The Conflicted Brain

BY JON WILKINS

When I played third base in Little League, ground balls used to come at me fast. Invariably, once a year, one would hit me in the eye, or nose, or mouth. In those cases, I would be positioned in front of the ball, but then, at the last moment, I'd flinch and look away. The ball would then bounce up and hit me in the face.

The problem was that different parts of my body were trying to achieve two different goals. My legs placed my body in front of the bouncing ball—with the goal of catching it. My face, on the other hand, was trying to get out of the way. If my entire body had committed to getting away from the ball, I could simply have moved aside and let the ball through. Better yet, if my entire body had committed to catching the ball, I would have kept watching it, and would have had my glove in the right position to catch it; keeping my eye on the ball metaphorically would have saved me from doing it literally.

Most people recognize this type of conflict: the feeling of being pulled internally in two directions. It's the tiny angel and tiny devil sitting on our shoulders, urging us to take disparate actions—we want to lose weight, but we also want to eat that donut. Recent research suggests that this sensation may have a basis in real mechanistic and evolutionary conflicts within our brains.

Brain-imaging studies suggest that different brain regions come into conflict with each other over certain decisions. At the same time, many genes that are expressed in the brain show evidence of having been in a long-term evolutionary conflict with each other. It is possible that when we feel as if we are of two minds, it is precisely because different sets of our own genes have effective control over different regions of our brains, and these different brain regions are exerting antagonistic influences on the decision-making process.

The idea of conflict in the mind is old. What is new is that we are beginning to understand some of the mechanisms through which these conflicts play. This new understanding undermines our preconceptions about human intelligence and our notions of the "self." In fact, it may turn out to be misleading to talk about the notion of individuals having a single "self" at all.

BATTLE OF THE NEURONS

On the basis of recent neuroeconomic experiments, researchers have suggested that difficult decisions might be made by a type of "voting" process within the brain. Typically, an experimen-

tal subject performs some behavioral task while his or her neural activity is monitored. This type of procedure has been used for decades to identify regions of the brain that are particularly active during specific cognitive or behavioral tasks.

One recent set of studies focuses on decision-making in difficult moral dilemmas. Subjects face a hypothetical situation: a train is rushing toward five people who are tied to the track. The only way to save those five people is to kill a different person (for example, by throwing him or her in front of the train). On the one hand, people sense that five lives are more valuable than one. On the other hand, there is something morally and emotionally distressing about the idea of actively participating in the death of the one person.

In the study, the subjects show increased activity in a region of the brain called the anterior cingulate cortex, associated with conflict resolution. Subjects also show increased neural activity in other regions. Some of these regions (such as the medial frontal gyrus and the posterior cingulate gyrus) are associated with the emotional response to the situation. Other regions (including the parietal lobe) are associated with higher cognitive functions—the "reasoning" part of the brain. Interestingly, the subjects who say that they would sacrifice the one to save the five show relatively higher levels of activity in this "rational" part of the brain. The subjects who would refuse to act show relatively more activity in the more "emotional" regions of the brain.

