INNATE

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How the Wiring of Our Brains Shapes Who We Are

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either innately or require maturation or experience to develop, then the list is long and much less contentious. Humans *tend to* walk upright, be active during the day, live in social groups, form relatively stable pair-bonds, rely on vision more than other senses, eat different kinds of food, and so on. A zoologist studying humans would say they are bipedal, diurnal, gregarious, monogamous, visual, and omnivorous—all of these traits are shared by some other species, but that overall profile characterizes humans.

And humans have *capacities* for highly dexterous movements, tool use, language, humor, problem solving, abstract thought, and so on. Many of those capacities are present to some degree in other animals, but they are vastly more developed in humans. The actual behaviors may only emerge with maturation and many depend to some extent on learning and experience, but the capacities themselves are inherent. Indeed, even our capacity to learn from experience is itself an innate trait. Though our intellect separates us from other animals—by enabling the development of language and culture, which shape all of our behaviors—our underlying nature is a product of evolution, the same as for any other species.

Simply put, humans have those species-general tendencies and capacities because they have human DNA. If we had chimp DNA or tiger DNA or aardvark DNA, we would behave like chimps or tigers or aardvarks. The essential nature of these different species is encoded in their genomes. Somehow, in the molecules of DNA in a fertilized egg from any of these species is a code or program of development that will produce an organism with its species-typical nature. Most importantly, that entails the specification of how the brain develops in such a way that wires in these behavioral tendencies and capacities. Human nature, thus defined, is encoded in our genomes and wired into our brains in just the same way.

This is not a metaphor. The different natures of these species arise from concrete differences in some physical properties of their brains. Differences in overall size, structural organization, connections between brain regions, layout of microcircuits, complement of cell types, neurochemistry, gene expression, and many other parameters all contribute in varied ways to the range of behavioral tendencies and capacities that characterize each species. It's all wired in there somehow. Human nature

thus need not be merely an abstract philosophical topic—it is scientifically tractable. We can look, experimentally, at the details of how our species-typical properties are mediated in neural circuitry. And we can seek to uncover the nature of the genetic program that specifies the relevant parameters of these circuits.

THE WORD MADE FLESH

To understand this genetic program, it is crucial to appreciate the way in which information is encoded in our genomes and how it gets expressed. It is not like a blueprint, where a given part of the genome contains the specifications of a corresponding part of the organism. There is not, in any normal sense of the word, a representation of the final organism contained within the DNA. Just as there is no preformed homunculus curled up inside the fertilized egg, there is no simulacrum of the organism strung out along its chromosomes. What is actually encoded is a *program*—a series of developmental algorithms or operations, mediated by mindless biochemical machines, that, when carried out faithfully, will result in the emergence of a human being.

This is not a reductionist view. The DNA doesn't do any of this by itself. The information in the genome has to be decoded by a cell (the fertilized egg, in the first place), which also contains important components required to kick the whole process off. And, of course, the organism has to have an environment in which to develop, and variation in environmental factors can also affect the outcome. Indeed, one of the most important capacities encoded in the genetic program is the ability of the resultant organism to respond to the environment.

Moreover, while the information to make any given organism and to keep it organized in that way is written in its genome, there is a web of causation that extends far beyond the physical sequence of its DNA. Its genome reflects the life histories of all its ancestors and the environments in which they lived. It has the particular sequence it has because individuals carrying those specific genetic variants survived and passed on their genes, while individuals with other genetic variants did not. A full map of what causes an organism to be the way it is and behave the way it does thus extends out into the world and over vast periods of time.

However, what we are after in this book is not a full understanding of how such systems work—how all those genetically encoded components interact to produce a human being with human nature. It is something subtly but crucially different—how *variation* in the genetic program causes *variation* in the outcome. Really, that's what we've been talking about when we've been comparing different species. The *differences* between our genomes and those of chimps or tigers or aardvarks are responsible for the *differences* in our respective natures.

INDIVIDUAL DIFFERENCES

The same can be said for differences *within* species. There is extensive genetic variation across the individuals in every species. Every time the DNA is copied to make a sperm or egg cell, some errors creep in. If these new mutations don't immediately kill the resultant organism or prevent it from reproducing then they can spread through the population in subsequent generations. This leads to a buildup of genetic variation, which is the basis for variation in all kinds of traits—most obviously physical ones like height or facial morphology. (Conversely, shared profiles of genetic variants are the basis for familial *similarities* in such traits.) Some of those genetic variants affect the program of brain development or brain function in ways that contribute to differences in behavioral tendencies or capacities.

We know this is the case because we can successfully *breed for* behavioral traits in animals. When wolves were tamed, for example, or when other animals were domesticated, early humans selected animals that were less fearful, less aggressive, more docile, more submissive—perhaps the ones that came nearest to the fire or that allowed humans to approach the closest without running away. If the reason that some were tamer was the genetic differences between them, and if those ones who hung around and tagged along with human groups then mated together, this would over time enrich for genetic variants predisposing to those traits. On the other hand, if the variation was not at least partly genetic in origin then breeding together tame individuals would not increase tameness in the next generation—the trait would not be passed on.

