Gene Tied to Excitable Personality

Evidence gleaned from twin and adoption studies over the past 20 years has led scientists to theorize that inheritance shapes various broad aspects of individual personality. Now, researchers assert that they have cornered for the first time a gene that participates in shaping a specific personality trait.

One version of the so-called D4 dopamine receptor gene, or *D4DR,* appears frequently in people who report high levels of "novelty seeking," according to two independent studies reported in the January NATURE GENETICS.

Some investigators conceive of novelty seeking as a discrete personality trait. People scoring high on this characteristic enjoy exploring new environments, are excitable and quick-tempered, and seek out thrilling sensations. Those scoring low are reflective, deliberate, and orderly.

"This work provides the first replicated association between a specific genetic locus involved in neurotransmission and a normal personality trait," contend Richard P. Ebstein of Sarah Herzog Memorial Hospital in Jerusalem and his colleagues. Ebstein's group performed one of the newly reported studies.

Both investigations took inspiration from a theory advanced by C. Robert Cloninger of Washington University School of Medicine in St. Louis. Cloninger argues for the existence of four independent temperamental traits—novelty seeking, harm avoidance, reward dependence, and persistence (SN: 3/5/94, p. 152).

Based on animal and earlier clinical studies, Cloninger proposed that the way brain cells handle the chemical messenger dopamine shapes an individual's propensity for novelty seeking.

Ebstein's group administered Cloninger's personality questionnaire to 124 unrelated Israeli adults, most of them Ashkenazi or Sephardic Jews. Each volunteer also donated a blood sample for genetic analysis.

Volunteers scoring high in novelty seeking were much more likely to bear a slightly longer form of the *D4DR* gene than low novelty seekers, the scientists maintain. The *D4DR* gene helps to regulate the formation of one class of receptors, or molecular gateways, for dopamine transmission in the brain. The longer gene may endow a person with receptors that respond to dopamine by promoting novelty-seeking behavior, Ebstein and his colleagues theorize.

In the other study, Jonathan Benjamin of the National Institute of Mental Health in Bethesda, Md., and his coworkers recruited 315 people in the United States, most of them pairs of male siblings. Volunteers completed a questionnaire that yielded scores on five personality traits—extroversion, openness to experience, neuroticism (being prone to distress and impulsiveness), agreeableness, and conscientiousness. Many psychologists currently favor this classification.

No single trait of the five showed an association with any *D4DR* variation. However, the long version of the *D4DR* gene corresponded to a substantially elevated frequency of answers to individual questions that signify novelty-seeking behavior, Benjamin's group asserts.

In a commentary accompanying the new results, Cloninger argues that they support the further use of his personality model for studying the genetics and neurobiology of personality.

Genetics alone does not determine personality, however. An individual's mix of temperamental traits affects responses to the environment and underscores character development throughout adulthood, Cloninger theorizes. In his model, character consists of commitments to goals, cooperativeness, and spiritual beliefs that transcend the self.

The identification of genes contributing to temperament may help to unravel the roots of some psychiatric disorders, Cloninger adds. For instance, a predisposition to novelty seeking may play a role in some cases of schizophrenia, he suggests. One antipsychotic drug, clozapine, specifically targets D4 dopamine receptors, which schizophrenic patients often possess in unusually high numbers. However, prior studies have found that the same patients do not exhibit a preponderance of any particular form of the *D4DR* gene.

It may be useful to reexamine *D4DR* in groups of schizophrenics to find how often the longer variety occurs together with novelty seeking, Cloninger contends. *— B. Bower*

New microcoil enhances NMR sensitivity

To a biological molecule, a nanoliter might as well be an ocean. But to molecular biologists, one-billionth of a liter is a volume so restricted that accurate chemical analysis of it can become an exercise in frustration.

To overcome such difficulties, Dean L. Olson and Jonathan V. Sweedler, chemists at the University of Illinois at Urbana-Champaign and their colleagues have fabricated a microcoil small enough to permit accurate molecular analysis of tiny samples with nuclear magnetic resonance (NMR).

"We think that the biggest impact of the NMR microcoils will be to enhance separation techniques," says Sweedler. Current NMR systems cannot be used to analyze samples produced during separation if the samples are smaller than about 50 microliters, Sweedler says.

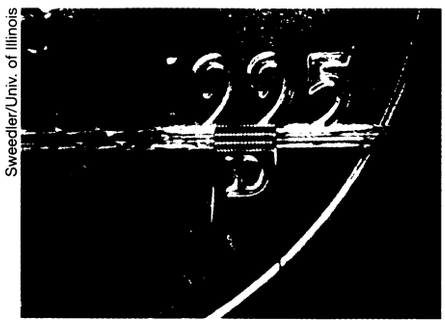
Using the diminutive NMR coils in conjunction with standard separation techniques adapted to small volumes—such as capillary electrophoresis or liquid chromatography—chemists can assay nanosamples with 100 times the sensitivity now possible with conventional NMR methods alone, Olson and Sweedler report in the Dec. 22, 1995 SCIENCE.

"The microcoils let us work with 5-nanoliter samples, which are 10,000 times smaller than samples currently used," Sweedler says. "You can measure some things that couldn't be measured before."

Sweedler predicts that the microcoil will greatly improve analysis of biological materials. "If you're isolating a peptide or trace component of a cell," he says, "you often don't have enough material to use conventional NMR."

"This is a very important contribution," says Charles S. Johnson Jr., an analytical chemist at the University of North Carolina at Chapel Hill. "NMR is an exceptional technique when it comes to chemical selectivity. But its sensitivity is poor in small samples, which has limited its use."

The magnets for an NMR system currently cost more than any other component, Sweedler adds. "With smaller coils, you can scale down the size of the magnets. That could cut the cost from more than $100,000 per magnet to less than $10,000. In the long run, that might make possible inexpensive bench-top NMR machines." *— R. Lipkin*



Sweedler/Univ. of Illinois

The size of the NMR microcoil in relation to a penny.