

# ON THE BRAIN

THE HARVARD MAHONEY NEUROSCIENCE INSTITUTE LETTER

## The Criminal Mind

**A**RE THE BRAINS of people who commit crimes different from the brains of people who don't? While the latest brain research indicates they are, Harvard Medical School specialists and others who study the criminal brain say the answer may not be that clear cut.

What neuroscience may one day tell us about the criminal mind is an enormous question, says Judith G. Edersheim, MD, JD, an assistant clinical professor of psychiatry at HMS and co-director of the Center for Law, Brain and Behavior at Massachusetts General Hospital. On one hand, cognitive neuroscience and neuroimaging are defining a link between brain abnormalities and certain criminal behavior. On the other, scientists are still not certain just what those abnormalities are.

"Some neuroscientists and psychiatrists are even challenging the idea that behavior is a product of free will—that you can decide to be a criminal or

not," says Edersheim, a forensic psychiatrist. "But, in our view, the jury's still out on that question."

### The go/no go paradigm

Scientists are using positron emission tomography and functional MRI, two neuroimaging tools, to study whether the brains of criminals are anatomically or functionally different from those of the rest of the population. The theory behind such research, says Edersheim, is that there may be an imbalance between the parts of the brain that mediate impulses and those that manage impulses. Essentially, these scientists are trying to determine if there is too much "go" and not enough "no go" in the brains of the criminals.

In most people, the drive to act impulsively is inhibited by the prefrontal cortex. This cortical region is responsible for what Edersheim calls pro-social behavior—self-control, concern for others, and empathy. "What we're studying with functional imaging," she says, "is whether that behavioral guidance system is out of whack in criminals."

Clinical substance abuse, particularly alcohol abuse, and other injuries to the prefrontal cortex can cause disinhibition of the no-go paradigm, while other illnesses as well as illicit drug use can hijack the go system and make it hard to curtail a particular behavior. In addition, a number of neurological syndromes affect our ability to initiate and stop actions, monitor and change our behavior, and understand the outcomes and consequences of our actions. Among these syndromes, found especially among convicted criminals, is antisocial personality disorder, also called psychopathy or sociopathy, in which a person cannot discern, or show regard for, right from wrong, and may behave violently.

Neuroscientists are unsure what drives people to behave in an antisocial manner, but a recent British study provides some clues. Two years ago,

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neuroscientists at King's College in London used diffusion tensor MRI to study two areas of the brain responsible for self-control and aggression. Among psychopaths, these brain areas appeared to be abnormal. The scientists' study determined that in psychopaths, a tract of white matter in the region that connects the amygdala, which directs our emotional responses, with the orbitofrontal cortex, which governs our decision-making capacity, was out of kilter. The researchers also found that people with more extreme forms of psychopathy showed even greater degrees of this abnormality. The findings suggest a possible biological explanation for the antisocial behavior of criminals.

"These people don't have the necessary filter to measure their impulses, analyze situations, and count to ten, as our mothers used to tell us to do, so they commit criminal acts that have consequences,"

*"The scientists' study determined that in psychopaths, a tract of white matter in the region that connects the amygdala, which directs our emotional responses, with the orbitofrontal cortex, which governs our decision-making capacity, was out of kilter."*

says Bruce Price, MD, an HMS associate professor of neurology, chief of neurology at McLean Hospital, and co-director of MGH's Center for Law, Brain and Behavior.

Other studies show that people with antisocial personality disorder have atrophy in regions of the cortex that control executive functions and in the amygdala. This loss of capacity may contribute to behaviors marked by a lack of remorse and self-control.

### **The moral dilemma**

While science can tell us about the function of the criminal brain, it can't, or can't easily, tell us whether criminals know right from wrong.

So much of the criminal act is contextual, says Price, that people who wouldn't otherwise act in a certain way do so when exposed to a particular level of intensity. "In some ways," he adds, "short of a diagnosis of psychopathy, it's hard to say

whether a criminal knows right from wrong at the time he or she commits a crime." One study discovered that the amygdala is not active in psychopaths who are thinking of moral dilemmas but is active in non-psychopaths pondering such dilemmas. These findings suggest that criminals have little capacity to feel remorse for their crimes or to discern the appropriateness of their actions.

"Criminals come in all flavors," says Edersheim. "Some are motive driven and know right from wrong, but still they choose to be antisocial. Others are impulsive and aggressive. So, different kinds of people commit different kinds of offenses."

As an example, consider the construction worker who cashes his paycheck, goes to a bar on Friday night, drinks five whiskeys, and gets into a fight. That sequence of actions—and the impetus behind them—is very different from someone who plans a bank robbery, wears a mask, and executes a well-orchestrated getaway.