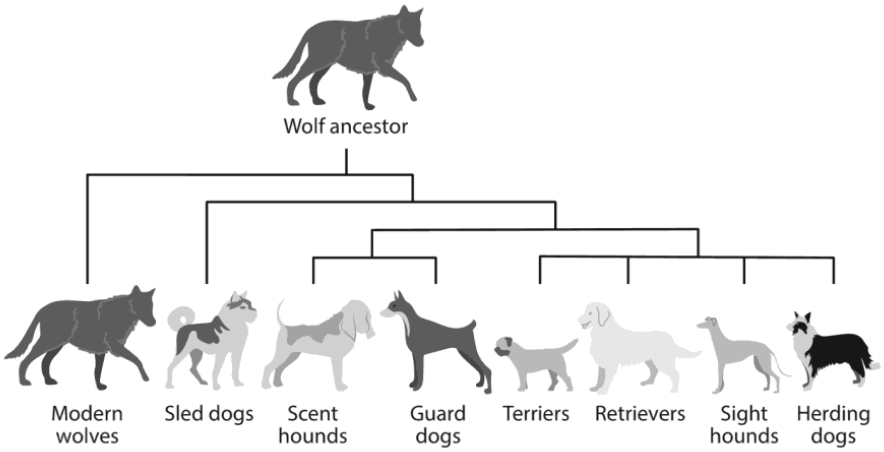

Figure 1.1 Selection of dog breeds for diverse behavioral traits.

Well, we know how that turned out—with modern dogs that have a nature very distinct from their lupine ancestors. And that process has been played out over and over again in the creation of modern dog breeds (see figure 1.1). These breeds were selected in many cases for behavioral traits, according to the functions that humans wanted them to perform. Terriers, pointers, retrievers, herders, trackers, sled dogs, guard dogs, lapdogs—all show distinct profiles of traits like affection, vigilance, aggression, playfulness, activity, obedience, dominance, loyalty, and many others. All these traits are thus demonstrably subject to genetic variation. The details of *how* genetic differences influence them remain largely mysterious, but the fact that they do is incontrovertible.

And the same is true in humans, as we will see in subsequent chapters. The empirical evidence for this is every bit as strong as it is in dogs. Even just at a theoretical level, this is what we should expect, based on the geneticist's version of Murphy's Law: anything that can vary will. The fact that our nature *as a species* is encoded in the human genome has an inevitable consequence: the natures of individual humans will differ due to differences in that genetic program. It is not a question of whether or not it does—it must. There is simply no way for natural selection to prevent that from happening.

BECOMING A PERSON

Just showing that a trait is genetic does not mean that there are genes "for that trait." Behavior arises from the function of the whole brain—with a few exceptions it is very far removed from the molecular functions of specific genes. In fact, many of the genetic variants that influence behavior do so very indirectly, through effects on how the brain develops.

This was dramatically highlighted by the results of a long-running experiment in Russia to tame foxes. Over 30 generations or more, scientists have been selecting foxes on one simple criterion—which ones allowed humans to get closest. The tamest foxes were allowed to breed together and the process repeated again in the next generation, and the next, and so on. The results have been truly remarkable—the foxes did indeed end up much more tame, but it is how that came about that is most interesting.

While they selected only for behavior, the foxes' appearance also changed in the process. They started to look more like dogs—with floppier ears and shorter snouts, for example—even the coat color changed. The morphological changes fit with the idea that what was really being selected for was retention of juvenile characteristics. Young foxes are tamer than older ones, so selecting for genetic differences that affected the extent of maturation could indirectly increase tameness, while simultaneously altering morphology to make them look more like pups.

This highlights a really important point. Just because you can select for a trait like tameness does not mean that the underlying genetic variation is affecting *genes for tameness*. The effect on tameness is both indirect and nonspecific, in that other traits were also affected. Though their identities are not yet known, the genes affected are presumably involved in development and maturation somehow.

The same kind of relationship holds in us. As we will see, the genetic variants that affect most psychological traits do so in indirect and nonspecific ways—we should not think of these as "genes for intelligence" or "genes for extraversion" or "genes for autism." It is mainly genetic variation affecting brain development that underlies innate differences in psychological traits. We are different from each other in large part because of the way our brains get wired before we are born.

and develop over decades, and our brains are literally shaped by the experiences we have over that period. It is common to view "nurture" as being in opposition to nature, such that the environment or our experiences act as a great leveler, to smooth over innate differences between people or counteract innate traits in individuals. I will describe an alternative model: that the environments and experiences we each have and the way our brains react to them are largely *driven by our innate traits*. Due to the self-organizing nature of the processes involved, the effects of experience therefore typically act to *amplify* rather than counteract innate differences.

With that broad framework in place, we will then examine a number of specific domains of human psychology in the second section. These include personality, perception, intelligence, and sexuality. These diverse traits affect our lives in different ways and genetic variation that influences them is therefore treated very differently by natural selection. As a result, their underlying genetic architecture—the types and number and frequency of mutations that contribute to them—can be quite different. Much of the variation in these traits is developmental in origin—the circuits underlying these functions work differently in part at least because they were put together differently. This means that random variation in developmental processes, in addition to genetic variation, also makes an important—sometimes crucial—contribution to innate differences in these faculties.

We will also look at the genetics of common neurodevelopmental disorders, such as autism, epilepsy, and schizophrenia. There has been great progress in recent years in dissecting the genetics of these conditions, with results that are fundamentally changing the way we think about them. Genetic studies clearly show that each of these labels really refers to a large collection of distinct genetic conditions. Moreover, while these disorders have long been thought to be distinct, the genetic findings reveal the opposite—these are all possible manifestations of mutations in the same genes, which impair any of a broad range of processes in neural development.

The final chapter will consider the social, ethical, and philosophical implications of the framework I've described. If people really have large innate differences in the way their brains and minds work, what does that mean for education and employment policies? What does it mean

for free will and legal responsibility? Does it necessarily imply that our traits are fixed and immutable? What are the prospects for genetic prediction of psychological traits? What limits does developmental variation place on such predictions? And, finally, how does this view of the inherent diversity of our minds and our subjective experiences influence our understanding of the human condition?

