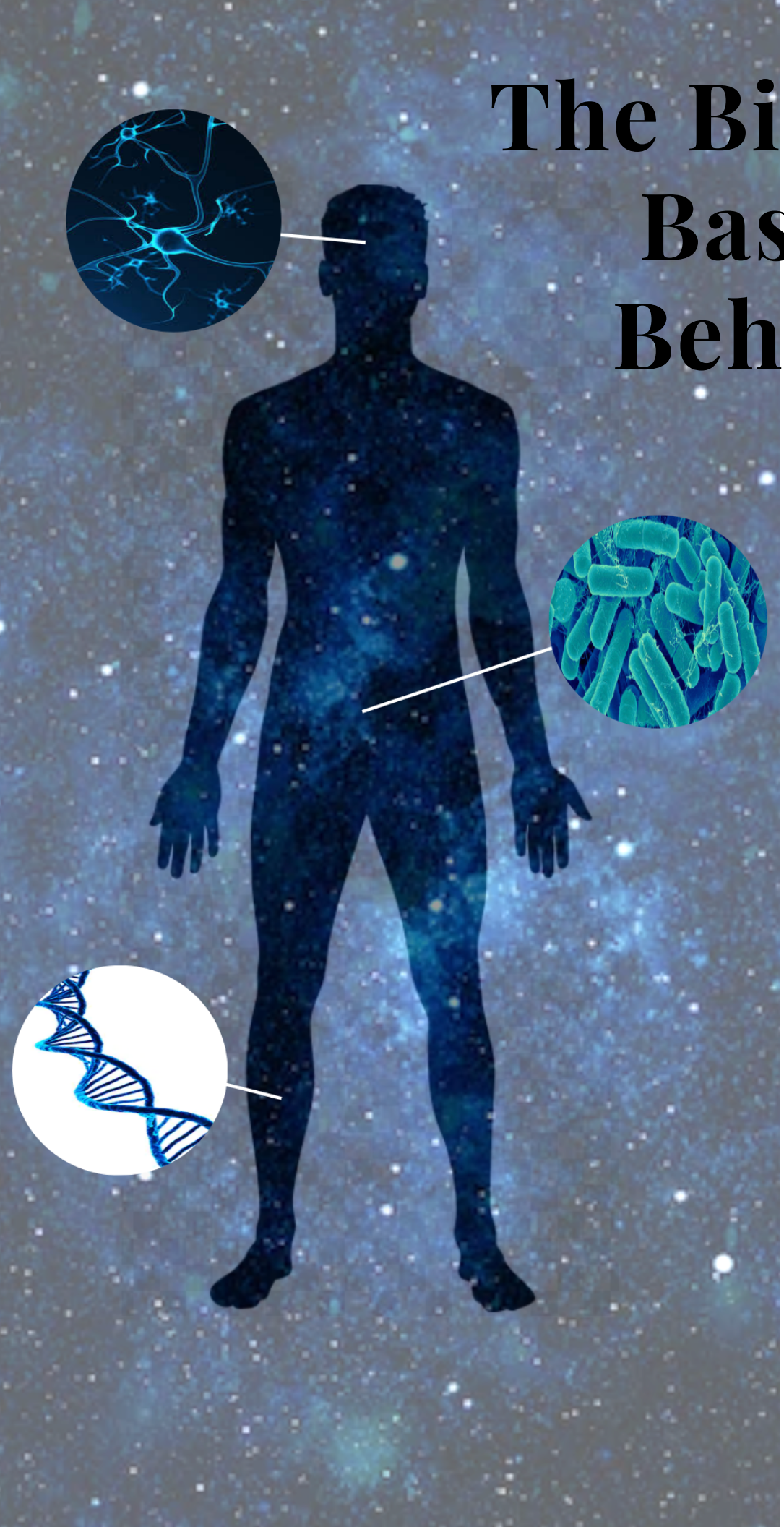


The Biological Basis of Behavior

How much do you know about what shapes your behavior? It may not be as straightforward as you think...

I stood in the kitchen trying to imagine apple pie. A rich buttery crust filled with soft warm apples, slightly sweet and spiced with cinnamon and cloves. Anything to make my mouth water. You don't realize how difficult it is to make your body produce saliva until you're trying to fill a not-so-small tube with spit. My mother and I had gotten our 23andMe kits soon after my grandmother started having memory issues. We wanted to see if we had the same mutations in the APOE gene that increase your likelihood of getting late-onset Alzheimers. 23andMe is a biotechnology and genomics company that offers information about ancestry and health traits based on genetic analysis.

