

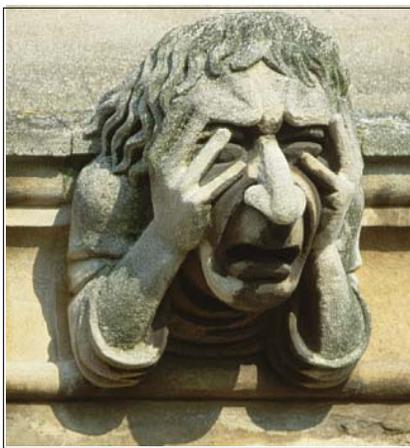
## THE RUNNERS-UP

This year's discoveries illuminated realms as small as a single molecule and as large as a gamma ray burst.

**#2 Decoding mental illness.** Schizophrenia, depression, and bipolar disorder often run in families, but only recently have researchers identified particular genes that reliably increase one's risk of disease. Now they're unraveling how these genes can distort the brain's information processing and nudge someone into mental illness.

The chemical messenger serotonin relays its signal through a receptor that's a target of antidepressant drugs. The gene for this receptor comes in two common flavors, or alleles, one of which had been tenuously linked to an increased risk of depression. This year, researchers revealed why the link had been so elusive: The allele increases the risk of depression only when combined with stress. Among people who had suffered bereavement, romantic rejection, or job loss in their early 20s, those who carried the vulnerability gene were more likely to be depressed than those with the other gene variant.

People with the high-risk allele have unusually heightened activity in a fear-focused brain region called the amygdala when viewing scary pictures. Together, these studies suggest that the gene variant biases people to perceive the world as highly menacing, which amplifies life stresses to the point of inducing depression.



**Agony antecedents.** New work links genes, brain activity biases, and mental illness.

A different brain area, the prefrontal cortex, is regulated in part by a gene called *COMT*, one of the handful associated with risk of schizophrenia. It encodes an enzyme that breaks down neurotransmitters such as dopamine. Two years ago, one version of this gene was shown to muddle the prefrontal cortex, which is necessary for planning and problem-solving skills that are impaired by schizophrenia. Even healthy people who carry the schizophrenia risk allele

have extra activity in the prefrontal cortex even when doing relatively simple tasks. The nonschizophrenia allele, which allows more efficient activity in the prefrontal cortex, appears to increase the risk of anxiety, suggesting that the two diseases lie at opposite ends of a spectrum.

Late in 2002, an allele of a gene for brain-derived neurotrophic factor (BDNF) was implicated in bipolar disorder, once known as manic depression. This year the allele was found to curb activity in the hippocampus, a structure necessary for memory that is shrunken in people with mood disorders. BDNF encourages the birth of new neurons in the hippocampus; other work this year showed that antidepressants require this neurogenesis to be effective. Through these and similar insights, researchers hope to understand brain biases underlying mental illnesses well enough to correct them.

## The Runners-Up: The News and Editorial Staffs\*

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