CHAPTER 2

VARIATIONS ON A THEME

If the typical nature of a species is written in its genome, then individual members of the species may differ in their natures due to genetic variation in that program. We saw some of the evidence for that in other animals in the previous chapter, but what about in humans? What kind of evidence could we use to determine whether genetic differences between people contribute to general differences in psychological traits? Well, one powerful method is to flip the question around and ask whether people who are more genetically *similar* to each other are also more similar in psychological traits. In short, if such traits are even partly genetic, then people should resemble their relatives, not just physically, but also psychologically.

That is a nice idea, but there is an obvious problem—people who are closely related to each other—like siblings, for example—also typically share similar environments, like being raised in the same family. So, if we know only that siblings resemble each other psychologically more than random people in the population, we cannot distinguish possible effects of nature from those of nurture. We need some way to dissociate these two effects—to test the impact of shared genes separately from the impact of shared family environment, and vice versa.

TWIN AND ADOPTION STUDIES

Twin and adoption studies have been developed for precisely that purpose. Adoption studies are the simplest to understand—the idea is that if shared genes are what make people more similar to each other, then adoptees will resemble their biological relatives, while if shared

environment is more important then they will resemble their adoptive relatives, especially adoptive siblings (children who are not biologically related but who are raised in the same family).

Twin studies take the converse approach—they compare people who have the same degree of shared environment, but differ in how similar they are genetically. Twins can be identical (or monozygotic [MZ], meaning they come from a single fertilized egg, or zygote, that has split into two embryos with the same genome) or they can be fraternal (or dizygotic [DZ], meaning they come from two different eggs fertilized by two different sperm and thus are only as similar to each other as ordinary siblings—they just happen to be conceived at the same time). As they grow up under similar conditions, these different types of twins make an ideal comparison to test the importance of shared genes.

If the environment you grow up in were the only thing that mattered for some trait, then the similarity between pairs of MZ twins should be about equal to that between pairs of DZ twins. DZ twins make the ideal comparison here because they grow up not just in the same household, but at the same time, and also share any possible effects of being twins, which, if they exist, would not be apparent in other siblings. By contrast, if variation in a trait is due to genetic differences, then MZ twins should be more similar to each other than DZ twins. Of course that is obviously true for physical traits, which is why we call MZ twins "identical." But is it true for psychological traits?

To answer this question, we need to do something that is much harder for psychological traits than for physical ones like height—we need to measure them. If we are to calculate how similar different people are for some trait, we need a number—some objective measure that captures or reflects variation in the trait of interest.

MEASURING PSYCHOLOGICAL TRAITS

There are many possible ways to do this, some of which are more direct than others. For example, we can simply ask people questions about their own behavioral patterns or predispositions and generate some kind of arbitrary numerical ranking or score from their answers, as in personality questionnaires. These typically ask people how strongly they

agree or disagree with statements like "I really enjoy going to parties and get energized by social situations," and give a score based on a five-point scale. If you analyze the responses to many such questions you can get an aggregate number that reflects the personality trait of extraversion.

These kinds of questionnaires were first developed by Francis Galton, the Victorian polymath, who was obsessed with measuring anything that could be measured, and who applied this to the study of variation in human faculties. He also devised ways of classifying fingerprints, created the first weather map, and even studied scientifically the best way to make a cup of tea. It was Galton who coined the phrase "nature versus nurture" and he foresaw the use of twin and adoption studies as a means to separate these effects. Later, he became a champion of the eugenics movement (having invented the term), which led to a dark chapter in the history of human genetics, not just with the well-known horrors in Nazi Germany, but also with the enthusiastic adoption of eugenic policies in the United Kingdom and the United States, involving forced sterilizations of "feeble-minded" people. Though the days of enforced government programs such as this are hopefully over, new genetic technologies are providing the means for individual action, in selection of embryos based on genetic information, for example. This raises a host of ethical and moral issues, which we will consider in chapter 11. In the meantime, we will see more of Mr. Galton in this and subsequent chapters.

An alternative to questionnaires is to measure performance on tests of, for example, intelligence or memory or empathizing—anything where a specific number emerges based on success in answering questions. This can be extended to all kinds of tasks in a lab where things like reaction time or quantitative differences in perception or task performance are measured. And these days we can go even further and directly measure differences in brain structures or brain activity under various conditions and consider such differences as traits of interest.

Finally, we can measure the actual occurrences of specific behaviors or of real-world outcomes that can act in some way as proxies for underlying traits. These might include things like educational attainment, number of times arrested, what time you get up in the morning, number of same-sex partners, whether you have ever been prescribed an antipsychotic medication, how much you drink, whether you write with your right or left hand, and so on.

which is called the *correlation* or *regression coefficient* (another invention of Francis Galton). This number ranges from 0 (if there is no relationship within pairs) to 1 (if the values are always identical within pairs).

If we make such plots and calculations for many pairs of adopted siblings, we tend to find a very modest correlation between them for many psychological traits. They are, for some traits, more similar to each other than random people, but typically only slightly and in many cases such similarity seems to be temporary—it is evident if the trait is measured while the siblings still live in the same home, but tends to disappear if they are measured as older adults. By contrast, if we plot adoptees versus their biological siblings, we see a much stronger correlation for many such traits. These findings indicate that sharing genes with other people really does make you more similar to them psychologically, and that this effect is not due to having similar upbringing. In fact, the effect of a shared family environment is remarkably modest for most such traits.

We can do a similar comparison between MZ and DZ twins. Typically what is found is that MZ twins are much more similar to each other than are pairs of DZ twins. As they share a family environment similarly in each case, this effect must be due to the fact that MZ twins share all their genetic material, while DZ twins share only 50% of it. Indeed, for many traits, MZ twins who have been reared apart are just about as similar to each other as ones who have been reared together. Again, the conclusion is that shared genes have a much bigger effect on psychological traits than a shared upbringing.

