

## Oxford Handbooks Online

### **The Gene-Culture Interaction Framework and Implications for Health**

Joni Y. Sasaki, Jessica LeClair, Alexandria West, and Heejung S. Kim

The Oxford Handbook of Cultural Neuroscience

*Edited by Joan Y. Chiao, Shu-Chen Li, Rebecca Seligman, and Robert Turner*

Print Publication Date: Dec 2015

Subject: Psychology, Cognitive Neuroscience, Personality and Social Psychology

Online Publication Date: Apr 2016 DOI: 10.1093/oxfordhb/9780199357376.013.20

### **Abstract and Keywords**

Based on the framework of gene-environment interactions (G × E), the gene-culture interaction framework demonstrates that a more complete understanding of thoughts and behaviors relevant to health may come from incorporating both genetic and cultural factors. Genes may interact with culture such that genetic predispositions lead to different outcomes depending on culture, and cultural differences on a given outcome may vary depending on genetic predispositions. We provide an overview of G × E research and some of the underlying biological mechanisms of these interactions. We explain the gene-culture interaction framework and discuss how culture is an important form of environment to consider that makes theoretical contributions unique from other forms of environment typically studied in G × E research. We discuss theoretical questions raised by gene-culture interaction research and specify how the gene-culture interaction framework can be applied to certain health issues.

Keywords: Gene-environment interaction, gene-culture interaction, determinants of health, framework, culture

Imagine two wine grape varieties across two different climates. Whereas the Cabernet Sauvignon variety may thrive in warm climates, the ideal climate for Riesling is relatively cooler. Knowing when and why grapes produce optimal fruit for good wine requires understanding the *interaction* of a number of factors, such as grape variety based on genes and climatic aspects of the environment: These grape varieties thrive in either warm or cool climates, depending on their particular variety. Similarly, variation in human thought and behavior relies on both genetic and environmental factors, as well as the interaction between the two. Focusing only on genetics as a source of variation ignores the reality that the same genetic tendency can lead to different outcomes according to the environment. Likewise, focusing on the environment as the sole

explanatory force overlooks the fact that the same environment can have different consequences for people depending on their genetic tendencies. In order to make predictions about when or why people think and behave the way they do, it is useful to consider their biological predispositions together with the particular environmental context in which they exist.

Among the many ways in which environments vary, culture—the part of the environment created and shared among social beings and passed down over generations (de Waal, 2001; Geertz, 1973; Herskovits, 1948; Triandis, 2007)—is one important aspect of environmental variation that has only recently been considered together with genes. Cultural psychology is a field that investigates cultural variation in systematic ways and has grown considerably in its breadth of topics and scientific approaches during the past 25 years. Recently, the emerging field of cultural neuroscience has built on cultural psychology, tackling questions on culture, mind, and the brain by integrating cultural psychological research with cutting-edge techniques and perspectives from neuroscience (for review (p. 280) and proposed framework of cultural neuroscience, see Kim & Sasaki, 2014). Using cultural psychology and cultural neuroscience as foundations, our research has examined gene-culture interactions, or the dynamic interplay of genes and culture as they jointly influence psychological outcomes (Kim, Sherman, Sasaki, et al., 2010; Kim, Sherman, Taylor, et al., 2010; Kim et al., 2011). Our perspective is that not only do both genes and culture act as independent sources of influence, but also, importantly, they interact to predict various outcomes. Therefore, the gene-culture interaction framework examines how culture can shape the way genetic tendencies are expressed and also how cultural influences may change depending on genetic predispositions.

Because the gene-culture interaction framework considers the sociocultural context as one source of psychological variation that interacts with biological predispositions, this framework may be important for understanding the complexities surrounding health within and across diverse societies. In particular, many issues relevant to physical and psychological health, including the determinants of health outcomes, treatments for health problems, and intervention strategies, may vary across cultures. Within any society, there exist groups of people that differ along multiple dimensions. In addition to ethnicity or nationality, which are the most commonly studied dimensions of culture, there are many other forms of culture (Cohen, 2009) that have important health implications, such as religion (Koenig & Larson, 2001; McCullough, Hoyt, Larson, Koenig, & Thoresen, 2000), region (Plaut, Markus, & Lachman, 2002), and social class (Adler, Epel, Castellazzo, & Ickovics, 2000; Adler & Stewart, 2010; Plaut, Markus, Treadway, & Fu, 2012). These different forms of culture vary not only within but also across societies, and therefore, a cultural perspective can help broaden understandings of health beyond the populations that tend to be studied most (i.e., “WEIRD” participants who are Western,

educated, industrialized, rich, and democratic; Henrich, Heine, & Norenzayan, 2010a, 2010b). At the same time, there are important individual differences in genetic predispositions, and these predispositions may predict health outcomes differently depending on the cultural context. Given that genes interact with environmental factors to influence health-related outcomes (e.g., Caspi et al., 2003; Johnson & Krueger, 2005; Kim-Cohen et al., 2006; Larsen et al., 2010; Miller et al., 2009; Schmid et al., 2010; Taylor et al., 2006) and that there are cultural differences in how people strive for and achieve a healthful life (Oishi & Diener, 2001; Plaut et al., 2012), the gene-culture interaction framework has great potential for predicting and explaining the complexity that surrounds health issues for diverse groups.

In this chapter, we first provide an overview of research on gene-environment interactions (gene  $\times$  environment, or  $G \times E$ ) and the biological mechanisms underlying these interactions. Second, we explain the framework of gene-culture interactions (gene  $\times$  culture, or  $G \times C$ ), including how this framework builds on gene-environment research and makes unique theoretical contributions. We also discuss some potential mechanisms of gene-culture interactions, review empirical evidence supporting the  $G \times C$  framework, and bridge the framework with a prominent theory in the study of genes and culture—that of gene-culture coevolution. In the next section, we discuss theoretical issues and questions raised by  $G \times C$  research, including implications for findings in cultural psychology and issues surrounding covariation of cultural and genetic differences. Finally, we specify how the  $G \times C$  framework can be applied to health research. In so doing, we explain the theoretical value of taking a cultural perspective in issues of health, suggest future areas of research relevant to health, and offer insight on how this research has implications for public health policy.

## Gene-Environment Interactions and Underlying Biological Mechanisms

The framework of gene-environment interactions ( $G \times E$ ) is one that should seem familiar to many psychologists, particularly in social and personality disciplines, and it also has certain advantages compared to other interactionist models of behavior. The idea that something about the person (in this case, genes) interacts with something in the environment (e.g., the social context) is reminiscent of classic work from person  $\times$  situation theory (Mischel, 1990; Mischel & Shoda, 1995), which addresses how personality can interact with situational contexts to influence behavior. Consideration of genetics from a similar perspective raises a number of novel questions and potential implications for psychology. Some of the underlying biological mechanisms of  $G \times E$

interactions, for example, may potentially be incorporated into theories of psychological phenomena. Genetics research also offers a particularly promising way to contribute to an understanding of cultural differences in basic (p. 281) psychological processes, including health-related outcomes.

The long-standing nature-nurture debate focuses on distinguishing the distinct influences of genes versus environment. Rather than treating the two factors separately, the  $G \times E$  interaction framework describes the phenotypic effects of interactions between individual genetic variation and the environment. The framework proposes that environmental conditions may moderate the psychological outcome of a particular genetic sequence or that genetic predispositions may moderate the relationship between the environment and an outcome (Caspi et al., 2002, 2003). In other words, an individual could be genetically predisposed toward a particular psychological outcome, but that outcome may only occur given specific environmental pressures. For example, Caspi and colleagues (2003) found that carrying the short (s) allele of the 5-*HTTLPR* polymorphism of the serotonin transporter (*SLC6A4*) gene promoter region increases the likelihood of showing depressive symptoms compared to carrying the long (l) allele, but only when coupled with exposure to life stress (for recent meta-analytic support of this  $G \times E$  finding, see Karg, Burmeister, Shedden, & Sen, 2011; but see also Risch et al., 2009).

Originally studied in the context of disease susceptibility, genes implicated in environmental sensitivity, such as the s allele of 5-*HTTLPR*, have been referred to as “risk” genes (e.g., Caspi et al., 2003). Recently, however, such genes have been reconceptualized as “plasticity” genes, rather than as linked to mostly positive or mostly negative outcomes, in order to highlight the malleability rather than valence of particular genetic predispositions (Belsky et al., 2009). In addition to 5-*HTTLPR* (Caspi et al., 2003; Cheon, Livingston, Hong, & Chiao, 2014; see also Chapter 17, this volume),  $G \times E$  interactions have been reported for various other genes, including the gene encoding monoamine oxidase A (*MAOA*) (Caspi et al., 2002; Foley et al., 2004; Kim-Cohen et al., 2006) and the dopamine D4 receptor (*DRD4*) gene (Bakermans-Kranenburg & van IJzendoorn, 2011; Sasaki et al., 2013). In a study of intervention effects on child behavior, a repeat polymorphism in *DRD4* moderated the effectiveness of the intervention (Bakermans-Kranenburg & van IJzendoorn, 2011), suggesting a differential susceptibility to environmental inputs dependent on genetic differences. Another study investigating the interaction between the environment and variants of the *DRD4* gene found  $G \times E$  interactions on even short-term exposure to environmental conditions: Participants carrying 2- or 7-repeat allele variants of *DRD4* were more susceptible to the influence of religion priming on prosocial behavior compared to participants without these variants (Sasaki et al., 2013). Across multiple genes and investigations, there is evidence that

people with certain genetic variants of “plasticity genes” may be more susceptible to environmental influence in particular domains.

At the molecular level, environmental factors may interact with genes by influencing the regulation of gene expression, which is a crucial link between genes and their phenotypes. Gene expression is the process of synthesizing a biologically functional molecule from DNA, and the capacity to adapt gene expression in response to physiological changes or environmental conditions is a basic biological mechanism. For instance, in response to being wounded, an injured organism might upregulate the expression of genes relevant to wound recovery (Slavich & Cole, 2013). Similarly, external social factors could activate biological pathways to regulate gene expression. Stress and social isolation, for instance, have long been associated with poorer immune system functioning (Seeman, 1996), and a study examining white blood cells provided evidence linking social to biological factors at the level of gene expression (Cole et al., 2007). In particular, among adults who felt less socially connected, pro-inflammatory genes were upregulated, whereas anti-inflammatory genes were downregulated, providing molecular evidence for the relation between social isolation and elevated risk for inflammatory disease.

Social signal transduction, first studied in the context of animal models (Robinson, Fernald, & Clayton, 2008), is a process explaining how social conditions might alter gene expression through transcription factors, which are proteins that regulate the transcription of DNA into mRNA (Slavich & Cole, 2013). Specifically, social signal transduction emphasizes that subjectively perceived social environment threats may affect hormone and transmitter levels, leading to changes in the activity of transcription factors. For instance, feelings of loneliness or social isolation have been linked to the activation of inflammatory genes and inhibition of antiviral genes (Slavich et al., 2010), and even the mere threat of social loss appears sufficient to alter gene transcription dynamics (Miller et al., 2008). The process of social signal transduction underscores the point that an individual’s subjective perception (p. 282) of social conditions as either threatening or nonthreatening may at times be more influential than what is objectively the case (see also Chapter 17, this volume).

