BOB SISKO

NIDA's search for new cocaine treatment medications has thus far focused in just two areas: agonists and antagonists. This is logical, given that they represent the dominant treatment paradigms in NIDA's toolbox. They form the very foundation upon which NIDA's theory of addiction treatment rest. Therefore, I would like to take a few minutes to discuss these two theories, and their application, from the addict perspective.

Remarks to the 56th meeting of the National Institute of Health's National Advisory Council on Drug Abuse, January 26th,1994

AS YOU KNOW, I am with an organization called ICASH, the International Coalition for Addict Self-Help. Our members and constituents are addicts and former addicts. Let me make this perfectly clear. We are not an anti-drug organization. In the area of drugs, we are pro-choice. We believe it is the right of the individual to self-medicate. We recognize however, that when an individual becomes addicted to drugs, he or she no longer has free choice. We believe that any person addicted to drugs who wishes to be free from that addiction should be able to have that choice. How does the paradigm relate to the issue of choice?

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Antagonists have never been popular among addicts. Trexon and other antagonists have never found acceptance among users. When people choose to use drugs, they don't want to have the pleasurable effects blocked. Though Trexon took years to develop, and no doubt cost millions, only a handful of addicts are willing to take it. What good is a medication if the person for whom it is intended refuses to take it? I sincerely doubt that the development of a cocaine blocker would have any real impact upon the problem (of cocaine addiction).

Now, the agonists are a different matter. We applaud NIDA's efforts to create a wide range of new cocaine analogs. I am especially excited to hear you are working on a cocaine analog with a longer duration of action. One of the main problems from cocaine use is that the effects of coke are so short lived. Addicts must use continually in order to maintain the high. I predict that a potent new long lasting analog would be popular among addicts, but might quickly end up on the streets, where it could be used as "cut", mixed in with cocaine to make the high longer-lasting. After all, the same illicit chemists who currently manufacture both powder and crack cocaine by the ton could easily manufacture NIDA's new cocaine analog as well.

Next to the idea of across-the-board legalization, the idea of developing a new stimulant compound which could be used as a medication for cocaine dependent people, much like methadone is used for heroin addiction, is probably the most radical idea around. As such, I support it. Though the idea would be popular among addicts, somehow, I don't think it will play in Peoria.

A third option

The problem with the yin-yang agonist-antagonist paradigm is that it excludes all other options. It acts as a blinder, obscuring a wider vision upon the treatment horizon. A third option exists, one that is neither agonist nor antagonist. It is that of the "interrupter", and represents an entirely different category of treatment modality. In its search for medications to treat cocaine dependency, NIDA has either overlooked or ignored the idea of the interrupter as a potential treatment option.

Nearly two years ago, NIDA's Medications Development Division (MDD) began the Biogenic Amine Transporter Project, the so-called BAT Project, to develop potential cocaine treatment agents. Since increased

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dopamine neurotransmission has been shown to be associated with the reinforcing effects of cocaine, the BAT Project is looking at agents that act at the dopamine transporter. Despite the fact that Broderick (1992) reported that ibogaine reduced cocaine-induced dopamine release in the brain's nucleus accumbens, ibogaine has been excluded from the BAT Project. It doesn't fit the mold. As reported by Woods (1990), it is neither an agonist nor an antagonist.

Dutch research

The Dutch, however, were not blinded by NIDA's dominant paradigms. Research supported by the European Addiction Research Institute and Erasmus University in Rotterdam sought to determine the potential anti-addictive properties of ibogaine utilizing the cocaine self-administration model in rats. The results indicated that "ibogaine or its metabolite(s) is a long-lasting interrupter of cocaine dependence, which supports similar observation from uncontrolled clinical studies." (Dzolic, 1993)

Part of the problem is that while terms like agonist and antagonist are well understood, there is no clear understanding or consensus among professionals as to what constitutes an interrupter. Just what is it, how can it be expected to work, how does it work, and what is its importance?

