion of different genes acting in males and females; however, environmental influences appeared to be shared. Understanding sex differences remains an important area of study in relation to aging; large, well-powered twin studies, including opposite sex pairs, and twin-family studies can help to answer questions about sources of these differences.

Continued importance of quantitative genetic studies in the genomic era

In the new post-genomic era, twin studies continue to be an important research methodology. As Andrew Heath discussed, multivariate and developmental twin studies still allow us to study many important questions about how genetic influences act, including how genes influence multiple behaviors, and how genetic influence unfolds over time. It is also important to embed twin studies in other major investigations of development, such as national surveys and longitudinal projects, to allow comparison of twins and singletons in representative samples, and to enhance the generalizability of twin studies. Large, population-based twin studies are also important to this end. Additionally, there is increased recognition of the importance of adding additional siblings into twin studies when possible, to enhance the power to detect both genetic and environmental effects.

Illustrating the important questions that continue to be addressed by twin studies, Matt McGue (University of Minnesota) and Kaare Christensen (University of Southern Denmark) fit latent growth curve models to depression symptomatology and physical functioning in the Danish cohort of twins. These models allow one to study genetic and environmental influences on both the mean level of the trait across time, as well as genetic and environmental influences on the rate of change in the trait across time. As Christensen pointed out, these analyses can also inform theories of aging: they found an increase in both genetic variance and common environmental variance in physical functioning over time, which supports both evolutionary and epidemiological theories of aging, respectively.

The use of endophenotypes and biomarkers

Longevity and disease related outcomes are distal variables often studied in relation to aging. However, efforts are underway to identify intermediate phenotypes that predict aging and/or survival. These endophenotypes or biomarkers may provide powerful quantitative indices of the aging process. Kaare Christensen reported on analyses of grip strength, a measure that correlates with indices of muscle strength and functioning, and mortality. Deborah Finkel (Indiana University Southeast) reported analyses of patterns of change among a number of biobehavioral variables, including forced expiratory volume, mean arterial pressure, grip strength, and motor functioning. She found that a linear model of change fit some measures, while others required nonlinear extensions. There

were also sex differences in rates of change, with men declining faster for some phenotypes. In addition to yielding quantitative indices of aging, studying patterns of change among biomarkers also has the advantage of providing dynamic endophenotypes for study. Interestingly, McGue reported that when disability was studied in relation to depressive symptomatology, disability was only weakly associated with depression; however, change in physical disability was a strong predictor of change in depression. Furthermore, this relationship was mediated environmentally, suggesting an important pathway for prevention and intervention efforts.

Need for multidisciplinary collaboration:

Bringing together skills and strengths from different fields of research is vital for progress. David Laibson (Harvard University) effectively spoke on the cross-over between diverse fields, by pointing out similarities between the goals of economists and those of behavior geneticists. Both fields have the goal of predicting behavioral outcomes; economists are interested in phenotypes such as asset accumulation; risk taking, as related to portfolio decisions; labor market outcomes, such as wages and retirement decisions; social network participation; and hedonics. To the extent that the significant influence of genes on a variety of behaviors has been demonstrated, economists are newly interested in capitalizing on genetic studies to inform prediction of behavioral outcome. Additionally, there is substantial methodological overlap between fields, as both fields largely work from a multiple regression framework.

The importance of collaboration between genetic researchers and social scientists is also underscored by the complexities involved in measuring the environment. Carol Ryff reminded us that most psychologists have, in fact, not focused on studying genetic influences, but rather have studied the environment. New interest in including environmental measures in genetically informative designs should encourage geneticists to seek the advice of outside environmental researchers in order to capitalize on their expertise in studying and measuring the environment.