### **The root of the matter**

Now that neuroscientists can see the working brain with functional imaging tools, they are trying to determine if the brains of criminals are less able to control impulses and to know right from wrong.

One downfall of expanding the use of functional imaging as evidence in the criminal justice system is that such imaging results are already working their way into courtrooms, Price says, where self-described experts are using them to absolve criminals of their responsibility for committing a crime.

Price and Edersheim in fact oversee a project at their MGH center that is focusing on neuroimaging, neurophysiology, and neuropsychology and their correlation with criminal responsibility. They are weighing whether data from these scientific disciplines should be used as evidence of whether a defendant is responsible for his or her actions against the knowledge that this still unreliable information could be overvalued and misunderstood by judges and juries. The project aims to develop scientific guidelines for the rational translation of neuroscience into law.

The answers to the many questions being raised, say Edersheim and Price, will not only change what we know about the criminal brain, but they may also revolutionize this nation's legal system. ♥

## Parents, Genes, Behavior, and the Brain

**M**OTHERS AND FATHERS often hope they will profoundly influence the behavior of their children. Recent genetics research at Harvard University and Harvard Medical School gives those hopes some substance. Scientists have found that the genes of both mother and father exert influence, but that they may do so in developmental shifts, with maternal genes playing a leading role in early development and paternal genes stepping on stage later, during adulthood.

The findings, published in 2010 in *Science*, suggest that a process called genomic imprinting, in which certain genes are expressed with a parent-of-origin specificity, can dramatically influence brain development and behavior. This type of gene expression may also contribute to a variety of brain disorders.

"It's not clear why genomic imprinting takes place or what the function of it is," says Christopher Gregg, PhD, a former HMS research fellow in genetics who co-authored the *Science* paper. "We do know that it's heritable and causes different patterns of expression depending on whether the gene comes from the mother or the father."

### Shifting biases

Nearly 20,000 genes are active in the brains of humans and other mammals. For the most part, these genes come as two-part units—one part from

mom and one part from dad—that function as one. Some genes, however, don't work like this. Instead, one part dominates. This parental bias is called genomic imprinting.

In their study, Gregg and Catherine Dulac, the Higgins Professor of Molecular and Cellular Biology at Harvard University, identified some 300 active genes in the brains of 15-day-old mice and in adult mice that exhibited some level of parental bias.

*"Scientists have found that the genes of both mother and father exert influence, but that they may do so in developmental shifts, with maternal genes playing a leading role in early development and paternal genes stepping on stage later, during adulthood."*

Although previous studies had indicated that fewer than 100 imprinted genes existed, 45 of them in the brain, Gregg and Dulac found that nearly a quarter of the neural regions that govern such behaviors as feeding, mating, pain sensation, and motivation are loaded with imprinted genes.

The two researchers found that more than 60 percent of the imprinted genes in the brains of young mice originated with the mother, suggesting

*This article is part of a series on the internal and external forces that affect the brain.*

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a strong maternal influence on brain development. To their surprise, however, the ratio flipped in adulthood, with nearly 70 percent of imprinted genes coming from the father.

"It's still unclear why maternal bias shifts to paternal bias," says Gregg, now an assistant professor of neurobiology and anatomy at the University of Utah. "Maybe it's the influence of changes during puberty or perhaps it's because genes that are active during development turn off in the adult brain. There are a lot of questions, but not yet many answers."

### **Parental control**

The process of genomic imprinting was first described in 1984, when two research groups discovered that a marker, or imprint, differentiates between certain genes on the maternal and paternal chromosomes and results in the expression of only one of the genes in offspring. Much of our knowledge about genomic imprinting rests on the

*"When we inherit a mutated copy of the imprinted gene from one of our parents—imprinting occasionally turns off the "good" gene in the pair—problems can occur, including a variety of neurologic disorders."*

kinship theory developed by David Haig, the George Putnam Professor of Organismic and Evolutionary Biology at Harvard, who participated in the Gregg and Dulac study. Haig's theory suggests that there is an evolutionary conflict between mammalian mothers and fathers over the expression of certain physiological and behavioral traits in their offspring. In early developmental stages, genes from the mother wrest control from genes from the father, primarily when it comes to the use of maternal resources.

"Mammals are unique," says Gregg, "because their offspring place so much demand on maternal resources, such as the placenta and mother's milk. Fathers, on the other hand, compete with each other and can mate with many females. Thus, the father invests in the litter, but the mother is saddled with providing life-sustaining resources."

In the mid-1990s, scientists at the Whitehead Institute for Biomedical Research at the

Massachusetts Institute of Technology discovered that genetic imprinting is associated with specific chemical changes in DNA, suggesting an important role for DNA in the regulation of gene expression during development.