Individuals may also vary in their signal-transducing potential depending on differences in their genes. For example, a study on the link between environmental adversity and health outcomes examined a single nucleotide polymorphism (SNP) in the promoter region of the human interleukin-6 (IL-6) gene, which is involved in the inflammatory response (Cole et al., 2010). Particularly within the promoter and enhancer region of genes, genetic sequence variations such as SNPs may alter the binding affinity of transcription factors. This SNP of IL-6 inhibits binding of the transcription factor *GATA1*, which typically activates in response to environmental adversity, and thus, people

carrying the low-binding-affinity variant of the IL-6 gene show an inflammatory response that is unrelated to exposure to environmental adversity.

Behavioral and health outcomes may also be influenced by epigenetics, which are processes that can affect gene expression without altering the underlying genetic sequence (Ledón-Rettig & Pfennig, 2012). Molecular-level processes, such as methylation, or the addition of methyl groups, may prevent transcription factors from accessing DNA, possibly preventing the synthesis of gene products. A key finding on how epigenetic processes contribute to behavioral variation showed that maternal care in rats is associated with differential methylation of the glucocorticoid receptor (GR) promoter region in the brain hippocampi (Weaver et al., 2004, 2005). The offspring of rat mothers who naturally exhibited greater pup licking and grooming behavior showed decreased methylation of the GR promoter region in the hippocampi. Greater methylation of the GR promoter has been found to reduce gene expression and to lead to a greater disposition for anxiety (Meaney, 2001; Weaver et al., 2004).

In humans, there is evidence that epigenetic regulation of genes may be involved in various social processes and mental health outcomes. For example, in a study investigating methylation status of a regulator region (CpG island) of the oxytocin receptor gene (*OXTR*) in peripheral blood cells and temporal cortex, individuals with autism showed increases in methylation compared to controls (Gregory et al., 2009). The increased methylation of this regulator region was specifically associated with decreased *OXTR* transcription in an area of the temporal cortex adjacent to the temporal parietal cortex and near the superior temporal sulcus (STS), a brain region implicated in social cognition (Allison, Puce, & McCarthy, 2000; Pelphrey & Morris, 2006). DNA methylation of *OXTR* may also play a role in individual variation in social information processing. The DNA methylation status of *OXTR* was found to predict neural activation of areas of the brain implicated in social processing in response to ambiguous social stimuli (Jack, Connelly, & Morris, 2012).

Unlike sequence variations, which are relatively stable across an individual's lifetime, there is emerging evidence that epigenetic modifications may occur dynamically in response to situational conditions. Immediately following a stressful experimental task, for instance, the methylation status of the stress-associated gene *OXTR* first increases, and then once the stressor ends, methylation status decreases below baseline (Unternaehrer et al., 2012). Epigenetic mechanisms may play an important role not only for long-term influences of environmental conditions on gene expression but also for short-term, rapid changes in gene expression in response to situational social stressors. Basic molecular mechanisms that underlie gene expression thus provide a biological

pathway for environmental influences to penetrate deeply, altering patterns of gene regulation and expression.

Advances in molecular biology have greatly increased scientific understandings of the mechanisms through which different social environments lead to changes in gene expression and thus behavior. In addition to investigating potential mechanisms more on the genetic side of the  $G \times E$  equation, our perspective is that incorporating a cultural approach in the  $G \times E$  framework adds the richness of cultural content to the environment side of the equation and may ultimately elucidate some of the psychological processes underlying  $G \times E$  effects.

## Gene-Culture Interaction Framework

Building on the gene-environment framework, the gene-culture interaction ( $G \times C$ ) approach provides one possible way of reconceptualizing the environment to include the cultural context (Kim, Sherman, Sasaki, et al., 2010; Kim, Sherman, Taylor, et al., 2010; Kim et al., 2011). The “environment” in the  $G \times E$  framework is a broad concept that can include anything from resource availability and weather variability to social environments in the family and the local society. Types of social (p. 283) environments can then be meaningfully partitioned into the *personal environment*, or individual variation in experiences and events, such as stress in the home setting (e.g., Taylor et al., 2006), and the *cultural environment*, or beliefs, values, practices, and products that constitute a shared system of meaning, such as the Western emphasis on independence and personal choice (e.g., Markus & Kitayama, 1991). Although there are many ways to potentially parse the environmental component of  $G \times E$ , we argue that focusing on the cultural part of the environment, as in the gene-culture interaction framework, is particularly important both theoretically and practically.

Although no one definition of culture is uniformly agreed upon, there are key components that many scientists are likely to endorse. Most would agree that culture is nonbiological—that is, nongenetic. Via evolutionary processes, social organisms may be biologically prepared with the capacity to develop culture (Tooby & Cosmides, 1992), and genes and culture may interact (Dressler, Balieiro, Ribeiro, & Dos Santos, 2009; Kim, Sherman, Sasaki, et al., 2010; Kim, Sherman, Taylor, et al., 2010; Kim et al., 2011; Kitayama et al., 2014; Sasaki, Kim, & Xu, 2011) and mutually influence each other in processes of gene-culture coevolution (Chiao & Blizinsky, 2010; Feldman & Laland, 1996; or dual inheritance: Boyd & Richerson, 1985; see also Cavalli-Sforza & Feldman, 1981; Durham, 1990, 1991; Fincher, Thornhill, Murray, & Schaller, 2008; Lumsden & Wilson, 1981) to

ultimately shape the neural processes underlying thought and behavior (see Chiao & Immordino-Yang, 2013). At the same time, however, culture can be separated from genes. Although culture influences and is influenced by biological processes, culture itself can be understood as beliefs, values, practices, and products that are socially created rather than genetically inherited by living beings (de Waal, 2001). Once socially created, these environmental features must then be socially transmitted to others and passed down over multiple generations such that they are maintained well beyond the lives of their original creators (Berger & Luckman, 1966). These characteristics, some have argued, are among the hallmarks of culture (de Waal, 2001; Geertz, 1973; Herskovits, 1948; Triandis, 2007).

Culture exists not only outside the self in the form of cultural products, or tangible, public representations such as art and media, but also inside the mind (Cohen, 2009; Kim & Markus, 1999; Shweder, 1995). In our approach, the  $G \times C$  interaction framework incorporates both aspects of the cultural environment. Thus, consideration of culture as a form of environment provides an understanding of how an individual's own beliefs and values are shared with others and how these mutually shared meanings allow people to interpret events and understand their experiences. Shared meaning constitutes an important part of culture that is unique from other forms of environment and is one of the main strengths of considering cultural and psychological factors in  $G \times E$  research.

## Mechanisms of the Gene-Culture Interaction Framework

Although the biological mechanisms of  $G \times C$  interactions have yet to be clearly elucidated, some of the known biological mechanisms of  $G \times E$  interactions may suggest possible mechanisms linking the cultural environment to genes. One way of conceptualizing culture is as socially shared patterns of mental processes and psychological responses, which can be applied to the process of social signal transduction. Just as the subjective perception of social conditions can affect patterns of gene expression (Slavich & Cole, 2013), differences in cultural expectations and norms could potentially affect perceptions of social situations and thus the way genes are expressed. For example, in the case of seeking social support, European Americans are more likely to confide in close others in distressing situations and directly ask for help compared to Asian Americans, who may be relatively more concerned about burdening their social networks (Kim, Sherman, & Taylor, 2008; Taylor et al., 2004). Thus, the same social situation—seeking social support—could be perceived as more or less threatening



depending on the cultural context (Taylor, Welch, Kim, & Sherman, 2007). One possibility is that such cultural variation in subjective experience could manifest in cultural differences in the activity of gene expression.

Cultural meanings, practices, and patterns of interactions could also have implications for epigenetic processes. Epigenetic differences in the genomes of monozygotic twins, for instance, can occur as a function of accumulated exposure to divergent life experiences (Fraga et al., 2005). Such epigenetic modifications result in different behavioral and health outcomes—in this case, differences between twins in disease onset. Similarly, individuals engaged in different cultural contexts may be systematically exposed to varying experiences that contribute to epigenetic change. For instance, a study comparing (p. 284) Asia and North America found that the cultural environment of the United States offered more frequent and potent opportunities to exert influence on one's surroundings compared to Japanese cultural environments, which provided more opportunities for adjusting to the situation (Morling, Kitayama, & Miyamoto, 2002). A lifetime of exposure to varying experiences could potentially result in culturally differing patterns of methylation, epigenetic modifications that in some cases may be transmitted across generations, providing an inheritance mechanism for the impact of environmental factors (see Franklin & Mansuy, 2010).

From the perspective of differential susceptibility, individuals may exhibit differences in their genetic predisposition to methylation and thus be more or less sensitive to environmental influences (e.g., Huang, Perry, & Laux, 1999). In a study of adults with traumatic experiences, increased methylation leading to decreased gene expression was found to moderate the association between serotonin transporter gene polymorphisms and depressive symptoms (van IJzendoorn, Caspers, Bakermans-Kranenburg, Beach, & Phillbert, 2010). The short variant of the *5-HTTLPR* gene predicted more feelings of unresolved loss but only when methylation levels were low. Thus, epigenetic processes, such as methylation, may operate at the interface of environmental exposure and psychological outcomes.

## Evidence for Gene-Culture Interactions

Evidence for  $G \times C$  interactions relevant to health outcomes derives from studies investigating a variety of genes and psychological processes. Building on the idea of environmental susceptibility,  $G \times C$  interaction research focuses on genes that have been implicated in environmental sensitivity and predicts that particular genetic variations will alter an individual's susceptibility to environmental influence. In a study of the

interaction between variants of the 2A serotonin receptor (5-HT<sub>2A</sub>) and depressive symptoms, the perception of one's family as a prototypically "good family" in Brazil negatively correlated with depressive symptoms (Dressler et al., 2009). The effect was enhanced for those individuals carrying the AA variant of 5-HT<sub>2A</sub> compared to individuals with AG or GG variants. Another study, which investigated G × C interactive effects on psychological well-being, found that religiosity was associated with greater well-being for those genetically predisposed to be environmentally sensitive (i.e., those carrying the GG variant of a particular oxytocin receptor gene polymorphism), but only for those from a cultural context in which religion tended to provide more frequent opportunities for affiliation (Sasaki et al., 2011).

Gene-culture interactions have also been shown for health-relevant behaviors, such as emotion regulation. Kim and colleagues (2011) compared emotion regulation approaches between the United States, where expressivity is more highly valued, and Korea, where suppression is valued more. Koreans with the environmentally sensitive variant (GG genotype) of the oxytocin receptor gene (*OXTR*) reported using more emotion suppression than those with the AA genotype, whereas European Americans showed the opposite pattern. Overall, it seems that through engagement in different cultural systems, individuals genetically predisposed to environmental sensitivity are the ones to most strongly adopt the particular psychological and behavioral patterns supported by a culture for certain psychological phenomena (Kim & Sasaki, 2012, 2014). Likewise, when comparing across multiple cultures, the most culturally divergent patterns of behavior relevant to a gene of interest appear to emerge among people with environmentally sensitive predispositions.