When we got our results back less than a month after sending in our kits, neither of us had any variants that would put us at higher risk for late-onset Alzheimers. But that's not all they told us. From my genetic profile, they predicted that I am more likely than the average person to be bitten by mosquitoes, prefer salty snacks to sweet ones, have a second toe longer than the rest of them, and probably wake up around 8:37 am. Apart from the fact that my alarm wakes me up about an hour earlier than predicted, they got almost everything else right.

Thanks to an improvement in genetic sequencing technology, researchers have found more and more traits with a strong basis in biology. Beliefs and characteristics that were once thought to arise as a result of the environmental factors, such as depression, religiosity, and likelihood to help others, have all been found to be related to the various genes and microorganisms often overlooked in our bodies. Now that's not to say that you can blame your unhelpful DNA when your housemates ask you to clean the kitchen; unfortunately, laziness wasn't one of the traits 23andMe linked to our genes.

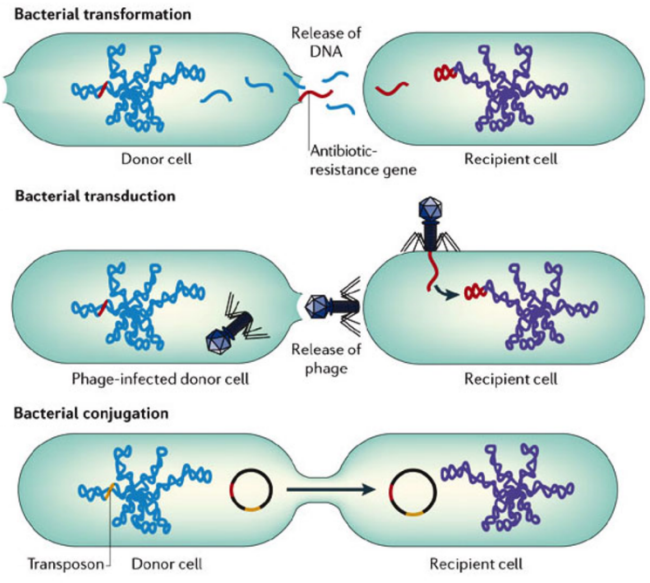
Obliging Organisms

When you finally decide to clean the kitchen, you may think you're the most helpful household member in the world, and you might be. But it could also be the thousands of microorganisms in your gut prompting you to help out for the greater good. Computer models developed by researchers at Tel Aviv University have shown that microbes that promote altruism, a behavior that hurts the giver but helps the receiver, outcompete microbes that do not produce that type of behavior. This seems counterintuitive. From an evolutionary standpoint, and all moral righteousness aside, why would anyone help anyone if they didn't get something in return? Using complicated mathematics to mimic the cost/benefit behaviors individuals do every day, researchers discovered that when a host organism helps another organism, they pass some of their microbes on to the organism they helped. This is a beneficial outcome for the microbes, which now have new hosts to colonize. Therefore, behavior that seems altruistic at the level of host organisms may not be so altruistic for the microorganisms driving the behavior.

In case computer models don't convincingly mimic the behavior of actual organisms, scientists at the French National Institute of Health and Medical Research studied living bacteria and observed similar results. Unlike humans, who do not mix DNA except during reproduction, bacteria can share genes through small circular bits of DNA called plasmids. These plasmids move from one bacterium to the next through a process called horizontal gene transfer. Whatever benefits might be gotten from the expression of the genes on a certain plasmid are quickly passed to an entire population of bacteria. Researchers first identified genes that contributed to the common good, or increased survival, since morality has yet to be observed in bacteria. Genome analysis of *Escherichia* bacteria, such as E. coli, showed that genes that are thought to be involved in social interaction and genes that encode antibiotic resistance are both more likely to be found on plasmids than on their chromosomal DNA. By tracing the movement of these plasmids, researchers found that bacterial populations favor cooperation.

Similarly, a group of Canadian researchers found that if they treat mice with antibiotics when they were young, the mice grew up to be more aggressive and display less socially cooperative behavior. Antibiotics are essential to kill bad bacteria in the case of infection or disease but are not discriminatory; they kill all types of bacteria, even the ones that are native to your body and extremely beneficial. In this experiment, mice were given low levels of penicillin at the very end stages of pregnancy and through the weaning period. This drastically changed the gut microbiome from what would be expected. Behavioral tests revealed that mice that had received antibiotic treatment were less likely to engage in social behaviors and were more aggressive, but those behaviors could be changed by treatment with certain types of bacteria. These results provide further evidence for the role of

gut microbes in cooperation and beneficial social interactions.



