Pain: Placebo Effect Linked to Endorphins

The mystery of why sugar pills and other inert "medications" can sometimes produce almost instant relief of severe pain has now been partially solved: As a result of expectations aroused by such placebos, some patients seem able to subconsciously activate their body's own pain-suppression system, releasing the recently discovered proteins called endorphins (SN: 7/23/77, p. 59). Discovery of this link is likely to expedite research into some of the body's regulatory systems and lead to more efficient treatment of pain.

Long before medicine became a science, the power of placebos was well established: The earliest witch doctors found that if a patient really believed that a treatment — almost any treatment — would work, it often did. Modern researchers quantified this finding several decades ago, demonstrating that a remarkably constant fraction of their patients — about one-third — received significant pain relief through the use of placebos.

The common explanation of this phenomenon was that the patients benefited "psychologically," that only their perception and not the pain itself had changed. But then came discovery of several physiological changes — such as improvement of stomach ulcers — under the influence of placebos, and the search began to see whether these treatments actually triggered some intrinsic curative or analgesic.

In the case of pain, the opportunity to test this hypothesis came with discovery of endorphins — literally, "the morphine within" — released by the brain and the pituitary gland. These substances appear to be modulators of the signals between nerve cells and act specifically on the same nerve receptors that are affected by morphine and other opiates. They not only relieve pain but also appear to help control body temperature and affect consciousness (SN: 7/28/78, p. 38). They have been implicated in acupuncture (SN: 11/20/76, p. 324). The pain-killing action of both endorphins and morphine can be blocked by a drug called naloxone.

Using naloxone as the tool to detect the presence of endorphins, a team of researchers at the University of California at San Francisco set out to investigate the effect of placebos on 50 patients recuperating from wisdom tooth extractions. In a double-blind experiment, some patients received the usual postoperative treatment with morphine, while others received naloxone or a placebo. The patients then reported changes in their pain, using a ten-point scale (from "no pain" to "worst pain ever").

As expected, about one-third of the patients receiving placebos reported a significant reduction of pain. Members of this group who were subsequently given naloxone reported a significant increase in pain — bringing their pain back up to almost the same level as that reported by patients who didn't respond to a placebo in the first place.

Since naloxone has no known effect by itself on these patients, the researchers conclude that the observed effect in the placebo-responsive patients resulted from that drug's ability to block the action of endorphins. Thus the conclusion is that endorphins have been produced in response to placebo treatment.

In a paper to be published this fall in LANCET, authors Jon D. Levine, Newton C. Gordon and Howard L. Fields suggest a striking interpretation of this result: that "variability among patients in reported pain intensity for a given pathology is due to differences in endorphin activity." Endorphin activity may prove a useful measure of pain and of placebo effects, allowing greater precision than patient reports of sensation.

Additional findings suggest even more possibilities for exploration of the relationship between placebos and the body's natural pain-suppression mechanism. No one has ever been able to pin down just what sort of person, under what circumstances, responds best to placebos. Perhaps the most common factor in successful cases is stress: A person who has just experienced a traumatic interruption of marriage, for example, is more likely to respond to a placebo. The authors say that stress appears to have played a significant role in their experiment. Similar investigations with experimentally induced pain in a laboratory — lacking the stress of a clinical situation — had produced only ambiguous results.

Investigations into the yet-unknown mechanisms by which placebos can activate endorphins are well underway, and the San Francisco researchers plan to publish further results soon. These studies may well reveal significant information about poorly understood functions of the brain and pituitary.

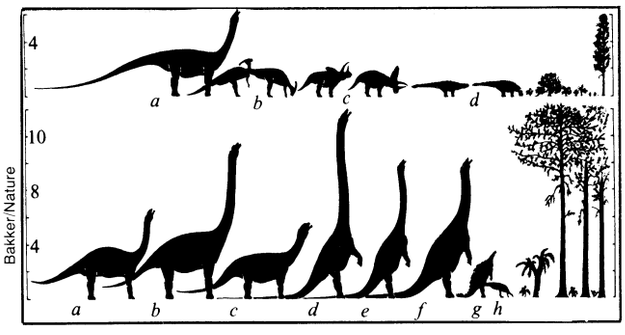
Levine summarized the potential impact for SCIENCE NEWS: "The importance of these results is that they shed new light on the body's own system for controlling pain. Further research along these lines should lead to more effective treatment of pain through a combination of methods, including drugs and psychological and physical treatment." □

Dinosaur tales: Flowers and a warm doom

Dinosaurs in their natural milieu provide a topic that will never yield to direct experimental investigation. Yet it's a tantalizing puzzle that continues to fascinate. How did those massive and powerful animals interact with their world? And why did they become suddenly (geologically speaking) extinct?

Fossil and geological records allow for structured speculation. Recently two novel ideas have been set forth. The first is from Robert T. Bakker, who is well known for his advocacy of the warm-blooded dinosaur (SN: 4/8/78, p. 218). He now suggests that the initial development of flowering plants was, at least in part, a direct result of dinosaur feeding habits. The eventual demise of the dinosaurs was the result of a short period of climatic warming, according to new information and a reappraisal of older data by Dewey M. McLean of Virginia Polytechnic Institute and State University. McLean warns that a modern warming trend, from human use of fossil fuels, over the next century or two threatens to initiate a Mesozoic-like period of worldwide extinctions.

Charles Darwin called the origin of flowering plants an "abominable mystery," because they seemed to appear abruptly without a clear hint of ancestry. Bakker now proposes that a swift change in dinosaur feeding behavior opened ecological opportunities for the rapid spread of those plants. An animal's height is most important in determining its selective pressure on vegetation, Bakker says. Tall animals, like a giraffe, will eat leaves, buds and fruit, but will rarely kill an adult plant. Short animals, however, concen-



Bakker/Nature

Jurassic dinosaurs (lower line) can stretch to nibble higher leaves than dinosaurs of the later Cretaceous period (upper line). Vertical scale is in meters.