### **Reversing the curse**

Like mice, all humans have imprinted genes, and all of them are active. For the most part, these genes have few adverse effects. Yet when we inherit a mutated copy of the imprinted gene from one of our parents—imprinting occasionally turns off the "good" gene in the pair—problems can occur, including a variety of neurologic disorders.

The two most common genetic disorders caused by the expression of mutated imprinted genes are the Angelman and Prader-Willi syndromes. Angelman contributes to autism-like disorders while Prader-Willi is linked to psychosis, mild-to-moderate mental impairment, and learning disabilities. Prader-Willi provides a useful example for understanding how genetic imprinting can contribute to the development of a neurologic disorder. In this syndrome, a large number of genes are deleted on a particular chromosome. When this deletion is inherited from the father, there is a maternal bias in gene expression. An infant born with this bias shows a failure to thrive and an aversion to nursing or eating. All this changes, however, around age two when the child's appetite becomes insatiable. Many children with Prader-Willi are so compelled to eat that they forage or steal food. This consumption behavior leads to obesity, which persists into adulthood.

Certain neurologic disorders, including multiple sclerosis, epilepsy, Huntington's disease, and schizophrenia, each of which affects one sex more than the other, have been linked to imprinted genes, although the molecular evidence for such a link has not been found.

Because the study of the relationship between genetic imprinting and disease is such a young field, Gregg says scientists are not yet certain if the process of imprinting can be reversed to stop disease. Evidence suggests that diet may modulate imprinting, he says, "so we may be able to develop drugs to stop the process or alter the diet to do so." Still, he adds, the evidence is not particularly strong as to whether genomic imprinting is hardwired in the brain or whether it can be silenced through drugs, genetic engineering, or other means. ♥

## A Whiff of the Past

**M**OST OF US have experienced it at some point in our lives: A memory flashes bright, sparked by a particular odor—freshly cut grass, a baking pie, or, perhaps, a certain perfume. The connection often is emotionally strong. But why? What ties a smell so firmly to a memory?

Odor and memory are inextricably linked for several reasons, says Sandeep Robert Datta, MD, PhD, an assistant professor of neurobiology at Harvard Medical School. Datta, who studies olfaction (the sense of smell) in mammals and the relationship between odors and instinctual behavior, says one reason for this link may be the close physical proximity in the brain of the region that processes odors from the outside world and the regions responsible for memory formation. They are near neural neighbors.

“Visual information that travels to the parts of the brain involved in memory or emotion must go through a lot of connections,” Datta says. “For smell, the number of connections is small—perhaps as few as two—so there’s very little processing needed.”

“Smell was the first sense to evolve,” he adds. “The brains of non-human animals are basically machines designed to process smell. For millions of years, animals have used this sense to determine food, friends, and what they should fear.” The behavioral reactions that animals have to odors from their predators—fear, avoidance, and stress—are in fact primitive forms of human emotions, Datta notes.

Much of what we know about the human sense of smell comes from the work of former HMS neurobiologist Linda Buck, who is now at the Fred Hutchinson Cancer Research Center in Seattle. The identification of olfactory receptors, for which she shared the 2004 Nobel Prize in Physiology or Medicine with Richard Axel at Columbia University, provided important insights into the underlying mechanisms of our sense of smell.

### The nose knows

The process for detecting a smell begins when our nostrils capture airborne molecules of vaporized odors and those molecules dissolve in the mucus at the roof of each nostril. Beneath this mucus lies the olfactory epithelium, a tissue layer studded with olfactory receptor neurons that are ready to capture the thousands of different chemical signatures defined in the dissolved molecules.

The receptor neurons transmit odor information along the olfactory nerve to the olfactory bulb

located at the base of the brain. Inside the olfactory bulb are nerve cells that send odor messages forward along two routes: to the brain’s limbic system and to its cortex. Odor messages to the limbic region largely target the amygdala, which is involved in the formation of memories of emotional experiences, while messages to the cortex involve the entorhinal cortex, which plays an important role in autobiographical and episodic memory, and the piriform cortex, a key player in identifying odors and mediating complex emotional behavior.

Certain odors trigger stronger neurologic—and behavioral—responses in the brain than others. A sour smell from milk, for example, signals that it’s unsafe for drinking, while an astringent musk warns that a skunk lurks nearby.



### Emotional bind

The rush of memories that smell can elicit is called “Proustian memory,” after the twentieth century French novelist Marcel Proust, who famously described the phenomenon in the opening of his novel, *Swann’s Way*.

Although the brain’s dorsolateral prefrontal cortex stores most memories, we retrieve memories using the right prefrontal cortex, a region located near the olfactory processing center. These two right-hemisphere centers are proximal to the

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## Sight Unseen

THE SCIENTISTS WERE astonished by what they were witnessing. A blind man, unaided by cane or companion, was making his way down a hallway strewn with furniture and was effortlessly maneuvering his way around each obstacle.