Credit: *Nature, Furuya and Lowy (2006)*

Types of Bacterial Gene Sharing

1. Bacterial transformation occurs when bacteria take up free bits of DNA from their environment.

2. Bacterial transduction requires viruses to act as DNA transporters. When a virus enters a bacterium, some of the bacterial DNA is incorporated into the viral DNA. When the virus leaves the bacteria to infect a new cell, it takes the bacterial DNA with it and can insert it into new cells.

3. Bacterial conjugation happens when two cells form a bridge between them and copy plasmid DNA from a donor cell into the recipient cell

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God Genes

In the same way that bacteria pass antibiotic resistance to each other because it helps their community, humans pass genes that promote the survival of the species from generation to generation. One trait that has had a strong evolutionary advantage is religion because it creates a sense of community and encourages people to look out for each other. For something to be acted upon by natural selection, the driving force of evolutionary change over time, it has to be a tangible unit that can be passed onto offspring. These tangible units are the genes in our DNA. If religion is something that has helped the human species survive as long as we have, it is likely passed from parent to offspring in some sort of genetic fashion.

Although many believe our religious beliefs are a result of whether or not our parents took us to church when we were young, it appears to be more complicated than that. Dean Hamer, director of the Gene Structure and Regulation Unit at the National Cancer Institute in Bethesda and author of the book "The God Gene", has proposed just that; a "God gene" that increases your likelihood of being religious[11]. The gene Hamer claims is responsible for someone's religious inclination is the vesicular monoamine transporter 2, VMAT2. VMAT2 is a membrane transporter that helps package monoamines such as dopamine and serotonin for release in the brain[3]. Hamer found that specific variants, changes in the nucleotides that make up the gene, in VMAT2 were more common in people who claimed to be religious and less common in less religious people. He does, however, qualify his claim, saying that VMAT2 is likely not the only gene that influences religiosity.

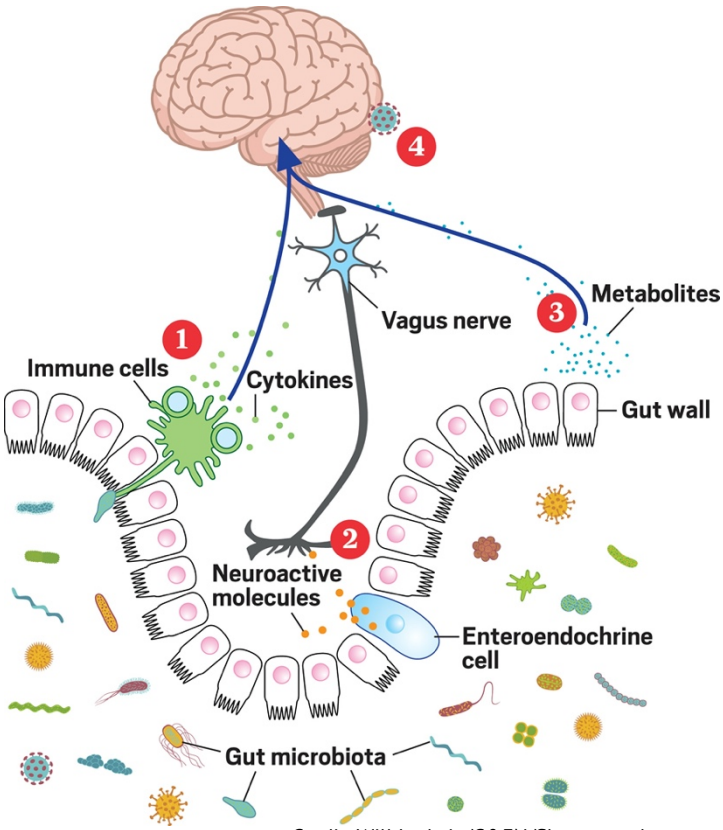
In fact, Dean Hamer and his research team are not the only ones to find a link between genes and religion. Although your genes won't determine whether you're Christian or Buddhist, they may influence your level of religiosity. Researchers at the University of Minnesota asked 169 pairs of identical twins and 104 pairs of fraternal twins questions about their religious activities at the time and

as children. Identical twins share 100% of their DNA while fraternal twins share only about 50%, as much as any set of siblings born at different times. All participants answered that they had similar religious views as the rest of their family (parents and siblings) when they were younger. However, identical twins were more likely than fraternal twins to keep the same level of religiosity when they grew up, suggesting a genetic component. When closely related people start getting the same disease or condition, the culprit is usually some mutation in the DNA that was passed through the family. This is especially true when people in the same family get the same diseases even once they no longer share the same environment. This is the principle that led researchers to conclude a genetic component for religion. Identical twins are more closely related than fraternal twins and, as expected in a genetically influenced trait, share religious views and practices more than other, less related, people. Michael McCullough, a psychologist at the University of Miami, told *New Scientist* that "...ultimately, we all decide what we're most comfortable with, and it may have more to do with our own makeup than how we were treated when we were adolescents".