These data directly show that people who are more genetically similar to each other tend to be more phenotypically similar to each other for psychological traits, and this correspondence is not due to being raised in the same family. From that, we can draw a more general inference by flipping back to considering differences rather than similarities. We can infer that genetic *differences* between people make a big contribution to *differences* in psychological traits across the population. By contrast, differences in family environments make a much smaller, often negligible, contribution. Now we are thinking not about what makes one individual a certain way or what makes two individuals similar to each other—we are instead thinking about what factors contribute to variation in a trait across the whole population. It is worth pausing a moment to consider what that shift in perspective means.

VARIATION ACROSS THE POPULATION

If we measure a trait in many individuals in the population, then we will see some variation in that trait and we can measure that too. For traits that have a continuous range of values, like height or IQ, we can plot the distribution of values across the population in what is known as a histogram. A histogram plots the values of the trait along the horizontal axis and the number of people who have that value on the vertical axis. Generally speaking, you find many more people near the average value and far fewer people as you go out to the extremes, giving the famous bell-shaped curve, or "normal distribution" (see figure 2.2).

All normal distributions have that general bell shape, but for some the bell is higher and narrower and for others it is lower and wider. A low and wide curve shows that there is more variability in that trait across the population. For example, if you plot the heights of all males in the population, you will have a distribution that ranges from well under five feet to over seven feet, with many more people in the middle of the range than at the ends. But if you were to plot the heights of professional basketball players, you would get a distribution with the average height shifted far toward the higher end and with much less variability—the bell curve would be narrower. (You can imagine a similar situation at the other end of the spectrum if you were to plot the heights of jockeys.)

The amount of variability seen in a distribution of values like that is called the *variance*. The variance is a precise number—it is calculated by measuring how far each point is from the mean, or average point, of the distribution, then squaring these values (so that any difference becomes a positive number) and adding them up. So, if the values are all clustered very close to the mean, the variance will be a small number. But if the values range more widely, the variance will be larger. And that is what we want to explain. What is it that causes that variability? What are the sources of variance in the trait?

Twin and adoption studies allow us to estimate how much of the variance in a trait is due to genetic differences between people, how much is due to differences in family environments, and, importantly, how much is unexplained even when those two factors are taken into account. For example, if we find that MZ twins are much more similar to each other

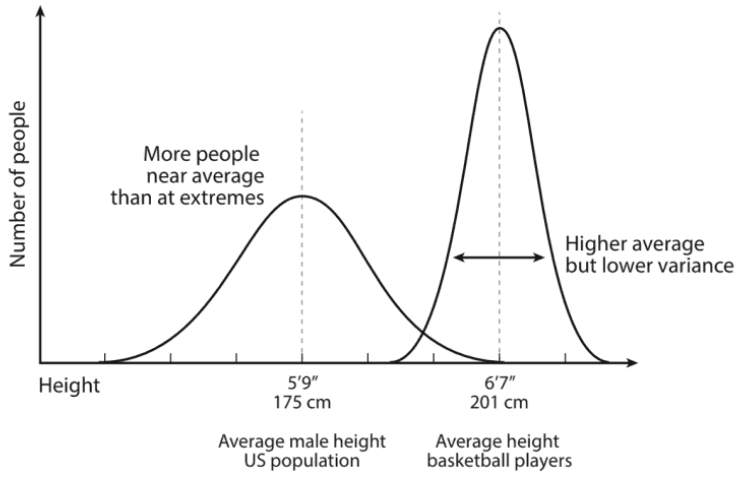

Figure 2.2 Variance. The distribution of heights across the general population follows a normal bell-shaped curve. The width of this curve reflects the variance of the trait. A selected population, such as professional basketball players, shows a higher mean value, but lower variance.

than DZ twins are, then we can infer that genetic differences make a large contribution to the variance in the trait across the population. Alternatively, if MZ twins are just a little more similar than DZ twins, then genetic differences must not play as large a role. Or if we find that adoptive siblings are just as similar to each other as biological siblings for some trait, that implies that a shared family environment is the key factor—that is, that differences in family environments can fully explain the variance in the trait that we observe across the population.

It's possible to go beyond just general statements, though. By mathematically comparing the values of the correlations between these different sets of pairs (MZ vs. DZ twins, or adoptive vs. biological siblings, or many other possible combinations), we can calculate the *percentage of the variance* accounted for by these various factors. The results from hundreds of such studies are remarkably consistent. In general, for psychological and behavioral traits, the percentage of variance accounted for by genetic differences ranges from modest (30%–40%) to very high (70%–80%). This last factor—the amount of variance in a trait that can

be attributed to genetic variation—is known as the *heritability*. It is a key concept in genetics but one that is often misunderstood—more on what it means and doesn't mean below.

Importantly, heritability can also be estimated by comparing phenotypes across thousands of people in the general population, relying on the fact that we are all distantly related, to varying extent. Even a small increase in relatedness above the average level is enough to cause a slight, but measurable, increase in phenotypic similarity. This effect can be measured by carrying out millions of pairwise comparisons across a population sample of thousands of people. Results from these kinds of studies confirm the heritability of psychological traits and also demonstrate that they are not caused by any artifacts or unusual aspects of twin studies.

These findings hold for all kinds of personality traits—conscientiousness, extraversion, impulsivity, aggressiveness, threat sensitivity, warmth, and on and on—as well as intelligence, memory, language ability, motor skill, balance, psychological interests, sexual orientation, sleep patterns, musicality, appetite, social attitudes, even how religious people are. It holds for behaviors like smoking, problem drinking, antisocial behavior, educational attainment, marital fidelity, and likelihood of divorce. And it is true for all kinds of psychiatric disorders, anxiety, drug abuse, even suicidal behavior. For all these traits or behaviors, genetic differences are a substantial cause of variation across the population. Within families, MZ twins are much more similar to each other than DZ twins, and biological siblings are much more similar to each other than adoptive siblings.

