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Effects of Heroin Self-Administration on Cigarette Smoking

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Abstract. Cigarette smoking increased during heroin self-administration in comparison to drug-free and methadone detoxification conditions in eight heroin addicts given naltrexone placebo ($P < 0.01$) and three heroin addicts given buprenorphine placebo. Cigarette smoking was stable across conditions for one subject who did not use heroin during naltrexone blockade of heroin effects. Five subjects smoked significantly more ($P < 0.01$) during the hour following a heroin injection than during the preceding hour, and two subjects in the same group smoked significantly less following a heroin injection ($P < 0.05$). Subjects smoked significantly more during the evening and night when self-administering heroin than during baseline conditions ($P < 0.05$), but subjects did not sleep significantly less during heroin self-administration. The peak of the intercigarette interval distribution remained between 16 – 30 min during baseline and heroin conditions. However, the increased smoking during heroin use appeared to reflect a higher rate of smoking rather than a generalized increase across intercigarette intervals. These data extend previous findings, that alcohol consumption is associated with increased cigarette smoking, to IV heroin self-administration.

Key words: Heroin addiction – Cigarette smoking – Polydrug use – Naltrexone – Buprenorphine

The interaction between cigarette smoking and other forms of drug use has been systematically studied only recently. Most research on smoking has examined tobacco use in isolation from other drugs (Gritz, 1979; Jaffe and Jarvik, 1978; Jarvik et al., 1977 for review). Although smoking often occurs independently of other drug use patterns, there is now compelling evidence that alcohol consumption induces increased cigarette smoking in alcohol addicts (Griffiths et al., 1976). These findings confirm the association between cigarette smoking and alcoholism indicated by self-report data (Dreher and Fraser, 1967; Maletzky and Klotter, 1974; Walton, 1972). Social drinkers, not addicted to alcohol, have also been shown to smoke more during periods of heavy drinking (Mello et al., 1979a). The covariance between smoking and drinking in a group of polydrug users appeared to be specific to alcohol and tobacco. Cigarette smoking did not covary with marijuana smoking, and marijuana use appeared to be independent of alcohol consumption when both drugs were simultaneously available (Mello et al., 1978, 1979a).

Several behavioral and metabolic hypothesis have been advanced, but there is no conclusive explanation for the covariance between cigarette smoking and alcohol consumption (Griffiths et al., 1976; Mello et al., 1979a). Indeed, there is still disagreement as to which constituent of tobacco makes it such an effective reinforcer (Kumar et al., 1977). However, most available evidence appears to favor nicotine as the primary reinforcer for cigarette smoking (Gritz, 1979; Gritz and Jarvik, 1977; Jaffe, 1978; Jarvik, 1977; Russell, 1976 for review). The apparent importance of nicotine in cigarette smoking suggests that alcohol may effect nicotine metabolism such that more nicotine is required to produce the desired effect during alcohol intoxication. Chronic alcohol consumption stimulates activity of microsomal enzymes which regulate drug metabolism (Lieber and DeCarli, 1968; Rubin et al., 1970), and an increased rate of nicotine metabolism occurs concomitant to the induction of hepatic mitochondrial activity (Russell, 1976). If nicotine were metabolized more (or less) rapidly when used concurrently with alcohol, each cigarette could be less reinforcing than usual. Alternatively, nicotine could become more reinforcing during alcohol intoxication in a manner analogous to the alleged post-prandial en-

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hancement of smoking satisfaction (Gritz, 1979). However, an alcohol-related change in nicotine metabolism could only account for one aspect of the reinforcing properties of cigarette smoking. It is recognized that many complex interacting factors, including expectancy, influence drug seeking, as well as the perceived consequences of drugs use (Jarvik, 1977; Jaffe, 1978; Marlatt and Rohsenow, 1979).

Nicotine has been shown to affect metabolism of several other compounds. For example, caffeine and theophylline are metabolized more rapidly by cigarette smokers than controls (Parsons and Neims, 1978; Jusko et al., 1978). Certain phenothiazines and benzodiazepines appear to be similarly effected by cigarette smoking (Boston Collaborative Drug Surveillance Program, 1973a, b, 1974). The effects of commonly abused drugs on nicotine metabolism remain to be determined.