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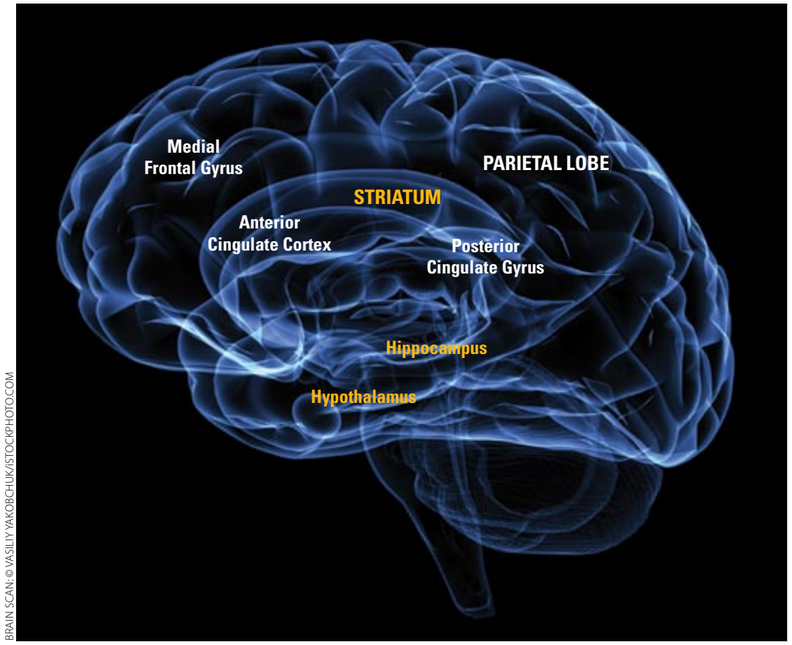
We are a long way from a complete understanding of this type of decision process. However, one possible interpretation is that the situation elicits two conflicting responses, and that these two responses are localized in distinct sites within the brain. It is as if one set of neural circuits is screaming out, "You must act! The lives of the five people on the track outweigh a single life!" while another set of circuits screams, "It is wrong to kill this man! The ends do not justify the means!" The decision that is ultimately made depends on which of the two sets of circuits screams louder.

WHY CAN'T WE ALL JUST GET ALONG?

Why might decision-making in the brain be structured like this? Is decision-making through competition adaptive, or is it a maladaptive byproduct of an evolutionary process? Most evolutionary explanations fall into one of two categories. These explanations assume (often implicitly) either (1) that this conflict is an adaptation, or (2) that it is a historical artifact. While there may well be some truth to either or both of these assumptions, both are rooted in a naïve understanding of natural selection that fails to capture the nuances of the evolutionary process. After briefly explaining these two simple classes of explanation, I will introduce a third possible explanation, one based on recent advances in molecular biology and evolutionary genetics: that this apparent neural conflict reflects a genuine evolutionary genetic conflict.

The first class of explanation assumes that competition is a powerful and robust way to make choices in a noisy and complicated world. Imagine that you face two choices, A and B. The brain receives a constant stream of information from the environment, most of which is irrelevant to the decision at hand. It must collect and evaluate the relevant information and follow the better of the two choices. One possible solution is to establish one apparatus that filters this stream and gathers all the evidence favoring choice A. A second apparatus would be dedicated to collecting evidence favoring B. Each would then produce a signal proportional to the weight of this evidence. If the signal favoring choice A outweighs that favoring B, choice A is followed, and vice versa.

This is like the principle upon which the Anglo-American criminal justice system is based. In principle, the goal is to reliably determine guilt or innocence on the basis of available evidence. The mechanism by which we attempt to reach an unbiased verdict, however, is an antagonistic interaction between biased advocates. One party is charged with gathering and presenting all of the evidence that the defendant is guilty. Another party collects the evidence that would exonerate the defendant. A third entity—the judge and/or jury—assesses which of the two has presented a more compelling case and rules accordingly.



BRAIN SCAN: © VASILIY YAKOBCHUK/ISTOCKPHOTO.COM

White text indicates locations of brain regions mentioned in the neuroeconomics studies. Orange text locates the human structures corresponding to the mouse brain regions mentioned in the genetic chimera experiments.