The clear biological basis for these traits suggests that twins and siblings behave similarly to each other because their brains are wired in similar ways. With new neuroimaging technologies we can now see that that is literally true.

VARIATION IN BRAIN STRUCTURE

Neuroimaging techniques allow us to see the structure of the brain in ever-increasing detail, and also to visualize its activity under different conditions. The most prominent of these techniques is magnetic resonance imaging (MRI). MRI works by using strong magnetic fields to

alter the states of atoms in a tissue, particularly hydrogen atoms. The single proton in the nucleus of each hydrogen atom acts like a tiny compass needle and aligns to the magnetic field. Radio waves are used to knock these protons out of alignment, and as they relax back into alignment they give off a radio wave signal that can be detected from outside the body. By using a graded and pulsed magnetic field, the radio wave signals can be localized with very high precision to create a high-resolution, three-dimensional scan of the tissue. Differences in these signals are caused as hydrogen atoms in different tissues realign at different speeds. This generates a contrast between different regions of a tissue—for example, between muscle and bone and tendon in your shoulder or your knee, or between gray and white matter in your brain.

"Gray matter" refers to areas of the brain where nerve cell bodies are densely packed and where the thin fibers that connect them (called *dendrites* and *axons*) are diffuse and local, intermingled among the cells. "White matter," on the other hand, refers to large bundles of axons that run quite separately from the nerve cell bodies and connect distant regions of the brain. They appear white because they are insulated with a fatty substance called myelin. The white matter is organized into major pathways through the brain—connecting, for example, the two cerebral hemispheres, the front of the brain to the back, the outer cortex to lower areas, or the brain to the spinal cord.

MRI scans can provide extremely detailed three-dimensional pictures of an individual's brain, from which we can extract all kinds of measurements. The most obvious is the volume or thickness or surface area of various brain regions, or the volume of specific white matter tracts. With these scans and measurements in hand, we can ask whether people who are genetically more similar to each other have brains that are structurally more similar. Outwardly, MZ twins look "identical" to each other—we can now clearly see that this similarity extends to the physical structure of their brains. Indeed, the brain scans of the two MZ twins shown in figure 2.3 look at first like scans of the same brain. Closer inspection reveals some subtle differences, but they are clearly much more similar to each other than are the brains of the DZ twins or siblings also shown. Importantly, the measurements we can derive from these scans allow us to quantify this similarity across large numbers of pairs of twins and assess their heritability, exactly as we did for psychological traits.

VARIATION IN BRAIN FUNCTION

Neuroimaging techniques can show us not just how people's brains are wired, but also how they work, at least at a gross level. A technique called functional magnetic resonance imaging (fMRI) is a powerful method that allows us to see which areas of the brain are active. It relies on the fact that active areas of the brain attract a flow of oxygenated blood, which has a different magnetic resonance signature to deoxygenated blood. Though this signal is much slower than the neuronal activity itself, it is a reliable proxy for that activity over a time frame of several seconds. This is the technique that is widely used to track which parts of the brain are involved in various functions. When you read about areas of the brain "lighting up" when you see a rattlesnake or hear music or think of serving a tennis ball, this is the signal they're talking about.

In reality, it relies on a lot of unglamorous statistical analysis to extract the signal from both the noise and the background activity. This raises a crucial point: though parts of the brain can be "activated" by various stimuli, this does not mean they are normally just sitting there, not doing anything. The brain is always active, even when a person is at rest—or even asleep, for that matter—a bit like a car sitting with its engine running, just idling.

That idling activity can also be detected by fMRI, and one of the things that people have noticed is that different parts of the brain sit there humming along at different frequencies. The fMRI signal shows a slow fluctuation or oscillation in each area, becoming slightly stronger or slightly weaker every 10–20 seconds or so. If you just let a person rest in the MRI scanner for about five minutes, you can track these fluctuations across all the areas of the brain. Then you can do something really interesting—you can see which areas of the brain are fluctuating *in synchrony* with each other.

When a person is engaged in some task, different parts of the brain may be coactivated. These usually reflect brain regions that make up an extended circuit or system involved in whatever that task is. It turns out that those functional relationships are also evident in the temporal correlations of the spontaneous fluctuations at rest. These are thought to reflect a past history of coactivation, meaning that if two areas are

fluctuating in synchrony with each other, they are likely part of an extended functional network. Importantly, while there is a general pattern to the subnetworks that emerge through these kinds of analyses, there are also important individual differences. Repeated imaging of the same people shows that such differences are highly reliable, reflecting stable differences in functional brain architecture, which are also highly predictive of the pattern of activity during various tasks across individuals. Indeed, these networks are so distinctive that they provide a kind of "neural fingerprint" that can be used to reliably identify individuals from brain scans, regardless of what the brain is actually engaged in during imaging.

Moreover, since the degree of temporal correlation gives a quantitative measure of the strength of functional connectivity between any two brain areas, these correlations can be used to derive a brain-wide *functional* connectivity network, just as for structural parameters. Structural and functional connectivity networks generally show very good correspondence, though many areas may be functionally "connected"—that is, talking to each other—even if they do not share a direct structural connection. And, again, multiple parameters of these networks can be measured and compared between people, including pairs of twins. The result, which is unlikely to surprise you at this stage, is that the brain networks of MZ twins are much more similar to each other than are those of DZ twins, such that both local and global parameters of functional connectivity show moderate to high heritability.

The upshot of all this is that the brains of people who are genetically related to each other are wired similarly and work similarly. Presumably this underlies their similarities in psychological traits. Once again, if we flip perspective, we can infer that a substantial proportion—often a majority—of the variance in the population in both brain traits and psychological traits is due to genetic differences. Now, it is important to delve a little deeper into this concept of heritability.