The purpose of this study was to determine if increased cigarette smoking also occurs during the use of addictive drugs other than alcohol. Cigarette smoking during a period of IV heroin self-administration was examined and contrasted with drug-free baseline and methadone detoxification conditions. Heroin is often described as a satiating drug which reduces interest in food and sex and produces a sense of tranquility (Jaffe, 1975). Exactly the opposite behavioral effects are commonly associated with alcohol intoxication (Mello and Mendelson, 1978). The contrast between the behavioral effects of alcohol and opiates, as well as differences in the route and frequency of administration, would suggest that cigarette smoking should be affected differently by each drug. However, heroin self-administration, like alcohol intoxication, was associated with increased cigarette smoking in comparison to baseline conditions.

Materials and Methods

Subjects. Twelve adult male volunteers with histories of heroin addiction and cigarette smoking gave informed consent for participation in studies of the effects of new pharmacotherapies on heroin self-administration in a clinical research ward setting. The long-acting narcotic antagonist naltrexone was compared with naltrexone placebo under double-blind conditions in 12 subjects. Only 9 of 12 were cigarette smokers. Three other subjects were involved in studies of buprenorphine, a new partial-agonist antagonist (cf. Jasinski et al., 1978). The effects of buprenorphine and buprenorphine placebo on heroin self-administration also were compared under double-blind conditions. Naltrexone and buprenorphine each significantly suppress heroin self-administration by heroin addicts under research ward conditions and these data are reported separately (Mello et al., 1979b; Mello and Mendelson, 1979; Meyer and Mirin, 1979). This report describes the effects of heroin and methadone on cigarette smoking in eight subjects assigned to the naltrexone placebo condition, one subject assigned to naltrexone, and three subjects assigned to the buprenorphine placebo condition.

Buprenorphine and naltrexone subjects were closely matched in age ($\bar{x}$ = 27 years, range 22–31) and social and educational background. Subjects had abused heroin for an average of 9.6 years (range 2–19 years). Subjects were fully informed about the nature and duration of each phase of the study and were free to withdraw at any time. All subjects were in good health and showed no evidence of psychiatric or medical abnormalities as determined by appropriate clinical and laboratory examinations. Subjects lived on a clinical research ward throughout the study.

Sequence of Drug Conditions. Each subject served as his own control during a drug-free baseline and each successive drug condition. Consequently, it was possible to compare the effect of heroin, methadone, and control conditions on cigarette smoking by each subject.

Naltrexone subjects were studied over 34 consecutive days in groups of four. The sequence of conditions for the naltrexone subjects was as follows: A 9-day drug-free baseline; a 10-day period of heroin availability during which naltrexone or naltrexone placebo was given; a 5-day detoxification phase during which methadone was given to subjects on naltrexone placebo; and 7 drug-free days, followed by 3 days of inpatient maintenance on naltrexone. Subjects given naltrexone during heroin availability continued to receive naltrexone throughout the study. Eight cigarette smokers were assigned to the naltrexone placebo conditions and each self-administered heroin. One cigarette smoker was given active naltrexone and did not self-administer heroin.

Buprenorphine subjects were studied over 39 consecutive days. The sequence of conditions for the buprenorphine subjects was as follows: A 5-day drug-free baseline; a 14-day period during which buprenorphine or buprenorphine placebo was administered in ascending doses; 10 days of maintenance with buprenorphine (8 mg/day) or placebo when heroin was also available; 5 days during which methadone was given to subjects on buprenorphine placebo and buprenorphine in decreasing doses was continued for subjects given active buprenorphine; and 3 drug-free days were followed by 2 days on naltrexone prior to discharge. Each of the three cigarette smokers were assigned to the buprenorphine placebo condition and each self-administered heroin.

Tobacco and Heroin Acquisition. Tobacco cigarettes were available during all phases of the study. Each subject purchased his preferred brand of cigarettes. However, the nursing staff retained the cigarettes and distributed them when requested. The time of each cigarette request was recorded. It was not possible to measure cigarette puff volume or duration in ambulatory subjects given unrestricted access to cigarettes over 34–39 days (Jarvik et al., 1977).

Subjects worked for heroin or for money on a simple operant task on a fixed interval (1 s) schedule of reinforcement (FI 1 s). Only the first response after a 1-s interval had elapsed counted as an effective response. Approximately 90 min of sustained performance on an FI 1-s schedule earned 18 purchase points which could be used to buy one dose of heroin or exchanged for $1.50 (U.S.A.) in cash upon completion of the study. Subjects could work for money during the baseline and during each drug availability condition. Points earned for money could not be exchanged for points for heroin. When both heroin and money were available, subjects chose to work for one or the other each time they activated the operant instrument. Details of the operant apparatus and procedures are presented elsewhere (Mello et al., 1979b).

