Chapter 13

Temperamental Contributions to the Development of Psychological Profiles: I. Basic Issues

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The bases for the properties all humans share, as well as the different reasons for the considerable variation, are two fundamental, unsolved scientific puzzles. Although experiences contribute to both outcomes, each child's pattern of temperaments represents the biological contribution to the variation. Most scientists define a temperament as a behavioral profile that originates in a distinctive biology that, at present, is a mystery. It is assumed, but not yet proven, that a majority of human temperaments appear during early childhood and are sculpted by experiences into a large, but, nonetheless, limited, number of possible personality traits. Although current theory assumes that most temperamental biases are the result of heritable variation in brain neurochemistry, or in some cases anatomy, some biases can be the products of prenatal events that are not strictly genetic. These causal conditions include season of conception and maternal infections or stressors, usually chronic, that alter the chemical environment of the embryo or fetus during gestation (Kagan & Snidman, 2004).

It is worth noting that the modern concept of heredity, which assumes that microscopic elements from each parent merge to contribute to the traits of the offspring, was not invented until the end of the eighteenth century. Indeed, sixteenth-century European scholars attributed the fact that "like begets like" to similarities in the circumstances surrounding conception and embryonic development. By contrast, the concept of atoms as the bases of the material world is more than 2300 years old (Muller-Wille & Rheinberger, 2012). One reason why scholars before Darwin found it difficult to imagine that material elements from the two parents could be transferred to offspring was that most children did not possess a large number of features that were identical to those possessed by one or both parents. The idea that

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the properties of all life could be traced to the four bases of DNA, which contain only four kinds of atoms (nitrogen, hydrogen, oxygen, and carbon) is extremely counter-intuitive.

American psychologists have not been friendly to the concept of temperament because it implies that children vary in their reactions to the same experiences. This premise is inconsistent with an egalitarian ethos which assumes that all children born healthy should be able to profit equally from the same events. The United States has been and remains a pragmatic society interested primarily in what can be changed to make things better; hence the dominance of learning theory for such a long time. The idea of temperament implies the presence of biological biases that are not changed easily.

Humans possess combinations of a large number of temperaments, some rare and some more common, most of which remain undiscovered. There are more than 290,000 combinations of the twelve blood types and their variants. Hence, the probability that any two people will have the same combination is .0003 (3 out of 10,000) (Lewontin, 1995). Because there are many more neurochemical profiles than blood types, the chance of any two individuals having the same pattern of temperaments should be extremely low.

HOW MANY TEMPERAMENTS?

The contemporary referents for a temperament are behavioral because we do not yet know the genes or brain properties that are the foundation of any known bias.

Infants vary in a relatively small number of observable behaviors that could be temperamental in origin. The most obvious are reactions to the uncomfortable states of pain, cold, and hunger. Infants vary in both the intensity and duration of distress to these aversive events, as well as in the ease of being soothed. This means that here should be four different temperamental biases: (1) infants who cry intensely and do not soothe easily; (2) infants who cry intensely but are soothed with minimal effort; (3) infants who are not seriously distressed but, nonetheless, do not soothe easily, and, finally, (4) those who are minimally distressed and easily soothed.

Another quartet of temperaments is defined by reactions to unfamiliar or unexpected events that are neither painful nor frustrating. These include new foods, smells, sounds, and sights. Some infants become active to these incentives; others remain still; some cry; others are quiet. The combinations of these reactions generate four additional temperaments. Infants also vary in their reaction to frustrations, such as losing the nipple they were sucking or being restrained by a blanket or a pair of hands. The combination of vigorous motor activity and crying to these frustrations yields an additional four temperaments. Four additional biases are defined by the predictability of the infant's behavior as well as the frequency of spontaneous babbling, smiling, or limb movements that occur without an external incentive.

These 16 temperaments are defined by behaviors rather than by psychological states that cannot be observed. It is likely, however, that infants also vary in the intensity of hedonic pleasure they experience to sweet tastes or gentle caresses, as well as the intensity of displeasure to bitter tastes or rough handling. The infants who have a larger than normal number of taste buds for sweet or bitter substances should experience more intense sensations to ice cream or turnips (Zhang et al., 2009). Future investigators may add these two biases to the 16 that are detected more easily.

However, 18 is a small number of temperaments considering the large number of possible biases; hence, it is likely that future investigators will discover many more biases than the ones nominated. It is relevant, therefore, to ask why psychologists have observed such a small number of biases when it is likely that there are many thousands of brain states, each linked to a distinctive neurochemical profile that could be the basis for a temperament. First, many brain profiles probably have no implications for a temperament. Second, there may be subtypes within each of the behavioral biases described. Some infants may scream at the pain inflicted by a diaper pin but not cry when hungry; some may smile when they are fed but not when playing peek-a-boo.

Because there are far fewer classes of behavior than potential causal conditions, each behavioral phenotype can be the product of more than one cascade of biological conditions. For example, the conditioned and spontaneous form of many responses that appear identical to observers, including body startle, orienting, and blinking, involve different circuits.

Moreover, the physical and social features of the child's settings have a profound influence on the moods and behaviors that reflect a temperamental bias. Thus, the observable signs of temperamental constructs should combine a class of behavior with a class of context. Unfortunately, most current temperamental concepts, such as excitability or regulation, are naked predicates free of any context. The conditions in modern societies may contribute a little to the psychologist's indifference to the significance of the setting on a behavior or mood. Visitors to zoos and aquaria see animals removed from their natural ecologies; visitors to museums view artifacts in glass cases rather than in their original locations; and photos on Facebook pages usually contain no information on the background of the person in the picture. These experiences support the idea that the setting of an animal, object, or person is irrelevant; all that matters is the entity of interest.

When future scientists discover the genes that are the foundations of many temperaments observed in infants they will not be able to predict the adult's personality because life experiences, including current circumstances, will have selected one profile of emotions and actions from the larger envelope of possibilities. That is, a particular profile is the result of a child with a particular set of temperaments growing up in a particular family in a particular cultural—historical setting. For example, the probability that an older adult who was depressed on one occasion would continue to be depressed for two additional years was

considerably higher in Italy than in neighboring Switzerland (Gallagher, Savva, Kenny, & Lawlor, 2013). This fact implies that the social conditions in a nation—unemployment rate, level of corruption, trust in government, level of income inequality—can influence the mood of its citizens and either maintain or alleviate the symptoms of melancholy.

Indeed, it is possible to defend the suggestion that the context often has important influences on the adaptive property of a biological feature. The minority of adults born with sickle-shaped red blood cells rather than the more frequent round shape have an advantage if they live in areas where malaria is common but are at a disadvantage if they reside in regions without the mosquito that carries the malarial parasite. Increased activity in the HPA axis and the sympathetic nervous system is adaptive for a soldier in a battle zone but not for a historian doing archival work in a library. A child born with a temperamental bias favoring a high threshold for uncertainty and anxiety is at risk for a criminal career if raised in a neglectful family and crime-ridden neighborhood but apt to become a productive leader if reared in an affluent, affectionate family in a quiet suburb. The cultural context can even determine whether a person who betrays those who believed they were friends should be classified as a psychopath or a great statesman.

The indeterminacy surrounding the relation between the presence of a gene with a known function and a psychological phenotype is supported by the recent, somewhat surprising, discovery that many adults who possess a large number of alleles known to contribute to physical diseases report no debilitating symptoms, probably because the risk genes are located in the context of other genes in the genome that are protective (Xue, Chen, Ayub, Huang, Ball, et al., 2012).

GENES AND NEUROCHEMISTRY

The human genome contains genes that code for at least 150 brain molecules and more than 2000 different receptors. The molecules that act directly on receptors on the postsynaptic neuron to initiate activity, such as glutamate and acetylcholine, are called neurotransmitters. Other molecules, called neuromodulators, such as serotonin and dopamine, modify the level of activity in a neuron already activated. Any one of the very large number of possible combinations of molecular concentrations and densities and locations of receptors could be the foundation of a human temperament.

Some of the important molecules are norepinephrine, dopamine, serotonin, corticotropin-releasing hormone, glutamate, GABA, opioids, vasopressin, oxytocin, prolactin, COMT, monoamine oxidase, and the sex hormones. If we assume conservatively, for the sake of illustration, that the concentration of a molecule and the density of the receptors to which it binds are low, moderate, or high, there can be nine possible profiles for each molecule. Hence, 150 different molecules would yield at least 1400 neurochemical profiles that could reciprocally influence each other and create the basis for a very large number of

temperaments. If we add the fact that most molecules can bind to several types of receptors in different locations the number of possible temperaments increases by a very large amount if we assume that at least some of these molecules contribute to temperament.

Consider a few examples of modest relations discovered between neurochemistry and behavioral signs of a temperament. Serotonin, secreted by the raphe nucleus, suppresses neuronal excitability in many sites, suggesting that infants or children with lower levels of brain serotonin should be more distressed. The duration of serotonin activity in the synapse is influenced by the serotonin transporter molecule which removes serotonin from the synapse. A large number of alleles of the gene for the serotonin transporter molecule—23 discovered thus far—could influence the amount of transporter produced. Two common alleles, called short and long, are located in the promoter region of the gene. The short allele (14 repeats of a 20 to 23 base pair string) is associated with less effective transcription of the gene than the long allele (16 repeats). Possession of the short allele implies the synthesis of less transporter and, therefore, serotonin will remain active in the synapse for a longer time. It is believed that this condition leads to suppression of activity in the raphe nucleus, or a decrease in the density of serotonin receptors, and, as a result, a lower tonic level of serotonergic activity. This condition is accompanied by greater excitability of the amygdala, as well as alterations in the circuit that connects the amygdala with the prefrontal cortex (Green et al., 2008; Hariri et al., 2002; Pezawas et al., 2005).

There is considerable variation across the world's populations in the frequency of the short and long alleles (Murdoch, Speed, Pakstis, Heffelfinger, & Kidd, 2013). Asian populations are much more likely than European or African pedigrees to possess the short allele (Gelernter et al., 1999). This fact, perhaps aided by other genetic differences between Asians and other groups, may contribute to the observation that four-month-old Chinese infants born in Beijing, as well as Chinese-American infants from Boston, were less likely than European-Caucasian infants to display high levels of vigorous limb movement, vocalization, and smiling to unfamiliar visual and auditory events (Kagan & Snidman, 2004). Serotonin increases the excitability of motor neurons in the face and spinal cord and modulates the excitability of the ventral pallidum which mediates limb activity. Hence, it is possible, though unproven, that infant carriers of the short allele, who presumably have lower serotonin levels in the brain, would display the less frequent smiling and limb activity observed in the Chinese infants (Perrier, Rasmussen, Christensen, & Petersen, 2013).