HERITABILITY—WHAT IT MEANS AND WHAT IT DOESN'T MEAN

One of the crucial things to keep in mind about heritability estimates is that they refer to *variance*, not to mean or absolute values of a trait. We use them to understand what makes people different from each other,

or different from the average value in a population—they say nothing about why that average value is what it is. That question comes back to our discussion about species-general traits; what we want to understand here is variation around those mean values, within a species. What drives the mean is still genetic in the sense that it still depends on our genomes—it's just not what we're interested in here. We are all generally human sized because of our human genomes—what heritability estimates are relevant to is the question of what makes some humans taller or shorter than others.

So, if we find that the heritability of a trait is, say, 60%, this does not mean that 60% of the absolute value of that trait in a particular individual comes from his or her genes. It would make no sense to say 60% of my height is genetic, for example. It means that, *across the population*, 60% of the variance (the deviation of individuals from the mean value of the trait) is due to genetic differences. So, if everyone in the population were genetically identical, the variance in the trait would be only 40% of what it actually is.

This brings up another crucial fact about heritability—it is a *proportional* measure. Say we have some trait that can be affected by both genetics and environment. Height is a good example, as there are strong genetic effects on a person's potential final adult height, but whether that height is actually attained can be affected by nutrition. If we measure heritability of height in a population where everyone has ready access to food, it will likely be quite high. Most of the variance in the trait will be due to genetic differences, partly because there are few differences in other factors that matter. But if we measure it in a population where access to food is highly unequal, then we may find the heritability is lower. This doesn't mean the genetic effects have been reduced in an absolute sense—just that their *relative* importance to the overall variation in the trait is lower, because the environmental variance is higher. Because of this, heritability estimates are always local and historical, applying only to the population in which the trait was measured. The number we find in any study is not a biological constant, equivalent to those we find in physics. It doesn't measure what factors *can* affect a trait; it only measures what factors actually *do* affect a trait, in a given population at a given time. The environment can still affect the mean value of a trait, but if it doesn't vary much then it won't contribute to *differences* in the trait.

Because heritability tells us only about sources of variance *within* a population and nothing about why the mean value is what it is, it also tells us nothing about sources of differences in mean values *between* populations. It is quite possible to have a trait that is highly heritable in two populations, but where the difference in the mean value between the populations is caused by nongenetic factors. Body mass index (a measure of weight relative to height) is a good example of this. It is highly heritable when measured within individual populations, but a comparison across countries shows huge disparity in average body mass index and percentage of the population that is overweight or obese. These differences are not genetic in origin; they are environmental or cultural. This issue is especially important when it comes to interpreting the heritability of intelligence and the possible causes of differences in average IQ across populations or over time. We will see in chapter 8 that an exactly analogous situation holds for intelligence as for body mass index.

Finally, it is important to emphasize that heritability is not the same as heredity or inheritance, or at least not always. For animal breeders, heredity is the important aspect—how strongly offspring resemble their parents. But heritability actually measures all genetic influences on a trait, not all of which are actually *inherited*. First, many traits are caused by multiple genetic factors acting together—the particular combinations of genetic factors may be crucial in determining the phenotypic outcome in each individual. Because each of our genomes represents a new combination of those genetic variants, these will be different from either of our parents. Second, we each also have new mutations in our genomes that arose in the generation of the sperm and egg cells from which we were formed. These also contribute to our individual traits but obviously do not contribute to parent-offspring similarity. Down syndrome provides a stark example of this; it is a condition that is rarely inherited from a parent—it most often derives from a new event in the egg or sperm that leads to an extra chromosome 21 being included—but it nevertheless has a completely genetic mechanism in the individual. Both these factors—the influence of new mutations and the importance of unique combinations of genetic variants—make large contributions in twin studies as MZ twins share all new mutations and also the exact same combinations of all genes.

NONGENETIC EFFECTS

I have been emphasizing the heritability of psychological and brain traits in humans, but twin and adoption studies also highlight *nongenetic* contributions to overall variance. These effects are often assumed to be "environmental" in origin, but we will see that that is not necessarily the case. The same comparisons of MZ and DZ twin pairs or biological versus adoptive siblings that are used to calculate heritability can also be used to estimate the variance explained by different family environments.

Consistently, and surprisingly, this turns out to be very low (usually not more than 10%–15%) and is often found to be zero. Generally speaking, adoptive siblings do not resemble each other for psychological traits any more than two strangers in the street. This is despite being raised in the same household, living in the same community, typically attending the same schools, and so forth. And for many traits, MZ twins who are reared apart are almost as similar to each other as those who have been reared together—sharing a family environment does not make them appreciably more similar.

This result has caused some consternation and even disbelief over the years since it was first highlighted by, for example, Judith Rich Harris and Steven Pinker. However, it is actually far less surprising if we consider the *kinds of traits* we are talking about. They are the very ones that, by definition, reflect some stable differences between people, some underlying dispositions that influence patterns of behavior over time. Any parent with more than one child will likely have noticed differences between them that cannot be traced to differences in parenting—in fact, these are an endless topic of conversation between parents. Why is one child studious and attentive while the other has his or her head in the clouds? Why is one cautious while the other is on a first-name basis with staff at the emergency room? Why is one so shy and quiet that you worry he or she will never have any friends while the other would happily stand talking to a post? Children have different temperaments, different talents, and different interests that simply seem to emerge of their own accord and to be largely resistant to any efforts to change them.

Academics love to find things that are counterintuitive—that conflict with our everyday experience and show how wrong we can be about the

CHAPTER 3

THE DIFFERENCES THAT MAKE A DIFFERENCE

When we say that genes influence behavior, what we really mean is that genetic *differences* contribute to *differences* in behavioral traits (which in turn influence patterns of behavior over time). So, what are these genetic "differences"? To answer that, we need to start with a more basic question: What are genes?