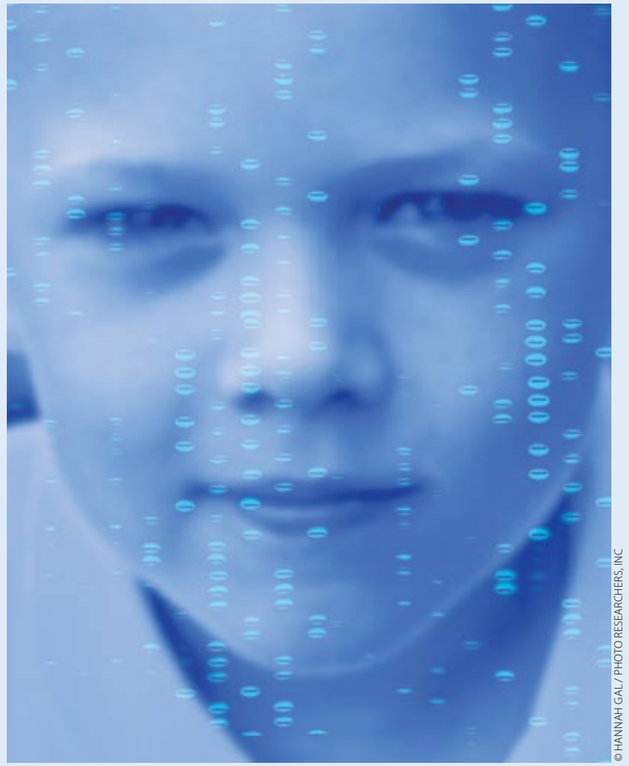
The second common explanation is that this conflict is an artifact of the evolutionary history of our brains. Our brains evolved through modification of an earlier primate brain, which was derived from an earlier mammalian brain, and so on. The human brain is necessarily descended from a long line of brains, each of which had to function well enough in its own environment to allow its bearer to survive and reproduce. Thus we have inherited a neural architecture that evolved in a very different context. It may simply be that when a complex organ is constructed in this way, by layering new functions on old, certain conflicts and incompatibilities will inevitably arise.

This second class is being invoked when researchers talk about conflicts between the "reptilian" and "mammalian" or the "emotional" and "cognitive" parts of the brain. In this scenario, our ancestors had a brain with certain heuristic rules that it used to navigate the world. Our modern brains contain regions that are homologous to those ancestral brains. We also have other regions that have evolved more recently, regions with their own set of heuristic rules. Sometimes, the old and new rules contradict each other. In this case, the conflict is not conceived as adaptive, but rather as an unfortunate limitation resulting from the historical path followed by evolution.

Now I'll suggest a third possible class of explanation—that the conflict is in some sense real. What I mean is that the conflict represents the direct outcome of natural selection, but that natural selection is acting differently on different parts of the brain. The apparent conflicts between regions of the brain are a manifestation of an underlying genetic conflict.

IMPRINTED GENES

We now understand that a conflict exists between the maternally and paternally inherited sets of genes within each of us. About one percent of genes in mammals (including humans) are subject to *genomic imprinting*. In the case of these imprinted genes, the gene copy, or *allele*, that came from your father functions differently from the allele that came from your mother, even if the



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This DNA autoradiogram superimposed over a child's face shows a pattern of bands produced during DNA analysis. It may represent genetic individuality, paternity testing, or biometric identification.

two alleles have identical DNA sequences. These functional differences are the result of *epigenetic* (meaning "on top of the genes") modifications to the DNA that are established in the germ line, and propagated through developments.

During *spermatogenesis* (the production of sperm), imprinted genes are marked with particular chemical modifications. During *oogenesis* (the production of eggs), these same genes are marked with different modifications. The offspring therefore inherits two functionally different alleles. When this individual grows into adulthood and has offspring of its own, these marks will be erased and reset on the alleles that it passes on to the next generation.

Why would a complicated mechanism like this exist? The most prominent explanation suggests that genomic imprinting is the outcome of an evolutionary conflict between these maternally and paternally derived alleles. The key to this conflict is the fact that natural selection acts to maximize the number of allele copies that are passed on to future generations. These copies can be passed on directly through the survival and reproduction of the individual organism carrying those genes, or through the reproductive success of related individuals who carry an identical copy of the allele. Since the maternally and paternally derived alleles are related to different individuals (e.g., cousins on your mother's side versus those on your father's), the strategy that maximizes the number of copies passed down differs between the two alleles.