Subjects self-administered a fixed dose of heroin IV under the supervision of a physician. Subjects could omit any heroin injection but could not receive doses larger or smaller than specified in the protocol. Medical considerations precluded unlimited access to heroin. Naltrexone subjects could take a maximum of 40 mg heroin each day in four 10 mg doses (at 8 a.m., 2 p.m., 8 p.m., and 2 a.m.). Buprenorphine subjects could take a maximum of 21 mg heroin in three doses during the first 5 days of buprenorphine (or placebo)

maintenance (7 mg at 9 a.m., 5 p.m., and 1 a.m.), and a maximum of 41.5 mg heroin (13.5 mg at the same times) during the second 5 days of buprenorphine maintenance.

Additional Assessments. These studies of smoking behavior were part of a series of multidisciplinary investigations of the behavioral and biological effects of naltrexone, buprenorphine, and opiates (Mello et al., 1979; Mello and Mendelson, 1979). A complete description of the physiological, neuroendocrine, and behavioral measures is not relevant to this report. However, sleep status was monitored and recorded every 30 min by the nursing staff 24 h each day. Phenomenological assessments of sleep and waking behavior have been shown to be sensitive to drug-related changes in sleep patterns and to be concordant with electroencephalographic sleep criteria (Mello and Mendelson, 1970).

Results

Baseline Tobacco Smoking. Ten of twelve heroin addicts were heavy smokers. One subject smoked 30 cigarettes or more per day and nine subjects smoked 20 or more a day during the drug-free baseline period. The other two subjects smoked less than 20 per day.

Effect of Drug Conditions on Smoking. The naltrexone placebo group smoked significantly ($P < 0.01$) more cigarettes per day during the 10 days of heroin availability than during the drug-free baseline as evaluated by *t*-tests. Average cigarette smoking during the period of heroin availability was also significantly greater than during methadone detoxification ($P < 0.001$). There were no significant differences in cigarette smoking during the drug-free baseline periods which preceded and followed heroin and methadone. Cigarette smoking during methadone detoxification also did not differ from the drug-free baseline periods. Consequently, the significant increase in cigarette smoking appeared to be specific to the heroin condition.

The one subject given naltrexone rather than naltrexone placebo did not take heroin during the period of availability, since naltrexone effectively blocked the subjective and physiological effects of heroin. Although this subject was on the ward with other subjects who were smoking more and taking heroin, there were no significant differences in his smoking behavior across conditions. This subject smoked an average of 25 cigarettes per day over the entire study. This suggests that heroin, rather than any nonspecific social interaction factors, accounted for the increase in cigarette smoking seen in the naltrexone placebo group.

Illustrative data for six naltrexone placebo subjects are shown in Figs. 1 and 2. Heavy smokers who smoked an average of over 20 cigarettes per day during baseline are shown in Fig. 1. Moderate smokers who smoked 20 a day or less during baseline are shown in Fig. 2.

Each of the heavy smokers shown in Fig. 1 smoked significantly more cigarettes during heroin use than during the drug-free baseline ($P < 0.01$). Two subjects