You might think there is a simple answer to that question, but there isn't. Defining what a gene is has in fact been a source of enormous confusion both within science and for the general public. The reason is that the term actually refers to two very different things. The original concept, famously devised by Gregor Mendel in the 1850s in studying various traits in peas, was of some physical thing that gets passed on from parent to offspring, and that determines the trait in question. From the patterns of inheritance he inferred that there must be distinct genes for whether peas had smooth or wrinkled shells, whether they were green or yellow, whether the flowers were white or purple, whether the plants were tall or short. He also was able to deduce that each plant inherited two copies of each gene—one from the mother and one from the father. Importantly, Mendel realized that each of these traits was controlled by a discrete inherited unit—different ones for different traits. The term "gene" was introduced later to refer to these units of heredity.

While Mendel knew that these units must have some physical substrate—genes must be a physical thing—he didn't know what they were made of. It was not until the 1940s that scientists figured out that the genetic material was DNA—deoxyribonucleic acid, a major chemical constituent of the chromosomes (literally, colored bodies) that were visible down the microscope in the nucleus of cells.

This fact is so well known now that it's hard to think of a time when it wasn't, but actually DNA was not even a front-runner in the betting for what substance carried the genetic information. It was deemed too simple, as it is composed of only four different chemical subunits, or bases, arranged in a long sequence along each chromosome. The preferred candidate was proteins, also present in chromosomes and throughout cells—these are much more complicated than DNA, as they are composed of 20 different amino acids strung together in long chains, which then fold back on themselves to form complicated three-dimensional shapes. While DNA just kind of sits there, proteins are properly impressive—they do all sorts of things inside cells, acting like tiny molecular machines or robots, carrying out tens of thousands of different functions.

Proteins thus seemed a much likelier candidate than DNA to be the genetic material. But a seminal experiment looking at how one type of bacterium could be transformed from a nonvirulent to a virulent (disease-causing) form clearly showed that it was DNA and not proteins that carried this genetic information. (It turns out the proteins associated with chromosomes are involved in packaging the DNA inside cells and in regulating which genes are expressed, but do not themselves carry the genetic information.) From our vantage point, in the digital age, this now seems unsurprising. The simplicity of DNA that led many to dismiss its information-carrying capacity can now be seen as ideal if the information is carried in the *sequence* of the bases that make it up, just as it is carried in a sequence of 1s and 0s in a computer. Moreover, the fact that it is chemically very inert—it just doesn't do much—is exactly what you want in order to safely and stably encode information over long periods, not just over the lifetime of an organism, but also over many generations spanning millions of years.

In fact, these properties were predicted on theoretical grounds by the physicist Erwin Schrödinger in a famous series of lectures on "What Is Life?" delivered in 1943 at Trinity College Dublin. He realized that what set living things apart from nonliving ones was that living things are organized. Both living and nonliving things are made of the same kinds of stuff—of atoms—it's just that in living things these atoms are organized into molecules and complexes of molecules and cells and organs. Keeping things organized is hard work, as the general trend in the universe is for things to get messier, if left to their own devices. It

requires energy to keep things organized, which all living things must take in, in some form or another, but it also clearly requires information. An organism must contain within it the information for *how* all those molecules and cells should be organized. And it must be able to replicate that information and pass it on to its offspring. Schrödinger realized that what he called an "aperiodic crystal" would be a perfect medium to store such information—that is, the material should be stable, like a crystal, and should contain within its structure a code, written in the nonrandom, nonrepeating sequence of different subunits.

THE STUFF THAT GENES ARE MADE OF

DNA fits that bill perfectly. The most obvious and direct thing encoded in DNA is, a little ironically, proteins. The recipes for all those impressive micromachines whizzing around in our cells are written in our DNA. And this brings us to the second definition of a gene—one derived from molecular biology, rather than the study of heredity. Here, a gene is a stretch of DNA that codes for a specific protein. Each chromosome in the cell is a single continuous molecule of DNA, like a long string, made of a series of the four different chemical subunits joined together. These subunits are called adenine, thymine, cytosine, and guanine, but are usually referred to as the "letters" of the DNA code: A, T, C, and G, respectively. Each of these molecules has a polarity to it—they have two ends where they can be chemically joined with the other bases—actually rather like the way we join letters together to make words.

The chromosome is made of two of these strands of DNA wound around each other in the iconic double helix. The information on each strand is complementary to the other due to the way that the chemical bases interact with each other: an A on one strand will be matched by a T on the other, while a C on one strand will pair with a G on the other. This gives an obvious mechanism for copying DNA—the double helix can be unwound and the two strands pulled apart, with each one then acting as a template for construction of another version of the other one, yielding two copies of the double helical molecule.

If you start at one end of a chromosome and scan along it (on one strand), you will soon come to a bit of the DNA that is special, because

