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## Reply to Stolerman and Jarvis

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We thank the editor for again allowing us the opportunity to participate in this important scientific debate and to respond to critics of our position. Stolerman and Jarvis (S&J) accurately described the difficulty in debating a topic with no generally agreed upon definition. The 1988 US Surgeon General's Report (USDHHS 1988) used one set of criteria to "prove" nicotine is addictive. West (1992) offers no clear definition, content with the concept that any behaviour that may be difficult to change should be labeled "addiction". Hughes (1993), S&J, and Dr. Kessler, the US FDA commissioner (1994) all offer additional definitions. The futility of debating an amorphous concept that cannot meaningfully differentiate the pharmacological and behavioural effects resulting from the abuse of heroin, crack, alcohol and barbiturates from the effects of consuming coffee, chocolate, cola and cigarettes should be obvious to anyone willing objectively to view the data. Apparently this is not the case. That is precisely why we wrote our original paper (Robinson and Pritchard 1992a), evaluating the clear distinctions outlined in the 1964 Surgeon General's Report (USDHEW, 1964) between addiction and habituation. We see nothing in the arguments of Hughes (1993) or S&J that alters our position.

Our original paper has been characterized as a series of "straw man" arguments (Hughes 1993), chosen for the ease with which we could tear them down. Our paper was written as a critical evaluation of the primary criteria, arguments and analogies used by the editors of the 1988 Surgeon General's Report (USDHHS 1988) to "prove" that nicotine is "addictive". We did not "choose" the criteria or the arguments presented in that report. The fact that the case for nicotine "addiction" crumbles upon close examination mixed with a little common wisdom serves as testament to the inherent weakness of the addiction proponents' arguments, not to the selection of the criteria we examined.

We offer the following in direct response to S&J:

**Definition:** Our critics realize that the distinctions we raise are meaningful and supported by the data, so we are instead accused of using "outdated" definitions of addiction and habituation. The addiction proponents offer a plethora of "definitions" that cannot distinguish crack smoking from coffee drinking, labeling as addictive any behaviour that may be difficult to change. As we stated in our "Reply to West" (Robinson and Pritchard 1992b) distinguishing addiction and habit highlights "important physiologic, pharmacologic and behavioral differences between smoking/nicotine and classically addicting drugs".

**Intoxication:** The concept of behavioral intoxication, disruptions in cognitive and motor performance, has been a defining feature of addictive drugs for decades. This was documented extensively in our original article because it serves as our key argument as to why smoking/nicotine and caffeine should be distinguished from classically addicting drugs. Since the addiction proponents realize that nicotine does not produce intoxication, they simply dismiss this key concept as not "relevant".

The data are clearly in support of our position in this area. Nicotine facilitates cognition and performance while the classically addicting drugs impair cognition and performance (i.e., intoxicate). We also take strong exception to the statement that under this distinction cocaine would be considered habituating rather than addicting. Prolonged abuse of stimulants can lead to a psychotic state resembling paranoid schizophrenia, definitely a form of intoxication. In contrast, smokers can smoke for decades with no evidence of cognitive or behavioral disruption.

**Compulsive nature:** The addiction proponents' views here are perplexing. Given the extent of current

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anti-smoking campaigns, is it any wonder that when smokers are asked "Would you like to quit?" they answer in the affirmative. To answer otherwise to a health official or service taker implies ignorance or certainly a "unique" way of thinking. Yet the addiction proponents accept these reports as "evidence" that smokers cannot give up their habit. How do they know smokers cannot quit? Because they said so! In contrast, the reports of the 43 million ex-smokers in the US who have successfully quit, 90% + without aid, are dismissed by S&J as "anecdotal". Labeling smoking as a habit does not imply that all smokers can easily quit. Quitting smoking requires a fundamental change in behaviour that may be difficult to accomplish and may require several tries to succeed.

A recent editorial in the Scripps Howard News Service addressed this issue quite eloquently. Leonard Larsen (1994), an ex-smoker wrote:

"By pretending that smokers are helpless addicts, slaves to a tobacco conspiracy, drug addicts unable to control their own actions, the addiction-conspiracy peddlers help make a very simple decision to stop become impossible.

There's actually no conspiracy but there's a secret about smoking.

To quit, you have to decide you want to quit.  
Then you quit".

In our view the addiction proponents cannot differentiate "can't quit" from "won't quit", seriously damaging their "compulsion" argument.

**Stimulus properties:** S&J contend that studies of "brain reward systems" demonstrate that "the psychopharmacological profile of nicotine has many points of extremely strong resemblance to classic addictive substances". They refer to the release of mesolimbic dopamine in response to nicotine administration and to reports that under limited circumstances nicotine can serve as a reinforcer in self-administration studies. This again highlights the danger of "argument by analogy". Just because certain general similarities at the neuronal level exist among compounds does not establish that these compounds result in similar cognitive or behavioral effects (see Bozarth 1994). Somehow the addiction proponents accept these general similarities as "evidence" but dismiss the critical differences we point to between nicotine and classically addicting drugs as unimportant.