## Bridging Gene × Culture with Gene-Culture Coevolution

Although the gene-culture interaction and gene-culture coevolution perspectives both investigate the relationship between biological and cultural variation, they address different aspects of this relationship, and there are some interesting points that arise from comparing these perspectives. Gene-culture coevolution theory (also known as dual inheritance theory) provides an explanation for the macro-level interactions between culture and genes by applying a Darwinian selection framework to culture. The theory proposes that similar to genetic variants, features of a culture could increase individual fitness and be transmitted through social learning in a system of inheritance not unlike genetic inheritance (Boyd & Richerson, 1985; Chiao & Blizinsky, 2010; Feldman & Laland, 1996). Thus, cultural features, which serve as adaptations to local environments

and conditions, could evolve much like genes evolve. Such cultural evolution may have been particularly important in the history of human evolution because cultural practices could have allowed for adaption to environments at a pace much faster than allowed by genetic evolution alone.

(p. 285) According to gene-culture coevolution, cultural systems contribute to creating environmental pressures under which genetic evolution occurs. One classic example is the coevolution of dairy farming practices and the lactase gene. The ability to digest milk proteins usually disappears after childhood. However, there is an association between a history of dairy farming and the frequency of genetic variants related to lactose tolerance in a population (Beja-Pereira et al., 2003; Myles et al., 2005), suggesting that the development of cultural practices supporting dairy farming and milk consumption contributed to evolutionary selection favoring alleles for adult lactose tolerance. Another example derives from research investigating the association between individualism–collectivism tendencies and the serotonin transporter gene polymorphism *5-HTTLPR* (Chiao & Blizinsky, 2010; for gene-culture coevolution evidence of cultural tightness vs. looseness and *5-HTTLPR* as explained by historical ecological threat, see Mrazek, Chiao, Blizinsky, Lun, & Gelfand, 2015). Previous studies have demonstrated that regions with historically greater pathogen prevalence tend to be more collectivistic (Fincher et al., 2008). Chiao and Blizinsky (2010) report that the cultural value of collectivism, which enhances social connectedness, is associated with a higher frequency of the s allele of *5-HTTLPR*, which has been linked to anxiety and mood disorders in certain populations. The development of collectivistic practices may have evolved to reduce exposure to environmental pathogens and thus may have also strengthened selection pressures for the s allele of *5-HTTLPR* if it buffers susceptible populations against genetic predispositions for affective disorders (see also Way & Lieberman, 2010).

The theory of gene-culture coevolution is complementary with the gene-culture interaction framework in that the two approaches operate at different levels of analysis. Gene-culture coevolution focuses on the macro-level evolutionary processes shaping cultural norms and genetic variants. In contrast, the gene-culture interaction framework addresses how culture and genetics interact to influence behavioral and psychological outcomes at the individual level. Through gene-culture coevolution processes, a particular adaptive cultural value may become common within a population, creating selective pressures for a particular genetic variant. However, genetic variation will still exist in the population. The gene-environment interaction framework explains how individuals within the same cultural context might think and behave differently depending on their genetic predispositions. For example, there may be a region-level correlation between the prevalence of the s allele of *5-HTTLPR* and collectivistic values (Chiao & Blizinsky, 2010), whereas at the individual level, s allele carriers versus l allele

carriers may be influenced by cultural norms differently, as predicted within the gene-culture interaction framework.

Research on gene-culture interactions is new, yet the perspective holds great promise for illuminating the processes underlying genetic and environmental influences on behavior. Investigations in molecular biology may inform understandings of underlying biological mechanisms, whereas cultural research may contribute to predictions about underlying psychological mechanisms. By bringing these two perspectives together, gene  $\times$  culture research may offer a more complete picture of the process through which cultural information, both inside and outside the head, can interact with genetic information to lead to different outcomes.

## Theoretical Issues and Questions Raised by Gene $\times$ Culture Research

As an emerging area of research, gene-culture interactions raise a number of important issues with theoretical relevance. First, there are some general patterns of results from gene  $\times$  culture research that may have implications for cultural psychology. Second, research on genes and culture raises interesting questions about genetic frequencies in different populations. Especially for addressing issues related to health, the combination of both genetic and cultural considerations holds great potential. Yet at the same time, the gene  $\times$  culture framework represents a departure from more classic cultural perspectives in some ways and raises important questions to be addressed.

### Implications for Cultural Psychology

Gene-culture interactions offer a way of understanding not only how genetic predispositions may manifest themselves differently depending on the cultural context but also how cultural factors may influence people differently according to individual differences at the level of genes. This framework captures how the content of culture can inform research in the realm of biology and behavioral genetics. However, that is not to say that the influence of culture is unvaried. Genes may constrain the effects of culture by providing people with a range of possible traits or behaviors, and the environment, (p. 286) including culture, can then select from that range of possibilities to lead to a particular outcome.

Gene  $\times$  culture findings have shown that some well-known cultural effects seem to occur more for people with certain genetic predispositions than others. Cultural differences in emotional support seeking (Kim, Sherman, Sasaki, et al., 2010) and emotion regulation (Kim et al., 2011), for instance, emerge among people with GG and AG genotypes of *OXTR* but not AA genotypes. In addition, previously found cultural differences in locus of attention (Choi, Koo, & Choi, 2007; Masuda & Nisbett, 2001) appeared only for GG and CG genotypes of *5-HTT1A* and not for CC genotypes (Kim, Sherman, Taylor, et al., 2010). This general pattern of results may have implications for cultural psychology more broadly because it is possible that many previously discovered cultural differences are stronger for those with certain genetic predispositions than others. Although it is probably not the case that a single gene leads people to be more or less culturally normative across all traits and behaviors, one possibility given our G  $\times$  C findings and other G  $\times$  E research is that sets of genes (e.g., oxytocin-related genes) may be related to culturally normative responses for specific outcomes (e.g., socioemotional sensitivity). This means that cultural differences on these outcomes may be more pronounced for people with certain genetic predispositions than others, but across outcomes, there should be no relationship between cultural normativity in general and any one set of genes, consistent with insights on why cultural differences are not always reducible to individual differences (Na et al., 2010).

### Covariation of Cultural and Genetic Differences

One intriguing question derives from observations combining cultural differences in psychological and behavioral tendencies with differences found in the distribution of specific genotypes across ethnic groups, such as people of East Asian versus European ancestry. Interestingly, many of the genes that have been commonly studied in psychology, such as *5-HTTLPR*, *OXTR*, and *DRD4*, have drastically different genotype distributions across ethnic groups. Sometimes these divergent genotype frequency distributions correlate with documented differences in cultural norms (Chiao & Blizinsky, 2010; Mrazek et al., 2015). However, when one considers the general set of psychological tendencies associated with any given polymorphism, the way in which genotype distributions within a cultural group align with their documented psychological tendencies varies considerably.

For instance, compared to groups with European ancestry, East Asian samples tend to have a much higher frequency of the *5-HTTLPR* polymorphism s allele, which is associated with stress reactivity (e.g., Caspi et al., 2003). East Asians are also known to be more avoidance oriented than North Americans with European cultural backgrounds (Heine et al., 2001; Lee, Aaker, & Gardner, 2000). Thus, the fact that the environmental

susceptibility genotype of *5-HTTLPR* is more common among people from East Asian cultures, which emphasize interpersonal influence (Morling, Kitayama, & Miyamoto, 2003) and the value of group harmony (Kim & Markus, 1999), seems to make sense intuitively.

At the same time, the G allele of *OXTR* rs53576 polymorphism is far more common among European Americans than among East Asians (e.g., Kim, Sherman, Taylor, et al., 2010; Kim et al., 2011). Given the association of the *OXTR* G allele with social bonding and affiliation (e.g., Bakermans-Kranenburg & van IJzendoorn, 2008; Rodrigues, Saslow, Garcia, John, & Keltner, 2009; but see Bakermans-Kranenburg & van IJzendoorn, 2014), as well as with greater environment susceptibility (Belsky, Bakermans-Kranenburg, & van IJzendoorn, 2007), it may seem counterintuitive to find a higher frequency of G alleles among European Americans, who are from cultural contexts that tend to emphasize independence and individualism, than among East Asians, who are from cultural contexts in which interdependence and collectivism are fostered.

To further complicate the matter, different variants of *DRD4* polymorphism (i.e., 2-repeat and 7-repeat alleles) in different ethnic groups are associated with similar functional and psychological characteristics (Reist et al., 2007; Wang et al., 2004), but the frequencies of these respective environment susceptibility genotypes are roughly compatible between European Americans and Asians (e.g., Kitayama et al., 2014; Sasaki et al., 2013).

Genetic profiles of different ethnic groups are no doubt the result of natural selection processes and specific challenges posed by the regional environment, but it is beyond the scope of this chapter to address how particular genes come to be more frequent in one ethnic group than another. In this chapter, we focus on what we can learn from the observation of diversity in genetic distributions among different ethnic groups and future research questions that may be inspired by these observations.

(p. 287) Given that the frequencies of genotypes for these susceptibility genes differ greatly, and sometimes against what seems to be the intuitive association with cultural tendencies, one can reasonably infer that cultural tendencies cannot be simply explained as averages of phenotypic tendencies of populations. That is, the frequency distribution of *OXTR* genotypes (Kim, Sherman, Sasaki, et al., 2010; Kim et al., 2011) probably does not explain why East Asians are more interdependent than European Americans. To the extent that there is any relationship between genotypic distributions and cultural tendencies, the relationships will be considerably more complicated, as proposed by other theoretical models such as gene-culture coevolution and gene-culture interaction. For example, there is evidence that the *DRD4* variant may moderate the cultural difference in independent versus interdependent social orientations such that 2- or 7-

repeat allele carriers tend to have greater independence for European Americans but greater interdependence for East Asians (Kitayama et al., 2014).

An additional point is that it is not always clear how specific the associations are between a gene and its psychological correlate. For example, stress reactivity is often discussed in relation to *5-HTTLPR*, although it is by no means the only gene that is associated with stress reactivity. There are other genes, such as *OXTR* (Rodrigues et al., 2009) and *MAOA* (Caspi et al., 2002), that influence one's sensitivity to environmental distress. Thus, although there seems to be some genetic specificity in the associations with different social behaviors, strongly inferring conceptually distinct and exclusive psychological outcomes from specific genes should be done with caution. Rather, there may be sets of genes with distinguishable but overlapping functions that predispose individuals to certain domains of sociocultural influence. It will be useful to adopt more reliable ways of investigating genetic influence, such as a polygenic approach examining the link between a trait and multiple genes and a pleiotropic approach examining how a single gene may be linked to multiple traits.

Moreover, considering gene-culture interactions in the context of genotypic distribution differences in ethnic groups raises the question of why sometimes only a small genetic minority in a cultural group seems to embody culturally normative tendencies. For example, the s allele of *5-HTTLPR* is relatively rare among European Americans, and the G allele of *OXTR* rs53576 is relatively rare among East Asians, yet both the *5-HTTLPR* s allele and the *OXTR* G allele seem to predispose people to be more susceptible to cultural influences. For this question, we propose that there are at least two possible answers.