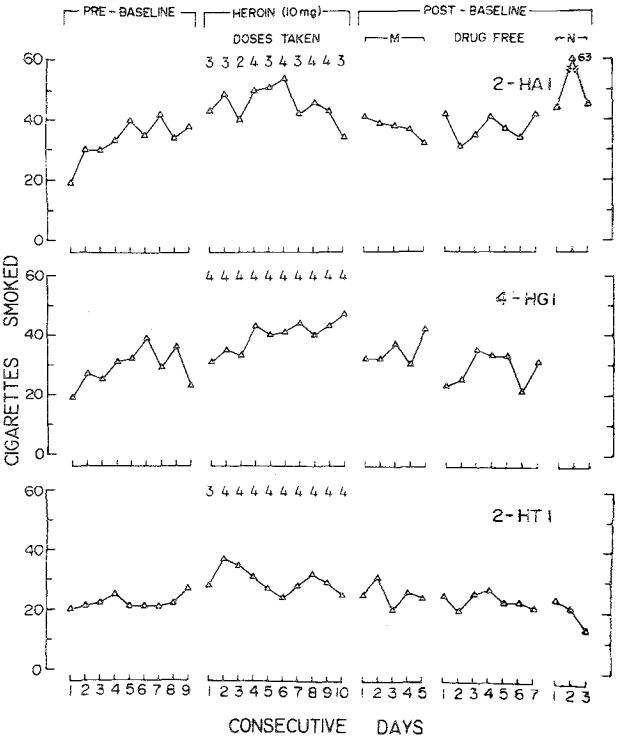

Fig. 1. Cigarette smoking across successive drug conditions. Cigarette smoking over 34 consecutive days is shown for three individuals who were heavy tobacco users. Each subject was given naltrexone placebo during heroin availability. The successive drug conditions (drug-free baseline, heroin + naltrexone placebo, methadone detoxification, drug-free baseline, and naltrexone availability) are shown across the top of the figure. The number of heroin doses taken each day by each subject is shown at the top of each row. The number of cigarettes smoked each day is shown on the ordinate

(4-HG 1 and 2-HT 1) took all or almost all of the four heroin doses available each day. Therefore, variations in cigarette smoking observed during heroin self-administration were not related to the specific daily dose of heroin. Although subject 2-HA 1 tended to smoke least on the days that he took the fewest heroin doses, the fluctuations in cigarette smoking did not appear to vary consistently with the daily dose of heroin. The increase in his smoking (to 63 cigarettes a day during the final naltrexone period) immediately before discharge was unusual and has not been observed in other heroin addicts studied under these conditions. Since the subject who was maintained on active naltrexone throughout the study did not show comparable elevations in smoking, it is difficult to attribute this finding to the effect of naltrexone per se.

Among the moderate smokers shown in Fig. 2, the subject 3-HT 1, who smoked least during baseline (an average 15 cigarettes per day), increased smoking most dramatically when heroin became available to an average 32 cigarettes per day ($P < 0.001$). This subject took all the available doses of heroin. Subject 1-HG 1

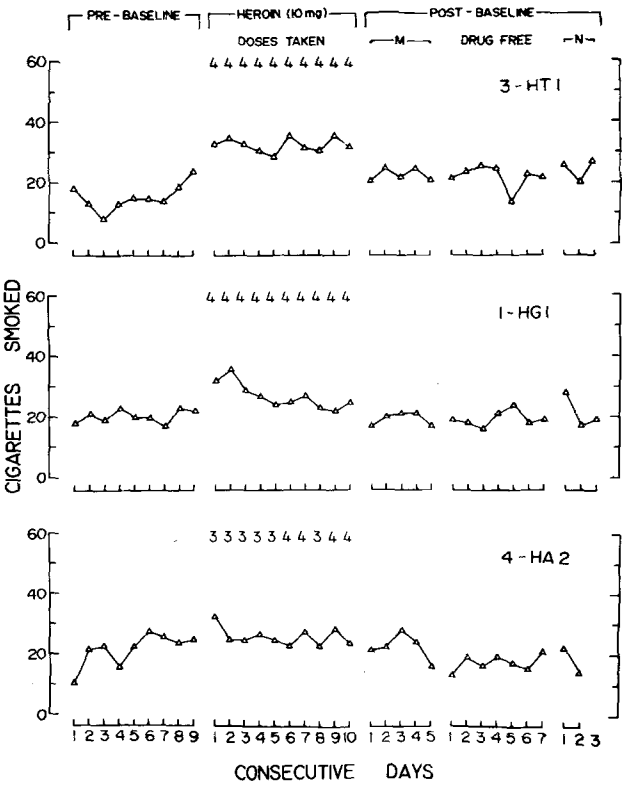

Fig. 2. Cigarette smoking across successive drug conditions. Cigarette smoking over 34 consecutive days is shown for three individuals who were moderate tobacco users. Each subject was given naltrexone placebo during heroin availability. The successive drug conditions (drug-free baseline, heroin + naltrexone placebo, methadone detoxification, drug-free baseline, and naltrexone availability) are shown across the top of the figure. The number of heroin doses taken each day by each subject is shown at the top of each row. The number of cigarettes smoked each day is shown on the ordinate

smoked an average 20 cigarettes per day during baseline. During the period of heroin availability, he took most of the heroin available and increased smoking by an average seven cigarettes per day ($P < 0.01$). Subject 4-HA 2 smoked an average of four cigarettes more per day during the period of heroin availability ($P < 0.05$) and also took most of the heroin available.

