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Caffeine: Preferential Consumption by Rats[1]

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VITIELLO, M. V. AND S. C. WOODS. *Caffeine: preferential consumption by rats.* PHARMAC. BIOCHEM. BEHAV. 3(2) 147–149, 1975. – The present experiment explored the effect of forced daily consumption of large amounts of caffeine (analogous to that of heavy coffee drinkers) upon the subsequent intake of caffeine in a free-choice situation. It was found that forced caffeine consumption is directly related to subsequent free-choice intake and that a flavor associated with the forced caffeine consumption is not preferred.

Caffeine Drug preference Flavor associations

ALTHOUGH caffeine is consumed in at least moderate amounts by millions of humans on a daily basis, little is known of the possible habit-forming qualities of the drug. The possibility of some sort of dependence upon caffeine given its chronic usage becomes more important in light of the recent evidence linking its consumption to a relatively high incidence of myocardial infarction [3, 4, 5, 9]. Although many behavioral and physiological effects of the drug have been well-investigated (e.g.,[7,11]), data dealing with the development of a possible caffeine dependence are few [1,2] and suggestive at best. The present experiment demonstrates that when rats are forced to consume caffeine in amounts similar to those of heavy coffee drinkers, a preference for the drug is established.

METHOD

Animals were 36 naive male Long Evans rats, approximately 120 days old. They were housed in individual stainless steel cages and received ad lib food throughout the experiment. They were randomly divided into 3 experimental and 3 control groups. Each group underwent the following basic procedure. Experimental rats received an aqueous solution of caffeine (U.S.P., Parke-Davis) of one of the following concentrations (0.17, 0.34, or 0.50 mg/ml) plus mocha flavoring (T. Noirot: 2 ml/1) continuously for fourteen days. This mixture was the only source of water during that interval. Control rats received ad lib water during the same interval. All rats were then given a continuous choice among 3 solutions for 8 days. The choices were caffeine in water (in the same concentrations as the experimental rats had already consumed), mocha flavoring in water, and water alone. One-third of the control rats received each concentration of caffeine. The relative positions of the 3 calibrated drinking tubes were randomly determined each day, and liquid consumption measures were obtained daily.

At the end of the 8-day free-choice session, the control rats which had received the 0.50 mg/ml caffeine solution were given the aqueous solution of caffeine (0.50 mg/ml) and mocha for 14 days and then were retested with a second 8-day, 3-solution choice as before.

RESULTS AND DISCUSSION

The consumption data were analyzed for the individual groups by ranking each rats' consumption of the three solutions and applying Friedman's test for ranks for matched groups [10]. Experimental rats which had received the two lower concentrations of caffeine during the 14-day forced consumption period (i.e., 0.17 and 0.34 mg/ml) did not differ from their respective control groups in that approximately equal consumption of caffeine, mocha and water occurred (see Table 1); i.e., a preference for one or another solution was not manifest by either experimental or control rats. Experimental rats which had been forced to consume the largest concentration of caffeine (0.50 mg/ml), on the other hand, consumed significantly more caffeine and significantly less mocha than their controls ($p<0.005$). These control rats were similar to the other two control groups in that no particular preference occurred. When this control group was given additional treatment (in the manner of the experimental group with the largest concentration of caffeine), a significant increase of its caffeine consumption and decrease of its mocha consumption occurred relative to its former values ($p<0.05$). Both of these experimental groups preferred caffeine at the expense of mocha on the first day and on each subsequent day of the trial period.

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TABLE 1

DAILY CONSUMPTION OF THE VARIOUS SOLUTIONS (IN ml) BY EXPERIMENTAL AND CONTROL GROUPS DURING THE 8-DAY, FREE-CHOICE PERIOD. VALUES ARE EXPRESSED AS THE MEANS PLUS AND MINUS THE STANDARD ERRORS OF THE MEANS. W = WATER; C = CAFFEINE SOLUTION; AND M = MOCHA-FLAVORED SOLUTION.

	Caffeine Concentration (mg/ml)						
	0.17		0.34		0.50		0.50*
	Experimental	Control	Experimental	Control	Experimental	Control	Experimental
W	14.8 ± 1.3	13.3 ± 4.3	16.6 ± 1.4	16.8 ± 1.0	17.8 ± 3.5	17.8 ± 0.9	16.0 ± 2.4
C	13.1 ± 0.8	12.5 ± 3.2	13.0 ± 0.7	12.3 ± 1.0	25.4 ± 3.8	17.0 ± 3.2	24.3 ± 3.4
M	13.9 ± 1.4	12.5 ± 2.9	17.4 ± 1.2	17.3 ± 1.1	6.3 ± 1.5†	17.8 ± 3.1	10.0 ± 2.5†

*The results of the former control group which was later given 14 days of forced-choice caffeine and mocha.
†There was a significant ($p<0.05$) increase of caffeine and decrease of mocha consumption in these two groups.

