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A primate model for Huntington's disease?

Huntington's disease is an incurable neurodegenerative disorder. Rodent models of Huntington's exist, but they do not reproduce the disease course and symptoms of affected humans very closely. This limits their applicability in evaluating the pathology and potential treatments for the disorder.

Now, a group of scientists from the Yerkes National Primate Research Center at Emory University (Atlanta, GA) has taken the first steps toward establishing a primate model for Huntington's. The group, led by Anthony Chan, bred five rhesus macaques carrying the mutation that causes Huntington's in humans. The transgenic monkeys had some characteristics of Huntington's disease: nuclear inclusions and neuropil aggregates in the brain, and clinical features such as chorea and dystonia (*Nature*, published online 18 May 2008; doi:10.1038/nature06975). Two of the monkeys died within one day of birth; a third survived for one month; and the remaining two lived for at least six months.

The macaques are the first primates that have been genetically engineered to have a human disease. Chan's group believes that the monkey model may help us to better understand how Huntington's develops and thus lead to new therapies and treatments. They chose Huntington's as a first target because of its relative genetic simplicity (linked to a mutation in one gene), but their approach may also open the door to creating primate models for other, more genetically complex neurodegenerative diseases.

What makes fruit flies hate fruit?

In most species, animals change their behavior as they develop. The fruit fly larva, for instance, hatches inside rotting fruit and immediately begins gorging itself. At some point, the larva suddenly loses interest in the fruit and migrates as far away from food as possible. Leaving the fruit is probably beneficial for larvae, as it keeps them from drowning in juice.

A study led by Ping Shen of the University of Georgia (Athens) reveals the chemosensory mechanisms underlying this behavioral switch (*Nat. Neurosci.* **11**, 676–682; 2008). The team investigated the role of the protein PAIN, which belongs to a family of receptors that has previously been implicated in larva food aversion. They found that larvae in which PAIN expression was disrupted did not leave rotting fruit, and that larvae were specifically averse to fructose. The researchers concluded that PAIN causes fructose aversion and that its expression is suppressed until larvae reach the age of migration.

These findings may yield insight into similar mechanisms in other animals. They may also be relevant for studies of pain in humans, as the neuropeptides that suppress PAIN production and fructose aversion in flies are homologous with human peptides that are thought to suppress pain.

Potential treatment for alcoholism

Gabapentin, an anticonvulsant drug used to treat epileptics, has already proven effective in the treatment of alcohol withdrawal in humans. A study led by Marisa Roberto of the Scripps Research Institute (La Jolla, CA) suggests that the same drug might be used to treat the hangover's cause: the tendency to drink excessively.

Roberto and colleagues examined the effects of gabapentin in an established rat model of alcoholism (*J. Neurosci.* **28**, 5762–5771; 2008). They induced ethanol dependence in rats by exposing them to alcohol vapor for several weeks in an inhalation chamber. They then trained rats to voluntarily self-administer ethanol. The researchers found that ethanol-dependent rats that received gabapentin drank significantly less alcohol than did ethanol-dependent rats that did not receive the drug. The drug also reduced anxiety-like behavior associated with alcohol withdrawal in dependent rats. Gabapentin had no effect on ethanol consumption in nondependent rats. When researchers compared brain slices of ethanol-dependent and nondependent rats, they found that the drug had opposite effects on neural synapses in the region involved in response to alcohol consumption.

According to the scientists, clinical trials for the efficacy of gabapentin as a treatment for alcoholism are currently under way.