PARENTAL CONFLICTS IN THE BRAIN

Our understanding of imprinted genes in the brain is still in its infancy. However, observations involving *genetic chimeras* (made up of two sets of cells with different genomes) suggest that our maternally and paternally derived genes are in conflict over how large particular brain regions should be.

Normal mammalian development requires the presence of both maternally and paternally derived complements of alleles. In mice, it is possible to make *gynogenetic* embryos (which contain two maternally derived sets of genes) or *androgenetic* embryos (which contain two paternally derived sets of genes) by removing the nucleus (containing the DNA) from one cell and injecting it into another. These uniparental embryos fail to develop beyond the first few rounds of cell division, since they have inherited two inactive copies of many imprinted genes (and are receiving double the normal dose from the rest).

However, it is possible to combine these cells with cells from a normal, biparental embryo. These mixed, or chimeric, embryos develop relatively normally. The inclusion of gynogenetic and androgenetic cells appear to have complementary effects on the development of the brain. When a chimera contains gynogenetic cells, those cells are overrepresented in particular brain regions, including the striatum, the hippocampus, and the neocortex. These regions (evidently favored by maternally inherited alleles) are involved in many higher cognitive functions, such as planning and problem solving.

In the other type of chimera, the androgenetic cells are overrepresented in different regions, including the mediobasal forebrain and the hypothalamus. The regions favored by these paternally inherited alleles participate in behaviors such as food seeking, mating, social aggression, and the expression of emotions.

Another set of observations concerns a genetic disorder called Turner syndrome. Girls with Turner syndrome inherit only one copy of the X chromosome (as opposed to the normal two). These girls suffer from a variety of problems, and generally perform less well than chromosomally normal individuals on various cognitive tasks. Relevant here is that there are significant differences in the extent to which different cognitive skills are impaired, depending on the parental origin of the single X chromosome. If the X chromosome is paternally, rather than maternally, inherited, the girls exhibited better verbal ability, social cognition, and behavioral inhibition.

These are only two of the experiments that suggest that imprinted genes affect the development of different brain regions, and the development of different sets of skills. Other experiments suggest conflicts over how much care to provide for offspring and how to value risk. If the neuroeconomists are right, some of our decisions may be determined by comparing the relative intensity of activity in two or more regions of the brain. Imprinted genes might effectively tip the scales to favor one type of decision over another by influencing the relative size of these different brain regions.

WHAT DOES IT ALL MEAN?

Based on the type of effects we see in other systems affected by genomic imprinting, we can speculate about how this conflict might have affected our brains.

First, we expect to find an escalatory "arms race" between different brain regions. If maternally derived genes are expanding one region to bias decisions in a particular way, paternally derived genes will counter by augmenting regions with the opposite effect. Eventually, we might expect this to produce an increase in overall brain size. In fact, this may have happened: over the past hundred million years, the size of the mammalian brain has increased disproportionately relative to body size.

We also expect this conflict to increase fragility. Different sets of genes are pulling hard in opposite directions; a mutation in any one of these genes can result in a dramatic shift in the system. Imprinted genes have been linked to many human behavioral dysfunctions, including schizophrenia, ADHD, autism, and bipolar disorder. These disorders may be much more severe and/or more common than they would be in the absence of genomic imprinting.

It is perhaps time to stop thinking of the human brain as evolution's crowning achievement and the physical embodiment of the "self." Rather, our brains are casualties of millions of years of internal conflict.

As humans, we routinely engage in a wide variety of self-destructive behaviors. We cheat on our diets. We don't exercise. We smoke and gamble and get addicted to a wide range of substances. It is perhaps time to stop thinking of the human brain as evolution's crowning achievement and the physical embodiment of the "self." Rather, our brains are casualties of millions of years of internal conflict. Every decision we make is argued out by at least two distinct evolutionary "selves." We may eventually discover that multiple personality disorder is simply the most extreme manifestation of a dynamic that governs even the most mundane behaviors in each of us. ◀

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