Canine Brains Offer Clue to Narcolepsy

In a strain of dogs that sleep excessively and collapse when they are excited, investigators have discovered a withering away of axons, the communication cables that convey signals between nerve cells. That degeneration, if also evident in human brains, may finally offer an explanation for narcolepsy, a sleep disorder that afflicts an estimated 250,000 people in the United States.

"This is really the first evidence that something gets destroyed in the [narcoleptic] brain," says Jerry M. Siegel of the University of California, Los Angeles and Sepulveda Veterans Affairs Medical Center, who presented the research at last week's Society for Neuroscience annual meeting in San Diego.

Though the condition provokes many jokes, narcolepsy can be a debilitating disorder: Narcoleptics sometimes fall asleep in the middle of conversations or physical activities. Symptoms appear during the teenage years, with excessive daytime sleepiness usually marking the onset of the disorder. Many narcoleptics then begin to suffer from cataplexy, a sudden loss of voluntary motor control stimulated by intense emotions such as anger, fear, or joy. A simple joke can cause a narcoleptic's knees to buckle, head to drop, and jaw to go slack.

Narcoleptic dogs, mainly Doberman pinschers, have served as a model of the condition since the 1970s. In these dogs, symptoms normally appear at about 2 months of age. Simply playing fetch can trigger a cataplectic attack.

Examining the brains of young dogs, Siegel and his coworkers found three regions in which narcoleptic dogs showed much more axon degeneration than do normal dogs.

Siegel et al.

At play a moment ago, this narcoleptic dog has lost voluntary motor control.

Investigators had previously linked the three affected brain areas—the medial septal nucleus, the diagonal band region, and the amygdala—to sleep inhibition, motor control, and the processing of emotions. "It's easy to explain the symptoms of narcolepsy with this damage," asserts Siegel.

The crucial issue, he acknowledges, is whether human narcolepsy results from similar degeneration. Since human narcoleptics live to normal ages, says Siegel, evidence of the axon degeneration could largely have disappeared by the time a patient dies, explaining why autopsies of narcoleptics have not revealed obvious brain abnormalities. With specific brain regions now implicated by the canine research, he says, investigators can more effectively examine human narcoleptics, either through brain imaging of live patients or detailed postmortem analysis.

Some narcolepsy investigators caution that the axon degeneration found in dogs may bear no relation to what causes human narcolepsy. "I don't think the dog has been a particularly excellent model," says Sharon L. Merritt of the Center for Narcolepsy Research at the University of Illinois at Chicago. "Maybe this will provide a lead, but considering the past, I'm skeptical."

Still, Merritt and other investigators agree on the need to fully explore the hypothesis of axon degeneration. Current therapies for narcolepsy—stimulants and antidepressants—alleviate some of the disorder's symptoms but do not provide a cure. "To develop better treatments, we need to know the mechanism of the disease," says Seiji Nishino of Stanford University's Sleep Disorders Research Center. —*J. Travis*

When pertussis is not a whooping cough

Pediatric textbooks traditionally liken pertussis to rubella, in that a single bout of infection or a vaccination against the microbe responsible is thought to confer lifetime immunity. A spate of new studies, however, indicates that pertussis can strike repeatedly throughout life; it just remains largely misdiagnosed because few victims apart from infants develop the signature whooping cough.

Two of these new studies took place in Germany, where until recently physicians did not routinely vaccinate children against the disease.

In the most recent study, Carl Heinz Wirsing von König of the municipal Institute for Hygiene and Laboratory Medicine in Krefeld and his coworkers monitored the spread of pertussis in households after the diagnosis of a case. In the Nov. 18 LANCET, they report that 55 percent of exposed children developed the highly infectious disease, as did 27 percent of exposed adults. Moreover, at least one-third of the 80 symptomatic adults recalled having had pertussis 20 or more years earlier.

To diagnose the disease in adults, the researchers tested for high concentrations of pertussis antibodies in individuals whose cough lasted at least 6 days. Compared to children, adults exhibited fewer episodes of prolonged coughing, vomiting, or whooping but proved more likely to develop headaches, sinus pain, and attacks of sneezing, sweating, or choking.

A second team also found high rates of adult pertussis in Germany, this time during a 3.5-year-long study of 900 households where children were vaccinated. Again, generally relying on antibody counts or the polymerase chain reaction (to identify DNA from the pertussis bacterium), researchers diagnosed the disease in 32 percent of adults who had a cough that had lasted more than 2 weeks. James D. Cherry of the University of California, Los Angeles School of Medicine and his coworkers describe their findings in the October CLINICAL INFECTIOUS DISEASES.

Three years ago, Cherry's group identified similar rates of pertussis—26 percent in a 30-month-long study—among UCLA students going to the school health service with complaints of a cough lasting at least 6 days. Unlike the German adults, most of these students had been vaccinated.

In this month's CLINICAL INFECTIOUS DISEASES, his group reports on 255 Californians exposed to pertussis at home. They diagnosed infection in 46 percent of patients with no symptoms, in 43 percent of those with mild respiratory illness, and in 80 percent of individuals, mostly infants less than 6 months old, exhibiting the classic whooping cough. The disease tends to be lethal only in this youngest group.

Cherry's data suggest that by age 20 everyone, even in the United States, has developed infectious pertussis. But he suspects that by initiating booster immunizations for adults—perhaps at age 15 and every 10 years thereafter—"you should decrease the major source of infection during the first year of life, which is parents." —*J. Raloff*