Identifying specific genes

Questions remain regarding the best way to identify genes involved in behavioral processes. Some researchers suggest that we should focus on finding genetic effects first, and only once genes have been identified should we attempt to elucidate environments that may modify their effects. Others feel that studies of gene-environment interaction should parallel and complement studies of genetic main effects, as the identification of specific genes may still be a long time in coming. Taking into account gene-environment interaction may actually help further the identification of specific genes. There is no consensus on the best strategy to find genes that influence behavior. Larger pedigrees are likely needed, in addition to well-formulated lists of candidate genes. The issues that emerged at the NIA meeting and are summarized in this report—better characterization of the dynamic nature of genetic factors, gender differences, environmental factors, complementary animal and human models, and better assessment—will certainly be important to this end. Additionally, researchers should begin to consider the benefits of

banking biological samples, such as brains, from existent twin studies to anticipate their potential for future research. Finally, interdisciplinary relationships will be critical in furthering our ability to identify specific genes involved in behavior. These collaborations, both between researchers using different model systems and researchers in different fields, are sometimes hampered by differences in methodology and language. There is a need for training programs and conferences with the specific goal of acquainting researchers who have complementary areas of research to familiarize one another with their respective methodologies and to foster integrative research.

Outline of individual presentations

Summarized below are conclusions from each of the presentations made at the meeting.

Session I: Behavior Genetics and Aging: Where Are We Now?

- Genetics, aging and social sciences: where should we be going?

C. Ryff -- We need an increased emphasis on gene-environment interaction. Twin studies should be embedded in other major investigations, such a national surveys and longitudinal projects. Gender specific models of aging are needed.

D. Laibson – Economists are also interested in understanding behavior. Phenotypes of interest to economists are asset accumulation, risk taking, labor market outcomes, social network participation, and hedonics. There is substantial methodological overlap between economics and the behavioral sciences.

- Multivariate structure of adult personality -- M. Stallings

Cohort comparisons suggest that strict factorial invariance holds for novelty-seeking across older age cohorts in the AARP sample (50-96 years). Results also suggest measurement invariance for harm avoidance and reward dependence in these older cohorts. Modest age differences in means for novelty seeking and PS were found, but no age/cohort effects were evident for harm avoidance and reward dependence. There was no evidence for age and cohort differences in genetic or environmental influences from age 55-75.

- Depressive symptomatology and life style factors in the LSADT – M. McGue

Depression is a function of overall vulnerability and time-specific risk factors. Overall vulnerability appears to be strongly genetically influenced, while time-specific risk appears to be strongly environmentally influenced. Change in physical disability is the strongest predictor of change in depression. This relationship is environmentally mediated and may moderate genetic vulnerability.

- Gender differences in the etiology of dementia – M. Gatz

Once age is controlled for, incidence of depression does not differ by gender. In women, both additive and dominant genetic influences are important for dementia; however, in men, shared environment may play a role in addition to additive genetic influences. There are gender differences in cognitive impairment consistent with the dementia findings and possibly suggesting different influences on cognitive decline for women and for men, which might represent either different genes or different environments.

- Discussion – A. Heath

Seven key discussion points were raised: (1) Studying twins remains important in the molecular era. (2) It is important not only to study twins, but also to study additional family members, such as siblings, as well. (3) We need to think carefully about how early we should start prospective studies. (4) Generalizability remains an important concern. (5) Gene-environment interaction is important to study. (6) There is need for multidisciplinary interaction. (7) Assessment is an important concern, especially in the study of aging.

Session II: Modeling the Genetics of Behavioral Aging

- Age trajectories of genetic variance in physical functioning: a longitudinal study of Danish twins aged 70+ -- K. Christensen

There is an increase in variance in physical functioning over time. There is an increase in additive genetic variance, which is in agreement with genetic-evolutionary theory. However, there is also an increase in environmental variance, which is in agreement with ”wear and tear” theory. However, there is no change in heritability.

- The influence of mortality on twin models of change – N. Pedersen

Data from SATSA demonstrate that correlations are more stable after data imputation. Furthermore, when mortality is imputed, apparent genetic influence becomes common environmental influence. This may reflect genetic influence on mortality in this age group. In the OCTO twin sample, MZ similarity was found to be due to a very selected group of twins: those who survive. When selection is controlled for, no within pair correlation is left, suggesting the initial correlation was an artefact completely driven by intrapair correlation in mortality.