The number of cigarettes smoked per day across the successive conditions of the study are shown for the three buprenorphine placebo subjects in Fig. 3. Since there were only three cigarette smokers in the buprenorphine placebo group, changes in cigarette smoking as a function of drug conditions were analyzed for individual subjects with *t*-tests. The introduction of buprenorphine placebo did not result in significant changes in cigarette smoking by any subject compared to baseline. Heroin self-administration was associated with an abrupt increase in cigarette smoking by all subjects. Each subject smoked more cigarettes on the average during heroin self-administration than during the drug-free baseline or during buprenorphine placebo. However, only one subject (1-HB 1) smoked significantly more during heroin use than during the immediately preceding buprenorphine placebo condition ($P < 0.001$). Two subjects (1-HB 1 and 2-HB 1) smoked significantly more cigarettes ($P < 0.01$) during the period of heroin self-administration than during the subsequent methadone detoxification period. The other subject (4-HB 1) left the study before the methadone detoxification period.

Temporal Patterns of Cigarette Smoking as a Function of Heroin Use. To determine if the significant increases

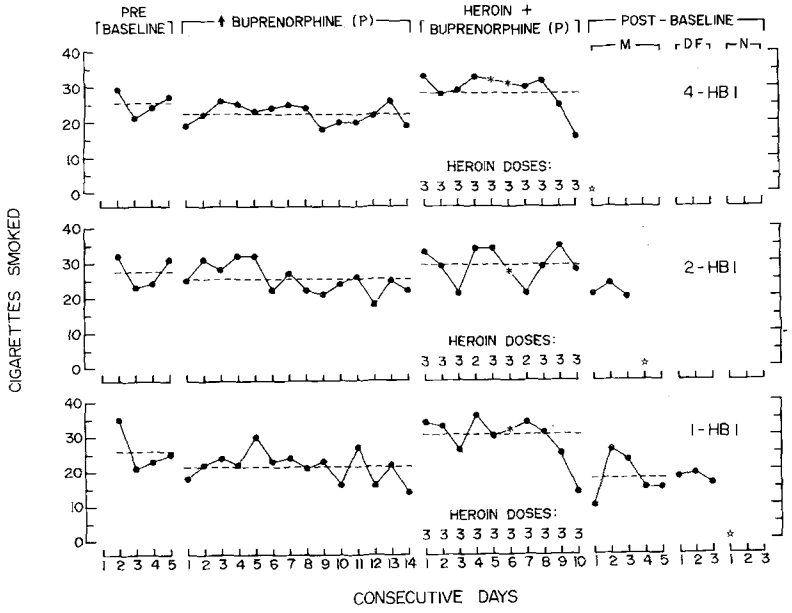

Fig. 3
Cigarette smoking across successive drug conditions. Cigarette smoking by three individual subjects is shown over 39 consecutive days. Each subject was given buprenorphine placebo prior to and during heroin availability. The successive drug conditions (drug-free baseline, buprenorphine placebo, heroin + burprenorphine placebo, and methadone detoxification) are shown at the top of the figure. The number of heroin injections taken each day by each subject is shown at the top of each row. The number of cigarettes smoked each day is shown on the ordinate. Missing data are indicated by an asterisk. The day on which each subject left the study is indicated by a star

in cigarette smoking by the naltrexone placebo subjects during heroin availability were generalized increases or were temporally associated with the heroin injection, two types of analyses were done. The number of cigarettes smoked before and after each heroin injection was compared, and the temporal distribution of cigarette smoking during baseline, heroin, and methadone conditions was examined.

The number of cigarettes smoked during the hour preceding and the hour following each heroin injection was tabulated, and the differences in cigarette smoking before and after heroin were evaluated for individual subjects. An analysis of variance showed that the time of day of the heroin injection did not result in significant differences in cigarette smoking. Therefore, it was possible to pool all pre- and post-heroin injection cigarette smoking data from each subject for matched *t*-test analysis.

Five of eight subjects smoked significantly more cigarettes during the hour immediately following heroin injection than during the hour preceding heroin self-administration ($P < 0.01$ versus 0.001). The other three subjects smoked fewer cigarettes immediately following a heroin injection and this decrease in smoking was significant for two subjects ($P < 0.05$).