**Cognitive enhancements:** The behavioral effects of smoking/nicotine are fundamentally different from those of addicting drugs. Nicotine facilitates cognition and motor performance while the classically addicting drugs impair cognition and performance (that is, they are intoxicating). S&J cannot recognize this incompatibility without surrendering to our viewpoint.

**Withdrawal syndrome:** In 1964 the US Surgeon General's report stated that following smoking cessation no

characteristic abstinence syndrome occurs, but that some people experienced a gamut of mild symptoms that might include increased nervous excitability, restlessness, anxiety, drowsiness, and difficulty concentrating. These symptoms are remarkably similar to what S&J reference as the nicotine withdrawal syndrome. We agree with the conclusion of the 1964 report: that these symptoms represent what would be observed "in any emotional disturbance secondary to deprivation of a desired object or habitual experience." In other words, abrupt changes in behavior can be accompanied by changes in mood. In addition, we would point out that a well-defined physical withdrawal syndrome occurs in the two to three cup a day coffee drinker who suddenly stops drinking coffee. Should we equate caffeine with cocaine and heroin because of this?

In sum, while certain vague similarities may exist, the critical cognitive and behavioral effects of smoking/nicotine are fundamentally different from those of classically addicting drugs. We are reminded of the fictitious King Dogma, who decreed all those lacking 20-20 vision to be blind, consigning terms such as "myopic" to the archives of history. Rather than consigning the term habituation to the same archives, we suggest it be resurrected to impart meaning to the word "addiction" and save the concept of addiction from increasing trivialization. True addiction to intoxicating drugs is a devastating phenomenon that should be distinguishable from eating chocolate, drinking coffee and colas, tobacco use and even eating carrots (Cerný and Cerný, 1992).

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The major evidence for nicotine's addictiveness resides in the tenacity of the smoking habit. In most smoking cessation studies over 80% of people who initially quit have relapsed by the end of a year. As Stolerman and Jarvis (this issue) indicate, most beginning smokers rapidly become heavy smokers and very few, probably less than 5%, smoke less than five cigarettes a day (dubbed "chippers" by Shiffman 1989). By contrast, alcohol is used casually by most people with only about 7% of regular users of alcohol considered alcoholic. The tendency towards escalation with cigarette smoking is extremely strong and certainly must be considered an important component of the addiction liability of cigarettes as it is with heroin and cocaine.

For some time now Warburton (1989a, b, 1992) and, more recently, Robinson and Pritchard (1992) have been willing to oppose the tide of public opinion that nicotine and cigarette smoking is addicting. In fact, it takes some intellectual gymnastics to argue that nicotine is not addicting; however, by championing an unpopular viewpoint Warburton and colleagues force those of us who feel that cigarette smoking is a dependence disorder (American Psychiatric Association, 1987) to examine our concepts more thoroughly. A good controversy sharpens the wits.

The original Surgeon General's report of 1964 was pretty soft on nicotine (USDHEW 1964). This report argued that smoking was an habituation and not an addiction. At that time social pressure in the United States was much friendlier to cigarette smoking than it is now. The writer of that section of the Surgeon General's Report was Professor M.H. Seevers of the University of Michigan, an authority on heroin addiction. However, Seevers, like many academics of his generation, was a cigarette smoker himself and not

likely to stigmatize himself with the pejorative title of "addict." It was not until 1988 that the Surgeon General's Report finally recognized that nicotine was addicting.

Various attempts have been made to tighten the definition of addiction or of its synonym, "dependence". The World Health Organization's definition is semi-operational in that the definition contains somewhat less controversial terms than the definitions. It includes such terms as compulsion, psychic, and discomfort, which are themselves ambiguous and require further definition. Jaffe (1990) writes "the term *addiction* has been used in so many ways that it can no longer be employed without further qualification".

We would define drug addiction as follows "An individual is addicted to a drug if he/she exerts significant effort to obtain the substance, ingests, injects or inhales it on a daily basis and exhibits a withdrawal syndrome when deprived for 1 day or more". Physiological withdrawal signs are necessary to diagnose addiction or dependence on a drug. By this definition nicotine is addicting.

Abrupt cessation of smoking will result within 24 h in a significant decrease in heart rate and other more subtle manifestations of sympathetic nervous system suppression. There may be increased appetite and weight gain, as well as increased somnolence. These signs are all indicated as choices in the DSM III-R and DSM IV list of nicotine withdrawal signs and symptoms. Of course, there are individual differences in reaction to withdrawal which may be a function of inborn or developmental distribution of cholinergic nicotine receptors and a baseline sympathetic tone.

It is hard to ignore the fact that Robinson and Pritchard work for a large tobacco company, R.J. Reynolds. It would be very surprising to find an employee of a tobacco company, under siege by anti-smoking advocates, who would be willing to describe smoking as addicting, not to mention as a dangerous cause of cancer or heart disease risk. But this point is an

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*ad hominem* argument about their logic, guilt by association, and should therefore be set aside.