A longitudinal study of Chinese-American and Caucasian children growing up in Boston who were assessed eight times between 3.5 and 29 months revealed that the Chinese- American children had a less variable heart rate at every assessment, stayed close to their mother for a longer time in unfamiliar settings, were more likely to cry to temporary separation from the mother, and, at 29 months, were described by their mothers as less likely to laugh and more

likely to be timid in unfamiliar settings (Kagan, Kearsley & Zelazo, 1978). It is worth noting that serotonin has an important influence on the embryo's neural crest cells which, in turn, affect the formation of the craniofacial skeleton (Moiseiwitsch, 2000). The average Chinese, infant and adult, has a craniofacial skeleton marked by a flatter face (the nose and jaw protrude less) than the average Caucasian or African.

A lively controversy surrounds the suggestion that a combination of the short allele and maltreatment during childhood renders the individual at risk for persistent depression (Uher, Caspi, Houts, Sugden, et al., 2011). Advocates of this hypothesis imply that this interaction applies to all individuals who meet both criteria, even though the original study was performed with a New Zealand population consisting of individuals with either a European or Maori pedigree; two groups that could have differed in both the prevalence of the short allele and family experience. When the sample was composed of Scandinavians, adolescents' reports of childhood maltreatment were the best predictor of a bout of depression, independent of any allele, and possession of the short allele had to be combined with possession of an allele of the gene for brain derived neurotrophic factor, or BDNF, to predict depression (Comasco, Aslund, Oreland, & Nilsson, 2013). The best predictor of depression in older German adolescents from disadvantaged families was both copies of the long allele together with the Val/Val allele of BDNF (Buchman, Hellweg, Rietschel, Treutlein et al., 2012).

An alternative position argues that carriers of the short allele are susceptible to more intense feelings when unpleasant events occur because of their more excitable amygdala. Hence, they might be biased to exaggerate the seriousness of mildly threatening experiences that a majority would ignore or treat as minimally distressing. This idea has support. Newborns homozygous for the short allele had a larger increase in cortisol to the brief pain of a heel prick (Mueller, Brocke, Fries, Lesch, & Kirschbaum, 2010). In addition, adult carriers of the short allele had a larger surge of blood flow to the amygdala when they saw a neutral, but ambiguous, stimulus (Heinz, Smolka, Braus, Wrase et al., 2007) and were more likely to report intense anxiety in their diary on days that contained a mildly stressful event, say a friend's cool reception, that carriers of the long allele could have experienced but ignored (Gunthert, Conner, Armell, Tennen et al., 2007).

If carriers of the short allele are vulnerable to exaggerating the seriousness of events that a majority treats as minor annoyances, investigators should gather objective, prospective evidence of childhood adversity and not rely solely on the adult's memories of experiences that occurred 10 to 25 years earlier. Most autobiographies begin by acknowledging that the author's memories of the childhood years are fallible. Yet some social scientists continue to treat these recollections as if they corresponded to what a camera would have recorded. In sum, the validity of the original hypothesis of an interaction between childhood maltreatment and possession of the short allele affecting persistent depression remains possible but is still unproven (Murphy, Maile, & Vogt, 2013).

The different classes of neuropeptides, secreted by the hypothalamus but stored in the pituitary, are relevant for temperaments. The opioids, for example, modulate the medulla which receives information from the body and transmits it to the amygdala and cortex. Variation in the density of opioid receptors in the medulla influences the intensity of the input to the pons, thalamus, and amygdala and, therefore, the probability that activity in the gut, autonomic nervous system, and muscles will enter consciousness. Infants born with a high density of opioid receptors should experience less frequent and/or less intense changes in bodily feelings than those with fewer receptors. The latter should be more vulnerable to a conscious state of tension or arousal, which they might interpret as anxiety (McNally & Westbrook, 2003.) The sight of a dangerous animal, say a tarantula, usually elicits activity in the amygdala, periaqueductal gray, anterior insula, anterior cingulate, bed nucleus of the stria terminalis, and autonomic nervous system. Opioids, as well as serotonin, can mute the level of activity in many of these sites (Miyawaki, Goodchild, & Pilowski, 2002; Mobbs, Yu, Rowe, Eich, FeldmanHall, & Dalgleish, 2010).

The neuropeptide oxytocin mediates relaxation of smooth muscle in the gut and cardiovascular system, and induces the expression of a gene responsible for a protein, called the regulator of G-protein signaling (RGS2), that reduces activity in the central nucleus of the amygdala. These processes should generate a feeling of relaxation. If the person happens to be in a social relationship, the feeling of relaxation should potentiate the pleasure of the social experience. However, feeling relaxed while meditating, hiking, or reading alone should contribute to the pleasure taken from these activities too. Hence, oxytocin should be regarded as the relaxing molecule rather than the social bonding molecule. Support for this claim comes from the fact that men given oxytocin displayed larger eye blink reflexes (than controls) to a loud sound (potentiated startle) while looking at unpleasant pictures, because of greater relaxation of the muscles of the eye (Striepens, Scheele, Kendrick, Becker, Schafer, et al., 2012). (See also Liu, Guastella, & Dadds, 2013).

Gamma-aminobutyric acid (GABA) suppresses neuronal excitability. The amygdala, which activates targets that produce signs of fear and anxiety, has a dense set of receptors for the GABA molecule. Infants born with a lower density should be more vulnerable to states of fear or anxiety (Auerbach et al., 1999). The insula, which receives and elaborates activity originating in the viscera, has a dense set of GABA A receptors that mute neuronal activity at this site. Hence, individuals with fewer GABA A receptors should experience more frequent activity in their heart and gut and forced to interpret this information. It is relevant that patients with panic disorder had fewer sites in the insular cortex that bound a benzodiazepine receptor ligand, implying fewer GABA A receptors (Cameron, Huang, Nichols, Koeppe, Minoshima, Rose, & Frey, 2007). However, individuals who have a damaged insula can still experience a variety of feelings because of the contributions of the hypothalamus and brain stem sites (Damasio, Damasio & Tranel. 2013).

Dopamine is among the most prominent molecules in the brain. Variation in dopamine release from the substantia nigra and ventral tegmental area and the density of the five dopamine receptors contribute to a wide variety of brain states, including the energizing or inhibiting of motor actions, states of reward, and the alerting that accompanies encounter with a novel or unexpected event. The five receptors belong to two categories. D1 and D5 are typically excitatory; D2, 3, and 4 are inhibitory. All anti-psychotic drugs block D2 receptors, resulting in less restraint on D1 receptors.

Unexpected or unfamiliar events typically evoke a phasic increase in dopamine that is inversely related to the tonic level of dopamine activity, especially in the striatum. The lower the tonic level, the larger the phasic increase in dopamine and the greater the probability that the individual will report a momentary feeling of pleasure.

Females, animals and humans, have more dopamine receptors in the striatum and frontal cortex that are occupied and, therefore, not available for activation by a momentary surge of dopamine (Kaasinen, Nagren, Hietala, Farde, & Rinne, 2001).

This condition is due, in part, to the fact that estrogen potentiates the synthesis, release, and turnover of dopamine and inhibits the dopamine transporter molecule (Becker, 1999; Jacobs & D'Esposito, 2011). The higher level of tonic dopaminergic activity in females, especially in the striatum, implies that an unexpected, but desirable, event will not generate as large a phasic increase in dopamine as typically occurs in males. As a result, females should experience a less intense surge of pleasure from a novel experience. It may not be a coincidence that fewer females than males engage in high risk activities, such as sport parachuting, drag racing, sexual activity with strangers, or high stakes gambling.

The relations described above represent a very small proportion of the possible neurochemical profiles that might contribute to a temperament. Unfortunately, the current immaturity of our knowledge frustrates any attempt to posit specific relations among genes, neurochemical profiles, and a temperament. At the present time, no gene, or collection of genes, has been discovered that accounts for more than 10% of the variation in a complex behavior or the symptoms of a mental illness. Most alleles account for even less variance. One likely reason is that each behavior or symptom can be mediated by a number of different genomes. It is likely that schizophrenia, depression, and social phobia are as genetically heterogeneous as leukemia. Moreover, the discovery of the epigenetic changes generated by certain experiences have complicated the simplistic view of genetic effects on brain and behavior biologists held only 25 years ago.

Most scientists assume that a large number of genes contribute to most psychological phenotypes, with each gene making a small contribution to each outcome (Manuck et al., 2004). The combined effects of the genes that code for 19 different brain molecules were required to account for 60% of the variation in avoidant behavior in a sample of rats (Ray, Hansen, & Waters, 2006).

Each temperamental bias, therefore, is probably the product of a pattern of alleles. One-year-olds with extreme levels of avoidant behavior to a stranger possessed both the two short alleles of the serotonin transporter gene, as well as the 7-repeat polymorphism of the dopamine D4 receptor (DRD4). Minimally avoidant children combined the two long forms of the serotonin transporter gene with the 7-repeat DRD4 polymorphism (Lakatos et al., 2003). Some children who display a timid, avoidant posture to unfamiliar events and settings are more likely than others to possess an allele of a gene called RGS2, responsible for a protein that modulates the G protein-coupled receptors that respond to serotonin and oxytocin in select sites (McGrath, Weill, Robinson, Macrae & Smoller, 2012).

The G protein-coupled receptors that modulate the amygdala are influenced by alleles of the RGS2 protein which are influenced, in turn, by the concentration of oxytocin which is influenced, in turn, by the presence of the corticotropin-releasing hormone (CRH) which is influenced, in turn, by GABA-ergic activity. Hence, investigators who measure only one of these biological products, which is the typical strategy, cannot obtain a faithful understanding of the relation between a phasic or tonic brain state and a psychological outcome.

The large number of inconsistent relations reported by different laboratories is the partial result of investigator decisions to measure only one allele or one molecule whose influence on an outcome required that it be part of a pattern (Arbelle et al., 2003). For example, the serotonergic and oxytocinergic systems are intertwined, implying that the therapeutic effects of SSRIs might require the contribution of oxytocin (Montag, Fiebach, Kirsch, & Reuter, 2011). Possession of one allele of the serotonin transporter gene and one allele of the BDNF gene represent a risk for depression in German adolescents who grew up in disadvantaged homes (Buchman, Hellweg, Rietschel, Treutlein et al., 2012). To add to the complexity, the concentrations of many brain molecules vary with the seasons (Praschak-Rieder & Willeit, 2012). Because most laboratories in the northern hemisphere test more subjects from September to May than during July and August there is always the possibility that the brain activity recorded from participants in November would be different if they were measured in July.

Finally, the sample sizes in most studies are too small to detect the contribution of an allele to a temperament. Investigators had to sample 180 single nucleotide polymorphisms (called SNPs) in 180,000 individuals in order to account for 10% of the variation in adult heights (Vrieze, Iacomo, & Mc Gue, 2012). A SNP is a deviation from expectation in a single base in a DNA sequence that occurs in at least one percent of the population. Geneticists believe that, on average, a SNP occurs about every 300 bases (there are 6.4 billion bases in the human genome and 3.2 billion base pairs) and two of every three SNPs involve replacing the base cytosine with the base thymine which can result in a different amino acid. This fact is important because epigenetic methylation of a base occurs only to cytosine. Hence, most SNPs reduce the probability that a gene will be silenced through methylation. If that gene contributed to a disturbance

in homeostasis, say excessive cell growth, the mutated SNP could result in an abnormal physiological process.