The average number of cigarettes smoked by the naltrexone placebo group during consecutive 6-h periods was tabulated for each of three conditions i.e., drug-free baseline, heroin availability, and methadone detoxification. The temporal distribution of group cigarette smoking during each of these conditions is shown in Fig. 4. There were no significant differences in number of cigarettes smoked as a function of the drug condition during the period from morning to early afternoon (8 a.m. – 2 p.m.) and during the afternoon to early evening period (2 p.m. – 8 p.m.). However, significantly more cigarettes ($P < 0.01$) were smoked during heroin use than during baseline in the evening and at night (8 p.m. – 2 a.m. and 2 a.m. – 8 a.m.). During heroin self-administration, significantly more cigarettes were smoked in the morning ($P < 0.05$) and at night ($P < 0.1$) than during methadone detoxification. Since heroin was given once every 6 h (at 8 a.m., 2 p.m., 8 p.m., and 2 a.m.), this shift in the temporal distribution of smoking could reflect the fact that subjects were awake longer and therefore smoked more. However, comparison of hours slept during baseline, heroin self-administration, and methadone detoxification revealed no significant differences (*t*-test). Consequently, the waking hours available for smoking were equivalent for each condition.

The temporal distribution of smoking for the buprenorphine placebo group was also analyzed as a function of consecutive 6-h periods during the drug-free baseline, buprenorphine placebo, and heroin availability conditions. These data are shown in the lower half of Fig. 4. Heroin injections occurred three times a day (at 9 a.m., 5 p.m., and 1 a.m.). Although more cigarettes were smoked during heroin use in the evening and at night than during the drug-free baseline, these differences were not statistically significant. There were also no significant differences in hours of sleep between baseline and heroin self-administration. However, these subjects did sleep significantly more during methadone detoxification than during heroin self-administration ($P < 0.05$).

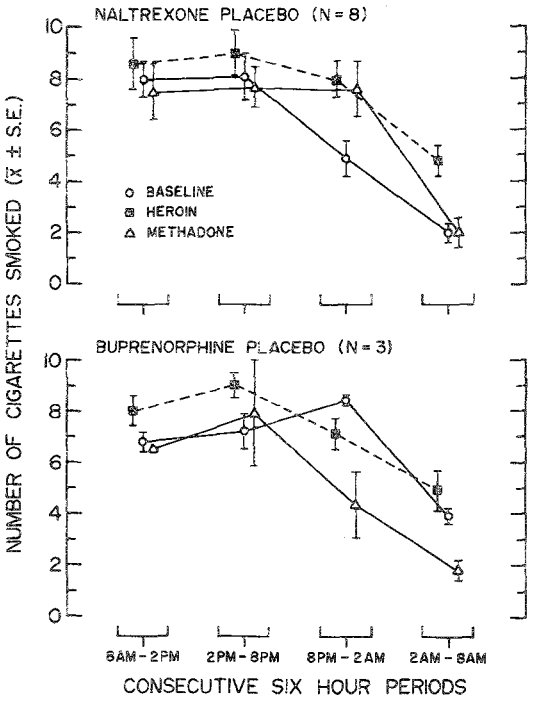

Fig. 4. Cigarettes smoked as a function of time of day. The number of cigarettes smoked ($\bar{x} \pm$ SE) are shown on the ordinate, and consecutive 6-h periods are shown on the abscissa. The top row shows the number of cigarettes smoked by the naltrexone placebo group ($n = 8$) during the drug-free baseline (○), the 10 days of heroin availability (▩), and the methadone detoxification period (△). The second row shows the number of cigarettes smoked by the buprenorphine placebo subjects ($n = 3$) during the drug-free baseline period (○), heroin availability (▩), and methadone detoxification (△)

Intercigarette Interval Analysis. To determine if there were marked changes in the overall rate of cigarette smoking as a function of heroin self-administration, the distribution of intervals between successive cigarette requests was examined for three naltrexone placebo subjects. The number of cigarette requests occurring at intervals of less than 15 min, 16–30 min, 31–45 min, and so on, were tabulated for the drug-free baseline condition and the period of heroin self-administration for individual subjects. The percent of the total number of cigarettes smoked during each condition at each

