A second cup of coffee

Coffee is among the world's most popular pick-me-ups, but until recently its effects have been poorly understood. Now scientists are reporting the first evidence that long-term consumption of caffeine — the psychoactive ingredient in coffee — causes significant changes in brain tissue, which may be responsible for caffeine headaches and other symptoms of dependency reported by heavy coffee drinkers. At the same time, another group of scientists say that they have found preliminary evidence of a second psychoactive substance in coffee — a chemical, present even in decaffeinated coffee, that appears to block the normal circulation of brain opiates.

In a recent experiment at the National Institute of Mental Health, biologist Paul Marangos gave mice a daily dose of caffeine (the equivalent of four or eight cups of coffee) for up to 40 days in order to measure the effects of chronic caffeine consumption on the brain. After two weeks, he found a dose-related proliferation of brain receptors for a neurotransmitter called adenosine, a potent natural sedative believed to work by triggering the release of several other neurotransmitters.

The increase in adenosine receptor sites suggests that caffeine is acting as a chemical "antagonist," blocking the normal action of adenosine; when such blockage takes place, Marangos told SCIENCE NEWS, the brain adapts by producing new sites. The result is a hyperactive adenosine system, which causes abnormal sedation (and a craving for caffeine) whenever the effects wear off. Marangos also found a less dramatic and transitory growth in the brain receptors that are involved in the control of anxiety.

Marangos's findings help explain why more and more coffee drinkers are choosing to decaffeinate themselves. But according to another group of scientists, that may not be enough to eliminate the beverage's effects on brain and behavior. J.H. Boublik, a medical researcher at Prince Henry's Hospital in Melbourne, Australia, reports in the Jan. 26 NATURE that another chemical compound — present in regular and decaffeinated coffee but not in tea or cocoa — inhibits the binding of the opiate antagonist naloxone to opiate binding sites in the brain. What this suggests is that the new (and as yet unidentified) substance is also an opiate antagonist; and because the average cup of coffee contains five times the active dose, Boublik and his colleagues say, drinking coffee may have behavioral effects (in addition to those of caffeine) that result from the blockage of brain opiates, which work as both painkillers and mood elevators.

— *W. Herbert*

More debate over clay layer's origin

A study of the mineral composition of the clay layer that marks the boundary between the Cretaceous and Tertiary periods suggests that the clay formed from ash deposited during a time of intense volcanic activity. The findings, reported in the Feb. 4 SCIENCE by Michael R. Rampino of NASA Goddard Space Flight Center in New York, and Robert C. Reynolds of Dartmouth College, are especially pertinent because they contribute to the ongoing debate over what happened about 65 million years ago, a time when many kinds of life on earth became extinct.

One hypothesis is that an asteroid struck the earth and that the clay layer is in part the remnant of a huge dust cloud that was strewn into the atmosphere when the asteroid struck (SN: 6/2/79, p. 356; 11/14/81, p. 314). Rampino and Reynolds contend that if the boundary clay was caused by an impact of the earth with a large extraterrestrial body, then it should contain material from both the asteroid and from the earth, and that the layer should be well mixed and similar in each location.

When they studied the mineralogy of the boundary in Denmark, Italy, Spain and Tunisia, the researchers found that the clay in the layer, found at varying depths or exposed at the earth's surface, does not contain "exotic" minerals that would be expected from an asteroid impact. Moreover, they found, the clay is not much different from the clays above and below the boundary in each location, and the layer's composition is different from place to place.

Rampino and Reynolds cite calculations by John O'Keefe and Tom Ahrens, both of Caltech, showing that most of the material thrown up during an asteroid impact would be solid fragments of mineral or rock, and that glassy particles would comprise only about 15 percent of an "impact-related boundary layer." The mineral analysis shows that most of the clay layer consists of smectite and smectite-illite, two clays known to be formed by the alteration of glassy volcanic ash. One cannot tell by studying only the clay minerals if the layer formed from volcanic ash or from material melted during an impact. Both kinds of material will form smectite, says Frank Kyte of UCLA. "The fact that they've done the mineralogy is important," he says, but he stresses that the findings do not disprove an asteroid impact.

O'Keefe says that a major impact could cause melted material to be ejected to high altitudes and that his models show that all of the material less than one micron could be melted. "It's very difficult" to predict the state of material below that size, he says. If an asteroid hit, one would expect different sites to exhibit a range of concentrations. "It's a very strong statement [by Rampino and Reynolds] to say that the material would be homogenous," he says. He and Ahrens find that up to 10 percent of the first material to exit the forming crater as an asteroid penetrated could consist of meteoritic material. As the crater grows, the fraction of meteoritic matter in the ejected material could fall to a small fraction of a percent. —*C. Simon*

Biosynthesis of a rabies vaccine

Scientists at Genentech, Inc. have completed the first step toward developing a genetically engineered rabies vaccine. They have synthesized the rabies virus glycoprotein, the protein that forms the virus's coat, by transferring the genes for its expression from the rabies virus to *Escherichia coli* bacteria. The bacteria synthesized both the full-length glycoprotein and a shorter glycoprotein that the researchers had devised, which excluded a portion of the protein's amino acid chain that might diminish the amount of the glycoprotein the *E. coli* produce.

Elizabeth Yelverton and colleagues of Genentech, South San Francisco, report in the Feb. 11 SCIENCE on the biochemical characteristics of the synthesized proteins. The natural glycoprotein is what causes the immunogenic response that raises antibodies against infection. Current rabies vaccines are produced by culturing the virus in a laboratory and inactivating it, but an effective synthetic vaccine for rabies-infected animals in the wild is still needed.

The researchers assayed the effects of both the full-length (G_{505}) and truncated (G_{427}) proteins by reacting them with rabbit antiserum and comparing these tests with those of natural glycoprotein reacted with antiserum. The original, insoluble fractions of the synthesized proteins were only 2 or 3 percent as effective as the natural glycoprotein per weight in binding themselves to antibodies. In order to increase the activity of the synthesized proteins, Yelverton and her colleagues used "a rather vigorous solubilization procedure." When the proteins were dissolved and retested, they became 30 times as active. The full-length glycoprotein, G_{505}, was about 90 percent as effective a reactant with antiserum as the natural product, and the truncated G_{427} tested at 70 percent.

The authors caution that they have not yet achieved a genetically engineered vaccine. They need to further purify the synthesized proteins and run more assays and animal inoculation tests to determine how well the proteins perform against live rabies infections. —*A. Chen*