In the case of ibogaine, the interruption of drug use begins immediately upon administration of the substance. Once ibogaine is administered, the compulsion to use drugs is immediately abated, and the interruption has begun. The subject becomes calm and relaxed for the duration of the treatment, and is able to detoxify without discomfort or craving for drugs. Ibogaine is quickly metabolized yet its action lasts somewhere between two and three days. Its effect as an interrupter continues long after the compound has left the body. This was noted by Stanley Glick (1991), who studied the effects and after-effects of intravenous morphine self-administration in rats. He observed "the aftereffect occurred at a time when ibogaine should have been entirely eliminated from the body and when there was no obvious indication of ibogaine exposure."

While Glick and Dzolic reported respectively on the inhibitory effects of ibogaine on self-administration of both morphine and cocaine in rats, ICASH and our European counterparts have firsthand experience not with animals, but with people. The results mirror one another. We have found, in the majority of cases, a clear and observable interruption of drug use and drug seeking behavior, for significant periods. How long are those periods? How long can an interrupter be expected to remain effective?

The answer is elusive. One can perhaps compute an average, after statistical evaluation of data. But the key is not to be found with the medication, but with the individual. What the medication does is to give the addict a kind of GRACE PERIOD after the detox stage, a hiatus from the incessant cravings which normally follow detox. It removes the compulsion, and replaces it with choice.

Results

Although I know of instances where individuals have returned to drug use immediately after treatment with ibogaine, they are not representative. There are also those who were treated with ibogaine and subsequently gave up drugs completely. But they, too, are a minority.

In the majority of cases with which I am familiar, those treated remained free from addiction for periods ranging, on average, from three to six months. During this time, the addiction is in check. It has gone into remission. All of a sudden, the person's life no longer revolves around the acquisition and use of drugs.

Many take this opportunity to attempt to put their lives back in order. Whether or not the individual will return to drug use, and eventually become re-addicted, has more to do with how effective the individual is in rebuilding his or her life during this grace period than with ibogaine itself. (The aftereffects of which we speak are, after all, limited in duration.)

When relapse occurred, our clients recognized it and sought re-treatment. Those who have been treated with ibogaine express a clear preference for it when it comes to re-treatment. There is currently widespread interest and acceptance among addicts for ibogaine as a treatment. It is the only treatment discovered and developed by addicts and ex-addicts.

Treating people two, three, or even four →

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times a year with ibogaine makes more sense than treating them every day with a substitute stimulant, the development of which is a declared goal of MDD's BAT Project. I believe that the development of either a cocaine blocker or a stimulant substitute for cocaine users is a futile, misguided approach which is doomed to failure. It will cost millions, take years to develop, and is almost guaranteed to fail. As such, it is little more than a smokescreen which gives the impression that new and meaningful treatments are being developed. Well, it's the same old stuff, presented in a different package, a repeat performance of yesterday's failures.

Finding and developing a pharmacotherapy capable of combating cocaine dependency is a difficult and challenging task. There is no real precedent, because there is no FDA-approved treatment for cocaine abusers, despite the fact that studies on cocaine abound.

In perhaps the most well-known cocaine study of all time, made famous by the Partnership for a Drug Free America, rats who were given free access to self-administered cocaine did so to the exclusion of all else, including food, water, and sex. Such unrelenting behavioral patterns are extremely difficult to overcome. However, in his work on the inhibitory effects of ibogaine on cocaine self-administration in rats, Dr. Dzolic reported a significant decrease in cocaine use for prolonged periods after administration. He identified ibogaine as a potential long-lasting interrupter of cocaine dependency. That sounds like a breakthrough to me, and to a lot of folks out there also. Dzolic came to Keystone, Colorado in 1992 to present preliminary data to a joint meeting of the Committee of Problems of Drug Dependence (CPDD) and International Narcotics Research Conference (INRC). Afterwards, he flew to Washington, DC to address the FDA advisory panel which met last August. Apparently, nobody at the BAT Project got the message.

The Interrupter

The compound they seek, one capable of altering conditioned patterns of cocaine abuse, has already been identified. Since it already exists, it doesn't have to be invented. That will cut years of development time. What's more, NIDA has significant supplies of ibogaine on hand for research. So what's the problem?

When a new plateau of knowledge is reached by enough people, the effects are irreversible. It cannot be ignored, and it won't go away, any more than atom bombs or home computers will disappear. The new word which has recently made its debut into the language of addiction science is INTERRUPTER. Pick it, and you will go to the head of the class. Ignore it, and you will fail. Guaranteed. •

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