The Interaction of Genes, Behavior, and Social Environment

For most people, the probability of having a physical or mental disability increases with age, as does the number of ailments they might have at any time—particularly after age 70. Memory loss and other cognitive impairments are more likely with age and, in addition, the elderly tend to be more socially isolated. These changes may occur because of genes, behavior, the environment, or interactions among these factors. Understanding the nature of these interactions could be the key to designing effective public health and medical interventions to slow or even reverse the onset of mental and physical conditions associated with aging. Knowing the extent to which genes counteract or exacerbate health risks such as smoking, obesity, or pollution may help doctors and public health officials target the most vulnerable populations, improving health in the later years of life for millions of people. The Division of Behavioral and Social Research at the National Institute on Aging supports research on the interaction of genes, behavior, and the social environment. This newsletter highlights recent results from research that assesses the effects of interactions among genes, behavior, and the environment.

What Is Gene-Environment Interaction?

In the context of gene-environment interaction research, the word "environment" refers to a broad social context, including relationships, communities, institutions, pollutants, diet, and medications. The environment also extends to conditions experienced while still in the womb. Genes work together with these elements of the environment to determine specific physical, behavioral, and health attributes (Boardman and Shanahan 2009).

Gene-environment research incorporates data on a person's genes into the study of observable physical, psychological, and biological traits—anything from skin color to depression. These traits are the result of both genes and the physical and social environment. By integrating genetic information into the study of a person's behaviors or characteristics, researchers aim to better understand and explain a variety of outcomes, ranging from levels of health and wellness to specific personality traits. Based on research findings to date, scientists generally agree that neither specific genes nor the sum total of a person's genes solely determines health or behavior. Instead, the interaction among environment, genes, and behavior produces an individual's observable characteristics and behavior (Shanahan and Boardman 2009). For example, a person may have a high genetic propensity for alcoholism but whether he or she becomes an alcoholic depends on lifelong patterns of stress, social support, self-control, and other factors.

Gene-environment interaction research is particularly important in the area of aging. Risky health behaviors and negative environmental effects may start to catch up with individuals at older ages, with interaction among genes, behaviors, and experiences contributing to poor health. Understanding the consequences of specific gene-environment interactions may enable researchers to develop treatments or recommend policies that reduce negative

consequences of aging and improve health and quality of life at older ages.

Inflammation

Inflammation is a widely used measure of injury or stress to the human body. As part of its response to negative stimuli like infection, injury, or irritation, the body sends fluids to the affected area producing symptoms such as swelling, pain, and fatigue. Although inflammation causes many of the negative results of injury or illness, inflammation itself is a positive sign of the body working to heal itself. However, these inflammatory responses take a toll, and the energy that healing from injury or infection requires can deplete the body. Differences in a person's genes can determine the extent to which inflammation causes harm. Some people may experience more long-term consequences of infection than others, depending on how each individual's set of genes reacts to injury or illness.

The two main types of inflammation that are of interest in gene-environment research are acute inflammation and persistent (chronic) inflammation. Acute inflammation occurs rapidly and there is usually a clear and distinct end to symptoms. Chronic inflammation may or may not occur as rapidly as acute inflammation and is characterized by its persistence and the symptoms' lack of resolution. Chronic inflammation occurs when the affected tissues are unable to overcome the negative effects of the stimuli. Research links many of the negative effects of aging and certain diseases to either the long-term consequences of acute inflammation that may emerge years after injury or infection or to the persistent effects of chronic inflammation.

The body's inflammatory responses can compound over the entire lifespan, including the time spent in the mother's womb, and can have detrimental effects on an individual's health at all ages. This compound effect might not show up until decades later and, as a result, may not be attributed to the specific injury or illness experienced earlier in life. For example, if an individual contracts an illness in childhood, the body responds to fight off the infection. Even after recovery, the stress experienced during the childhood illness can have a negative effect on health later in life, possibly contributing to the cause of death decades later.

Survivors of early childhood illness and injury are burdened by the remnants of genetic matter associated with their body's response to these conditions and by the body's attempt to heal and remove the materials that caused inflammation. For these survivors, the presence of these substances and the body's response begin in childhood and continue into adulthood. A reduction in chronic infections, and thereby in inflammation, has been linked to overall improvements in life expectancy since 1850. Because inflammation is linked to most of the chronic diseases prevalent among the elderly, reducing the number of infections and inflammation-inducing stimuli would both increase life expectancy and decrease the prevalence of chronic diseases like cancer and atherosclerosis (hardening of the arteries) in old age (Finch 2012).