This dramatic demonstration of “blindsight” took place during an experiment conducted by an international team of neuroscientists that included Beatrice de Gelder, PhD, an instructor in radiology at Harvard Medical School and a cognitive neuroscientist at Tilburg University in the Netherlands.

*“Blindsight results from sensory messages that move directly from the retina to a subcortical region of the brain, rather than traveling through the primary visual cortex.”*

Blindsight, which is the capacity to sense movement, location of objects, and even emotions on other people’s faces in the absence of the more usual neural pathways, results from sensory messages that move directly from the retina to a subcortical region of the brain, rather than traveling through the primary visual cortex. Relying on a so-called subconscious visual pathway, blindsight is thought to kick in when the visual cortex or other key areas of the brain involved in vision are

damaged, but the eyes and the optic nerve remain intact and are still capable of gathering and sending sensory information to unaffected parts of the visual system.

Previous research has reported this curious phenomenon in people with damage to one of the brain’s two visual areas—there is a visual processing area in each of the brain’s hemispheres. The damage left them blind on only one side of their visual field. But de Gelder’s study is the first to show blindsight in a person whose bilateral centers for visual processing had been completely destroyed, in this case by a stroke.

“Our findings are significant,” she says, “for they tell us that this visually based behavior has to be implemented by some other visual structure.”

### Subconscious sight

In humans, visual processing usually follows what is considered to be a conscious pathway that takes information gathered by cells in the retina and sends it to the primary visual cortex. But in addition to sending information to the visual cortex, the retina also projects information into subcortical regions of the brain that include the superior colliculus, which processes eye movements and performs other vision-related functions. De Gelder and colleagues, testing whether blindsight works because it exploits the information from this secondary pathway, have shown that the superior colliculus is indeed essential for translating visual signals that cannot be consciously perceived.



In 2010, de Gelder described these findings in *Scientific American*, writing that "...the superior colliculus acts in the human brain as an interface between sensory processing (sight) and motor processing (leading to the patient's action), thereby contributing to visually guided behavior in a way that is apparently separate from pathways involving the cortex and entirely outside conscious visual experience."

Using blindsight, a person can identify simple shapes, the orientation of lines, movement, and color. The phenomenon is strongest when visual details are about the size of a quarter and are viewed at distances of 5 to 15 feet.

Researchers have also found that people with emotional blindsight can recognize facial expressions and other gestures or non-verbal signals in those they encounter. Using advanced imaging techniques such as diffusion tensor imaging, researchers have traced the neural pathways of the visual signals that produce this type of blindsight

and have identified small collections of neurons that connect the superior colliculus to the amygdala, the brain's emotional headquarters.

De Gelder and others have found that people with what is called emotional blindsight can reliably determine facial expressions, such as a smile or a frown, but that they can't identify such characteristics as identity or gender. Their findings suggest that the subcortical regions of the visual system can recognize not only objects but social signals as well.

De Gelder says her research may one day help blind people and those with certain brain injuries become more independent, and she adds that training may also help people who have lost their sight because of an injury or illness that has damaged the vision-processing regions of the cortex. Learning to use this secondary system may provide these people with the skills they need to tap their subconscious visual pathways—and to better see their world. ♥

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### *A Whiff of the Past*

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amygdala-hippocampal complex. If location does influence association, the nearness of the centers for odor processing, memory storage, and memory recall may help explain the strong link between a smell and a memory.

Several studies have shown that our most vivid autobiographical memories tend to be of emotional events. Unlike more neutral memories, autobiographical memories tend to be recalled frequently and with great clarity and detail. This sort of memory retention has been preserved through human evolution, helping us link smells to situations that could threaten our survival. Over time, protective patterns of behavior were reinforced through life-and-death situations, eventually becoming genetically embedded in the amygdala. The well-known fight-or-flight response is the result of eons of learning how best to survive.

Datta says it's almost certain that humans and other animals can form deeply embedded memories from just about any smell. Researchers studying the fruit fly, for example, are unable to alter its innate repulsion for carbon dioxide, he

says, regardless of the rewards they provide the flies. Such a finding suggests that you can't "learn" to change your behavioral response to particular smells. "That said," adds Datta, "there are many innately aversive odors, including predatory odors, that you can train an animal to consider attractive."

### **Context is key**

The strength of an odor-linked memory quite possibly depends more on the context than the smell itself, says Datta. "Certain smells evoke your grandmother's kitchen," he says, "because your grandmother's kitchen is such a strong contextual cue."

It's a good thing that context plays a role or we would be deluged with smell-triggered memories. The ambient air is chock full of small odor molecules, but because the context in which we identify and process these odors is often unimportant, we don't notice these smells acutely—and we don't remember them. We instead link smells with experiences that count, and, in savoring those memories, survive. ♥

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