Behavior

The subtle strength of placebos

What is the best way to study the effects of administering inactive substances, also known as placebos, on the pain-reduction mechanisms in the brain? Most researchers have compared groups receiving a placebo for pain to others receiving no treatment or those receiving pain medication. A few studies have included subjects who are given an infusion of placebo by a person hidden in an adjacent room to control for subjects' — and experimenters' — expectations of the outcome.

Jon D. Levine and Newton C. Gordon of the University of California at San Francisco report, however, that open and hidden doses of placebo reduce pain equally well. They suggest that investigators compare the two treatments with preprogrammed machine injections of placebo to better understand pain-reduction responses.

Levine and Gordon administered placebo, morphine or naloxone, a drug that blocks opiate action, to 96 dental patients as their surgical anesthesia was wearing off. Groups of 12 patients received open, hidden or machine-regulated doses of the substances.

The researchers note in the Dec. 20 NATURE that while self-reports of pain intensity decreased similarly in groups receiving open or hidden placebo doses, reported pain increased after machine-controlled placebo doses. Pain also increased after administration of naloxone under all conditions. Morphine, administered only through a machine in doses of 8 and 12 milligrams, resulted in pain decreases. Open and hidden placebo doses reduced pain to the same degree as about 8 milligrams of morphine.

The results suggest that the natural opiates in the brain that are hindered by naloxone play a role in the placebo response, says Levine. Other scientists have proposed that opiate action increases after dental surgery as a result of stress rather than placebo administration (SN: 12/3/83, p. 359). Further experiments with machine-injected groups may clear up the data, points out Levine.

More important, he adds, this experimental approach shows that subtle cues can elicit a pain-killing reaction even when the subjects cannot see the people administering the placebo. The cues are so subtle that subjects and experimenters are often not consciously aware of them, observes Levine. After his study, for example, patients were unable to identify any cues signaling when hidden doses were given or what substance had been administered.

More money for less medication

Efforts to find the lowest effective dose of antipsychotic medication for schizophrenic patients received a shot in the arm recently when the National Institute of Mental Health (NIMH) announced that it will fund a five-year, $5 million collaborative study of alternative treatments for schizophrenia. Researchers at four medical centers will compare the effects of continuous standard doses of this powerful medication to two other approaches: the continuous use of significantly lower doses and the short-term use of medication when there are early signs that schizophrenic symptoms are about to worsen.

Preliminary studies indicate that, in many cases, an antipsychotic drug known as fluphenazine is most effective at doses up to one-tenth of those usually prescribed (SN: 11/10/84, p. 297). Compared with patients on a standard dose, a majority of low-dose patients reported fewer schizophrenic symptoms and better social adjustment with their families.

The NIMH collaborative effort will include families in its analysis. Some families of schizophrenic subjects will be given basic information about the disorder and told of ways to deal with stressful reactions to it. Other families will take part in supervised sessions to help them apply this knowledge.

Environment

New clues to diesel exhaust's potency

Vehicle exhaust sampling has focused primarily on measuring a class of compounds called polycyclic aromatic hydrocarbons (PAHs), many of which cause cancer when metabolized in an animal's body. Gasoline-engine vehicles belch out two to three times the PAHs that equivalent-sized heavy-duty diesels do. However, diesel exhaust's mutagenicity — perceived as a rough clue to its possible carcinogenicity — has, per microgram (μg) of particulates, generally been much higher than the gasoline engine's. Reasoning that PAHs alone were not accounting for the higher diesel mutagenicity, Takashi Handa and colleagues at Science University of Tokyo in Japan decided that more and stronger mutagens must be present in diesel exhaust.

The researchers sampled emissions from the exit sides of two long tunnels — one having an average uphill grade of 0.4 percent, the other a downhill slope of 1 percent — on the Tomei Expressway, one of Japan's busiest. The selected grades required vehicles — most of which cruised by at speeds close to the posted 50 miles per hour — to operate under engine load conditions that were, respectively, higher and lower than average. This study, sponsored in part by a cancer research grant from Japan's Ministry of Health and Welfare, suggests what it is that accounts for the diesel emissions' potency.

Reporting in the December ENVIRONMENTAL SCIENCE AND TECHNOLOGY, the researchers found that emission levels, as measured in micrograms per hour, per vehicle, were higher for heavy-duty (truck and bus) diesel engines than for light-duty gasoline-engine passenger vehicles — even when displacement differences between engine types were taken into account. Clues as to why diesels were higher came from measurements not only of PAHs but also of a host of other carcinogenic or mutagenic compounds, such as direct-acting mutagenic NPAHs (formed by the exposure of PAHs to nitrogen oxides), heterocyclic hydrocarbons (AHHs) and polycyclic quinones (PQu's) that may form when PAHs are acted upon by oxygen in an engine's hot environment. The chemists discovered that, although on a μg/hour basis the gasoline vehicles produced about twice the PAHs and benz-anthrones (derived from a PQu compound) that diesels do, the diesels produced 10 times more NPAHs and up to 10 times more AHHs for a particulate mass totaling 14 times that issued by gasoline engines. And particulate emissions were generally higher for all vehicles under the high-load conditions.

How algae may protect crops

Though chemicals that kill insects or discourage their ravenous appetites occur naturally in many terrestrial plants — caffeine being among the most recently identified (SN: 10/13/84, p. 229) — few such compounds have been isolated from marine plants or algae. But a chance observation by three Egyptian chemists will now add brown algae *(Dictyota dichotoma)* to the growing list of natural pesticide sources.

While a crude mixture of volatile chemical components extracted from the algae through steam distillation of fresh plants showed some insecticidal effect on houseflies, cotton leaf worms and rice weevils, the mixture proved especially effective in curbing the appetite of the cotton leaf worm. University of Cairo biochemists Mahmoud Abbas Saleh and Nadia M. Abdel-Moein, together with Nagy A. Ibrahim of the Egyptian agriculture ministry's research center in Giza, report on their finding in the November/December JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY. Gas chromatography and mass spectrometry identified the most active appetite suppressant as an azulene-based compound with the unwieldy name 1-(1, 3, 4, 5, 6, 7-hexahydro-4-hydroxy-3, 8-dimethyl-5-azulenyl) ethanone. What led the researchers to look for this compound in the first place was the observation that houseflies selectively ignored this species of algae when it was left for four days to air dry.