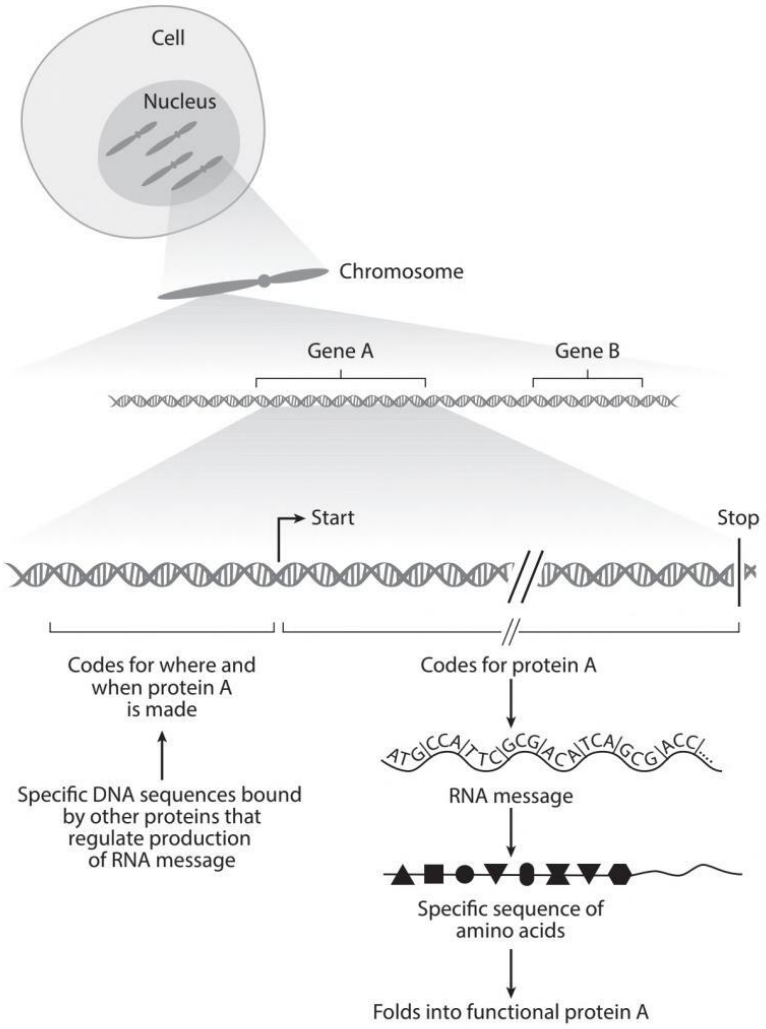

Figure 3.1 The physical structure of genes. Spread out along each chromosome are genes—stretches of DNA that code for proteins. The sequence of DNA bases—A, C, G, and T—codes for a sequence of amino acids in the corresponding protein. DNA sequence in regulatory regions controls protein expression.

the sequence of bases here encodes a protein. That is, the sequence of letters is a code that tells the cell which amino acids to string together, in what order, to make protein A or protein B, and so on. It took a while to work out, but we now know that each successive three-letter stretch of the DNA sequence corresponds to a different amino acid. There are also three-letter codes that tell the cell where the code for a particular protein starts and where it ends. So, if you keep scanning along the DNA, you will also come to the end of the section that codes for whatever that protein is. Figure 3.1 illustrates the structure of a gene.

From a molecular biological point of view—the perspective that aims to understand how cells work rather than how traits are inherited—that stretch of DNA is a "gene." We have about 20,000 different genes spaced out along our 23 chromosomes, which collectively make up the human genome. They code for proteins like collagen, hemoglobin, insulin, metabolic enzymes, antibodies, ion channels, neurotransmitter receptors—all the things that cells need to do their various jobs.

TURNING GENES ON AND OFF

Now, things are about to get more complicated. When I said that a gene encodes a protein, that is true, but the gene itself doesn't make the protein. As I mentioned above, DNA is an incredibly inert molecule—it just stores the information. In order for that information to be acted upon, or expressed, it must be read out by the cell and decoded. The machinery that does that is itself composed of other proteins in the cell. (If you're starting to see a chicken and egg problem, you're right.)

These other proteins include, first of all, an enzyme that makes a direct copy of the stretch of DNA that codes for a protein. This process is called *transcription* because the code is essentially the same, though the physical substrate carrying this copy is not DNA, but its cousin molecule, RNA (ribonucleic acid). This RNA copy, called a message, is then transported out of the nucleus of the cell—the information storage compartment—to the cytoplasm of the cell, which is where proteins are made. The RNA message is, like a tape, gradually passed through a complicated molecular machine called the ribosome (made of proteins and other types of RNA molecules) and at each successive three-letter

the protein, which impairs its function, causing the disease sickle-cell anemia. So, from different perspectives, the gene "for" hemoglobin is also the gene "for" sickle-cell anemia. When we're talking about genes "for" traits or diseases being inherited, we are really talking about inheritance of a version that contains one of those differences in the DNA sequence.

So, where do these differences come from? Simply put, from mutation. Geneticists use the word "mutation" to refer to both the process whereby some change occurs in the DNA sequence and to the resultant change or difference itself. There are many sources of mutation. Thanks to comic books and movies, people often think of mutation as involving some external causative agent, like gamma rays or toxic chemicals. It is certainly true that such factors, or others like ultraviolet light, can indeed induce mutations, which is why they increase the risk of cancer. But it is also true that mutations just happen.

Whenever DNA is copied, when cells are dividing, some mistakes occur. The process is simply not 100% accurate. Our genome has three billion letters of DNA to be replicated—the enzymes that do that job are incredibly faithful but, still, some errors can arise each time a new copy is made. To put that number in context, the famously lengthy novel *War and Peace* has approximately 587,000 words. With an average of five to six letters per word, this amounts to about three million letters. Imagine if you had to copy *War and Peace*, by hand, letter by letter, but multiply the length by a thousand—that is the scale of the job that a dividing cell has to do when replicating its genome. You'd probably forgive yourself a few errors.

Most of the errors in DNA replication involve a simple change to one letter of the DNA code—perhaps an A is inserted in the new copy where a C should have been. Or sometimes a letter is left out or an extra one is inserted. These "point mutations" are fairly simple typos and the cell has proofreading enzymes and DNA repair enzymes that detect and correct many of these errors. But not all of them. A few creep through, just as I am sure some typos will creep through in this book. Figure 3.2 shows some of the different types of mutation that can occur.

There are also more drastic mutations that involve deletions or duplications of larger segments of DNA, affecting not just a single letter, but whole sections of chromosomes. These are more like missing or