Letters

Naloxone Antagonism as Evidence for Narcotic Mechanisms

In her excellent Research News article, "Analgesia: How the body inhibits pain perception" (4 Feb., p. 471), Jean L. Marx reports on recent data which have been interpreted as indicating that acupuncture analgesia is mediated by the same neural mechanisms as those participating in the analgesia resulting from the administration of narcotics. The inference that acupuncture and narcotics share common neural processes is based primarily on the observation that the analgesia produced by both procedures is antagonized by naloxone, a drug commonly represented to be a specific antagonist of narcotic effects.

In view of the considerable public interest that acupuncture analgesia has generated, statements about its possible mechanisms of action should be based on more definitive lines of evidence. As Marx points out, recent work in our own and other laboratories suggests the existence of at least two physiologically distinct mechanisms capable of modulating responses to painful stimuli. Such demonstrations highlight the need for rigorous research strategies to distinguish narcotic from nonnarcotic mechanisms of analgesia.

Several considerations suggest that conclusions are premature regarding the commonality of neural mechanisms mediating acupuncture and narcotic analgesia. First, there is a growing body of evidence which makes suspect the contention that naloxone antagonizes only the effects of narcotics by preventing the binding of narcotic drugs to their specific receptors. Naloxone has been shown to antagonize the analgesic consequences of a variety of nonnarcotic manipulations. In addition to acupuncture, these manipulations have included the administration of nitrous oxide, lanthanum, cannabinoid analogs, and acetylcholine, as well as electrical stimulation of the brain (*1*). Aside from studies using analgesic measures, naloxone has been shown to interact with a variety of other effects. For example, naloxone has been reported to antagonize fatigue in the guinea pig ileum (which is commonly used to study narcotic action), in addition to antagonizing other responses produced by cholinergic agents, glutamate, and *d*-amphetamine (*2*). Alternatively, since excitatory and facilitatory effects of the drug even at modest doses cannot be excluded (*3*), it is also possible that certain cases of naloxone antagonism could result from activation of some opposing system rather than from pharmacological competition for narcotic receptor sites. We wish to point out, however, that we do not rule out the possibility that some or all of the above effects are mediated by interactions with endogenous opiate-like substances or their receptors.

We wish to emphasize, also, that in certain situations naloxone antagonism may be a necessary condition to infer activation of a narcotic system, since to our knowledge naloxone has not failed to antagonize narcotic analgesia. Thus experiments in which naloxone does not antagonize the effects of an analgesic manipulation at least provide evidence against involvement of a narcotic system.

To summarize, it has long been recognized in careful pharmacological studies that naloxone antagonism is necessary but not sufficient to infer a narcotic mechanism of action. While the need for additional lines of evidence has not been universally ignored (*4*), we feel this approach should be given more explicit attention in current behavioral and physiological research.

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Myelin Basic Protein: Clinical Trials

We wish to correct an impression that may be given in the Research News article of 11 March (p. 769) about multiple sclerosis by Thomas H. Maugh. Contrary to a statement in the article, a clinical trial of myelin basic protein in multiple sclerosis patients has not begun at the University of Toronto.

A trial has been proposed to clinicians in the neurology program at the university; however, the protocol is still in the developmental stage, so that a date for commencing a study cannot be forecast.

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Uranium Resources

The long-run marginal cost of uranium oxide (U_3O_8) is a key factor in major policy questions regarding the development of nuclear energy. Current debates about the economic desirability of breeder reactors, spent fuel reprocessing, and plutonium recycling all hinge critically on the question of how much uranium can be produced at what cost. Advocates of the new technologies argue that rapidly growing demand and limited resource supplies necessitate prompt action to permit continued use of nuclear fission energy (*1*). Critics argue that demand has been overstated and supply understated and, consequently, that there is no need for an early decision to undertake recycling or reprocessing or to proceed more rapidly with breeder development (*2*).

There *is* a great deal of uncertainty about the supply of uranium. Very large amounts of high-cost uranium (forward costs of more than $125 per pound of U_3O_8) evidently exist in the Tennessee shales and Conway Granites. The relevant policy question is, however, whether substantially more low-cost ores (forward costs of less than $50 per pound) remain unexploited (*3*). M. A. Lieberman, in his article "United States uranium resources—an analysis of historical data" (30 Apr. 1976, p. 431), utilizes the so-called "Hubbert" hypothesis to estimate the ultimate recoverable uranium resources available from the western sandstone deposits, where most domestic production has occurred in the past. Lieberman characterizes this approach as "prudent" and the resulting estimates as "objective" and concludes that the