# Pessimism linked to poor health

Disappointment, misfortune and tragedy intrude into all lives at some time. But the habitual ways in which people explain the bad events that befall them may put them at risk for poor physical health by middle age, according to a 35-year study reported in the July JOURNAL OF PERSONALITY AND SOCIAL PSYCHOLOGY.

The investigation, initiated in 1946 with recent graduates of Harvard University, reveals that individuals who explain bad events pessimistically in early adulthood have substantially more illness at age 45 than those who offer rosier explanations for bad events. The relationship between pessimism and poor health declines somewhat in the following years but remains statistically significant through age 60, say psychologists Christopher Peterson of the University of Michigan in Ann Arbor and Martin E.P. Seligman of the University of Pennsylvania in Philadelphia and psychiatrist George Vaillant of Dartmouth University in Hanover, N.H.

Peterson and his colleagues analyzed the responses of 99 Harvard men to an open-ended questionnaire completed in 1946, when they were about 25 years old. The questionnaires asked about experiences during World War II. The men are part of a larger, ongoing study of adult development in which physical health is charted annually.

Questionnaire responses were rated for "explanatory style." There are three main elements of a pessimistic explanatory style: invoking a stable, long-lasting cause for misfortunes; assuming the cause of a bad event will have a ruinous effect on most areas of one's life; and identifying the cause's source as oneself rather than other people or circumstances.

In an extreme example of such pessimism, a subject might explain his lack of advancement in the military by saying, "I seem to be unwilling to face reality," and then noting the pervasiveness of this fault, which he believes has kept him from firmly pursuing a postwar career.

Studies of college students conducted in the last decade indicate pessimistic as well as optimistic explanatory styles remain relatively stable as individuals progress into adulthood, says Peterson.

In the Harvard sample, pessimism at age 25 predicted more severe types of physical illness (a full range of disabling and nondisabling disorders was tracked) between the ages of 45 and 60. Peterson notes that a total of 13 men have died, not enough to allow meaningful analysis of any links between explanatory style and mortality.

While the study is an "impressive demonstration of a relationship between pessimism and poor health in middle age," it remains unclear how explanatory style affects physical well-being, Peterson acknowledges. Perhaps pessimistic people become passive in the face of illness and do not take care of themselves, he suggests. Studies of college students who developed colds or flus show that pessimistic subjects are less likely to seek medical advice, take simple medical precautions or curtail activities.

Studies also indicate pessimistic individuals are socially withdrawn and have fewer supportive friends and relatives, a factor that may importantly influence health over the long haul, Peterson says.

Further studies of pessimism's link to health need to include a broader spectrum of subjects, he notes. The investigators are now evaluating explanatory styles of 1,500 men and women recruited in the 1920s for a long-term study organized by Stanford University psychologists. This sample is also limited, however, because subjects were selected on the basis of having high childhood IQs.

The similarity of pessimistic explanatory style to other personality measures linked to poor health, such as Type A behavior and hostility, remains unclear, Peterson says. — *B. Bower*

# Gene control: Curiosity and the cat box

Researchers this week reported new and surprising observations about a family of proteins that control gene activity in human and other cells. Their report provides a glimpse of one of the most fundamental "on-off" switches in the biological machine, and suggests that mechanisms of gene regulation are even more mysterious and subtle than previously assumed.

Scientists have known for decades that within DNA strands reside coded instructions for a spectrum of biological functions, from DNA replication to the production of enzymes and other proteins. In a simplified view, segments of DNA, called genes, serve as blueprints for the production of particular proteins. But the process is not a one-way street; certain specialized proteins themselves bind to DNA, where they can regulate the activity, or "expression," of genes.

Little is known about these DNA-binding proteins, but one thing is clear: They are critical to any "decision" by a piece of DNA to either replicate itself or initiate transcription — the first stage in the process that leads to a protein's production. An understanding of this mechanism of gene regulation might someday enable scientists to control or correct a host of genetic errors, from embryo defects due to aberrant protein synthesis to cancer — the result of uncontrolled DNA replication and cell division.

Robert Tjian of the Howard Hughes Medical Institute at the University of California, Berkeley, and his colleagues worked with a family of DNA-binding proteins that specifically bind to a DNA region featuring the base sequence code GCCAAT. Scientists find the GCCAAT motif (often called the CCAAT-box) in various places along DNA strands in viruses, yeasts, mammals and other organisms, where it has been associated with DNA transcription and replication. The researchers cloned for the first time several individual members of this mixed family of DNA-binding proteins, and found to their surprise that even a single variety of protein could initiate both transcription and replication.

"Before this we had a family of proteins, and we could say members of this family are involved in both transcription and replication. However it was not clear whether . . . all of them showed the same activities or whether some would do one thing and others would do another," says Nicolas Mermod of the research team. "Now we know that the same protein can do it all."

In related studies, the researchers appear to have settled a longstanding question by showing that in the family they examined, a single gene can code for a spectrum of CCAAT-box-binding proteins. Molecules of messenger RNA — key "middlemen" in the process of protein synthesis — apparently can be cut into pieces, "shuffled" and then spliced together in more than one way before being used as templates in the protein production process. This method of creating a variety of proteins, or "family members," from a single gene has never before been associated with genes affecting transcription. It provides a mechanism for a single DNA site to respond to different, related proteins.

The research, which appears in the July 21 NATURE, provides a new generation of questions about gene regulation. What is the significance of the different forms of regulatory proteins? If a single version can perform at least two distinct functions, what factors determine the job it will actually do? And perhaps most intriguing: What regulates the splicing of messenger RNA, and thus regulates the ultimate diversity of these regulatory proteins?

For now, says Nicholas J. Short of King's College, London, the functional differences between the family members "remain obscure," although "it is conceivable that each form could have subtly different effects on transcription or DNA replication, perhaps by interacting in different ways with some of the other protein factors involved in these processes." In an editorial accompanying the research, he adds, "The potential complexity of the system is staggering."

— *R. Weiss*