Finally, copy number variants, defined by deletions, additions, or inversions of a sequence of nucleotides, often more than a thousand, can be risk factors for a mental illness. Some SNPs and copy number variants are novel mutations that occurred for the first time in the gametes of one of the parents or in the developing embryo and are absent in other members of the family pedigree.

Analyses of the genomes of 1,092 individuals from 14 different human populations revealed a great deal of variation among groups living in different world regions. Europeans had the largest number of very rare variants (less than 0.5% of the individuals possessed the variant); whereas Africans possessed more variants that had a low frequency (from 0.5 to 5% possessed the variant) (1000 Genomes Project Consortium, 2012). Any two randomly selected humans differ in about 6 million bases out of a possible 6.4 billion bases, or .001% of the genome.

The many studies reporting heritability coefficients of 30 to 50% for an anxiety or mood disorder are based on the degree of similarity in verbal report or behavior between genetically related individuals—twins, siblings, or a parent and child—usually measured with questionnaires. Most of the related individuals in these studies share the same home environment, social class, and neighborhood. Moreover, parents describing twin siblings are biased to exaggerate the differences between fraternal twins and to minimize the differences between identical twins. This bias produces an exaggerated estimate of the heritability value. In addition, investigators rarely measure each person's life history and current circumstances. Hence, the high heritability coefficients that are based on heritability equations that use questionnaire evidence are rough estimates of similarities that originated in shared biology and experience. Because these estimates ignored the contributions of epistasis and interactions between biology and experience, they should be called *family similarity coefficients* rather than *heritability coefficients.* The latter term implies that the coefficient reflects the degree of similarity in a property that is due to similarities in the genes of the related individuals. This premise is misleading. The heritability equation assumes, for example, that monozygotic twin girls have identical genomes. But it turns out that the pattern of the inactivated X chromosome in the body cells of twin sisters, one from the father and one from the mother, is not identical in the two embryos. Hence, the twin girls are not genetically identical (Richards & Hawley, 2011).

OTHER ORIGINS OF TEMPERAMENTS

Although many scientists believe that inherited variation in brain chemistry is the most frequent basis for a temperament, it is not the only source. There is preliminary evidence suggesting that subtle variations in the patterning of gyri and sulci in the orbitofrontal cortex are associated with behaviors that could reflect

a temperamental bias (Whittle, Bartholomeusz, Yucel, Dennison, Vijayakumar, & Allen, 2012).

Season of conception might contribute to some temperaments because the pregnant mother's physiology is influenced by the more rapid rate of change in the hours of daylight that occurs during the spring and fall. When daylight is decreasing faster than usual, from early September to late October in the Northern Hemisphere, prospective mothers secrete larger amounts of melatonin and women differ in the amount of melatonin they secrete as dusk approaches. Embryos conceived from late February to late April, when the hours of daylight are increasing, are exposed to smaller amounts of melatonin. Melatonin has profound influences on the embryo's brain and body, including the protection of mitochondrial functions, activation or silencing of genes, and the synthesis of molecules, such as cortisol, that influence the developing brain (Chotai & Asberg, 1999; Torres-Farfan et al., 2004). Thus, embryos whose genomes rendered them especially vulnerable to high or low concentrations of melatonin should be affected by the season of conception. The evidence supports that conviction. Children conceived during the fall in the Northern Hemisphere, or during the period from early March to late April in the Southern Hemisphere, are at a slightly higher risk for becoming extremely shy children and for having suicidal thoughts as adults (Gortmaker, Kagan, Caspi, & Silva, 1997).

In addition, maternal infections, extreme stress, abuse of alcohol or drugs, or certain medicines taken during the pregnancy could create conditions that lead to neurochemical, anatomical, or immune disturbances that can create temperamental biases in the infant (Hanley, Brain, & Oberlander, 2013; Patterson, 2006).

SOURCES OF EVIDENCE

The validity of every inference is influenced by the source of evidence and, therefore, the method that generated the observation. Each source of evidence awards unique properties to any inferred concept. Thus, the meaning, and therefore the truth value, of the statement, "A proportion of young children consistently avoid adults they do not know", depends on whether the evidence came from questionnaires or interviews, which are the usual source, or from direct observations. Psychologists studying children before 1950 were more likely than contemporary investigators to base their inferences on observations of behavior.

Verbal reports have become over the past 25 years the usual source of evidence for human temperaments, most often a parent's descriptions of an infant or young child, but also descriptions of older children provided by teachers, peers, or the youths themselves. Unfortunately, the agreement among different informants is often poor for many, but not all, traits (Rubin, Althoff, Walkup, & Hudziak, 2012). For example, observations of a large group of three-year-olds revealed that girls were more sociable and displayed more smiling than boys. But the mothers of these children rated the two sexes similarly on these two traits (Olino, Durbin, Klein, Hayden & Dyson, 2013).

In a great many studies one parent, usually the mother, is the source of all the evidence, which might include her socialization practices, personality, and perception of the home environment, as well as descriptions of her child's traits (Lemery-Chalfant, Kao, Swann, & Goldsmith, 2013). Australian scientists asked more than 6,000 mothers of six-month-old infants to rate signs of dysregulation (for example, colic, sleeplessness, feeding problems) and years later to rate the frequency and seriousness of internalizing or externalizing behaviors in their five-year-old children. A group of five-year-olds who had been described as dysregulated infants were rated as high in externalizing or internalizing traits. But the mothers of this small group of five-year-old children were younger and poorer than the majority in the sample. Hence, it is possible that the mothers' worries and personalities colored their ratings of their infants and older children (Hyde, O'Callaghan, Bor, Williams, & Najman, 2012).

When parental descriptions of children are the basis for a diagnosis of ADHD in the United States, the prevalence of this syndrome is significantly higher in the states east of the Mississippi than in those to the west. Because it is unlikely that the genes that place a child at risk for ADHD are more prevalent in the east it is necessary to conclude that parental biases are responsible for this fact. That is why it is necessary to check on the validity of all parental descriptions.

The usual failure to obtain these checks is reminiscent of a story about an adolescent who asked the man who rang the town's church bells every day at noon how he could be certain of the correct time. The man said that every morning after breakfast he went by the watchmaker's shop and set his watch by the time on the clock in the window. The youth then went to the watchmaker and asked how he could be certain that the time on the clock in the window was correct. The watchmaker replied that he relied on the ringing of the church bells at noon to set the time on his clock.

Behavioral observations in the laboratory, home, or school setting to supplement verbal descriptions are infrequent, despite the fact that Goldsmith and colleagues have developed a procedure, called the Lab-TAB, that generates behaviors that may have a temperamental contribution (Gagne, Van Hulle, Aksan, Essex, & Goldsmith, 2011). Moreover, responses to questionnaires do not contain the valuable information about mood and attitude that can be gained from interviewing a person directly and attending to prosody, spontaneity, posture, and facial expression (Mitchell & Ross, 2013). The importance of this information explains why most adults prefer to attend a play or see a film rather than read the script. Support for the claim that parental descriptions of children on questionnaires are not an acceptable proxy for direct behavioral observations comes from a longitudinal study of a large number of MZ and DZ twin pairs on whom both extensive behavioral observations and parent reports of behavioral inhibition had been gathered at 14, 20, 24, and 36 months. The behavioral evidence implied increasing heritability over age and a large portion of the variance attributable to non-shared experiences at every age. By contrast, the parent reports implied decreasing genetic influence over age and no variance assigned

to non-shared events at any age (Smith, Rhee, Corley, Friedman, Hewitt, & Robinson, 2012).

The degree of correspondence between reports provided by the self, parent, or teacher, on the one hand, and observations of corresponding behaviors, on the other, ranges from negligible to modest (Connelly & Ones, 2010; Durbin & Wilson, 2012; Edelman & Baker, 2002; Kagan & Snidman, 2004; Rescorla et al., 2012; Reynolds, Ortengren, Richards & de Wit, 2006; Schwerdtfeger, 2004; Uher, Perlis, Placentino, Dernovsek, Henigsberg et al., 2012). Despite the questionable validity of verbal reports, some investigators define childhood aggression, which most scientists and citizens understand to refer to observed behaviors, by the answers mothers provide on the Child Behavior Checklist or CBL (Thomas & Pope, 2013).

The information from the CBL often reveals that children described as internalizing are also described as externalizing. This finding is so common investigators have become accustomed to it and fail to appreciate that they would be puzzled if they actually observed a number of shy, timid children who also displayed aggressive actions frequently. Scientists often make discoveries when they try to understand a puzzling phenomenon. Behaviors contain more puzzles than answers on questionnaires. I suggest that a psychologist who saw an adolescent girl purposely cut her skin with a knife would experience a stronger feeling of puzzlement than if he/she read the youth's questionnaire reply stating that she occasionally harms herself. The millions of Americans who are not surprised by reading an article stating that a suicide bomber in Baghdad killed 30 guests at a restaurant would be surprised if they actually witnessed the event. Reading about a massacre of innocent civilians in a war zone does not generate PTSD. Words bleach the feeling of perplexity from uncommon events.

At least six conditions compromise the correspondence between parental descriptions of their children's behaviors and direct observations. Firstly, the parents' descriptions are influenced by their conceptions of the ideal child. Those who want sociable children will be threatened by a very quiet one and will be tempted to deny their young child's timidity and exaggerate his sociability. Secondly, parents are sensitive to the logical consistency of their multiple answers to a questionnaire. If a mother says that her daughter smiles a lot on an early question, she might resist acknowledging on later questions that her child shows signs of sadness or anxiety. All answers to questions are influenced in a major way by a respondent's automatic bias for preserving a semantic coherence that need not be faithful to the perceptual and visceral schemata that are activated when a person replies to a question. When the former are inconsistent with the latter a force favoring semantic coherence usually wins. A mother who possesses a semantic representation of her son as bold and daring will suppress her schemata of his occasional timidity when confronted by older boys and rate him on a questionnaire as bolder than observations would reveal.