One possibility is that the maintenance of culturally normative tendencies may be shaped by multiple genes in conjunction with each other. Examination of multiple polymorphisms in combination, including genes that are more or less common in a given population (e.g., G allele of *OXTR* or s allele of *5-HTTLPR* among East Asians), is likely to yield a more normally distributed genetic profile at the cultural group level (cf. Belsky et al., 2013), evening out skewed distributions of each polymorphism. In other words, the genetic basis of cultural susceptibility itself is probably similarly and normally distributed among many cultural groups. Given that, it would be unwise to infer that any single gene is responsible for a broad range of cultural differences or that a gene or even a group of genes are responsible for a broad category of social behaviors, such as cultural conformity, without further specifying the exact processes. It is more likely that a particular gene or set of genes predispose each individual to be sensitive to a small aspect of cultural environment, and only as a whole, we may be able to see cultural patterns.

This issue of single gene research is not limited to research in cultural genetics. The single gene approach has been fruitful in leading the initial examination of the

excruciatingly complex process of genetic influence, allowing investigators to formulate theory-driven predictions in a relatively parsimonious manner. However, the field is moving toward examining how multiple genes together influence psychological and behavioral tendencies. Yet, there is currently no clear model to examine multiple genes in conjunction with each other. It is unclear if the genes function in additive, interactive, or compensatory ways, although there are some notable efforts to deal with this issue. For example, Belsky and colleagues (2013) selected multiple genes based on results of genome-wide association studies (GWAS) and examined how they predict particular health-related behaviors, such as smoking and obesity, using an additive model. Also, genome-wide complex trait analysis (Yang, Lee, Goddard, & Visscher, 2011) was developed to address the “missing heritability” problem as a way to utilize GWAS data for estimating and partitioning complex trait variation. Although these models offer promise, to date there has not been a compelling study using multiple genes along with environmental input to predict social behaviors. (p. 288) As the field moves forward, there will no doubt be empirically and biologically informed ways to examine multiple genes to further uncover the role of genes and environment in shaping social and cultural behaviors, and researchers will then be able to answer questions with greater certainty.

An additional possibility is that much of the culture-specific norms have not been stable for long enough to be reflected directly by a set of genes. The time frame for genetic divergence among ethnic groups is more than 40,000 years (Bowcock et al., 1991). Thus, much of the genetic composition of each ethnic group seems to predate certain components of the established culture, at least in terms of cultural values, institutions, and assumptions based on specific historical antecedents. Of course, as research on gene-culture coevolution shows, cultural practices may have a detectable influence on genetic distribution in specific cases (e.g., Beja-Pereira et al., 2003) within a relatively brief evolutionary time frame. Nevertheless, it is likely that changes in thoughts and behaviors at the individual level, and even cultural practices and norms at the group level, are much more malleable and quick-paced than changes in genetic characteristics of populations. Given that, the link between genetic profiles of a particular ethnic group and their cultural characteristics may be fairly unstable, and this is an important possibility to keep in mind.

The ways in which genes and culture are related with each other are numerous, as shown in this very brief review. Currently, much remains unknown in terms of how genes work to eventually lead to traits, and there are a number of caveats to consider in formulating new theories. The field will benefit in the future from combining multiple perspectives, including psychology, behavioral genetics, population genetics, and anthropology, to address questions about the mind and behavior.



## How Can the Gene × Culture Framework Be Applied to Health Research?

Due to the growth of cultural psychology, there is now a relatively large body of research to draw upon for investigations of health using a gene-culture interaction perspective. In this final section, we discuss cultural research relevant to health, promising avenues of future research, and implications for public health policy.

### Culture and Health

Cultural differences exist even in basic psychological phenomena, many of which have important implications for understanding what people consider healthful and how they ultimately achieve positive health outcomes. For instance, it is well-known that social relationships have strong implications for health (Cohen, 2004), and this general link may be true in every culture. The meanings embedded in relationship contexts, however, may vary across cultures and thus have relevance for understanding a range of health-related issues, from the way people draw on their social networks to cope with difficulties (Kim et al., 2008) to the extent to which one's well-being is contingent on others (Plaut et al., 2012). In addition, given that certain genes or sets of genes may be linked to social sensitivity in particular contexts (e.g., Bartz, Zaki, Bolger, & Ochsner, 2011), it may be especially useful for gene-health research to consider the cultural contexts that shape norms and expectations in social relationships.

Research from a cultural perspective has also shown more directly that there are cultural differences in health outcomes, the willingness to seek different kinds of treatment, and the effectiveness of different treatments. Given that perceived discrimination contributes to health disparities (Major, Mendes, & Dovidio, 2013; Pascoe & Smart Richman, 2009; Williams & Mohammed, 2009), it is important to consider intergroup dynamics for investigations on culture and health. For instance, it is well documented that people from lower social class contexts tend to fare worse than those from a higher social class on certain health outcomes, in part due to greater exposure to stress and other health-debilitating risks (Williams & Collins, 1995; for review, see Matthews & Gallo, 2011). In addition, minorities may seek mental health treatment less often compared to majority group members, even after acculturating to a new culture (B. Kim, 2007; Mills, 2012), and for those who do seek medical care, there is evidence that ethnic minorities tend to receive lower-quality treatment on average (Williams & Sternthal, 2010). Some minority groups, such as Black Americans, continue to face lower average life expectancies

compared to White Americans, even after taking social class into account (Williams & Sternthal, 2010), raising the possibility that minorities may face greater health risks due to perceived discrimination. However, some immigrant groups, such as those with Mexican backgrounds, tend to have equivalent or better health outcomes than the mainstream White population, despite the fact that they face greater risk of poverty and low-quality health care (p. 289) (a phenomenon termed the “Hispanic paradox”; Markides & Eschbach, 2005).

People from different cultures may also show different symptomatology for mental health problems and have different beliefs about treatment (Ryder, Ban, & Chentsova-Dutton, 2011). Studies of people with depression across cultures have found that the Chinese tend to somaticize depression symptoms more than do Westerners (Chang, 1985; Tsai, Simeonova, & Watanabe, 2004). Also, European Americans who are depressed tend to show decreased emotional reactivity, whereas East Asians who are depressed show heightened emotional reactivity (Chentsova-Dutton et al., 2007). With regard to support seeking, people from Japan tend to be less likely to seek support from close relationships and from professional services compared to Americans, and this difference may be explained by cultural differences in willingness to disclose problems (Mojaverian, Hashimoto, & Kim, 2013) and relationship concerns, such as disrupting harmony or saving face (Taylor et al., 2004). In addition, a longitudinal study of pregnant women found that the Japanese, compared to Americans, are more likely to experience certain positive pregnancy outcomes when they believe that close others have control over decisions surrounding their pregnancy (Morling et al., 2003). These findings emphasize the importance of understanding how culture may shape the expression or presentation of certain health conditions, as well as how beliefs about appropriate treatment may have consequence for health outcomes.

From the perspective of cultural neuroscience, a more complete picture of how people conceptualize health, make decisions regarding their health, and ultimately achieve positive health outcomes may come from examining the interaction of cultural and biological factors (e.g., Chiao, Cheon, Pornpattananangkul, Mrazek, & Blizinsky, 2013). Gene-culture interactions may be a particularly promising area of research within cultural neuroscience that explains diverse psychological responses (Sasaki, 2013). For example, research suggests that situating the individual within an intergroup context may potentially have implications for health and that people with certain genotypes may be more sensitive to stressful features of this context than others. Specifically, research by Cheon and colleagues (2014) found that people who had prior negative contact with out-groups and perceived that the social world is dangerous were more likely to report intergroup biases, but this relationship was stronger for carriers of the more stress- or threat-sensitive s allele of *5-HTTLPR* compared to those homozygous for the l allele. This

research highlights the importance of considering how an individual perceives the self in relation to other groups in an intergroup context, as well as one's genetic predispositions to be sensitive to stress in this context.

Genes represent one component of biology but are certainly not the only important factor to consider for questions surrounding health. As a field, cultural neuroscience examines the complex ways in which culture and biology interact (Chiao & Ambady, 2007), and it is crucial to consider specific findings of gene-culture interactions within the context of cultural neuroscientific frameworks more broadly in order to understand health disparities (Cheon, Mrazek, Pornpattananangkul, Blizinsky, & Chiao, 2013; Chiao et al., 2013). A recent review of cultural neuroscience (Kim & Sasaki, 2014) proposes a framework for understanding how genetic and environmental inputs affect psychology via neural processes and how culture shapes these processes at multiple levels and is constrained by the processes of evolution. Because it is clear that culture plays a role in health outcomes in multiple ways, the next challenge for future research is to incorporate a cultural approach while anchoring findings within a broader theoretical framework.

### Future Research on Gene-Culture Interactions

There are many ways to conceptualize culture (Cohen, 2009), and future research on gene-culture interactions should thus explore other methods of examining culture in addition to using cultural group comparisons. For instance, measures of subjective experience may be one way to consider culture in investigations. As previously described, a  $G \times C$  study of cultural consonance, or the degree of match between one's own life and the broader shared culture, found that lower cultural consonance was associated with greater depressive symptoms, and this was especially the case for people with a potential genetic link to depression-related conditions (Dressler et al., 2009). This study raised the important point that disparities between subjective experiences and the norms prescribed by the broader culture can have implications for health outcomes.

Other cultural psychological approaches include cultural task analysis to test implicit indicators of cultural differences (Kitayama, Park, Sevincer, (p. 290) Karasawa, & Uskul, 2009), continuous measures of educational attainment to measure social class as culture (Grossmann & Varnum, 2011), and cultural priming to test causal effects of cultural information on psychological outcomes (Hong, Morris, Chiu, & Benet-Martínez, 2000; Oyserman & Lee, 2008). Cultural priming may present an especially promising future direction for gene-culture interaction research because it allows for causal inferences about the relationship between cultural information and an outcome for people with different genetic predispositions (for a  $G \times E$  example of environmental priming in a

laboratory setting, see Sasaki et al., 2013). All these examples of cultural approaches could potentially be used in conjunction with the  $G \times C$  framework.

Future research should also examine the mechanisms through which gene-culture interactions occur, and the  $G \times C$  framework may provide good opportunities to address this issue. The framework of  $G \times C$ , like that of  $G \times E$ , makes predictions about moderation by formalizing how the same genetic predisposition can be linked to different outcomes depending on one's culture and also how the same cultural background may predict different outcomes depending on one's genetic predisposition. As Baron and Kenny (1986) explained, the best moderators are those that suggest possible mediators, revealing something about the underlying mechanisms involved in a psychological phenomenon. Culture is a moderator with such potential because numerous cultural psychological studies have revealed mediating processes. In research on culture and motivation, for instance, Heine and colleagues (2001) initially established an interaction between a situation (receiving success vs. failure feedback) and culture (Japan vs. North America) on task persistence and additionally showed that the interaction seemed to suggest motivation as a potential mediator. Specifically, they showed that North Americans seemed to experience greater motivation following success (vs. failure) feedback, allowing them to persist more on a task compared with Japanese participants. On the other hand, Japanese participants seemed to be more motivated by failure than success compared with North Americans. Furthermore, cultural differences in motivation were explained by between-group differences in lay theories about the utility of effort. Because cultural differences in a given outcome (e.g., task persistence) pointed to differences in an underlying process (e.g., motivation) and revealed potential explanations for cultural differences (e.g., lay theories), this example illustrates how a cultural approach can be useful for elucidating basic psychological processes.