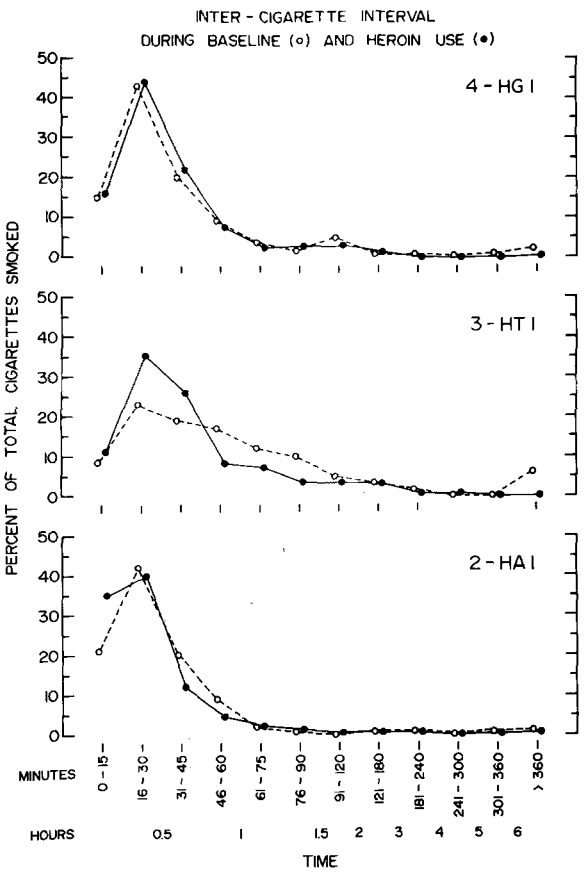

Fig. 5. Distribution of intercigarette intervals during baseline and heroin use. The interval between successive cigarette requests is shown on the abscissa. The percent of the total number of cigarettes smoked during the 9-day baseline period and 10 days of heroin availability is shown on the ordinate. Intersmoking interval data are presented for three naltrexone placebo subjects who were moderate or heavy smokers

intercigarette interval was then calculated. The distributions of intersmoking intervals are shown in Fig. 5.

Subject 3-HT 1 increased cigarette smoking during heroin self-administration by an average of 17 cigarettes per day or 113% (cf. Fig. 2). The peak of the intercigarette interval fell between 16–30 min during both baseline and heroin conditions. However, during baseline, 19% more of the total number of cigarettes were smoked at intervals of 46–60 min, 61–75 min, and 76–90 min than during heroin self-administration. Moreover, 6% of the cigarettes were smoked at intervals of 6 or more hours during baseline. When heroin became available, this subject smoked more cigarettes more frequently, i.e., 72% of all cigarettes were smoked at intervals between 0–45 min. During baseline, he only smoked 50% of his total cigarettes at this rate.

Subject 2-HA 1 smoked an average of ten more cigarettes per day during heroin self-administration than during baseline, and averaged 45 cigarettes per day (cf. Fig. 1). The peak and form of the distribution of intercigarette intervals during baseline and heroin conditions were very similar. However, 12% more cigarettes were smoked at 0–30-min intervals during heroin self-administration than during baseline.

Subject 4-HG 1 also smoked an average of ten more cigarettes per day during heroin self-administration than during baseline, and averaged 39 cigarettes per day during that period (cf. Fig. 1). However, there was no appreciable change in the distribution of intercigarette intervals, except that somewhat fewer cigarettes were smoked at intervals of 3–6 h during heroin self-administration than during baseline.

These distributions of intercigarette intervals suggest that increased smoking during heroin self-administration reflects a more rapid rate of smoking, rather than smoking more cigarettes at long intervals of 3 h or more. The consistency of the peak of the distribution of intersmoking intervals within and across subjects and across conditions indicates that these moderate to heavy smokers most often smoke a cigarette every 15 or 30 min.

Discussion

In view of the satiating effects believed to be associated with chronic heroin intoxication (Jaffe, 1975), it was somewhat surprising to find that cigarette smoking consistently increased during heroin self-administration and increased significantly over baseline in 6 of the 11 heroin users studied. Increased cigarette smoking appeared to be specific to heroin use since comparable smoking increments were not observed during methadone detoxification or in the subject who did not use heroin during naltrexone blockade.

Although these data are analogous to previous reports of alcohol-induced increments in cigarette smoking in alcoholics (Griffiths et al., 1976) and social drinkers (Mello et al., 1979a), it is difficult to suggest a common factor which could account for both opiate- and alcohol-related changes in smoking behavior. Chronic heroin and alcohol intoxication produce similar increases in anxiety and dysphoria (Mello, 1978 for review), but these affective changes probably can not account for the abrupt increase in smoking at the beginning of heroin use, or the covariance between smoking and drinking in nonalcoholic subjects.