Thirdly, the nouns and verbs on questionnaires in English refer to abstract behavioral categories, such as aroused, regulate, good, bad, and fearful, that

are indifferent to the form the trait assumes, the context in which it is displayed, the participants, or the relation to a particular brain profile (Kawabata & Zeki, 2004). No title in any paper in the February 2013 issue of *Psychological Science* informed the reader about the species, age, or ethnicity of the subjects or the kind of evidence gathered. By contrast, many titles in the March 2013 issue of *The Journal of Neurophysiology* specified the species and source of evidence; for example, "Action of dopamine on synaptic transmission in mouse prefrontal cortex". Most words also make it difficult for a parent to describe blends of behaviors or emotions. There is no English word that describes the emotional state of a child who hopes for parental forgiveness for a misdemeanor but is afraid of being punished. Human languages contain the largest number of words for personality traits that refer to those who display socially approved or disapproved behaviors or capture the difference between energetic compared with passive individuals (Saucier, Thalamayer, Payne, Carlson, et al., 2013). Humans seem to be especially concerned with individuals who adhere to or violate local mores and attempt to cope with a challenge or remain passive. It is not a coincidence that this fact matches the observation that evaluations of a large number of nouns representing objects, animals, and people on 20 scales anchored at each end by a pair of antonyms, provided by adults speaking many different languages, revealed that humans are preoccupied, first, with the goodness or badness of an event and, secondarily, with whether a person, animal, or object has the potency to change current conditions. Natural phenomena, however, do not award special significance to these two factors. It is important to distinguish between statements that engage the good- bad and potent-impotent continua (for example, "Mary is very aggressive") and judgments that do not ("Mary has brown hair"). Evaluations of the validity of the former statements require behavioral evidence.

Fourthly, every question requires informants to make a comparison. Usually a parent compares one child with another. One source of error in these judgments is that if the child being judged is only a little different from a comparison child the informant will exaggerate the difference. For example, if the child being rated is a little more disobedient than his brother the parent will be tempted to exaggerate the level of disobedience of the former child (Cogan, Parker, & Zellner, 2013). A second form of comparison involves two activities. Parents who read the question, "Does your child like to go to parties?" unconsciously compare that preference with others their child might enjoy. If one parent compares "going to parties" with an activity that the child dislikes, whereas a second parent compares "going to parties" with an activity the child prefers, the former is more likely than the latter to endorse that item strongly, even though both children might like going to parties to an equivalent degree.

Fifthly, young parents who have not had extensive experience with infants or children have a less accurate basis for judging their first child than those who have had two or three children. Moreover, inexperienced mothers who have become accustomed to frequent bouts of irritability in their infant are less likely

to notice and report this trait than mothers with less irritable infants who notice that their infant was very distressed over the past two weeks (Hane, Fox, Polak-Toste, Ghera, & Guner, 2006).

Finally, parents differ in their understanding of the meanings of some words on questionnaires. This is especially true for words such as anxious, sensitive, aggressive, regulate, and understand. One of my students once asked adolescents who had watched two actors compete in a 20-minute film, "Which actor was more anxious?" Some adolescents interpreted the term anxious as meaning "eager to perform well"; others interpreted the same word as meaning "fearful". Some mothers interpret the term shy as implying that their child is sensitive to the moods of friends; others interpret the same word as meaning that the child is cautious when interacting with others; still others interpret shy as meaning "fear of unfamiliar adults".

These are some of the reasons why parent or teacher descriptions of children have a poor to modest correspondence with comparable information based on direct behavioral observations (Klein, 1991). Over 40 years ago, Marian Radke-Yarrow and colleagues found that parental recollections of what their children were like only several years earlier were generally inaccurate (Radke-Yarrow, Campbell, & Burton, 1970). Yet, some investigators continue to rely only on this evidence and do not acknowledge that the validity of the verbal report "My son is timid" or "I am timid" depends on a web of relations among direct observations and words describing the observations. The fact that a parental statement such as "My son is callous" has consensual meaning in a particular language community tells us nothing about its validity. Fourteenth-century European Christians had a shared understanding of the meanings of Devil and Purgatory but neither concept named a natural phenomenon.

Adults will answer verbal queries about feelings or ideas to which they have given little or no thought. I suspect that more than 90% of adults would provide an answer to a questionnaire item that asked, "How coherent has your life been over the past 20 years? Please rate on a 10 point scale", even though most informants had never posed that query to themselves and were not sure of the meaning of a "coherent life". Put simply, most conclusions that are based on verbal reports are unlikely to correspond to conclusions that would be inferred from behavioral evidence.

The ambiguous meaning of a person's verbal statement is revealed by a comment Ludwig Wittgenstein made to a relative as the philosopher lay dying. As some readers may know, Wittgenstein was profoundly depressed and anxious most of his life and as a younger man had written in a private notebook that he could not imagine a future that contained any joy or friendships. Nonetheless, one of his last comments to a friend as he lay dying was: "Tell them I've had a wonderful life." (Waugh, 2008).

In sum, psychologists want to predict and understand five classes of phenomena: the behaviors of agents in particular settings, their store of knowledge, competences, ethical values, and feeling states. Verbal reports alone are

insufficiently accurate indexes of all five. Like children's drawings, the correct interpretations of written verbal replies are not always transparent.

Most of the words across the world's languages that are intended to describe human psychological traits are not rich enough to capture all the important feelings, thoughts, and behaviors that actually occur. Physicists had to invent new words that were not in the popular lexicon, including quark, boson, lepton, and dark energy, to describe the elements of the material world.

Most words throw away too much of the variability in observed behaviors among those who are categorized as conscientious, anxious, open to ideas, extraverted, or agreeable. Even the verb selected can influence a reader's understanding of a person assigned to a category. The sentence, "Mary has social phobia" implies that avoidance of social settings is only one of Mary's traits. The sentence, "Mary is a social phobic" implies that avoidance of others is her most defining trait. A similar contrast is present in the comparison between "Humans have two legs" and "Humans are bipeds".

The tendency to invent new constructs that can be studied with questionnaires and to avoid thinking about concepts that cannot be probed with verbal queries is a serious disadvantage of current practices. For example, adults are unable to remember how long they experienced an intense state of arousal after a failed exam, lost friendship, or insult that occurred years earlier and so investigators do not brood on this process. Many psychologists are reluctant to acknowledge the serious limitations of a sole reliance on questionnaire data. Natural scientists are, by and large, more conscious than social scientists of the importance of the variance attached to a specific procedure and are reluctant to rely on the evidence from one procedure to validate a novel or important concept. Our understanding of the universe would be inadequate if astrophysicists relied only on the observations generated by ground based optical telescopes; our understanding of genes would be inadequate if biologists relied only on X-ray crystallography. For the same reason a fuller understanding of human temperaments, behaviors, talents, emotions, and beliefs requires gathering more than one source of evidence.

THE ENTHUSIASM FOR BIOLOGY

Although temperamental biases have a partial origin in biological processes the forms the biases assume in the older child and adult are dependent on the person's life history. The current hyping of the biological contributions to temperaments and mental illnesses has been accompanied by an indifference to each person's interpretations of their feelings, actions, life history, and local circumstances. This neglect of subjective interpretations and the contexts in which they occur is distorting the public's understanding of the determinants of psychological phenomena. It is not a coincidence that the variation in poverty rates among the 50 states tracks quite well the rate of teenage pregnancies and the prevalence of Type 2 diabetes due to obesity. All three conditions are among

the highest in the southern states and among the lowest in New England and the upper Midwest. By contrast, the incidence of violent crimes is highest in the western states where gun ownership is high and lower in the states where a much smaller proportion of residents own guns. The population density of a state even affects the probability of a fatality in an automobile accident. The odds are much higher in less populated states with long distances between cities and cars traveling at high speeds (Nebraska has the highest rate) and lowest in densely populated eastern states (Massachusetts has the lowest fatality rate). These facts, available on government web sites, point to the significance of the social context, not genes, on behaviors that lead to these important outcomes.

It is a bit paradoxical that at the same time investigators who study variation in human behaviors are awarding increasing influence to genes, those who study animals in their natural habitats are emphasizing the importance of the environment in creating variation. One team, for example, reported that group size interacted with the genomes of members of a large group of wild baboons living in the Amboseli basin to affect patterns of gene expression (Runcie, Wiedmann, Archie, Altmann, Wray, Alberts, & Tung, 2013).

The nature of the world's problems in 2014 has contributed to the ascent of biological accounts and a descent in the explanations referring to environmental forces that social scientists provide. The public is concerned with finding new forms of energy, keeping the WEB safe from hackers, paying for the healthcare costs of an aging population, preventing epidemics of infectious illnesses, slowing climate change, and protecting citizens from terrorists. Coping with these problems requires the technologies and concepts of natural science.

By contrast, north Americans and Europeans in 1950 lived in a more peaceful time with plentiful gasoline, no inkling of the coming rise in sea and air temperatures, no terrorists, no epidemics of AIDS or SARS, and a small proportion of the population living past 75 years of age. Finding ways to be happier, preventing school failures, reducing crime rates, and making the society more egalitarian were the primary preoccupations. The solutions to these problems seemed in 1950 to be the responsibility of psychologists and sociologists. The academy is a collection of individuals who are experts on specific problems. History determines which experts are needed during a particular era.

All scientists agree that feelings, evaluations, and actions emerge from brain activity. But the representations linked to a person's life history, gender, ethnicity, culture, and historical moment can impose idiosyncratic meanings on the brain profiles accompanying an event (Leknes, Berna, Lee, Snyder, Biele, & Tracey, 2012). Cambodians who witnessed the atrocities committed by the Khmer Rouge from 1975 to 1979 interpreted these events in ways that were unlike the ones imposed by American soldiers in Iraq who witnessed similar atrocities (Chhim, 2012).

Adults listening to music and watching film clips suggestive of six emotions (e.g., fear, sadness, amusement) relied, as most humans do, on the concepts of valence and arousal when they rated the emotion they believed they experienced

to each stimulus. But each person's pattern of 16 autonomic measures (which included skin conductance, heart rate, gastric activity) to each stimulus did not correspond to these two symbolic dimensions. This fact suggests that the psychological categories individuals impose on emotional experiences transcend the information contained in the reactivity of heart, respiratory system, skin, and stomach (Kragel & La Bar, 2013).

The scientists who argue that physical exercise has therapeutic effects on anxiety and depression usually explain this relation as due solely to the physiological processes that accompany muscle use (Moylan, Eyre, Maes, Baum, Jacka, & Berk, 2013). These authors typically ignore the important fact that the use of the skeletal muscles has to be voluntary if it is to be therapeutic. Similar levels of muscle activity that occur in the workplace or under coercion are not therapeutic. When an action is voluntary the person feels he or she is in control and the brain assumes a profile that differs from the profile seen when the same action is demanded or imposed by another (Brass, Lynn, Demanet, & Rigoni, 2013). The nineteenth-century concept of *will* has returned after over a century of exile. The facts imply that the beneficial consequences of physical activity are due to a combination of a special psychological state (choosing to exercise and feeling in control) and the physiology that accompanies muscle activity under those circumstances (Kemper, Umbach, Schwager, Gaschler, Frensch, & Sturmer, 2012).

A person's understanding of why they are physically active and whether they chose this response participates in any benevolent outcome of the behavior. Hence, one cannot assume that only one physiological pattern accompanies walking a mile or lifting heavy objects. A similar process is operative when a person takes a medicine or enters a cryogenic chamber for three minutes searching for a cure for an ailment. The patient's understanding of the possible therapeutic effects of a pill, or the feeling of cold and the expectation that it will be beneficial, contribute to its biological and psychological consequences (Geuter, Eippert, Hindi, & Buchel, 2013). Adults who expected a taste to be only mildly aversive showed a smaller activation of the insula to a highly aversive taste than they would if they had anticipated the highly aversive taste (Sarinopoulos, Dixon, Short, Davidson, & Nitschke, 2006).