Moody Microbes

Another example where environmental factors may not tell the whole story is in depression. While an impending divorce, the death of a loved one, or pressure from work or school certainly does nothing to improve mood, bacteria in your gut play just as important a role. A 2016 study published in Nature took germ-free mice, or mice with no native gut bacteria, and gave them either a "depression microbiota" or a "healthy microbiota". The different microbiotas were cultured directly from human patients that were either clinically depressed with major depressive disorder (MDD) or healthy. Mice that were given gut bacteria from patients with MDD began to display depressive behavior, as measured by decreased activity in behavior tests. MDD mice also displayed more anxious behavior. Mice given healthy bacteria displayed no difference in their activity in the behavior tests over time nor their anxiety levels. The researchers believe that their results "provide an original perspective to uncover the pathologic mechanism(s) underlying depression as well as revealing the need for innovative gut-mediated therapies for depression".

Researchers still weren't sure whether it was a presence of good bacteria or an absence of bad bacteria that caused changes in MDD patients. A study conducted in 2019 offered a more specific analysis showing which bacteria are absent in the guts of those with depression. Researchers at the Rega Institute for Medical Research in Belgium asked over 1,000 participants questions measuring their quality of life and depression levels and simultaneously analyzed their gut microbes. Two genera of bacteria, *Coprococcus* and *Dialister*, were consistently found to be more prevalent in those with a better quality of life and less prevalent in those with depression. Researchers speculate that these bacteria are important because they produce butyrate, a short-chain fatty acid that plays a crucial role in maintaining gut and brain health. Butyrate-producing bacteria decrease gut inflammation and prevent "leaky gut", a condition in which your intestines become more permeable to bacteria from your gut, causing them to leak into the bloodstream, which would certainly be depressing.



Credit: Will Ludwig/C&EN/Shutterstock

How Your Gut Communicates with Your Brain

1. Microbes interact with immune cells in the gut, causing them to make cytokines, substances secreted by immune cells that act on other cells. These cytokines can circulate through the blood to the brain.

2. Microbes interact with enteroendocrine cells in the gut which produce neuroactive peptides and molecules. These substances interact with the vagus nerve, which sends signals to the brain.

3. Microbes in the gut produce neurotransmitters and metabolites such as butyrate. When they travel to the brain, some of them are small enough to cross the blood-brain barrier, while others alter cell activity directly at the barrier itself.

4. In 2018, researchers at the University of Alabama at Birmingham reported that they had found gut bacteria in human brain tissue, suggesting that microbes can make their way into the brain.

Some bacteria in your gut can be more harmful than they are helpful. According to a 2019 review in the *European Journal of Neuroscience*, neuroinflammation is a key contributor to depressive behavior, and some gut bacteria can be key contributors to systemic inflammation. Gut microbiota can influence levels of T helper cells, important cells in your immune system which recognize foreign antigens and activate other immune response cells, by binding to cells that activate the immune system. One pathway T cells are important for is inflammation. In the case of an invading pathogen, inflammation serves to increase blood flow and bring more cells to the affected area in order to fight off infection and disease. However, excessive production of inflammatory signaling chemicals can make their way to the brain and act on neuronal and glial receptors, changing how the brain responds to stimuli. The key to mediating clinical depression is finding the perfect balance of gut bacteria, a feat many of us seem to achieve with little to no thought of the tiny microorganisms silently influencing our mood.

Further Findings

Every few months I get a new email from 23andMe, telling me that there is a new trait they can give me information about based on my genes. The human genome was finally mapped in 2003 thanks to the Human Genome Project, so it's no surprise that this field is rapidly evolving. While we are learning so much about behavior from our genes and microorganisms, it is certainly not an exact science. Much of this research is done on bacteria or mice because, for good reason, it is not ethical to edit the DNA of human fetuses or make people depressed just to see what

biological changes happen. Because of this, studies done in humans are typically correlational rather than causational and although results can be promising, there are literally an infinite number of variables that differ between people that could also be contributing to any changes seen. This doesn't mean that the studies and results discussed above don't matter; there is a clear biological basis to many of our traits and behaviors. Next time you help someone out with seemingly no benefit to you, think of your microorganisms trading bits of DNA with microorganisms on the person you're helping. When you argue over religion at the next family gathering, remember some of the genes in the 2 meters of DNA held in each cell that influence what you believe. And when you're in a particularly good mood, thank some of the 100 trillion bacteria in your gut decreasing inflammation and improving your quality of life.