During 1918 and 1919, a flu pandemic swept the United States, killing nearly 1 percent of the total population. Many of the flu deaths were from secondary infections that caused pneumonia, especially in pregnant women. Mazumder and colleagues (2010) examined the cohort born during the flu pandemic and found a higher prevalence of chronic disease in adulthood, likely as a result of the maternal infections experienced in utero. The cohort born to flu-infected mothers who survived the pandemic had lower education levels and earnings, as well as an increased risk of neurodevelopmental defects, including schizophrenia and autism, than the cohort born before or after the pandemic. Men were more susceptible to chronic disease than women born in the same cohort, a fact the researchers attributed to the interaction of predominantly male behaviors (for example, smoking) with the effects of the flu encountered in the womb.

Several studies have linked inflammation to atherosclerosis. One study (Nazmi et al. 2010) examined infections associated with inflammation and found that the number of infections was a more important predictor of inflammation than the independent contribution of each of the particular infections observed. This research suggests that atherosclerosis may be related not only to a person's environment but also to the amount of stress a person's system is under. However, Gurven and colleagues (2009) found that cardiovascular disease was not present in a preindustrial indigenous population

with a high load of inflammation and infection. In this population, even with many of the risk factors that are associated with chronic heart conditions (such as high c-reactive protein), low caloric intake and high levels of physical activity appeared to counteract the detrimental effects of chronic inflammation.

Health Disparities

Researchers are also interested in the health differences among individuals based on their race and ethnicity. Diez-Roux and colleagues (2009) examined differences between older whites and minorities using telomere length, a genetic measure of stress on a person's body. The telomere is a protein structure found on the ends of chromosomes. It protects against DNA degradation and when measured can indicate the number of times a cell has replicated. The shorter the telomere, the more times the cell has divided and the higher the level of measurable stress on that cell. Even after controlling for factors of physical health, socioeconomic status, diet, and body mass index, the telomere length of black and Hispanic participants was shorter than for whites. However, telomere length did not differ among black, white, and Hispanic newborns, suggesting that racial differences in telomere length may emerge and increase with age.

King, Morenoff, and House (2011) also explored measures of an individual's overall risk for adverse health events, or cumulative biological risk, as a way to study racial and ethnic disparities in health. They created an index of cumulative biological risk from eight indicators that were set to a level considered to be at risk of negative health outcomes. They found substantial racial and ethnic differences in the cumulative biological risk of individuals, even after controlling for sociodemographic characteristics and health behaviors. However, no significant differences existed among racial and ethnic groups from socioeconomically similar neighborhoods. These results highlight an important element of an individual's health: his or her physical environment. Some elements of an individual's environment can be improved—lowering pollution, increasing access to healthy food and clean water, and increasing the availability of safe places to exercise and play. Not all the negative health outcomes may be improved by changing individual behavior. The physical environment at home and at work also plays a major role in individual health.

Cognitive Decline and Memory Loss

Memory loss and other elements of cognitive decline are likely to affect many older adults as life expectancy increases

and people live longer than previous generations. Even in the healthiest individuals, some degree of aging-related mental decline is inevitable (Small et al. 2012). Cognitive decline at older ages ranges from less serious conditions—loss of episodic (personal events) memory, semantic (general knowledge) memory, or slowed speech—to more serious ailments such as Alzheimer's disease and other forms of dementia. To varying degrees, all these types of cognitive decline may negatively affect an older person's life by limiting independence and the ability to engage in everyday activities.

In a study of twin pairs, McArdle and Plassman (2009) found that memory loss at age 75 and older was related to genetic differences and not to environmental influences. The researchers gave word-recall tests up to three times over a 12-year period to 6,000 twin pairs who were ages 59 to 75 at the start of the study. They found that memory loss before age 75 was different between twin pairs, suggesting that an individual's lifetime environmental influences contributed to memory decline before age 75. However, memory decline at age 75 and older was more similar between twin pairs. They concluded that genetics play the more important role in memory decline at age 75 and beyond. Understanding the genetic component to memory decline at older ages may be an important step to stopping or reversing memory loss and more serious conditions, including dementia.