The events that are classified as stressors also depend on the agent's mental state. Caring for an unwanted infant is stressful; caring for an infant that was desired for many years is typically satisfying. The confinement and noise experienced during the seven or eight hours of a transatlantic flight are accompanied by different consequences in the holiday traveler who has never been abroad and the bank executive who must make this trip twice each month. The different psychological and biological consequences associated with controlling the delivery of an event versus being a passive recipient have been demonstrated in many mammalian species. Mice, for example, who receive injections of the drug Ecstasy in certain brain sites contingent on an operant response show patterns of gene expression in the brain that differ from those shown by yoked

controls receiving the same drug (Fernandez-Castillo, Orejarena, Ribases, Blanco, et al., 2012). A knife piercing the skin, acupuncture, strenuous exercise, spicy food, and orgasm all have the potential to release endorphins. The amount of release and its benevolent effects on mood depend on the person's prior mental state.

Agents who are in control of their actions can anticipate and prepare for future events and, therefore, experience an illusion of power. The driver of an automobile traveling at a fast speed, for example, usually feels more secure than a passenger. Individuals in control should experience less activation of the amygdala, be protected from a chronic state of vigilance, able to pursue a desired goal, and freed from anger over being coerced by others.

The biological and psychological consequences of being strapped to a post and whipped are different for a victim of torture and a masochist who requested the whipping. Adolescents who sense they have lost control of the events in their current setting are at risk for developing anorexia as a way of regaining control of at least one aspect of their lives. The economically disadvantaged, who are more often salaried employees without permanent job security living in neighborhoods with more violent crime, may have a less secure sense of control than the affluent. I suspect that the current habit of sending frequent electronic messages to friends gives the sender a sense of control over the relationship, even if that belief is illusory.

The increased sense of control over edible food, potable water, body temperature, and medicines for an illness is one of the most significant differences between early and modern humans. Having become accustomed to a feeling of control, an unknown proportion of contemporary populations may be seriously threatened by regular media reports of polluted water and food, climate changes promising extreme temperatures, new viruses and bacteria that resist all drugs, pandemics, dirty nuclear bombs, IEDs, identity theft, and cyber attacks on banks and government agencies. It is easy to imagine these sources of concern potentiating anxiety in those with existing worries and leading to an increase in the prevalence of anxiety disorders without any changes in genomes.

Despite the repeated demonstrations of the importance of an agent's mental state, this family of psychological phenomena lost causal power after scientists developed ways to measure a variety of biological variables. Once one could measure activity in the HPA axis, sympathetic nervous system, and brain sites, scientists with an attraction to physiological explanations ignored the cascade that began with an agent's thoughts or feeling of control and made the biological response the primary definition of stress, as well as a significant origin of psychological or physiological outcomes (Chrousos, 1998). Soon increasing numbers of scientists claimed that any event they classified a priori as capable of disturbing the body's homeostasis was a stressor, independent of the person's psychological state. For example, a large rise in salivary cortisol in a person told to make a speech in front of strangers became an index of a stressful state. Most investigators simply ignored the very modest correlations among the biological

indices of stress and a person's subjective evaluation of their level of stress across types of settings (McEwen & Seeman, 1999).

The small number of social scientists who studied the gradient relating a person's social class to their health, however, insisted that a person's state of mind, especially a sense of control in the workplace and level of trust in others, was a major cause of the physiological processes that define a chronically stressed bodily state (Marmot, 1999). This is one reason why most DSM diagnoses are more prevalent among the disadvantaged who, as I noted, are more likely to feel that they have lost control over many of the events in their lives.

Although understanding why a person initiated an action or experienced an event has to have a foundation in the brain, scientists are not close to discovering that profile. When they do it is likely to involve large sections of the temporal and frontal lobes which act as moderators of the brain's response to an acute or chronic experience. This function is analogous to the role of enhancers and promoters in the genome which determine where and when a protein-coding gene will be transcribed as well as the level of transcription.

Some readers may not appreciate that the notion that psychologically stressful events could generate the symptoms of a mental illness originated in the late eighteenth-century when major social changes wrought by industrialization and urbanization led many eminent scholars to argue that new social conditions had generated abnormal bodily states that were leading to increases in mental illness (Rosen, 1959). These commentators understood, implicitly, that for most of the history of our species a majority of humans lived with frequent hunger, cold, disease, premature deaths of children and spouses, and attacks by animal and human predators. But these early humans assumed that these conditions were natural and, therefore, their distress states were not abnormal.

When western societies began to alleviate some of the sources of distress that plagued their ancestors, and life for an increasing proportion of the population in nineteenth-century Europe and North America was became physically less distressing and somewhat more predictable, the concept of stress assumed the new meaning of a psychological state marked by chronic worry, tension, and uncertainty attributable to the pressures of modern life.

The current definition of stress as an abnormal biological state characterized by a disturbance in the body's homeostasis, usually marked by excessive activity of the sympathetic nervous system and the HPA axis, is indifferent to the agent's thoughts or feelings. This idea became popular after Hans Selye published his theory of the general adaptation syndrome in 1946 which was based primarily on the physiological consequences of injecting rats with foreign substances. Although most biologists ignored Selye's concept because it did not differentiate among different types of stressors operating in different species, psychologists were attracted to its abstract quality, which implied that the nature of the threat (famine or loss of a friend) or the animal studied (rat or human) were of minor importance (Karatoreos & McEwen, 2013).

On reflection, therefore, the term stress is far more ambiguous than most scientists acknowledge in their writing. This concept is defined by two criteria. Stress is a physiological state that deviates from a presumed optimum and places a person or a population at risk for an unwanted or undesirable outcome. This definition requires stipulating the states that are naturally optimal. The problem is that what is optimal varies with the species and its local ecology. The Indians who have lived in the Andes for generations possess hemoglobin with features that are not shared by most humans, but these features are adaptive if one lives at 10,000 feet. It is easier to list the small number of biological properties that permit stipulating the values that are both abnormal and potential risks—blood pressure and blood glucose levels—than to name many psychological states that meet this pair of criteria. A chronic fear of God's wrath was normative among Christians in medieval Europe and was accompanied by a feeling of well-being. The minority who did not possess that fear were at risk for a bout of depression or anxiety. Contemporary Europeans who fear God's wrath are deviant and at risk for the same symptoms.

This discussion reveals the slippery nature of the concept of a psychological stressor or a state of stress in contemporary writing. It also points to the need, which is usually unmet, to specify the species, the local ecology of a population within a species, the nature of the stressful event, its presumed undesirable consequences, and whether biological or psychological measures are used to infer the abnormal state that places an individual or a group at risk for an unwanted outcome. The biological state of a rat who has been restrained in a narrow tube for six hours or the state of an infant monkey separated from its mother for 24 hours is not to be equated with the psychological state of a 25-year-old woman, who believes that her mother rejected her when she was a young child, or the state of a soldier who witnessed horrible atrocities and did nothing to stop them. Each is experiencing a qualitatively different state of stress.

Some readers may not appreciate that between 1910 and 1960 many papers in leading psychological and psychiatric journals concerned with personality or pathology centered on the influences of the family and the experiences linked to a person's social class (Kagan & Moss, 1962). During the 50-year interval when Freudian ideas were popular, adults with anxious or depressive symptoms were told that their distress was due to repression of sexual ideas and suppression of sexual activity. The eventual rejection of this explanation by historical events required the invention of a new culprit. The dominance of biology in the current Zeitgeist made it likely that genes would be nominated as the villainous cause of the symptoms that had been attributed to inhibition of sexual ideas and behaviors. However, because one in three American women who display no evidence of either a repressed libido or possession of risk alleles report at least one bout of anxiety or depression in their lifetime, we have to include conditions in the society as contributing to these symptoms.

These conditions include large numbers living in densely crowded urban areas far from family and childhood friends in societies with large Gini

coefficients, weak hierarchies, and uncertainty over the ethical rules that should always be honored. This relatively recent development in the history of our species has an analogue in the relatively recent selection of alleles that potentiate the ability of the immune system to deal with the increasing variety of disease-producing viruses and bacteria, but exact the cost of rendering those harboring these alleles vulnerable to an inflammatory illness, such as Crohn disease, celiac disease, multiple sclerosis, lupus, psoriasis, ulcerative colitis, or Type 1 diabetes (Raj, Kuchroo, Replogle, Raychaudhuri, Stranger, & De Jager, 2013).

The biological determinism that penetrates most current discussions of psychopathology is the result of four, relatively independent historical developments. Firstly, the social scientists who advocated the power of experience relied too heavily on habits gave conditioned responses. They ignored the implicit, more private, representations that comprise identifications with family and symbolic categories for gender, class, and ethnicity, as well as other inferences extracted from life conditions.

Secondly, many who argued for the importance of experience continued to rely on crude evidence from questionnaires and interviews which yielded categories that were too heterogeneous in origin to be the basis for fruitful theoretical constructs. Hence, totally experiential accounts lost some appeal and both scientists and the public were receptive to new explanations. Biology's success in explaining so many physical diseases made genes and brain profiles logical candidates to account for mental illnesses too.

Social scientists also failed to develop technologies that might uncover novel phenomena, especially less conscious representations of self and others. The celebrated biologist Sydney Brenner noted that progress in science depended on new techniques, new discoveries, and new ideas, usually occurring in that order. Francis Crick and James Watson could not have discovered the structure of DNA in 1953 if X-ray crystallography had not been invented early in the same century.

A reluctance to blame victims of poverty or prejudice for their misfortunes is a third reason for the influence of biology. If genes and compromised brains were the primary cause of depression or anxiety—states that are more prevalent among the disadvantaged—no one can blame patients suffering from these moods, or their families, for contributing to these states. This position, which makes it difficult for the marginalized to accuse scientists of racial or class prejudice, is politically more attractive. The New York Times of April 1, 2013 reported that diagnoses of ADHD are much greater in Louisiana, Alabama, Georgia, and South Carolina (one in four boys in these states received this diagnosis) than in New Mexico, Nevada, Colorado, and California. But the author of this essay failed to note the obvious fact that the former states have a large proportion of African-American youth and the latter states have large numbers of Hispanic children. I suspect that this omission was motivated by a reluctance to accuse clinicians in the Southern states of an ethnic bias in their diagnoses or to imply that black children are more restless and less attentive than Hispanic

children. Either suggestion would have been politically incorrect. A paper on the consequences of being a victim of bullying, or behaving like a bully, among North Carolina youth also omitted any analysis of race or ethnicity, even though the sample had both black and white youth and the risk for a psychiatric diagnosis was related to the family's social class (Copeland, Wolke, Angold, & Costello, 2013).