The variables which account for the heroin-related increase in cigarette smoking seen in these heroin addicts are unclear. Since the last heroin injection of each day occurred at 1 or 2 a.m., and subjects smoked more during the evening in both the naltrexone placebo ($P < 0.05$) and the buprenorphine placebo groups, it seemed possible that changes in sleep patterns could

have accounted for the increase in smoking. If subjects were awake more hours during heroin self-administration, increased smoking could have reflected more time for smoking rather than a drug-related effect. However, there were no significant differences in hours of sleep across conditions and no obvious differences in sleep patterns. Subjects stayed up late watching television most evenings throughout the study.

Efforts to examine the temporal association between IV heroin injection and cigarette smoking yielded somewhat equivocal results. Although five of the subjects who smoked significantly more during heroin availability also smoked significantly more within 1 h following heroin self-administration than during the preceding hour ($P < 0.01$), the other three subjects smoked less during the hour following heroin injection. The decrease in smoking following heroin injection was statistically significant in two subjects ($P < 0.05$).

The frequency pattern of cigarette smoking was similar during the drug-free baseline and heroin self-administration. Analysis of the interval between successive cigarette requests during each period indicated that most smoking occurred within 16–30 min of the preceding cigarette request. This smoking pattern is consistent with the time course of nicotine metabolism. The plasma half-life of nicotine is about 20–30 min (Jaffe, 1978). Increased cigarette smoking during heroin use occurred primarily at shorter intercigarette intervals rather than being distributed equally across the range of intervals studied (15 min to 6 or more h).

The question remains as to whether more cigarettes are smoked during heroin intoxication because they are more reinforcing or because their effects are attenuated and more are required. It is possible that heroin may increase the rate of nicotine metabolism so that it is necessary to smoke more to achieve the accustomed effect. However, there is no direct evidence that heroin affects nicotine metabolism. The fact that another opiate, methadone, did not produce similar increases in cigarette smoking would tend to argue against a metabolic change hypothesis.

It is also possible that nicotine and heroin may act in a complementary and mutually facilitory way. There are both similarities and differences in the spectrum of action of each drug (Mansky, 1978; Jaffe, 1975; Volle and Koelle, 1975; Russell, 1976). Nicotine stimulates, alerts, arouses, and decreases distractibility (Jaffe, 1978; Russell, 1976; Volle and Koelle, 1975). Acute doses of opiates to former addicts have also been shown to increase activity, arousal, and feelings of energy (Mansky, 1978). Consequently, it could be postulated that increased smoking during heroin self-administration is a reflection of a generalized increase in activity levels. These subjects did not appear sedated following heroin injections and worked longer hours, and earned significantly more points at the operant task during heroin self-administration than during the drug-free baseline (Mello et al., 1979b).

It is difficult to compare the actions of heroin and nicotine since effects will differ as a function of relative dose and the biphasic action of each compound. However, chronic heroin intoxication is usually associated with sedation, drowsiness, and "mental clouding" (Mansky, 1978; Jaffe, 1975). These behavioral effects are clearly discordant with those usually ascribed to nicotine.

These data on heroin and smoking, as well as previous reports of covariance between alcohol intoxication and smoking, may reflect a common aspect of polydrug use. There are considerable anecdotal and self-report data which suggest that concurrent use of drugs from different pharmacological classes, with divergent or even contradictory effects, is not uncommon (Benvenuto et al., 1975; Goldman, 1974). Since there has been little direct observation of "gourmand" polydrug use patterns in a clinical research setting, this impression may be of limited generality (Mello et al., 1978). Multiple drug use which involves substances with conflicting or antithetical behavioral effects is more difficult to reconcile with traditional views of drug abuse than the concurrent use of drugs with complementary or mutually enhancing pharmacological effects. We have suggested elsewhere that it may be useful to think of drug use in terms of a stimulus-self-administration framework (Mello, 1977, 1978). The reinforcer for drug use may be a change in state, and the direction of that change may be less important than the occurrence of the change itself. This notion parallels the observation of Wikler and Rasor, over 26 years ago, that opiate addicts describe one goal of heroin use as to "get off the normal" (Wikler and Rasor, 1953). The applicability of a stimulus-self-administration concept to polydrug use involving heroin and nicotine can only be evaluted by further behavioral analyses of multiple drug use.

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