- Behavior genetic analysis of patterns of change in biobehavioral markers of aging – D. Finkel

Studying a variety of biobehavioral markers of aging, monotonic changes with age were found for forced expiratory volume, mean arterial pressure, and grip strength. Gender differences were found in intercept and slope for forced expiratory volume and grip

strength. There was an acceleration in decline with age for motor functioning and well-being. These findings suggest that aging is a cumulative product of multiple basic mechanisms. There are different patterns of aging for different markers of aging. There is evidence for both genetic and environmental influences on rates of decline in markers of aging.

- Nonlinear dynamic models and twin data – S. Boker & M. Neale

Dynamic models are an exciting new methodological tool. Applying these models to echocardiogram data, change in echocardiogram data was found to be due largely due to common and unique environmental components. More sophisticated models are possible, such as those allowing for dynamic genetic components and dynamic common environmental components.

- Discussion – J. McArdle

Recent papers demonstrate important increases in the sophisticated integration of developmental, genetic, and statistical concerns -- pointing to reliable results. We need to characterize and expand upon the built-in assumptions and limits of developmental genetics. We can do much more with the dynamic models, including kinetics, in studies of the "determinants". Expansion of the models to include even more family configurations remains important. These are difficult studies that will benefit from advances in measurement, such as environmental impacts.

Session III: Environment and context in behavior genetic studies of aging

- Environmental considerations in the study of genetic influences on aging – T. Wachs

We must use a systems context of development, and incorporate state of the art measures of the environment in our studies. Studying the environment in relation to the elderly poses many unique challenges. The elderly have a multilevel environment. At advanced ages, there is likely an increase in the importance of the physical environment. We must go beyond the study of family influences and incorporate additional aspects of the environment. The subjective environment must be assessed. There must be an understanding of active person-environment covariance. Finally, research should be directed toward maximizing the fit between the person and the environment.

- Contextual decomposition of environmental variance in quantitative genetic research – K. Whitfield

Preliminary data from the Carolina African-American Twin Study of Aging was presented to illustrate several of the challenges of assessing the environment in

genetically informative designs. We must understand chronic effects of environmental influences, and the influence of environmental exposure over time. We must be careful in selecting behavioral versus objective measurements. The meaning of context could be key, both in terms of the individual and the community. We must work on ways to integrate context into genetically informative designs.

- Discussion – S. Hofer

Research in the social sciences has essentially been conducted in two bodies: those who study the environment and ignore genetic influences, and those who study genes, largely ignoring the environment. We must work on assessing environment across the lifespan and better understanding the taxonomy of the environment.

Session IV: Discussion – Where should we be going? Other phenotypes and questions for genetic studies of aging?

- D. Laibson Both economists and behavior geneticists are largely concentrating on the same goal—understanding and predicting behavior. There is substantial methodological overlap between the fields. Economists are interested in incorporating genetic influence into their models to maximize their power and improve prediction. This underscores the need for multidisciplinary collaboration.

- C. Ryff We must not forget the importance of resilience, in the context of studying individuals who are at genetic risk but do not manifest problems. Additionally, it is important to study the reverse—individuals who have encountered a number of environmental risk factors but do not suffer adverse effects. It is important to apply genetically informative designs to the study of social inequality and health.

Session V: Model organisms and animal studies to understand genetics of behavior and aging

- Gene mapping and gene expression in studies of aging mice – R. Miller

Using full sibling mice, genes have been identified whose effects are limited to early or later stages of life, and genes whose effects are sex-specific. Biomarkers measured at 18 months can predict life span, whereby, regardless of the cause of death, mice died early; genes for this phenotype have been mapped to chromosomes 4 and 13. This suggests that aging should be viewed as a process, rather than within a disease construct. Finally, genes have been identified in dwarf mice that influence delayed aging. New gene array techniques are being used to look for genes differentially expressed in normal and dwarf mice.