The number of childhood adversities, especially neglect, abuse, a parent with a mental illness, or exposure to frequent violence, predicts the number of psychiatric diagnoses in the adult. But the authors of this finding were reluctant to acknowledge explicitly that both the adversities and the diagnoses are more common in families with marginal educations and incomes than in families where both parents have a college degree and a joint income of over $200,000 a year. These investigators did not think it was important to report the correlation between the social class of the 10,000 American adolescents interviewed and their adversities and illnesses. This decision allowed readers to conclude that the adversities qua adversities compromised their biology and contributed to later mental symptoms (McLaughlin, Green, Gruber, Sampson, Zaslavsky, & Kessler, 2012). They did not acknowledge that children from advantaged families who suffered the same adversities might be less likely to possess the same number of mental illnesses because an adversity among the poor is part of a pattern that is missing among the privileged.

Authorities in eighteenth-century England and France recognized that the prevalence of infectious diseases was far more prevalent among the poor than the affluent because of the unhygienic conditions in which they lived and worked and regarded this burden on the less advantaged as a responsibility of the larger society (Rosen, 1959). However, contemporary authorities are reluctant to acknowledge that the high rate of depression among the poor in most societies is due, in part, to social conditions and a greater morbidity burden that the larger community could ameliorate if it wished. At the moment, these communities prefer to attribute the reasons for this epidemiological fact to genes and events within the family.

Finally, most Western scientists remain friendly to the popular premise that physical entities whose features are detectable—atoms, genes, neurons, molecules—are the foundation of all natural phenomena. Thoughts and feelings, by contrast, are immaterial, transient events that cannot be observed directly. Hence, it seemed wise to classify them as epiphenomena and deny them much causal potency. This premise is one reason why the discovery of the conditioned reflex had to wait until 1902 when some of Pavlov's army of medical student assistants demonstrated that a neutral stimulus, say a tone, could acquire the power to cause a dog's salivary glands to secrete saliva.

The many talented physiologists in 1902 who were studying unconditioned reflexes must have noticed that they salivated at the smell of freshly baked bread. But they never thought of demonstrating this phenomenon with animals or humans in the laboratory because such an experiment would require them to

invent or use a vocabulary that was foreign to physiology. Even Pavlov wrote that the physiological bases of the dog's conditioned reflexes were dissimilar from the bases of the reflexes that appeared to resemble human responses because humans were symbolic creatures who thought (Babkin, 1949).

The materialistic premise Pavlov advocated is seen in a recent paper reporting that released criminals who stated on a popular questionnaire that they had little respect for society's rules were most likely to be rearrested for a crime. But the neuroscientists who found that these recidivists also showed reduced activity in the anterior cingulate during a go/no-go task concluded that the biological marker was the significant sign of risk for a future crime, even though this brain measure was far less predictive of re-arrest than the criminals' confessions that they had little motivation to conform to social rules (Aharoni, Vincent, Harenski, Calhoun, Sinnott-Armstrong, Gazzaniga, & Kiehl, 2013). But because those anti-social attitudes were immaterial these authors preferred to award the causal power to the brain measure.

The current attraction to biological explanations is seen in the fact that the authors of a recent book on the origins of antisocial behavior placed the genetic, neurochemical, and anatomical contributions to aggressive behavior in the opening chapters, despite the robust fact that social class, income inequality, and neighborhood ambience are far and away the best predictors of these actions in every community studied (Thomas & Pope, 2013). The automatic habit of attributing an outcome to a compromised brain is revealed in a paper claiming that juvenile offenders who did not show a skin conductance response during fear conditioning had an impaired central nervous system despite the fact that many healthy persons do not display this response during conditioning (Syngelaki, Fairchild, Moore, Savage, & Goozen, 2013).

An article in The New York Times of March 1, 2013 celebrated the fact that scientists discovered four SNPs (out of millions examined) that were shared by patients diagnosed with schizophrenia, bipolar disorder, autism, or ADHD. The two SNPs that had a possible rationale accounted for less than one percent of the variance in the occurrence of these diagnoses (Cross-Disorder Group of the Psychiatric Genomics Consortium, 2013). When social scientists find that the education of the mother and father and the quality of schools attended by their offspring account for about 20% of the variation in the occurrence of ADHD, criminality, substance abuse, learning problems, or low IQ scores, few newspapers treat these findings as worthy of dissemination. All of these events came together to persuade the public that explanations of psychological phenomena that mention genes and brain processes are more valid (Weisberg, Keil, Goodstein, Rawson, & Gray, 2008).

One reason why scientists have been unable to detect reliable and robust relations between measures of brain and a psychological outcome is that they have not paid sufficient attention to the context in which the brain measures are gathered. A pattern of neuronal oscillations evoked by seeing a scene in a film portraying torture can be accompanied by different outcomes if, for example,

the person is alone at home, with a friend in a theatre, or sitting next to a stranger on a plane. Even the laboratory in which blood flow profiles are measured can have an important influence on the pattern recorded (Friedman, Stern, Brown, Mathalon, et al., 2008).

Unfortunately, most of the current evidence on the human brain's reaction to an incentive is gathered in a very unusual context; namely, the person is lying supine and alone in a narrow tube. Therefore, it is not possible to know what psychological outcome might emerge if the same incentive occurred in one of the person's natural settings where he or she was free to assume a variety of postures (Zimmerman, Toni, & de Lange, 2013). For example, a majority of studies of cerebral blood flow in humans present the participant with a stimulus, say a face or an object, and record the resulting BOLD signal. This procedure induces a mental set to classify the stimulus (what is it?) rather than to act on it. These two mental states evoke different patterns of blood flow (Cavina-Pratesi, Goodale, & Culham, 2007). A face with a fearful expression and no background provokes an intention to classify it. The same facial expression on a spouse who is staring at a cockroach on a counter provokes an intention to act in order to alleviate the spouse's fear.

The conditions in modern society may have contributed to an indifference to setting. Visitors to zoos see animals outside their natural ecologies; visitors to museums see artifacts taken from their usual location and put in glass cases; and photos or scenes on Facebook contain no information on the context in which the photographs were taken. These experiences make it easy to dismiss the importance of the usual setting in which an event occurs.

Predictions of the outcome of a large air mass pose the same problem. A collection of molecules of water and air at a particular average temperature, velocity, and direction of movement could move several tons of sand, create 10 foot waves, or tear the roof from a house depending on the setting in which the air-water mass was moving. Analogously, the basis for a thought, feeling, or action rests with the relations among an incentive, a brain pattern, and the social context. There has been a significant increase over the past 20 years in the number of deaths due to patients accidentally taking an overdose of a physician-prescribed drug. This statistic is best explained by noting that doctors are prescribing more kinds of pain killers to more patients. The presence of these pills in the medicine chest represents a context that increases the probability that a person will ingest too many when they are in distress or pain.

Missing from almost all discussions of mental illness is the fact that humans cannot help but think about the psychological properties they *ought* to possess and the experiences they *ought* to have enjoyed. Humans are the only species that live in two realities: the natural world of hunger, cold, warmth, pain, sweet tastes, and moving objects as well as a symbolic space where sensations, events, and things can be good or bad, potent or impotent, respected or demeaned. Even Charles Darwin could not suppress the temptation to impose an ethical

evaluation on evolution—in several places in *The Origin* he writes that natural selection can only act for the good of each organism.

The brain honors these two realities by placing neurons responsive to sensations and those responsive to the symbolic forms of cognition in different places. For example, pain and visceral activity are processed by the posterior half of the insula; whereas the anterior half contributes to the feelings accompanying worry (Simmons, Avery, Barcalow, Bodurka et al., 2012).

The properties of the symbolic world are one reason why adults who had childhood experiences that generated intense shame are at a higher risk for a mental illness (Matos, Pinto-Gouveia, & Duarte, 2012). If the British psychologist Stuart Sutherland had not believed that jealousy was irrational and a serious violation of his notion of the ideal man, he would not have suffered a serious depression when he found himself unable to control bouts of jealous rage after discovering that his wife was having an affair with one of his friends (Sutherland, 1976). An American adolescent who is shy with strangers and quiet at parties knows that he or she is supposed to be sociable and talkative. If most American youths believed, as many middle-class, seventeenth-century Europeans did, that children and adolescents should be initially shy and quiet with strangers, the prevalence of social anxiety disorder would plummet.

The high prevalence of bouts of depression among American undergraduates—close to 20%—is due, in part, to the current emphasis on the importance of having many friendships. This value implies that the loss of a relationship, or having no relationships, will be interpreted as a violation of an ethical norm and an incentive for some of the biological signs of stress. But if these individuals did not believe that they ought to have many friends the perception of friendlessness would not be an incentive for disappointment. A fifteenth century Christian who believed that he had offended God would experience a bout of guilt and the stress that guilt brings. But this sequence required that he believe in an omniscient God that punished those who offended Him. History, not biology, made the perception of friendlessness an origin of unhappiness and the biological changes that accompany that state. Pascal once wrote that happiness was only possible for those who were able to enjoy being alone in a quiet room for several hours.

Thus, friendlessness is not to be classified as a biological deprivation, such as hunger. The unhappiness that accompanies the lack of friends requires a belief that one ought to have friends. That suggestion does not mean that loneliness is an innocent psychological state, only that it should be classified as a source of stress that history created. Four events that contributed to that history are: the increased competitiveness of women with men and with each other, high rates of geographic mobility, the recognition that important accomplishments require being a member of a team and/or having friends in positions of power, and, finally, the absence of ethical imperatives that the person regards as binding under all conditions. These events came together

like a perfect storm to catapult friendships into a prominent place in the psychic economy of youth in developed societies and to render their absence a serious stressor.

It is even possible to argue, albeit in a speculative vein, that the dramatic rise in diagnoses of anxiety and depressive disorders among economically secure Americans born after 1950, most of whom enjoyed lives free of serious deprivation, trauma, chronic disease, the wounds of war, and restraints on sexuality, is due partly to an uncomfortable feeling generated by a sense that they did not deserve a life bereft of serious suffering. The Old and New Testament state in many places that suffering builds character. The Biblical figure Job is virtuous because, despite being a repeated victim of pain and loss, he retains his faith in God. Luke 14:27 states: "Whoever does not bear his own cross … cannot be my disciple." The Roman philosopher Seneca advocates a similar ethic: "Fire is the test of gold, adversity of strong men."

Nineteenth-century Europeans and Americans, however, regarded the suffering of slaves, children and adults working 15 hour days in crowded, poorly ventilated factories, and victims of torture as morally unacceptable and their governments eventually passed laws making such conditions illegal. After these unjust bases for suffering were eliminated, Americans turned their attention to the unjust treatment of African-Americans. An empathic concern for their suffering led to the Civil Rights movement and relevant legislation. The empathic mood was extended a generation later to all individuals who suffered injustice, frustration, or anxiety because of their gender, religion, country of origin, or a compromising physical or mental property.

