# Study finds connections between genetics, brain activity and preference

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A team of researchers from Massachusetts General Hospital (MGH) has used brain imaging, genetics and experimental psychology techniques to identify a connection between brain reward circuitry, a behavioral measurement of preference and a gene variant that appears to influence both. The report in the August 4 issue of *Archives of General Psychiatry* describes how variations in a gene involved with the brain's reward function are associated with the activity of a key brain structure and, in parallel, with the effort study participants 'invest' in viewing emotion-laden facial images. The findings have implications for how genes may influence healthy or dysfunctional behavior involving choices in many different areas.

"This work helps connect our psychological understanding of why we like some things and not others with the genetic mechanisms that define our range of behaviors," says Hans Breiter, MD, senior and corresponding author of the study and principal investigator for the Phenotype Genotype Project in Addiction and Mood Disorders, an interdisciplinary project involving the MGH Departments of Radiology, Psychiatry, and Neurology. "In the ongoing discussion about how much the environment versus genetics determine behavior, this study points to how the interaction between these factors influences our judgment and decision-making."

The current study is part of a decade-long effort to link studies of reward and aversion in animal models to human psychology and neuroscience. In the mid-1990s, Breiter and other MGH researchers used functional

magnetic resonance imaging (fMRI) techniques to demonstrate how structures deep within the brain were involved with the experience of reward, how that experience was connected to motivated behavior, and how the reward system could be co-opted in situations like drug addiction.

In 2001, Breiter collaborated with Daniel Kahneman, PhD, of Princeton University and Peter Shizgal, PhD, Concordia University, Montreal, to show how the brain's reward/aversion circuitry followed the principles of what is called prospect theory when responding to the anticipation and receipt of a financial reward, helping to lay the groundwork for the field now called neuroeconomics. Kahnemann was a co-recipient of the 2002 Nobel Prize in economics for his earlier development of prospect theory, which describes the different ways people evaluate positive and negative outcomes in uncertain situations.

The current report connects molecular genetics with earlier studies of choice and preference and with investigations of the brain's reward circuitry. The researchers focused on a gene called CREB1 that has been implicated in animal studies of the brain's reward/aversion function. Study lead author Roy Perlis, MD, medical director of the MGH Bipolar Program, and colleagues previously found that depressed men with a particular variation near the gene coding for CREB report greater difficulty suppressing anger. Another study of theirs associated the same variation with a threefold greater risk of suicidal thinking in major depressive disorder patients soon after beginning antidepressant therapy. The 28 participants in the current study had no evidence of any psychiatric disorder or physical disorder that might influence brain activity.

In addition to analyzing each participant's version of the CREB1 gene, the researchers conducted a set of experiments. As the participants viewed facial expressions reflecting different emotional states – happy,

neutral, sad, fearful and angry – fMRI scans were taken to examine the activity of brain structures associated with processing pleasant or unpleasant experiences. In another test, participants viewed the same pictures and could change how long they viewed an image by the way they pressed keys on a keyboard. Many earlier studies have established the keypress experiment as a quantitative measure of preference. In the version used in this study, keypress responses reflected participants' judgment and decisions about how much or how little they preferred the facial expressions.

The fMRI study showed that, during the viewing of angry faces, the activity of a structure called the insula, involved in the response to unpleasant situations, depended on which version of the CREB1 gene a participant inherited. In the keypress experiment, responses indicating a preference against the angry expression paralleled the CREB1-affected fMRI activity seen in the insula in the first experiment and also differed depending on the CREB1 variant that had been inherited.

"We were surprised to see that variation in the CREB1 gene would account for more than 20 percent of the difference in how healthy participants weighed different options and expressed specific preferences," says Perlis. "Our previous studies and the work of other groups suggested that variation in this gene could be important for judgment and decision-making by the brain, but we needed to connect this to a measurable decision-making effect in both behavior and brain activity."

Breiter adds, "This study connects quantitative measurements across three levels of observation – brain activity, genomic variation and the expression of preference. We now are investigating the potential role of other genes and will go on to assess how this relationship across three levels of observation may be affected by conditions such as depression and addiction."

Source: Massachusetts General Hospital