- Choosy females, killer males: an evolutionary perspective on sex and death -- D. Promislow

Mate choice is costly for males; many of the traits that females choose on (i.e., bright plumage in birds) are costly for males. Reproduction is costly for females. Females that do not mate tend to live longer; this has been demonstrated in flies and there is some suggestion that this may be the case in humans, as well. Sex specific genes have been identified for longevity in flies, which may reflect sexual conflict.

- J. McClearn – Commonalities between animal and human studies: prospects and limitations

Animal models have the potential to elucidate aging mechanisms that may be acting in humans. There is a need for bi-directional interaction and communication between human and animal researchers. There are many examples of gene-environment interaction in animal models. Cooper and Zubek's 1958 study on maze-bright and maze-dull mice provides a classic example of gene-environment interaction. Although the exact interactions may not translate to human work, animal models provide illustrations of the dynamic processes that are likely influencing the human aging process.

- J. Carey – Discussion

Several topics related to the study of aging were discussed. Firstly, a new end-of-life behavior in the medfly was reported; supine behavior predicted time-to-death in male Mediterranean fruit flies. Secondly, the co-evolution of sociality, longevity and behavior was discussed. Extended longevity is a precondition for the evolution of incipient sociality. Sociality, in turn, creates conditions for the evolution of further extensions in longevity, which then creates conditions for the evolution of even greater degrees of sociality. Behavioral changes are inextricably tied to changes in longevity extension and sociality. Finally, there was general discussion and thoughts on the study of the life span. The extension of life has led to the addition of new age classes, causing increased need to understand dementia and neurological disorders. There has also been an emergence of robust elderly, leading to new issues regarding retirement and later life. Life cycle modification has raised new life-course issues regarding care-giving.

Genetics, Behavior and Aging Meeting Agenda
March 29, 2002

National Institute on Aging
Gateway Building, 5th floor conference room
7201 Wisconsin Avenue, Bethesda, MD

Time	Session Title	Speaker
8:00	Coffee	
8:10-8:25	Welcome and Introductory Remarks	R. Suzman/J. Harris
8:25-09:55	**Session I: Behavior Genetics and Aging: where are we now?**	
	Genetics, aging and social sciences: where should we be going?	C. Ryff /D. Laibson
	Multivariate Structure of Adult Personality	M. Stallings
	Depressive Symptomatology and Life Style Factors in the LSADT	M. McGue
	Gender Differences in the Etiology of Dementia	M. Gatz
	Discussion	A. Heath
09:55-10:05	Break	
10:05-11:45	**Session II: Modeling the Genetics of Behavioral Aging**	
	Age Trajectories of Genetic Variance in physical functioning: a longitudinal study of Danish Twins Aged 70+	K. Christensen
	The Influence of Mortality on Twin Models of Change	N. Pedersen
	Behavior genetic analysis of patterns of change in biobehavioral markers of aging	D. Finkel
	Non-linear Dynamic Models and Twin Data	S. Boker & M. Neale
	Discussion	J. McArdle
11:45-12:30	Lunch	
12:30-13:25	**Session III: Environment and Context in Behavior Genetic Studies of Aging**	
	Environmental considerations in the study of Genetic Influences on Aging	T. Wachs
	Contextual Decomposition of Environmental Variance In Quantitative Genetic Research	K. Whitfield
	Discussion	S. Hofer

13:25-13:45	**Session IV: Discussion - Where should we be going? Other phenotypes and questions for genetic studies of aging?**	D. Laibson/ C. Ryff
13:45-13:55	Break	
13:55-15:15	**Session V: Model Organisms and Animal Studies to Understand Genetics of Behavior and Aging**	
	Gene Mapping and Gene Expression in Studies of Aging Mice	R. Miller
	Choosy females, killer males: an evolutionary perspective on sex and death	D. Promislow
	Commonalities between animal and human studies: prospects and limitations	J. McClearn
	Discussion	J. Carey
15:15-16:00	**Session VI: Wrap up and Future Directions**	**Discussants & Participants**