Social Interaction

Social consequences of aging also may negatively affect older people. Older people may withdraw from social situations when they feel sick or have limited mobility. However, some evidence also suggests that poor health outcomes are not the cause of social withdrawal but the result. When a person is sick, a cellular response occurs in the brain that signals "sickness" (such as fatigue and aches) associated with illness. This response makes individuals rest and avoid other people. These behaviors help the recovery process and prevent others from becoming infected. Inangaki and colleagues (2012) found that when an individual's brain is stimulated by a response to inflammation, he or she avoids negative social stimuli and ultimately withdraws, suggesting that inflammation might be the cause of the avoidance behavior.

The same avoidance behavior that aids in physical healing may be an outcome of cognitive decline. Small and colleagues (2012) found that withdrawal from social situations in the older population is an active-reactive relationship: Engaging in social activities may serve to buffer some of the negative consequences of aging but older people with poorer

cognitive performance may withdraw from some social situations due to their poor memory or their slowed speech. In this study, researchers were interested in the timing of withdrawal from physical or social activities and the onset of slowed speech and memory loss. If they could identify which came first, they could pinpoint interventions to help prevent these types of cognitive decline. Whether the withdrawal preceded the memory loss and slowed speech or the slowed speech and memory decline came before the withdrawal was not important. In either case, older people can benefit from engaging in social situations. For people experiencing problems with memory loss, engaging in social and physical activities may serve to slow this deterioration; for those not yet experiencing memory loss or slowed speech, engaging in activities might serve to protect them from these outcomes. The researchers suggest that individuals be aware of their abilities and continue to engage in social activities as much as possible.

Looking at the population more broadly and not just at the elderly, genetic stratification of the human population may have consequences for health behavior. Genetic stratification is known to be the result of geographic sorting and the tendency for people to reproduce with others that share similar traits. One study (Fowler, Settle, and Christakis 2011) examines the possibility that other types of associations may produce genetic stratification. This study looks at six different types of genes and shows that even after accounting for genetic stratification in the population, two genes are useful in guessing who befriends whom. Individuals with one of these genes (DRD2) are likely to associate with others with the same gene, whereas individuals with another gene (CYP2A6) are not likely to associate with others that also have the CYP2A6 gene. Fowler and his colleagues suggest that the finding with respect to DRD2 may be related to differences among the social networks of drinkers and nondrinkers. DRD2 has been associated with alcoholism, and it is possible that drinkers are drawn to social environments that nondrinkers avoid.

Modeling of genetic variation in human social networks has provided some insight into the way that genes affect human behaviors and how these behaviors spread from person to person. Based on differences between genetically identical twins and same-sex twins that share only 50 percent of genes, some studies have found that genes appear to play a role in personality, intelligence, and several other behavioral traits. Fowler, Dawes, and Christakis (2009), using a similar design, found that genetic factors play a substantial role in determining how many times a person

in a social network is named as a friend. They also found that genetic factors partially explain how likely it is that a person's friends know each other. The reasons behind genetic differences in the ability to attract friends or the desire to introduce friends is not clear, but investigating the relationship between genetic traits and the type of social networks a person generates may be helpful in understanding more about how social networks contribute to emotions and health behaviors (such as smoking, drinking, or obesity).

Genetic Buffers

An important consideration of gene-environment research is the direction of the observed relationships. Sometimes genes dictate the environment's effect, instead of the environment affecting the way genes are expressed. Cole and his colleagues (2011) found that in older adults, the presence of certain genes combined with adverse socioeconomic conditions (particularly high-crime and high-poverty neighborhoods) increase the inflammatory response to the environment. However, the same genes and socioeconomic conditions do not increase inflammation for people of all ages. The particular gene that causes an inflammatory response in adults acts to desensitize adolescents to the adverse effects of their socioeconomic and environmental conditions. This may explain why genes that are associated with poor health in adults still

exist today: For young people these same genes act as protective factors that aid survival to adulthood.

With genetic information, researchers can begin to determine the gene-environment interactions that result in poorer health in an individual. Even under identical circumstances, some individuals may contract certain illnesses while others may not. Cole (2009) examined the types of human genes that may be expressed differently depending on a person's environment. Future research will likely begin to more accurately identify which genes are subject to social regulation and which are not. With a greater understanding of which genes interact with which elements of the social environment, steps may be taken to prevent and perhaps reverse some of the negative consequences of the aging process.

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National Institute on Aging research goals
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Integrating genetic data into behavioral and social research
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