Psychological and Psychiatric Consequences of Opiates

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History
The powerful effects of opiates have been well known from the dawn of human existence. The poppy art of Assyria from 4000 B.C. to the increasing popularity of heroin in present times illustrates the tenacious hold opiates have on our lives. Opium, the Latin derivation of the Greek opo, meaning juice, has long been associated with sleep. Opiates are the natural alkaloids of the opium poppy (Papaver somniferum). They include such substances as codeine and morphine. Narcotics are a broader group of opiate-like drugs which include synthesized substances like methadone, fentanyl, heroin, and meperidine. However, “narcotics” is often loosely used in common parlance to refer to any illicit drug.

The bulk of human experience with opiates lay mainly in eating or smoking raw opium. The era of patent medicines (late 19th and early 20th centuries) brought us new concoctions such as “laudanum,” a mixture of opium and alcohol. Such medicines were widely available and unregulated before the Pure Food and Drug and the Harrison Narcotic Control Acts were passed by the U.S. Congress early in the 20th century. Compared with other medical treatments at the time (bloodletting, high doses of laxatives, calomel, and radium water), “[t]he sweet effect of opium in fevers, inflammatory disease, delirium tremens, insanity, depression, convulsions, poisoning, hemorrhages, and venereal disease must thus have appeared in many cases superior to [these alternatives]” (Musto, 1987, p. 198). These tonics were popularized and are frequently associated with noted individuals such as Elizabeth Barrett Browning, Samuel Taylor Coleridge, and Thomas DeQuincey. DeQuincey, who describes his experience with opium in Confessions of an English Opium Eater, was an avid supporter of opium use and at one time used more than 20 grams of opium per day (Karch, 1989).

Three momentous events during late 19th century brought new dimensions to our experience of opiates: (1) the invention of the hypodermic syringe, (2) isolation of specific alkaloids from raw opium, and (3) the synthesis of heroin from morphine. These events brought us the ability to isolate pure alkaloids, synthesize more potent drugs from them, and directly administer these drugs into the circulation, bypassing both digestion and “first-pass” metabolism. The ability to rapidly deliver a large amount of potent opiate drug to
the brain by injection greatly increases addiction liability.

Even though regular opiate use leaves the user anxious, dysphoric, and at risk for the so-called pains of withdrawal, the powerful reinforcing effects of opiates in spite of the many risks of use encourage continued self-administration (Gold, 1995). Public health concerns began to mount as the numbers of persons addicted to opiates rose in the late 19th century. Our recent experience with crack cocaine parallels the American experience with opiates 100 years ago. Today, we have seen a time of toleration of cocaine use during the 1970s and early 1980s when cocaine users were mainly young professionals using the drug “recreationally” or to “enhance performance.” The invention of crack cocaine brought our association of the drug to poor, inner-city African Americans. When this occurred, public opinion of cocaine came to view cocaine as a public anathema. Opiate use similarly grew rapidly in the United States during a time of drug toleration.

Pharmacology

Use in Medicine

The use of opiates as a therapeutic agent is as old as the drug itself. Opiates have probably always been used for their analgesic and anesthetic qualities. Laudanum was an invention of Paracelsus in the early 16th century; he knew that sleep and analgesia are part of curing disease. Freud was initially a popular supporter of opium as a near-panacea; he later advocated cocaine (see Karch, 1989). The most important property of opium and its alkaloids is their unparalleled ability to relieve pain. They have contributed significantly to the progress of modern medicine by allowing patients to tolerate otherwise painful procedures and to live with previously crippling illnesses. They also have been and still are used as antitussive, antidiarrheal and antiemetic agents. Modern research in molecular biology has elucidated the important role that opioids play in homeostasis. Discovery of opioid receptor antagonists allows us to study the role that opioids play in regulation of rewarding activities including eating, drinking, and copulation. In addition, the expanding list of opioid receptor subtypes has increased our understanding of the role that opioids have in the mechanisms of drug reinforcement. Opioids are postulated to modulate reward in continued self-administration of cocaine, marijuana, nicotine, alcohol, PCP, and other drugs.

Mechanism of Action

Opiates bind to specific sites in the brain and body that cause the numerous and seemingly diverse effects (Hughes, 1975; Pert & Snyder, 1973; Simon, Hiller, & Edelman, 1973). The effects of opiates on diarrhea, cough, mood, and pain can now be explained as a result of binding to specific sites in central and peripheral locations known to involve control of these events (Watson, Akil, Khachaturian, Young, & Lewis, 1984). Identification of these receptors led to the discovery of naturally occurring endogenous substances that possess opiate activity (Childers, 1991; Cox, Goldstein, & Li, 1976; Mains, Eipper, & Ling, 1977). The first substances discovered were called endorphins, a contraction of “endogenous morphine.” Discovery of endorphins led many to question why every vertebrate and some invertebrates possess opioid receptors, whether endorphins are neurotransmitters or hormones (Mains et al., 1977), and why authentic morphine and codeine have been found in the mammalian nervous systems (Donnerer, Oka, Brossi, & Spector, 1986).

Opioid drugs exert their actions by binding to receptors on cell membranes of neurons and other cells (Koob & Bloom, 1988). These opiate receptors are diverse in type and function. They have been divided into mu, kappa, delta, and lambda subtypes. These receptors are thought to be a part of the G-protein receptor super-family. These receptors, when activated, stimulate GTPase activity and are naloxone sensitive. Both GTP and sodium have been demonstrated to decrease agonist but not antagonist binding. The agonists inhibit adenylyl cyclase; a GTP-dependent and pertussis-toxin-sensitive effect. A summary of the purported