A similar approach can be used in the context of health for  $G \times C$  research. For example, one of our previous  $G \times C$  studies described previously found that culture moderates the link between *OXTR* and emotional seeking among those who experience greater distress (Kim, Sherman, Sasaki, et al., 2010). This finding of cultural moderation could potentially illuminate social processes in relation to oxytocin more broadly because it suggests that people who may be predisposed to be more socially sensitive only directly seek more emotional social support in cultural environments that endorse this behavior as appropriate. Although initial oxytocin findings seemed to suggest that higher levels of oxytocin generally encourage people to socially connect with others in positive ways (Kosfeld, Heinrichs, Zak, Fischbacher, & Fehr, 2005), later research has demonstrated that oxytocin can also have negative effects, particularly in the context of in-group-out-group competition (De Dreu, Greer, Van Kleef, Shalvi, & Handgraaf, 2010; Declerck, Boone, & Kiyonari, 2010) or for individuals lacking optimal resources to deal with social

stressors (Bartz, Zaki, Bolger, et al., 2010; Bartz, Zaki, Ochsner, et al., 2010; Bartz, Simeon, et al., 2011). In reality, the influence of oxytocin is complicated and should therefore be applied with caution (Miller, 2013). The social effects of oxytocin appear to be highly dependent on aspects of the context and the individual (for review, see Bartz, Zaki, et al, 2011); in addition, our research suggests that oxytocin may lead people to interact with others in ways that are sanctioned by the sociocultural context (Kim, Sherman, Sasaki, et al., 2010; Kim et al., 2011; Sasaki et al., 2011).

These  $G \times C$  findings further support theories about how social support processes may not function in the same way across cultures, and more broadly, they demonstrate that genetic predispositions may manifest themselves in different ways according to what is normative in the cultural context. As in the case of the culture, *OXTR*, and emotional support-seeking study described previously (Kim, Sherman, Sasaki, et al., 2010), the act of seeking emotional social support can have different meanings depending on the cultural context (for review of culture and social support processes, see Kim et al., 2008).  $G \times C$  research demonstrates that the relationship between genetic predispositions and behaviors may depend on the cultural (p. 291) meanings of behaviors rather than on actual behaviors per se.

### Implications of Gene $\times$ Culture Research for Public Health Policy

The utility of  $G \times C$  research goes beyond the advancement of theory and development of new methodology; it also has practical applicability to health issues, particularly in its ability to inform public health policy. Here, we explore how  $G \times C$  research can be applied to the policy areas of defining health and developing goals for public health policy and providing effective care in a targeted, cost-efficient manner. In so doing, we also discuss implications and potential recommendations based on past studies and identify questions for future research to address.

#### Defining and Delivering Health

Before developing policy, public health policymakers throughout the world should address the following questions: What constitutes optimal health? How is it best fostered in a given population? Answering these questions is far from straightforward, and much research on cultural differences strongly suggests that peoples' responses to these questions can vary in important ways. The World Health Organization's (WHO) recent emphasis on addressing "social determinants of health," or social factors that contribute to health inequities throughout the world (Commission on Social Determinants of Health, 2008), is consistent with this idea that effective public health policy must take the sociocultural context into account. WHO also defines health as "a state of complete

physical, mental, and social well-being and not merely the absence of disease or infirmity” (World Health Organization, 2003), but across cultures, the meaning of well-being might vary greatly. For example, a study of conceptions of health in New Mexico and Colorado found that Hispanic villagers highly emphasized fulfilling role obligations according to one’s age and sex, and the primary repercussion of illness was that it interfered with the ability to fulfill one’s obligations, not that it affected the sick individual (Schulman & Smith, 1963). When addressing the concept of health among First Nations or Aboriginal North Americans, a common model is the medicine wheel, which depicts health as a holistic balance among social, mental, physical, and spiritual elements—the latter being a factor that does not commonly appear in Western concepts of health (Roberts, Harper, Tuttle-Eagle Bull, & Heideman-Provost, 1998; Waldram, 2006). Furthermore, cultural variation also exists in the conception of a specific component of health—that is, mental or subjective well-being (Fulmer et al., 2010; Oishi & Diener, 2003; Uchida & Kitayama, 2009). Lay concepts of subjective well-being in Western cultures often tend to center on the “pursuit of happiness” and avoidance of unhappiness for oneself (Diener & Diener, 1995; Suh, Diener, Oishi, & Triandis, 1998). In some Eastern cultures, however, subjective well-being is achieved through fulfilling role obligations and finding a balance between happiness and unhappiness (Lu, 2005; Suh et al., 1998; Uchida & Kitayama, 2009). These findings suggest that public health policy aimed at highly maximizing the population’s happiness may increase the psychological well-being of a Western population, but it may not have the same effects in an Eastern population, where such policy may be less appropriate.

Beyond considerations of the definitional components of health, cultural psychological research also sheds light on differences in the ways to achieve optimal health. For example, Eastern cultures’ emphasis on balance and dialecticism might apply to attitudes toward health and the desired goals of public health. In research on topics such as emotional experience (Uchida & Kitayama, 2009), reasoning and logic (Ji, Nisbett, & Su, 2001; Peng & Nisbett, 1999), and self-concept (Heine & Lehman, 1997; Spencer-Rodgers, Williams, & Peng, 2010), it has been shown that Asians tend to be more tolerant of contradiction, think of events in terms of cycles rather than linearly, and place importance on the balance of opposing forces that are viewed as mutually dependent. It is possible, then, that learning to accept illness and disability when they occur is an important part of achieving health in some Asian populations. The issue of achieving optimal health is further complicated by the possibility that cultural differences in certain phenomena may be moderated by genetic predispositions (Kim & Sasaki, 2014). Thus, policy aimed solely at eradicating illness and disability may be incomplete, missing important differences in cultural attitudes and beliefs and the possibility that these cultural differences could potentially vary by genes.

However, it is also important to consider the individual differences that exist between people within a culture. People may have certain predispositions in terms of their biology, personality, and behavior; thus, it will be important for public policy to allow for flexibility in accommodating (p. 292) within-group variation. For example, individual differences in extraversion versus introversion have been linked to a dopamine receptor gene, *DRD2*, with carriers of the A1 allele being significantly more extraverted than noncarriers (Smillie, Cooper, Proitsi, Powell, & Pickering, 2010). People who vary on levels of extraversion would likely also differ in the types of situations and behaviors that best foster social and mental well-being (Diener, Oishi, & Lucas, 2003; Moskowitz & Coté, 1995). In terms of health policy, what may contribute to optimal health for a more extraverted A1 allele carrier, for instance, may not work as well for someone without this allele. It is a further possibility that genes may express themselves differently depending on a person's cultural environment (e.g., Kim, Sherman, Sasak, et al., 2010); thus, a thorough understanding of how best to promote the health of a population may require policy that takes both individual predispositions and cultural influences into account.

### Providing Effective, Efficient Care

Whether implemented at the local, regional, or national level by governments and institutions, public health policy aims to promote health and prevent disease and illness in a population. Due to the spread of health-related ideas and tools throughout the world, people are sometimes faced with the challenge of adapting policy that has been imported from other populations. However, effective policy involves far more than finding a one-size-fits-all prescription for well-being. Policy must be tailored to fit various types of populations, within which there will be differences in genetic predispositions and cultural backgrounds. Although a highly personalized care system may be ideal for allowing each person in a society to strive for better health in his or her own way, the reality is that public health policy is bound by limited resources and is therefore under pressure to maximize its efficiency. Negotiating a balance between the ideal of effective, personalized care and the limitations surrounding its provision is a difficult challenge for public health policymakers, but helping to do so may be one of the greatest promises of  $G \times C$  research.

There is much public interest in genetics as a potential tool to identify health risk factors. Although such an approach has much promise,  $G \times C$  findings caution against the assumption that genetic associations with health outcomes are uniform. The findings of  $G \times C$  research provide a more nuanced understanding of how multiple factors interact in relation to health outcomes, and this knowledge can be used to create more streamlined policy that delivers effective care while limiting the waste of resources. By its mandate,  $G \times C$  research investigates micro- and macro-level influences on the individual in order to predict outcomes. However, it goes beyond an additive model of these influences,

demonstrating how one level moderates the other and uncovering information about potential mediators. In doing so, this research clarifies when predictions based solely on genes or culture are likely to be qualified due to an existing interaction. In terms of health policy, this means preventing the misappropriation of resources that can occur when genes and culture are considered in isolation. To give a hypothetical example, imagine that Japanese policy based on genetic studies conducted in Germany led to individuals with a particular gene being identified as at-risk and given an intervention, when in actuality, that gene was not a risk factor given the cultural environment in Japan. Another example is a scenario in which certain cultural elements in the United States were found to account for a higher prevalence of a disorder in that country, so an intervention policy aimed at widespread change was enacted, even though only people with certain genetic predispositions would be negatively affected. In both situations, the efficiency and effectiveness of policy are compromised by considering genes and culture separately rather than adopting a  $G \times C$  perspective. Of course, there will certainly be cases in which a person's genes or culture alone may predict a large portion of the variance in certain health outcomes, but  $G \times C$  research can help predict when any particular association is qualified due to the interaction of genes and culture.

Utilizing a  $G \times C$  framework can be effective for addressing health issues related to etiology, course, and outcome in different cultures. Clinical depression has been associated with certain genetic precursors, such as the presence of an s versus an l allele of the *5-HTTLPR* polymorphism, depending on the environment: Having an s allele puts one at higher risk of depression if coupled with environmental risk factors, such as loss, interpersonal conflict, or a stressful childhood environment (Caspi et al., 2003; Taylor et al., 2006). As Maselko (see Chapter 23, this volume) explains, various risk factors in the early environment may biologically calibrate a person in a way that can prove maladaptive and increase risk of neuropsychiatric disorders in later life. However, the prevalence and manifestation of depression and other mental health disorders (p. 293) show considerable variability between nations and between groups within nations, suggesting that cultural factors may also play a role in a person's susceptibility (Chiao & Blizinsky, 2010; Kleinman, 1982; Maselko, Chapter 23, this volume; Tsai & Chentsova-Dutton, 2002; see also Chapter 22, this volume). In fact, as Yang and Benson (Chapter 22, this volume) note, clinical diagnoses based on culture-specific symptoms may be more appropriate for determining the actual prevalence of certain disorders. Yet it is not enough to know about the genetic and cultural influences on depression independently if one hopes to predict its occurrence. As discussed in this chapter, genes and culture sometimes interact and therefore should be considered in concert. This has been shown to be the case in depression, as the presence of the s allele of *5-HTTLPR* is actually associated with lower prevalence of the disorder in more collectivistic cultures, perhaps due to the buffering effect of collectivistic cultural values (Chiao & Blizinsky, 2010). Thus,



a thorough understanding of how and when not only genetic and cultural factors but also their interactions predict health outcomes can be instrumental in developing effective, efficient policy.

