

in the central amygdala and other limbic sites—has taken place after long-term cannabinoid administration. If unmasked by administration of a cannabinoid antagonist, the neuroadaptation can be observed at the cellular, neurochemical, neuroendocrine, and behavioral level. The effects are qualitatively the same as those we have observed during withdrawal from cocaine, ethanol, and opiate use; whether they are quantitatively the same remains to be explored. Nonetheless, these data raise the specter that the same changes are occurring with long-term high-dose cannabinoid receptor activation.

By no means does the lack of cannabinoid self-administration in rats invalidate these data. Many behavioral and pharmacological properties of a drug contribute to abuse liability, none of which is predictive by itself. Moreover, as was the case with ethanol and nicotine, valid animal models of self-administration often take a long time to develop. Neither does the argument that rats “do not like cannabis” hold up to close scrutiny. While anxiogenic and aversive effects are indeed common after high doses, low doses of psychoactive cannabinoids not only activate brain reward mechanisms, but can produce conditioned place preference and induce anxiolysis in rats (1). In fact, two of the common neurobiological elements associated with addiction—activation of the brain reward system upon short-term administration and activation of brain stress systems during withdrawal from long-term administration—have been demonstrated with cannabinoids. In particular, the convergence of the effects of stress and drugs of abuse (2) is highly informative for the understanding of factors that maintain drug addiction or lead to relapse. Enhanced behavioral and neuroendocrine reactivity to stress is not only a reliable index of vulnerability to psychostimulant self-administration in laboratory animals (3), but approximately 75% of relapse in human drug abuse takes place in situations of stress, conflict, and social pressure (4). It must be of concern, therefore, that in vulnerable individuals continuous high-dose use of THC can engage stress systems and thereby augment susceptibility to future drug abuse.

Statistics show that 9% of THC users become substance dependent using DSM-III-R criteria (5), and a recent study revealed the same incidence (9%) of presentation of a withdrawal syndrome in a large sample of users (6). That study confirms that despite the slow elimination of THC, a distinct behavioral cannabinoid withdrawal syndrome can be observed in humans. In the history of drug abuse re-

search, significant motivational signs of withdrawal have often been overlooked because of a preoccupation with physical withdrawal symptoms that may be largely irrelevant (7). When vulnerable populations are explored, cannabis dependence becomes more apparent. In a recent structured assessment of 229 substance-dependent adolescent patients who had serious conduct problems, more than 70% met criteria for cannabis dependence. More than two-thirds of the cannabis-dependent individuals complained of withdrawal, and one-fourth of the cannabis-dependent persons reported using cannabis to relieve withdrawal symptoms (8).

Because of the substantial political, social, and public health implications, we could not agree more with admonishments to “let us take all due care in cannabinoid science.” However, this goes for those on either side of the issue. Inflammatory rhetoric invoking visions of law enforcement “crackdowns” on marijuana users as a result of this research does not serve the need for dispassionate and scientifically objective debate about cannabis. The conclusions drawn by us follow from the data and stand independent of the issue of marijuana’s legal status. There is an urgent need to advance the scientific understanding of both the “good and evil” that may be lurking in this drug. In this endeavor, clinical, epidemiological, and neurobiological studies all have their rightful place.

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Hawksbill Turtles in Cuba

In his article “Turtle project can’t outrun bureaucracy” (News & Comment, 20 June, p. 1785) Jeffrey Mervis states that Cuba is seeking limited trade of hawksbill sea turtles on the grounds that its population is self-contained. The Cuban proposal at the 10th meeting of CITES (Convention on International Trade in Endangered Species of Flora and Fauna) in Harare did not say that hawksbills in Cuban waters were a closed population; it argued that the data were consistent with some hawksbills being relatively residential in those waters.

The main grounds for the Cuban proposal were that hawksbills in its waters were well managed and that the proposed quota for trade was conservative, almost a tenth of the harvest levels that had been sustained for more than two decades. These are more important matters than whether some turtles cross international boundaries. However, to the extent that such movements do occur, one would think that other Caribbean nations would give Cuba some credit for having reduced its harvest by about 90%. And, in fact, although the Cuban proposal did not obtain the two-thirds majority necessary for CITES approval, more parties voted for it than against it.

Sustainable use as a conservation method has been effective with vicunas and crocodiles; it should be given a chance with sea turtles.

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