Mutation revealed for adult Tay-Sachs

Scientists have discovered the genetic mutation responsible for the adult form of Tay-Sachs disease, a rare, degenerative brain disorder most commonly seen in its childhood form. The finding, along with the recent discovery of two mutations that can cause the childhood disorder, may allow screening of people who carry a Tay-Sachs gene to tell them which form of the disease they carry, says study coauthor Richard L. Proia, a biochemist at the National Institutes of Health.

People with late-onset Tay-Sachs suffer progressive mental and motor deterioration, with symptoms that vary from stuttering and falling to depression, schizophrenia and premature death. "But [adult Tay-Sachs] is nothing like infantile Tay-Sachs," which leads to death in early childhood, says biochemist Elizabeth F. Neufeld of the University of California, Los Angeles.

To contract either form of Tay-Sachs, a person must inherit a defective gene from both parents. The most common Tay-Sachs carriers, Ashkenazi Jews, frequently choose to take an enzyme test screening for this incurable disease and, if positive, usually opt for prenatal diagnosis or, in rare cases, not to conceive children. Genetic testing would be most useful in prenatal diagnosis, because the enzyme test may yield ambiguous results in fetuses predisposed to develop the adult form of the disease, says biochemist Eugene E. Grebner of Thomas Jefferson University in Philadelphia.

Both adult and infantile forms of the disease are caused by defects in an enzyme called beta-hexosaminidase. In the infantile disorder, brain cells do not produce this enzyme, and in the adult case, they produce a poorly functioning enzyme. In both, brain cells degenerate because they accumulate a membrane lipid normally metabolized by beta-hexosaminidase.

To find the adult mutation, Proia and geneticist Ruth Navon examined DNA from an adult Tay-Sachs patient who also carries the gene for infantile Tay-Sachs. The small amount of beta-hexosaminidase RNA his cells made from the late-onset mutant gene allowed the scientists to isolate the mutant. Sequencing the gene revealed the oddity: one changed base pair, a mutation for which eight additional adult Tay-Sachs patients proved positive and 20 asymptomatic individuals tested negative, the scientists report in the March 17 SCIENCE.

In separate work, Neufeld and Michael M. Kaback of the University of California, San Diego, found the same mutation. Their findings will appear next month in PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES. — *I. Wickelgren*

Fading remembrances of television past

A psychologist has come up with a happy ending for the plethora of prime-time television programs axed after one year on the major networks. He uses them to illuminate the nature of long-term memory over as many as 15 years.

His findings establish for the first time that forgetting can be gradual and continuous for many years after learning, particularly if there was limited, intermittent exposure to the learned material, reports Larry R. Squire of the Veterans Administration Medical Center in San Diego, in the March JOURNAL OF EXPERIMENTAL PSYCHOLOGY: LEARNING, MEMORY AND COGNITION.

Squire devised a multiple-choice test based on one-season television shows aired from one to 15 years previously. He administered the test to a different group of 20 to 32 subjects for nine consecutive years, from 1978 to 1986. Each annual test contained an average of 70 questions and was updated to include canceled programs from the prior year. The test asked people to choose a former show from four titles, three of them fabricated.

A question for the year 1974, for example, provides the following choices: "Mandrake," "Shipmates," "Private Nelson" and "Lucas Tanner." The last title is the correct response.

Squire combined the average percentage of correct responses for each of the preceding 15 years across the nine test groups. The percentage of correct scores for each program was then statistically adjusted according to the number of weeks it remained on the air.

Subjects recognized about three-quarters of the shows from the year before taking the test. Two-thirds of the responses were correct for shows canceled five years previously. Correct responses bottomed out at 58 percent for 15-year-old programs.

Evidence for the gradual forgetting of television-program names contrasts with research showing that although some Spanish learned in high school is soon forgotten, after several years a substantial amount of knowledge remains and is accessible for 25 to 50 years (SN: 3/10/84, p.149).

Gradual forgetting may not extend beyond a few years for material learned over several years with repeated exposures, such as a foreign language, Squire suggests. But for facts, names and events to which one has limited exposure, gradual and continuous forgetting appears the rule, he maintains. — *B. Bower*

Window on the chemistry of cracking glass

If glass were flawless, it would be much stronger than steel. However, most glass is full of tiny cracks that can slowly creep along or suddenly shoot across at shattering speeds. To predict how glass will stand up over time, engineers are studying how it cracks and what factors determine the way cracks grow.

Several years ago, Bruce Bunker and Terry Michalske of Sandia National Laboratories in Albuquerque, N.M., developed models describing what happens to individual molecules when glass cracks. Now, they have gained a better understanding by taking into account the way outside chemicals alter the surface of cracks and influence their growth. They presented their findings in Houston this week at the International Conference on Fracture.

Bunker and Michalske's earlier work focused on the very tip of a crack, where the silicon-oxygen network of simple glasses can tear apart at one-trillionth of an inch per hour, then suddenly accelerate to 50 or 60 miles per hour. The researchers looked at how various corrosive chemicals — especially water — speed up the process.

But that model couldn't satisfactorily predict glass behavior over 10 or 20 years, especially in more complex glasses. Such glasses tend to be more vulnerable to corrosion by water and other chemicals. Corrosives add elements to the crack surface and leach out components of the glass, giving rise to a chemically distinct "alteration" layer. To test the role of this alteration layer in corrosion and cracking, Bunker and Michalske exposed different kinds of glass to different chemicals. They measured how fast the alteration layers formed and how fast cracks grew in each case. They also determined how much the alteration layers stressed the glass by measuring how the corrosive agents warped it.

The researchers found they could predict how long glass would hold up by analyzing the structure of the alteration layer. Generally, if the alteration layer is more compact than the surrounding glass, it will contract the crack surface and pull the crack apart. Other alteration layers expand the crack surface, squeezing the crack shut.

Michalske suggests the work will enable engineers to design glass products taking the expected lifetime into account. In addition, it may lead to new glasses with a chemistry that prevents alteration layers or encourages an alteration layer that hinders cracks. — *F. Flam*

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