### Conclusions on Gene × Culture Research and Public Health Policy

Genes play an important role in determining health risks and outcomes. As such, in matters of how to protect and promote the health of a population, genetic research provides indispensable recommendations about how to create good policy. However, it is important to realize that public health policy is a part of culture—it is an institutional force that shapes and is shaped by the values, norms, and beliefs of a people. Changes made to public health policy change the cultural context in which a population lives. Given that cultural research investigates how the cultural context affects health, it is clear that cultural research on health may have important recommendations for effective public health policy. However, it is not enough to consider genetic and cultural influences on health in isolation and then utilize the information in an additive manner to create policy. In many cases, it is likely that genes and culture interact with each other to influence a person's health, and only future research will be able to determine when this should be expected. Therefore, the G × C framework promises to provide a richer understanding of health for people across diverse societies.

## Acknowledgment

Preparation of the manuscript was supported by National Science Foundation grant BCS-1124552 to Heejung S. Kim.

## References

- Adler, N. E., Epel, E. S., Castellazzo, G., & Ickovics, J. R. (2000). Relationship of subjective and objective social status with psychological and physiological functioning: Preliminary data in healthy White women. *Health Psychology, 19*, 586–592.
- Adler, N. E., & Stewart, J. (2010). Health disparities across the lifespan: Meaning, methods, and mechanisms. *Annals of the New York Academy of Sciences, 1186*, 5–23.
- Allison, T., Puce, A., & McCarthy, G. (2000). Social perception from visual cues: Role of the STS region. *Trends in Cognitive Sciences, 4*, 267–278.

Bakermans-Kranenburg, M. J., & van IJzendoorn, M. H. (2008). Oxytocin receptor (OXTR) and serotonin transporter (5-HTT) genes associated with observed parenting. *Social Cognitive and Affective Neuroscience*, 3, 128–134.

Bakermans-Kranenburg, M. J., & van IJzendoorn, M. H. (2011). Differential susceptibility to rearing environment depending on dopamine-related genes: New evidence and a meta-analysis. *Development and Psychopathology*, 23, 39–52.

Bakermans-Kranenburg, M. J., & van IJzendoorn, M. H. (2014). A sociability gene? Meta-analysis of oxytocin receptor genotype effects in humans. *Psychiatric Genetics*, 24(2), 45–51.

Baron, R. M., & Kenny, D. A. (1986). The moderator-mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology*, 51, 1173–1182.

Bartz, J. A., Simeon, D., Hamilton, H., Kim, S., Crystal, S., Braun, A., et al. (2011). Oxytocin can hinder trust and cooperation in borderline personality disorder. *Social Cognitive and Affective Neuroscience*, 6, 556–563.

Bartz, J. A., Zaki, J., Bolger, N., Hollander, E., Ludwig, N. N., Kolevzon, A., et al. (2010). Oxytocin selectively improves empathic accuracy. *Psychological Science*, 21, 1426–1428.

Bartz, J. A., Zaki, J., Bolger, N., & Ochsner, K. N. (2011). Social effects of oxytocin in humans: Context and person matter. *Trends in Cognitive Sciences*, 15, 301–309.

Bartz, J. A., Zaki, J., Ochsner, K. N., Bolger, N., Kolevzon, A., Ludwig, N., et al. (2010). Effects of oxytocin on recollections of maternal care and closeness. *Proceedings of the National Academy of Sciences of the USA*, 107, 21371–21375.

Beja-Pereira, A., Luikart, G., England, P. R., Bradley, D. G., Jann, O. C., Bertorelle, G., et al. (2003). Gene-culture coevolution between cattle milk protein genes and human lactase genes. *Nature Genetics*, 35, 311–313.

Belsky, D. W., Moffitt, T. E., Baker, T. B., Biddle, A. K., Evans, J. P., Harrington, H., et al. (2013). Polygenic risk and the developmental progression to heavy, persistent smoking and nicotine dependence: Evidence from a 4-decade longitudinal study. *JAMA Psychiatry*, 70, 534–542.

Belsky, J., Bakermans-Kranenburg, M. J., & van IJzendoorn, M. H. (2007). For better and for worse: Differential susceptibility to environmental influences. *Current Directions in Psychological Science*, 16, 300–304.

Belsky, J., Jonassaint, C., Pluess, M., Stanton, M., Brummett, B., & Williams, R. (2009). Vulnerability genes or plasticity genes? *Molecular Psychiatry*, 14, 746–754.

Berger, P. L., & Luckmann, T. (1966). *Social construction of reality: A treatise in the sociology of knowledge*. Garden City, NY: Anchor Books.

Bowcock, A. M., Kidd, J. R., Mountain, J. L., Hebert, J. M., Carotenuto, L., Kidd, K. K., et al. (1991). Drift, admixture, and selection in human evolution: A study with DNA polymorphisms. *Proceedings of the National Academy of Sciences of the USA*, 88, 839–843.

Boyd, R., & Richerson, P. J. (1985). *Culture and the evolutionary process*. Chicago: University of Chicago Press.

Caspi, A., McClay, J., Moffitt, T. E., Mill, J., Martin, J., Craig, I. W., et al. (2002). Role of genotype in the cycle of violence in maltreated children. *Science*, 297, 851–854.

Caspi, A., Sugden, K., Moffitt, T. E., Taylor, A., Craig, I. W., Harrington, H., et al. (2003). Influence of life stress on depression: Moderation by a polymorphism in the 5-HTT gene. *Science*, 301(5631), 386–389.

Cavalli-Sforza, L., & Feldman, M. (1981). *Cultural transmission and evolution: A quantitative approach*. Princeton, NJ: Princeton University Press.

Chang, W. C. (1985). A cross-cultural study of depressive symptomatology. *Culture, Medicine and Psychiatry*, 9, 295–317.

Chentsova-Dutton, Y. E., Chu, J. P., Tsai, J. L., Rottenberg, J., Gross, J. J., & Gotlib, I. H. (2007). Depression and emotional reactivity: Variation among Asian Americans of East Asian descent and European Americans. *Journal of Abnormal Psychology*, 116, 776–785.

Cheon, B. K., Livingston, R. W., Hong, Y-y., & Chiao, J. Y. (2014). Gene × environment interaction on intergroup bias: The role of 5-HTTLPR and perceived outgroup threat. *Social Affective and Cognitive Neuroscience*, 9(9), 1268–1275.

Cheon, B. K., Mrazek, A. J., Pornpattananangkul, N., Blizinsky, K. D., & Chiao, J. Y. (2013). Constraints, catalysts and coevolution in cultural neuroscience: Reply to commentaries. *Psychological Inquiry*, 24, 71–79.

Chiao, J. Y., & Ambady, N. (2007). Cultural neuroscience: Parsing universality and diversity across levels of analysis. In S. Kitayama & D. Cohen (Eds.), *Handbook of cultural psychology* (pp. 237–254). New York: Guilford.

Chiao, J. Y., & Blizinsky, K. D. (2010). Culture-gene coevolution of individualism-collectivism and the serotonin transporter gene. *Proceedings of the Royal Society B: Biological Sciences*, 277(1681), 529-537.

Chiao, J. Y., Cheon, B. K., Pornpattananangkul, N., Mrazek, A. J., & Blizinsky, K. D. (2013). Cultural neuroscience: Progress and promise. *Psychological Inquiry*, 24, 1-19.

Chiao, J. Y., & Immordino-Yang, M. H. (2013). Modularity and the cultural mind: Contributions of cultural neuroscience to cognitive theory. *Perspectives on Psychological Science*, 8, 56-81.

Choi, I., Koo, M., & Choi, J. (2007). Individual differences in analytic versus holistic thinking. *Personality and Social Psychology Bulletin*, 33, 691-705.

Cohen, A. B. (2009). Many forms of culture. *American Psychologist*, 64, 194-204.

Cohen, S. (2004). Social relationships and health. *American Psychologist*, 59, 676-684.

Cole, S. W., Arevalo, J. M., Takahashi, R., Sloan, E. K., Lutgendorf, S. K., Sood, A. K., et al. (2010). Computational identification of gene-social environment interaction at the human IL6 locus. *Proceedings of the National Academy of Sciences of the USA*, 107, 5681-5686.

Cole, S. W., Hawkey, L. C., Arevalo, J. M., Sung, C. Y., Rose, R. M., & Cacioppo, J. T. (2007). Social regulation of gene expression in human leukocytes. *Genome Biology*, 8, R189.

Commission on Social Determinants of Health. (2008). *Closing the gap in a generation: Health equity through action on the social determinants of health. Final report of the Commission on Social Determinants of Health*. Geneva: World Health Organization.

De Dreu, C. K. W., Greer, L. L., Van Kleef, G. A., Shalvi, S., & Handgraaf, M. J. J. (2010). Oxytocin promotes human ethnocentrism. *Proceedings of the National Academy of Sciences of the USA*, 108, 1262-1266.

de Waal, F. (2001). *The ape and the sushi master: Cultural reflections of a primatologist*. New York: Basic Books.

Declerck, C. H., Boone, C., & Kiyonari, T. (2010). Oxytocin and cooperation under conditions of uncertainty: The modulating role of incentives and social information. *Hormones and Behavior*, 57, 368-374.

Diener, E., & Diener, M. (1995). Cross-cultural correlates of life satisfaction and self-esteem. *Journal of Personality and Social Psychology*, 68(4), 653–663.

Diener, E., Oishi, S., & Lucas, R. E. (2003). Personality, culture, and subjective well-being: Emotional and cognitive evaluations of life. *Annual Review of Psychology*, 54(1), 403–425.

Dressler, W. W., Balieiro, M. C., Ribeiro, R. P., & Dos Santos, J. E. (2009). Cultural consonance, a 5HT2A receptor polymorphism, and depressive symptoms: A longitudinal study of gene × culture interaction in urban Brazil. *American Journal of Human Biology*, 21(1), 91–97.

Durham, W. H. (1990). Advances in evolutionary culture theory. *Annual Review of Anthropology*, 19, 187–210.

Durham, W. H. (1991). *Coevolution: Genes, culture and human diversity*. Stanford, CA: Stanford University Press.

Feldman, M. W., & Laland, K. N. (1996). Gene-culture co-evolutionary theory. *Trends in Ecology and Evolution*, 11, 453–457.

Fincher, C. L., Thornhill, R., Murray, D. R., & Schaller, M. (2008). Pathogen prevalence predicts human cross-cultural variability in individualism/collectivism. *Proceedings of the Royal Society B: Biological Sciences*, 275, 1279–1285.

Foley, D. L., Eaves, L. J., Wormley, B., Silberg, J. L., Maes, H. H., Kuhn, J., et al. (2004). Childhood adversity, monoamine oxidase a genotype, and risk for conduct disorder. *Archives of General Psychiatry*, 61(7), 738–744.