Much of the hazard from cigarette smoke resides in the tar, especially carcinogenic potential. But nicotine alone is not totally benign, since it may cause excessive stimulation of the sympathetic nervous system; release of catecholamines can exacerbate cardiovascular disease. There is considerable evidence that nicotine can produce or increase cardiac dysrhythmias. In doses only a little higher than those habitually inhaled by cigarette smokers it will cause nausea and vomiting.

Daily acute tolerance occurs and is lost every night. Long lasting chronic tolerance develops to nausea and vomiting and possibly to other effects. There is no longer any doubt that a specific nicotine withdrawal syndrome exists. There are individual differences in the strength of various components. The idea that sudden cessation of long term nicotine use will be followed by a withdrawal syndrome is no longer controversial. As Stolerman and Jarvis point out, nicotine replacement by nicotine gum or nicotine patch has been shown to alleviate withdrawal symptoms and enables smokers to abstain more successfully during the period in which the replacement occurs.

As Stolerman and Jarvis have noted, the exact conditions under which a drug is administered or self administered will have a strong influence upon its reinforcing properties. Thus, nicotine apparently has a combination of both rewarding and aversive properties and it takes clever scheduling and appropriate routes and rates of administration to achieve the optimal positive reinforcing effect in animals. It has been difficult to engineer animal self-administration procedures for nicotine that seem to be effective. Only a moderate degree of success in inducing monkeys to smoke has been obtained (Jarvik 1967; Deneau et al. 1969; Ando and Yanagita 1981) Goldberg et al. (1989), by skillfully manipulating the scheduling, has succeeded in getting squirrel monkeys to self administer nicotine. Corrigan (1991) by similar techniques has induced rats to self-administer nicotine intravenously.

Human cigarette smokers are able to modulate the type of administration by first developing tolerance to many of the aversive effects of nicotine. They then deliver nicotine in large bolus rapidly into the circulatory system but always stopping below an aversive threshold level. This is a protective property of nicotine. The aversive components of a drug like cocaine are far less evident than those seen with nicotine thus cocaine is more dangerous.

It would be illogical to insist that nicotine's properties be identical to cocaine or to heroin for it to qualify as an addicting substance. After all, many of the properties of heroin and of cocaine are also considerably different. However, nicotine, cocaine and heroin share one property: they are actively sought and self-administered in regular frequent daily doses and abrupt cessa-

tion results in a drug-specific dysphoric withdrawal syndrome.

Stolerman and Jarvis point out that strong reinforcing effects of nicotine may not become manifest unless an interaction between nicotine and other organismic demands are met. Thus nicotine may (arguably) improve some cognitive abilities. Animals that are placed in a barren Skinner box with only an intravenous catheter that delivers nicotine and a lever are not likely to need significant cognitive enhancing effects. On the other hand, a mathematician, who is also a smoker, trying to solve a difficult problem may find his or her task facilitated by smoking. It remains to be shown that nicotine given to non-smokers can enhance this type of performance. However, during withdrawal there is reliably cognitive impairment. Relief of this withdrawal symptom may stimulate smoking or facilitate relapse.

Stolerman and Jarvis, citing Jaffe (1990) as well as Warburton, imply that nicotine cannot produce disabling intoxication. However, J. Wilbert (1987) describes, graphically tobacco smoke-induced trance states and hallucinations in south American Indians which are undoubtedly manifestations of nicotine intoxication. Of course, these Indians take in large quantities of smoke very quickly to induce these states. In contemporary American smokers the first cigarette of the day often produces dizziness or light-headedness which could well be considered a mildly disabling form of intoxication.

There are many lines of evidence that indicate that nicotine does have a strong resemblance to more classically accepted addicting psychostimulants such as amphetamine and cocaine. For one thing, in drug discrimination studies rats will generalize responses from amphetamine to nicotine. In other words, they identify nicotine as amphetamine. Secondly, there is evidence that the release of dopamine in mesolimbic pathways, including the nucleus accumbens, is an important feature of reinforcement by nicotine and by amphetamine and cocaine. Nicotine has been shown to facilitate intracranial self stimulation to cocaine and amphetamine (Clarke and Kumar 1984; Huston-Lyons and Kornetsky 1992).

Although I feel that Robinson and Pritchard have embraced a lost cause in championing the innocuous character of nicotine (and cigarette smoking), their efforts, and also those of Warburton, are valuable in forcing the proponents of nicotine addiction status to examine all of the logical underpinnings of their arguments. There are still considerable problems with understanding nicotine reinforcement, particularly since it has been difficult to get animals to self administer nicotine or to inhale cigarette smoke. But other drugs which are frequently self-administered by humans, such as tetrahydrocannabinol or LSD, are not self administered by animals. It may be that the addictive nature of certain drugs such as nicotine may only become mani-

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fest when there is an interaction with a certain peculiar human or cognitive state. Only further research will clarify the nature of reinforcement and addiction.

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