The muting of the emotions linked to the traditional moral imperatives forbidding homosexuality, abortion, divorce, and adultery created an ethical vacuum. The declaration that all suffering was amoral helped to fill that vacuum. This attitude was helped by the media's frequent and dramatic presentations of the suffering of Jews in Nazi Germany and black slaves in the antebellum south. It was also relevant that, unlike conditions in the United States 100 years earlier, by the 1980s the percentage of victims of poverty or virulent prejudice had dropped below one-third of the population and had become a deviant property. This fact allowed those who held a liberal ideology to hope that all suffering might be eliminated.

The increasing level of sympathy toward victims of suffering eventually led many Americans to award them a measure of moral authority. All six adults that Americans nominated most often as highly admired twentieth-century citizens accomplished something important despite a handicapping feature. It was poverty for Mother Teresa, membership in an oppressed minority group for Martin Luther King and Albert Einstein, and a physical compromise for John F. Kennedy, Helen Keller, and Franklin Roosevelt. The community's willingness to award a badge of virtue to those who achieved greatness despite suffering from a handicapping feature was facilitated by the loss of moral authority held 50 years earlier by Supreme Court justices, bankers, clergy, scientists,

physicians, professors, and writers. Humans need a few heroes and heroines as well as moral directives.

Contemporary films affirm the suggestion that Americans have become receptive to awarding victims whose suffering was not their fault a form of heroism that renders them especially attractive. The popular 2003 film *The Station Agent* portrays a self-sufficient, adult dwarf who evokes genuine affection from a lonely male food vendor and an equally lonely woman separated from her husband. The same theme is present at the end of the 1988 film *Rain Man* when Charlie Babbitt develops genuine affection for his autistic brother. The various women in the 2012 film *Sessions* who care for a man paralyzed from the neck down because of polio, including his sex therapist, fall in love with him, presumably because his ability to maintain an optimistic mood awards him a spirituality that makes him attractive to those who are healthy but a little less happy.

I suggest that the historical events of the past half-century led many Americans to extend sympathy towards those who suffered from anxiety or depression. As a result, these mood states contained a hidden attractiveness for the small proportion of Americans who had not met, or had violated, one or more of their principled ethical standards. This phenomenon used to be called the secondary gain of an illness. This claim is supported by evidence indicating that guilt can provoke acts of self-harm in otherwise normal adults from diverse societies (Gilbert, McEwan, Irons, Bhundia, et al., 2010; Hamza, Willoughby, & Good, 2013; Schwerkoske, Caplan, & Benford, 2012). This dynamic was what motivated suicide among a number of Chinese women who concluded that their improper behavior disrupted family harmony (Zhang & Ma, 2012).

A mother in one of my studies found her three-year-old son pinching himself with a force that generated pain. When she asked why, he replied, "I don't like myself". The boy was unusually aggressive with peers in the neighborhood and was aware that the children and their parents disapproved of him and his behavior. This phenomenon can be captured in the laboratory. Adults who had written about an action that produced guilt administered more intense electric shocks to themselves, compared with students who had written about a sad or neutral experience. In addition, the former students reported feeling less guilty after the self-administered shocks (Inbar, Pizarro, Gilovich, & Ariely, 2013).

This argument implies that unconscious thoughts, which are not usually revealed in questionnaire or interview data, can have formative power. Imagine a steel cylinder containing three internal shelves. The top shelf has holes two inches in diameter, the holes of the middle shelf are one inch in diameter, and the holes of the bottom shelf are only one-half inch in diameter. If balls with diameters of 2, 1, and 0.4 inches had been placed on the top shelf of the cylinder only the smallest balls would emerge at the bottom, leading observers to conclude that these were the only objects in the cylinder.

There are, at present, too many open parameters in theoretical arguments presumed to explain the relation between a brain profile and a psychological state or action. The current descriptions of brain profiles that are offered as

explanations are crude schematic diagrams that lack details. Despite the robust evidence indicating a universal preoccupation with good and bad among humans, evidence for the brain's representation of these concepts was missing from the blood flow patterns of five Americans looking at several hours of films representing 1,705 different categories of objects and actions (Huth, Nishomoto, Vu, & Gallant, 2012).

Some investigators resist this assessment of the field. One team of scientists spent considerable time and money searching for the alleles that might predict which depressed patients, who varied in gender, social class, and nationality, would benefit most from a variety of drug therapies administered by physicians who had different levels of rapport with their patients. Not surprisingly, they did not find a single allele that predicted a better or a poorer outcome (GENDEP investigators; MARS investigators; STAR*D investigators, 2013). A second team did not find one SNP, out of 1.2 million SNPs examined, in 9,240 adults with depression and 9,519 healthy controls that was shared by those suffering from depression (Ripke, Wray, Lewis, Hamilton, et al., 2013).

A third team found only one copy number variant (CNV) that was shared by .094% of a very large group of schizophrenics (a deletion on chromosome 16 consisting of many thousands of bases). But .015% of a control group whose members had no schizophrenic symptoms possessed the same deletion (Guha et al., 2013). One reason for the small amount of variance linked to the genes shared by those assigned to a current illness category is that each disorder is heterogeneous in etiology and has more than one set of alleles and life experiences that are risk conditions. The genetic heterogeneity among those assigned to current psychiatric diagnoses resembles the heterogeneity among those suffering from headaches, cramps, or a locomotor disability. It is hard to understand, given this evidence, why some investigators continue to believe that the current DSM categories cut nature at its joints.

In contrast to most American psychiatrists, Japanese clinicians are sensitive to the contribution of work conditions to serious symptoms. The Japanese Supreme Court in 2000 ordered a Japanese firm to pay more than 1.5 million dollars to the family of a man who committed suicide because his supervisor asked him to work an excessive number of hours for a prolonged period (Kitanaka, 2012).

A few younger clinical scientists are beginning to rebel against the heavy burden of biological reductionism that dominates their profession (e.g., Bracken, Thomas, Timini, Asen, Behr, et al., 2012). Four facts frustrate current attempts to arrive at strong statements about the relation between either genes or brain patterns and a class of human behavior, emotion, or cognitive process.

Firstly, the brain's massive anatomical interconnectivity makes it hard to localize a psychological function in one location. It is important to appreciate that the absence of connectivity between two sites based on anatomy is not synonymous with estimates of functional connectivity inferred from blood flow patterns. The latter only implies that one of the two sites was not hyper-aroused.

Thus, a reduced connectivity between the orbitofrontal cortex and the amygdala among adults with a particular allele, based on fMRI data, should not be interpreted as meaning that there was no anatomical connection between these two sites (Wang, Saalmann, Pinsk, Arcaro, & Kastner, 2012). The density of anatomical connections between the amygdala and the medial prefrontal cortex grows with age but the functional connectivity between these sites when children or adolescents are viewing fearful faces decreases with age (Gee, Humphreys, Flannery, Goff, et al., 2013).

Secondly, most brain molecules have diverse functions that are intertwined with the activity of other molecules.

Thirdly, robust relations found in one species, say mice or rats, are not always replicated in monkeys or humans because of important differences between the brains of rodents and primates (Asan, Steinken, & Lesch, 2013). White college students are the usual participants in experiments designed to localize a psychological process. It is not obvious that forty-year-olds from Nigeria or Indonesia would provide the same evidence (Han, Northoff, Vogeley, Wexler, Kitayama, & Vairum, 2013).

Finally, every psychological outcome studied thus far can be the result of more than one set of conditions (Fiorillo, Song, & Yun, 2013). This claim is based, in part, on the fact that the BOLD signal is influenced by conditions that have nothing to do with the task or stimulus presented. Some of these nuisance variables are the person's heart rate and breathing, level of activity during the baseline interval, the ambiguity of the task, the physical features of the incentive, and the degree to which the input stimulus is concrete and evocative of images or schemata (Ash, Suckling, Walter, Ooi, et al., 2013; He, 2013; Neta, Kelley, & Whelan, 2013). If, for example, the word "disgust" evokes greater activity than the word "serene", it could be because the former evokes more images and not because it created an emotion. The journey has just begun.

There is insufficient appreciation of the fact that some of the evidence provided by fMRI, MEG, PET, or EEG fits Shannon and Weaver's definition of information. But information is not synonymous with meaning. The blood flow pattern in adults reading scenarios describing an agent committing a moral violation—harming another, lying, or acting in a disgusting way—differed from the patterns generated when neutral scenarios were read. But there was no difference in blood flow patterns to each moral vignette between actions that the participants judged as morally wrong and those judged as acceptable (Parkinson, Sinnott-Armstrong, Koralus, Mendelovici, McGeer, & Wheatley, 2011). Hence, the blood flow information did not measure the moral meaning each person imposed on the narratives.

The pattern of blood flow evoked by an event is also influenced by the person's mental state. The fusiform face area is activated in participants who see a face, expect to see a face, or infer a face that is not present (Cox, Meyers, & Sinha, 2004; Summerfield, Egner, Mangels, & Hirsch, 2006). The sites activated by a photograph of a face with a fearful expression differ from the pattern

activated when participants see a film of a face with a fearful expression or see both the face and body. Most observers are more accurate in inferring an intense feeling in another caused by an unpleasant or pleasant event when they use cues from the body rather than the face (Aviezer, Trope, & Todorov, 2012; Faivre, Charron, Roux, Lehericy & Kouider, 2012). Yet faces with neither a body nor background are the stimuli most often used in studies of the relation between a brain profile and a person's emotional state.

Equally important, a large number of human actions are based on the person's anticipation of how he or she will feel in some future situation. I suspect that the brain profile accompanying the anticipation of seeing a person with an angry facial expression is palpably different from the profile evoked by seeing an angry face. The profile evoked by the receipt of an electric shock is dissimilar from the profile seen when a person is anticipating an electric shock. Yet much of what we know about the brain's reaction to an incentive is based on the neuronal response to particular events (an angry face, memory task, or speech) rather than the response to an anticipation of those events in the distant future. One reason for this asymmetry is that this strategy permits a more confident generalization from animals to humans.

The fact that one collection of neurons received more blood flow than another does not necessarily mean that those neurons fired more often, were the primary cause of an outcome, nor even that they were the most important bases for an outcome (Horovitz, Skudlarski, & Gore, 2002). The midbrain superior colliculus receives input from seven sites when a visual stimulus evokes a saccade. But the proximal cause of a saccade resides in the brain stem to which the colliculus projects. Because the brain stem site receives less blood flow than the colliculus, investigators are tempted to conclude that the latter site is the "cause" of the saccade. It is also important that the absence of an increase in blood flow to a site does not necessarily mean that the neurons at this site were not activated, as evidenced by information from MEG (Swettenham, Muthukumaraswamy, & Singh, 2013).

The introduction of fMRI, MEG, PET, and EEG should not replace the psychologist's strategy of trying to understand the relations among incentives, the agent's biology, and the products of past experience, on the one hand, and the resulting feelings, judgments, and actions on the other. It is chastening to note that in 1967 the members of the newly formed American College of Neuropsychopharmacology made wild, generally incorrect, predictions about the use of drugs, legal and illegal, in the year 2000. These included the belief that drugs would be used broadly to control aggression and in poor countries cocaine would be distributed to mute hunger pangs (Hirschbein, 2012).