Fraga, M. F., Ballestar, E., Paz, M. F., Ropero, S., Setien, F., Ballestar, M. L., et al. (2005). Epigenetics differences arise during the lifetime of monozygotic twins. *Proceedings of the National Academy of Sciences of the USA*, 102, 10604–10609.

Franklin, T. B., & Mansuy, I. M. (2010). The prevalence of epigenetic mechanisms in the regulation of cognitive functions and behaviour. *Current Opinion in Neurobiology*, 20, 441–449.

Fulmer, C. A., Gelfand, M. J., Kruglanski, A. W., Kim-Prieto, C., Diener, E., Pierro, A., et al. (2010). On “feeling right” in cultural contexts: How person-culture match affects self-esteem and subjective well-being. *Psychological Science*, 21(11), 1563–1569.

Geertz, C. (1973). *The interpretation of cultures*. New York: Basic Books.

Gregory, S. G., Connelly, J. J., Towers, A. J., Johnson, J., Biscocho, D., Markunas, C. A., et al. (2009). Genomic and epigenetic evidence for oxytocin receptor deficiency in autism. *BioMed Central Medicine*, 7, 62.

Grossmann, I., & Varnum, M. E. W. (2011). Social class, culture, and cognition. *Social Psychological and Personality Science*, 2, 81–89.

Heine, S. J., Kitayama, S., Lehman, D. R., Takata, T., Ide, E., Leung, C., et al. (2001). Divergent consequences of success and failure in Japan and North America: An investigation of self-improving motivations and malleable selves. *Journal of Personality and Social Psychology*, 81, 599–615.

Heine, S. J., & Lehman, D. R. (1997). The cultural construction of self-enhancement: An examination of group-serving biases. *Journal of Personality and Social Psychology*, 72(6), 1268–1283.

Henrich, J., Heine, S. J., & Norenzayan, A. (2010a). The weirdest people in the world? *Behavioral and Brain Sciences*, 33, 61–83. doi:10.1017/S0140525X0999152X

Henrich, J., Heine, S. J., & Norenzayan, A. (2010b). Most people are not WEIRD. *Nature*, 466, 29.

Herskovits, M. J. (1948). *Man and his works: The science of cultural anthropology*. New York: Knopf.

Hong, Y.-y., Morris, M. W., Chiu, C.-Y., & Benet-Martínez, V. (2000). Multicultural minds: A dynamic constructivist approach to culture and cognition. *American Psychologist*, 55, 709–720.

Huang, T. H. M., Perry, M. R., & Laux, D. E. (1999). Methylation profiling of CpG islands in human breast cancer cells. *Human Molecular Genetics*, 8(3), 459–470.

Jack, A., Connelly, J. J., & Morris, J. P. (2012). DNA methylation of the oxytocin receptor gene predicts neural response to ambiguous social stimuli. *Frontiers in Human Neuroscience*, 6, 1–7.

Ji, L. J., Nisbett, R. E., & Su, Y. (2001). Culture, change, and prediction. *Psychological Science*, 12(6), 450–456.

Johnson, W., & Krueger, R. F. (2005). Genetic effects on physical health: Lower at higher income levels. *Behavior Genetics*, 35, 579–590.

- Karg, K., Burmeister, M., Shedden, K., & Sen, S. (2011). The serotonin transporter promoter variant (5-HTTLPR), stress, and depression meta-analysis revisited. *Archives of General Psychiatry*, 68, 444–454. doi:10.1001/archgenpsychiatry.2010.189
- Kim, B. S. K. (2007). Adherence to Asian and European American cultural values and attitudes toward seeking professional psychological help among Asian American college students. *Journal of Counseling Psychology*, 54, 474–480.
- Kim, H., & Markus, H. R. (1999). Deviance or uniqueness, harmony or conformity? A cultural analysis. *Journal of Personality and Social Psychology*, 77, 785–800.
- Kim, H. S., & Sasaki, J. Y. (2012). Emotion regulation: The interplay of culture and genes. *Social and Personality Psychology Compass*, 6, 865–877.
- Kim, H. S., & Sasaki, J. Y. (2014). Cultural neuroscience: Biology of the mind in cultural contexts. *Annual Review of Psychology*, 65, 24.1–24.28.
- Kim, H. S., Sherman, D. K., Mojaverian, T., Sasaki, J. Y., Park, J., Suh, E. M., et al. (2011). Gene-culture interaction: Oxytocin receptor polymorphism (OXTR) and emotion regulation. *Social Psychological and Personality Science*, 2(6), 665–672.
- Kim, H. S., Sherman, D. K., Sasaki, J. Y., Xu, J., Chu, T. Q., Ryu, C., et al. (2010). Culture, distress, and oxytocin receptor polymorphism (OXTR) interact to influence emotional support seeking. *Proceedings of the National Academy of Sciences of the USA*, 107(36), 15717–15721.
- Kim, H. S., Sherman, D. K., & Taylor, S. E. (2008). Culture and social support. *American Psychologist*, 63, 518–526.
- Kim, H. S., Sherman, D. K., Taylor, S. E., Sasaki, J. Y., Chu, T. Q., Ryu, C., et al. (2010). Culture, the serotonin receptor polymorphism (5-HTT1A) and locus of attention. *Social Cognitive and Affective Neuroscience*, 5, 212–218.
- Kim-Cohen, J., Caspi, A., Taylor, A., Williams, B., Newcombe, R., Craig, I. W., et al. (2006). MAOA, maltreatment, and gene-environment interaction predicting children's mental health: New evidence and a meta-analysis. *Molecular Psychiatry*, 11, 903–913.
- Kitayama, S., King, A., Yoon, C., Tompson, S., Huff, S., & Liberzon, I. (2014). The dopamine receptor gene (*DRD4*) moderates cultural difference in independent versus interdependent social orientation. *Psychological Science*, 25(6), 1169–1177.

- Kitayama, S., Park, H., Sevincer, A. T., Karasawa, M., & Uskul, A. K. (2009). A cultural task analysis of implicit independence: Comparing North America, Western Europe, and East Asia. *Journal of Personality and Social Psychology*, 97, 236–255.
- Kleinman, A. (1982). Neurasthenia and depression: A study of somatization and culture in China. *Culture, Medicine and Psychiatry*, 6(2), 117–190.
- Koenig, H. G., & Larson, D. B. (2001). Religion and mental health: Evidence for an association. *International Review of Psychiatry*, 13, 67–78.
- Kosfeld, M., Heinrichs, M., Zak, P. J., Fischbacher, U., & Fehr, E. (2005). Oxytocin increases trust in humans. *Nature*, 435, 673–676.
- Larsen, H., van der Zwaluw, C. S., Overbeek, G., Granic, I., Granke, B., & Engels, R. C. M. E. (2010). A variable-number-of-tandem-repeats polymorphism in the dopamine D4 receptor gene affects social adaptation of alcohol use: Investigation of a gene–environment interaction. *Psychological Science*, 21, 1064–1068.
- Ledón-Rettig, C. C., & Pfennig, D. W. (2012). Antipredator behavior promotes diversification of feeding strategies. *Integrative and Comparative Biology*, 52, 53–63.
- Lee, A. Y., Aaker, J. L., & Gardner, W. L. (2000). The pleasures and pains of distinct self-construals: The role of interdependence in regulatory focus. *Journal of Personality and Social Psychology*, 78, 1122–1134.
- Lu, L. (2005). In pursuit of happiness: The cultural psychological study of SWB. *Chinese Journal of Psychology*, 47(2), 99–112.
- Lumsden, C. J., & Wilson, E. O. (1981). *Genes, mind and culture: The coevolutionary process*. Cambridge, MA: Harvard University Press.
- Major, B., Mendes, W. B., & Dovidio, J. F. (2013). Intergroup relations and health disparities: A social psychological perspective. *Health Psychology*, 32(5), 514–524.
- Markides, K. S., & Eschbach, K. (2005). Aging, migration, and mortality: Current status of research on the Hispanic paradox. *Journal of Gerontology Series B*, 60B, 68–75.
- Markus, H. R., & Kitayama, S. (1991). Culture and self: Implications for cognition, emotion, and motivation. *Psychological Review*, 98, 224–253.
- Masuda, T., & Nisbett, R. E. (2001). Attending holistically versus analytically: Comparing the context sensitivity of Japanese and Americans. *Journal of Personality and Social Psychology*, 81, 922–934.



- Matthews, K. A., & Gallo, L. C. (2011). Psychological perspectives on pathways linking socioeconomic status and physical health. *Annual Review of Psychology*, 62, 501–530. doi: 10.1146/annurev.psych.031809.130711
- McCullough, M. E., Hoyt, W. T., Larson, D. B., Koenig, H. G., & Thoresen, C. E. (2000). Religious involvement and mortality: A meta-analytic review. *Health Psychology*, 19, 211–222.
- Meaney, M. J. (2001). Maternal care, gene expression, and the transmission of individual differences in stress reactivity across generations. *Annual Review of Neuroscience*, 24, 1161–1192.
- Miller, G. (2013). The promise and perils of oxytocin. *Science*, 339, 267–269.
- Miller, G. E., Chen, E., Fok, A.K., Walker, H., Lim, A., Nicholls, E. F., et al. (2009). Low early-life social class leaves a biological residue manifested by decreased glucocorticoid and increased proinflammatory signaling. *Proceedings of the National Academy of Sciences of the USA*, 106, 14716–14721.
- Miller, G. E., Chen, E., Sze, J., Marin, T., Arevalo, J. M., Doll, R., et al. (2008). A functional genomic fingerprint of chronic stress in humans: Blunted glucocorticoid and increased NF-κB signaling. *Biological Psychiatry*, 64(4), 266–272.
- Mills, M. L. (2012). Unconventional mental health treatment: Reexamining the racial-ethnic disparity in treatment-seeking behavior. *Psychiatric Services*, 63, 142–146.
- Mischel, W. (1990). Personality dispositions revisited and revised: A view after three decades. In L. A. Pervin (Ed.), *Handbook of personality: Theory and research* (pp. 111–134). New York: Guilford.
- Mischel, W., & Shoda, Y. (1995). A cognitive-affective system theory of personality: Reconceptualizing situations, dispositions, dynamics, and invariance in personality structure. *Psychological Review*, 102, 246–268.
- Mojaverian, T., Hashimoto, T., & Kim, H.S. (2013). Cultural differences in professional help seeking: A comparison of Japan and the U.S. *Frontiers in Cultural Psychology*, 3, 615. doi:10.3389/fpsyg.2012.00615
- Morling, B., Kitayama, S., & Miyamoto, Y. (2002). Cultural practices emphasize influence in the United States and adjustment in Japan. *Personality and Social Psychology Bulletin*, 28, 311–323.