The psychologists who, with Roger Sperry, continue to believe that psychological processes emerge from a cascade of brain events in different locations and require a distinctive vocabulary find themselves intimidated by the growing number of scientists who are replacing psychological definitions of concepts with a vocabulary that makes brain states the referent for the same

concept. For example, activation of the nucleus accumbens is replacing the traditional behavioral meaning of the concept of reward; activation of the HPA axis is replacing the concept of stress; activation of the amygdala replaces the emotion of fear; activation of the insula replaces detected feelings; activation of the hippocampus replaces recall of the past; activation of the brain's hedonic detection system replaces a depressed mood; and activations of varied sites in the prefrontal cortex replace evaluation, reflection, regulation, and planning. I confess to a moment of surprise when I read a paper claiming that the pattern of increased blood flow in adults whose arm was stroked with a watercolor brush as they lay in a scanner reflected the psychological state these adults would have experienced when they received an "affective touch" from the fingers of a lover in the privacy of a home or a hotel room (Gordon, Voos, Bennett, Bolling, Pelphrey, & Kaiser, 2013).

I am not sure that the brain profile displayed by adults lying in a PET scanner being masturbated to orgasm by their heterosexual partner sitting outside the scanner would resemble the profile that occurred when these same partners had mutual orgasms during sexual intercourse in their bedroom (Huynh, Willemsen, & Holstege, 2013).

One problem with this word substitution is that changes in these brain sites are not always accompanied by a change in the relevant psychological state. A person's report of a psychological state, or performance on a task, is not always accompanied or preceded by the expected change in brain state. For example, equivalent performances on a set of cognitive tasks were accompanied by significantly different patterns of blood flow in different individuals (Sutton, Twyman, Joanissen, & Newcombe, 2012). There is no single pattern of activated sites in 100 adults reporting that a painting is ugly or beautiful (Kawabata & Zeki, 2004). Moreover, brain profiles that accompany a low level of activity in the HPA axis (inferred from salivary cortisol) can characterize individuals who are under low stress or are victims of chronic stress (Gunnar & Herrera, 2013).

The brain is being cast as the most important origin of all that is psychological as more investigators ignore the detailed and complex interplay between the first psychological product of the initial brain response to an event and the cascade of subsequent brain and psychological profiles. Yes, the brain is the foundation of all psychological phenomena, as the sun is the origin of all life on this planet. But evolutionary theorists accept the sun's importance and proceed to fill in the significant details that might explain how the first living cells were created and how birds might have evolved from reptiles without ever mentioning the sun. Analogously, psychologists and neuroscientists cannot explain many psychological phenomena, such as worry over losing a child, an autobiographical memory of maltreatment, or the narrative structure of a recalled dream, by declaring that these phenomena had an origin in the brain—case closed. Anthropologists and archaeologists contend that the adults in most early human societies believed that each person possessed a life force, individuals, places, and objects varied in level of sacredness, and some ways of life

were superior to others (Flannery & Marcus, 2012). None of these beliefs can be explained by pointing to particular genes or brain profiles.

One of Niels Bohr's great insights was to recognize that the context in which an event occurs is an integral part of the total phenomenon. This principle applies whether the context is a laboratory, bedroom, historical era, the country to which a Pakistani emigrates, the background of a person who displays closed eyes together with a clenched fist, or the fitness of an organism. The biologists who typically write about the "inclusive fitness of an animal" tempt unsophisticated readers to assume that this feature is an inherent property of a single animal. They readily acknowledge, however, that fitness is relative because it always depends on the animal's ecology, and, therefore, can be temporary. Dinosaurs and coral reefs were perfectly fit until their ecology changed. Thus, the context has as much power to shape the phenotype as the animal's biological properties, which is why Darwin chose the term "natural selection".

Younger readers may not appreciate that from 1900 to the 1930s most geneticists rejected the idea that an animal's ecological setting made a contribution to speciation. They insisted that mutations were the only important factor in evolution. Fortunately, by the 1940s geneticists and naturalists agreed on a synthesis that acknowledged the joint contribution of genetic mutations and ecological change to evolution. The fields of psychology and biology are ready for their synthesis and an admission by the biologists that genes and brains alone cannot explain the variation among phenotypes. It is necessary to measure the contexts in which individuals develop and the circumstances in which they are presently acting.

The person's immediate setting functions like a priming stimulus, for it selects from a large collection of possibilities the small number that are relevant to that context. It is not a coincidence that Pavlov discovered the conditioned salivary reflex—he had been studying the secretions of the dog stomach and salivary glands for years. When the forms selected refer to a person's knowledge networks, these representations dominate the others in that context. That is why a person can feel confident and secure in one social setting and unsure and insecure in another.

Neuroscientists, by and large, regard all of a person's stored representations as equally available when they present an incentive to a participant. They would rather not acknowledge that the unusual context in which they gather their data selects representations that might not be dominant in the life settings of their participants. The many attempts to find a single brain site that is the primary origin of a psychological process, independent of the ethnicity, age, or culture of the participants, shares features with attempts to locate the enthusiasm of a crowd at a football game or the investment firm responsible for the Dow Jones average at the end of a particular day.

One team of Canadian investigators did not think it was necessary to inform readers about the class, ethnicity, or age of the 19 adults asked to listen to unspecified 30-second musical excerpts while lying in a scanner in order to

conclude that increased activity in the right nucleus accumbens explains one-third of the variance in the human aesthetic evaluation of music (Salimpoor, van den Bosch, Kovacevic, McIntosh, Dagher, & Zatorre, 2013). Their conclusion implied that any group of 19 adults listening to any collection of music in any setting would show the same result, even though Danish and Chinese college students show different patterns of blood flow when asked to judge the personal appropriateness of a social role (Ma, Bang, Wang, Allen, et al., 2012).

Differences in social conditions, not genes or brain profiles, explains why 65-year-olds in Italy who develop a bout of depression are more likely than 65-year-olds in neighboring Switzerland to maintain their melancholic mood for two years (Gallagher et al., 2013). Nor will variation in genes or brains explain the different personas of adults born with the same low reactive temperamental bias who grew up either on a farm in rural Montana or a densely crowded neighborhood in Los Angeles.

Put plainly, an infant's temperamental biases can be sculpted into any of a large number of adult forms because each child is embedded in a particular family which is embedded in a community which is embedded in a larger culture embedded in a historical era. The four settings in which each child develops—family, community, culture, and era-—impose significant influences on the final psychological outcome of all inherited temperaments, as promoters and enhancers in the genome impose significant influences on when, where, and how much of a protein coding gene will be expressed.

A large number of scientists studying variation in human properties do not like this model. They prefer to find a single condition which their intuition or popular theory suggests makes the critical contribution. Hence, they perform covariance analyses in order to remove the contributions of the conditions they regard as less important in order to arrive at an estimate of the potency of the favored factor. This popular practice rests on the flawed premise that the favored condition possesses a causal power that does not depend on it being a part of a pattern. A tulip bulb, however, cannot generate a blossom unless it is part of a pattern that includes being planted in earth and receiving water and sun. Analogously, the consequences of being a victim of bullying or harsh socialization depends in a major way on the victim's other properties, which include his or her social class, peer groups, minority status, gender, grades, physical attractiveness, and all the family's practices. The aesthetic power of a speech in a play, a nude figure in a painting, or a chord sequence in a symphony also depends on the entire composition in which it is only a part.

Life experiences, particularly times and places which lie outside the genome and require a special vocabulary, select the forms that will be privileged to develop from the larger envelope of possibilities contained in a person's genome. A feeling of deviance or marginalization in a community, which can lead to anti-social actions or teenage pregnancies, usually requires the possession of observable properties that are deviant from those valued by the majority (Kearney & Levine, 2012). The same person might not feel marginalized in a different community.

Despite the reasonableness of the suggestion that a person's beliefs and knowledge networks, acquired in a particular place and time, are an important origin of some behaviors and moods, gathering this evidence does not attract much attention or research support. A team of social scientists requesting one billion dollars (less than the cost of the Human Genome Project) for a Human Psychonome Project that promised to discover the classes of schemata, semantic networks, beliefs, and values shared by all contemporary humans, along with the major differences among them, would probably be denied these funds, even though the results would be useful to the Defense Department, State Department, CIA, and epidemiologists concerned with preventing epidemics. Beliefs, not genes, were responsible for the tragedy of 9/11, the Arab Spring, and the 2013 bombings at the Boston marathon.

The problem is that mental events are invisible, immaterial phenomena; whereas genes and brain molecules and neurons are material things whose features can be described in detail and altered. A fair proportion of natural scientists, therefore, find it counterintuitive to award a causal force to ideas, moods, and desires and prefer to treat them as derivatives of biological events. These scientists might reflect on the fact that almost all biologists during the 1940s rejected as counterintuitive the possibility that nucleic acid could be the basis for all life since it was composed of only four different atoms arranged in patterns that represented only seven molecules. How could such a simple chemical foundation be the origin of all life forms?

The main point is that the principles governing the brain, and the vocabulary used to state these principles, are not the principles and vocabulary that describe psychological phenomena. The metrics for the brain include microvolts, frequency bands, oxygen consumption, and connectivity. The metrics for psychological phenomena include the valence and intrusiveness of feelings, size and coherence of semantic networks, frequency of occurrence of actions, and latencies to respond to varied incentives. It is not yet obvious how these metrics are related to those used for the brain.

Put differently, the neuroscientists' conceptualizations of the brain do not correspond closely to the psychologists' conceptualizations of their phenomena. The neuroscientist relies on the brain's gross and fine anatomy, patterns of anatomical connectivity, neurochemistry, level of neuronal activity and patterns of gene expression in different sites to particular inputs, and the presumed functions of each site. Each of these six ways to think about the brain has different implications for explaining psychological events.

Psychologists typically choose among five ways to conceptualize their domain. They rely on the distinctive properties of their three major phenomena: actions, verbal reports, and biological reactions. The other four refer to the functions these three classes of phenomena serve, the agent's level of consciousness, degree to which the phenomenon is dependent on experience or is biologically prepared, and the adaptive quality of the phenomenon.

It is possible to map the form of the phenomenon (action, thought, or feeling) on several of the categories for the brain but far more difficult to do so for the remaining four properties that neuroscientists rely on when they theorize about the brain. We do not yet know the material foundations of consciousness and neuroscientists cannot differentiate between a speech at a dinner party that was adaptive or maladaptive by measuring the brain of the speaker, because its adaptive quality depends on the evaluations of the guests. Thus, at the moment the two domains are separated by a chasm that makes it difficult to relate most psychological outcomes to a particular collection of brain properties, not unlike the chasm between the principles that explain atomic phenomena and those that explain the velocity, size, and direction of an area of low pressure moving west across the Atlantic ocean in late summer. The distinctive phenomena of brain and mind can be likened to the power of tigers and sharks. Each is potent in its own territory but impotent in the territory of the other.

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