- Morling, B., Kitayama, S., & Miyamoto, Y. (2003). American and Japanese women use different coping strategies during normal pregnancy. *Personality and Social Psychology Bulletin*, 29, 1533-1546.
- Moscowitz, D. S., & Côté, S. (1995). Do interpersonal traits predict affect? A comparison of three models. *Journal of Personality and Social Psychology*, 69, 915-924.
- Mrazek, A. J., Chiao, J. Y., Blizinsky, K. D., Lun, J., & Gelfand, M. J. (2015). Culture-gene coevolution of tightness-looseness and allelic variation of the serotonin transporter gene: The dual influence on morality. *Culture and Brain*.
- Myles, S., Bouzekri, N., Haverfield, E., Cherkaoui, M., Dugoujon, J. M., & Ward, R. (2005). Genetic evidence in support of a shared Eurasian-North African dairying origin. *Human Genetics*, 117, 34-42.
- Na, J., Grossman, I., Varnum, M. E. W., Kitayama, S., Gonzalez, R., & Nisbett, R. E. (2010). Cultural differences are not always reducible to individual differences. *Proceedings of the National Academy of Sciences of the USA*, 107, 6192-6197.
- Oishi, S., & Diener, E. (2001). Goals, culture, and subjective well-being. *Personality and Social Psychology Bulletin*, 27, 1674-1682.
- Oishi, S., & Diener, E. (2003). Culture and well-being: The cycle of action, evaluation, and decision. *Personality and Social Psychology Bulletin*, 29(8), 939-949.
- Oyserman, D., & Lee, S. W. S. (2008). Does culture influence what and who we think? Effects of priming individualism and collectivism. *Psychological Bulletin*, 134, 311-342.
- Pascoe, E. A., & Smart Richman, L. (2009). Perceived discrimination and health: A meta-analytic review. *Psychological Bulletin*, 135, 531-554. doi:10.1037/a0016059
- Pelphrey, K. A., & Morris, J. P. (2006). Brain mechanisms for interpreting the actions of others from biological-motion cues. *Current Directions in Psychological Science*, 15, 136-140.
- Peng, K., & Nisbett, R. E. (1999). Culture, dialectics, and reasoning about contradiction. *American Psychologist*, 54(9), 741-754.
- Plaut, V. C., Markus, H. R., & Lachman, M. E. (2002). Place matters: Consensual features and regional variation in American well-being and self. *Journal of Personality and Social Psychology*, 83(1), 160-184.

- Plaut, V. C., Markus, H. R., Treadway, J. R., & Fu, A. S. (2012). The cultural construction of self and well-being: A tale of two cities. *Personality and Social Psychology Bulletin*, 38, 1644–1658.
- Reist, C., Ozdemir, V., Wang, E., Hashemzadeh, M., Mee, S., & Moyzis, R. (2007). Novelty seeking and the dopamine D4 receptor gene (*DRD4*) revisited in Asians: Haplotype characterization and relevance of the 2-repeat allele. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics*, 144B, 453–457.
- Risch, N., Herrell, R., Lehner, T., Liang, K.-Y., Eaves, L., Hoh, J., et al. (2009). Interaction between the serotonin transporter gene (5-HTTLPR), stressful life events, and risk of depression: A meta-analysis. *JAMA*, 301, 2642–2471.
- Roberts, R. L., Harper, R., Tuttle-Eagle Bull, D., & Heidemann-Provost, L. M. (1998). The Native American medicine wheel and individual psychology: Common themes. *Journal of Individual Psychology*, 54, 135–145.
- Robinson, G. E., Fernald, R. D., & Clayton, D. F. (2008). Genes and social behavior. *Science*, 322, 896–900.
- Rodrigues, S. M., Saslow, L. R., Garcia, N., John, O. P., & Keltner, D. (2009). Oxytocin receptor genetic variation relates to empathy and stress reactivity in humans. *Proceedings of the National Academy of Sciences of the USA*, 106, 21437–21441.
- Ryder, A. G., Ban, L. M., & Chentsova-Dutton, Y. E. (2011). Towards a cultural-clinical psychology. *Social and Personality Psychology Compass*, 5, 960–975.
- Sasaki, J. Y. (2013). Promise and challenges surrounding culture–gene coevolution and gene–culture interactions. *Psychological Inquiry*, 24, 64–70.
- Sasaki, J. Y., Kim, H. S., Mojaverian, T., Kelley, L. D., Park, I., & Janušonis, S. (2013). Religion priming differentially increases prosocial behavior among variants of dopamine D4 Receptor (*DRD4*) gene. *Social Cognitive and Affective Neuroscience*, 8, 209–215.
- Sasaki, J. Y., Kim, H. S., & Xu, J. (2011). Religion and well-being: The moderating role of culture and the oxytocin receptor (*OXTR*) gene. *Journal of Cross-Cultural Psychology*, 42, 1394–1405.
- Schmid, B., Blomeyer, D., Treutlein, J., Zimmermann, U. S., Buchmann, A. F., Schmidt, M. H., et al. (2010). Interacting effects of *CRHR1* gene and stressful life events on drinking initiation and progression among 19-year-olds. *International Journal of Neuropsychopharmacology*, 13(6), 703–714.

Schulman, S., & Smith, A. M. (1963). The concept of "health" among Spanish-speaking villagers of New Mexico and Colorado. *Journal of Health and Human Behavior*, 4, 226-234.

Seeman, T. E. (1996). Social ties and health: The benefits of social integration. *Annals of Epidemiology*, 6, 442-451.

Shweder, R. (1995). Cultural psychology: What is it? In N. R. Goldberger & J. B. Veroff (Eds.), *The culture and psychology reader* (pp. 41-86). New York: New York University Press.

Slavich, G. M., & Cole, S. W. (2013). The emerging field of human social genomics. *Clinical Psychological Science*, 1, 331-348.

Slavich, G. M., O'Donovan, A., Epel, E. S., & Kemeny, M. E. (2010). Black sheep get the blues: A psychobiological model of social rejection and depression. *Neuroscience and Biobehavioral Reviews*, 35, 39-45.

Smillie, L. D., Cooper, A. J., Proitsi, P., Powell, J. F., & Pickering, A. D. (2010). Variation in *DRD2* dopamine gene predicts extraverted personality. *Neuroscience Letters*, 468(3), 234-237.

Spencer-Rodgers, J., Williams, M. J., & Peng, K. (2010). Cultural differences in expectations of change and tolerance for contradiction: A decade of empirical research. *Personality and Social Psychology Review*, 14(3), 296-312.

Suh, E., Diener, E., Oishi, S., & Triandis, H. C. (1998). The shifting basis of life satisfaction judgments across cultures: Emotions versus norms. *Journal of Personality and Social Psychology*, 74(2), 482-493.

Taylor, S. E., Sherman, D. K., Kim, H. S., Jarcho, J., Takagi, K., & Dunagan, M. S. (2004). Culture and social support: Who seeks it and why? *Journal of Personality and Social Psychology*, 87, 354-362.

Taylor, S. E., Way, B. M., Welch, W. T., Hilmert, C. J., Lehman, B. J., & Eisenberger, N. I. (2006). Early family environment, current adversity, the serotonin transporter promoter polymorphism, and depressive symptomatology. *Biological Psychiatry*, 60(7), 671-676.

Taylor, S. E., Welch, W. T., Kim, H. S., & Sherman, D. K. (2007). Cultural differences in the impact of social support on psychological and biological stress responses. *Psychological Science*, 18, 831-837.

- Tooby, J., & Cosmides, L. (1992). The psychological foundations of culture. In J. Barkow, L. Cosmides, & J. Tooby (Eds.), *The adapted mind: Evolutionary psychology and the generation of culture* (pp. 19–136). New York: Oxford University Press.
- Triandis, H. C. (2007). Culture and psychology: A history of the study of their relationships. In S. Kitayama & D. Cohen (Eds.), *Handbook of cultural psychology* (pp. 59–76). New York: Guilford.
- Tsai, J. L., & Chentsova-Dutton, Y. (2002). Understanding depression across cultures. In I. Gotlib & C. Hammen (Eds.), *Handbook of depression* (pp. 467–491). New York: Guilford.
- Tsai, J. L., Simeonova, D., & Watanabe, J. (2004). Somatic and social: Chinese Americans talk about emotion. *Personality and Social Psychology Bulletin*, 30, 1226–1238.
- Uchida, Y., & Kitayama, S. (2009). Happiness and unhappiness in East and West: Themes and variations. *Emotion*, 9(4), 441–456.
- Unternaehrer, E., Luers, P., Mill, J., Dempster, E., Meyer, A. H., Staehli, S., et al. (2012). Dynamic changes in DNA methylation of stress-associated genes (OXTR, BDNF) after acute psychosocial stress. *Translational Psychiatry*, 2, e150.
- van IJzendoorn, M. H., Caspers, K., Bakermans-Kranenburg, M. J., Beach, S. R., & Phillibert, R. (2010). Methylation matters: Interaction between methylation density and serotonin transporter genotype predicts unresolved loss or trauma. *Biological Psychiatry*, 68, 405–407.
- Waldram, J. B. (2006). *Aboriginal health in Canada: Historical, cultural, and epidemiological perspectives*. Toronto: University of Toronto Press.
- Wang, E., Ding, Y.-C., Flodman, P., Kidd, J. R., Kidd, K. K., Grady, D. L., et al. (2004). The genetic architecture of selection at the human dopamine receptor D4 (*DRD4*) gene locus. *American Journal of Human Genetics*, 74, 931–944.
- Way, B. M., & Lieberman, M. D. (2010). Is there a genetic contribution to cultural differences? Collectivism, individualism and genetic markers of social sensitivity. *Social Cognitive and Affective Neuroscience*, 5, 203–211.
- Weaver, I. C., Cervoni, N., Champagne, F. A., D'Alessio, A. C., Sharma, S., Seckl, J. R., et al. (2004). Epigenetic programming by maternal behavior. *Nature Neuroscience*, 7(8), 847–854.
- Weaver, I. C., Champagne, F. A., Brown, S. E., Dymov, S., Sharma, S., Meaney, M. J., et al. (2005). Reversal of maternal programming of stress responses in adult offspring

through methyl supplementation: Altering epigenetic marking later in life. *Journal of Neuroscience*, 25, 11045–11054.

Williams, D. R., & Collins, C. (1995). US socioeconomic and racial differences in health: Patterns and explanations. *Annual Review of Sociology*, 21, 349–386.

Williams, D. R., & Mohammed, S. A. (2009). Discrimination and racial disparities in health: Evidence and needed Research. *Journal of Behavioral Medicine*, 32, 20–47. doi: 10.1007/s10865-008-9185-0

Williams, D. R., & Sternthal, M. (2010). Understanding racial-ethnic disparities in health: Sociological contributions. *Journal of Health and Social Behavior*, 51, S15–S27.

World Health Organization. (2003). *WHO definition of health*. Retrieved from .

Yang, J., Lee, S. H., Goddard, M. E., & Visscher, P. M. (2011). GCTA: A tool for genome-wide complex trait analysis. *American Journal of Human Genetics*, 88, 76–82.

**Joni Y. Sasaki**

Joni Y. Sasaki Department of Psychology, York University, Toronto, Ontario

**Jessica LeClair**

Jessica LeClair Department of Psychology, University of California Santa Barbara, Santa Barbara, California

**Alexandria West**

Alexandria West Department of Psychology, York University, Toronto, Ontario

**Heejung S. Kim**

Heejung S. Kim Department of Psychology University of California Santa Barbara Santa Barbara, California