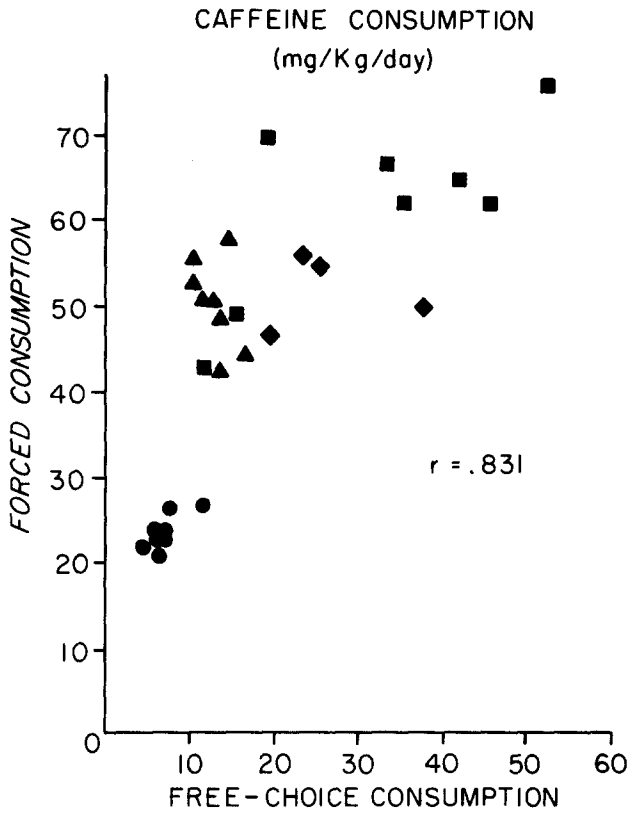

FIG. 1. Caffeine consumption (in mg/kg/day) for the individual experimental rats on both the forced consumption and free-choice intervals. Circles represent rats receiving 0.17 mg/ml of caffeine; triangles represent those receiving 0.34 mg/ml of caffeine; squares represent those receiving 0.50 mg/ml of caffeine; and diamonds represent the former control group which later received 0.50 mg/ml of caffeine during forced consumption.

Mean consumption of caffeine in mg/kg body weight/day during the 14-day forced exposure period and the subsequent 8-day free choice periods are depicted for the individual experimental rats in Fig. 1. The correlation between the two measures is 0.83 ($p<0.01$), indicating that a greater caffeine consumption during forced exposure led to a greater subsequent free-choice caffeine consumption. The conversion factor for approximate coffee consumption by humans is 0.87, assuming a 70 kg man and 100 mg caffeine/cup of coffee; i.e., a value of 20 mg/kg/day represents around 17 cups of coffee/day. However, this estimate is quite conservative since rats metabolize drugs

many times more rapidly than humans. A more reasonable estimate, therefore, would include a considerably smaller conversion factor. A value of 20 mg/kg/day would therefore represent between 5 to 10 cups of coffee/day.

Therefore, consumption of caffeine can lead to the development of a preference for the drug. It is noteworthy that the rats did not prefer the flavor associated with the caffeine, even on the first day of the free-choice period, for there is considerable evidence indicating that the aftereffects of drugs are readily associated with flavors [6,8]. Mocha, a noncaffeine-containing artificial coffee flavoring, was in fact consumed in a significantly less amount when caffeine was preferred. This may have implications for the use of low-caffeine coffee-flavored beverages by humans.

REFERENCES

1. Collins, E. and G. Turner. A suggestion for reducing the incidence of habitual analgesic consumption. *Med. J. Austral.* **28:** 863, 1973.
2. Colton, T., R. E. Gosselin and R. P. Smith. The tolerance of coffee drinkers to caffeine. *Clin. Pharmac. Ther.* **9:** 31–39, 1968.
3. Dalerup, L. H. Coffee and myocardial infarction. *Lancet* **1:** 104, 1973.
4. Jick, H., O. S. Mettinen, R. K. Neff, S. Shapiro, O. P. Heinonen and D. Slone. Coffee and myocardial infarction. *New Engl. J. Med.* **289:** 63–67, 1973.
5. Postron, R. N. Coffee and myocardial infarction. *Lancet* **1:** 45, 1973.
6. Revusky, S. H. and J. Garcia. Learned associations over long delays. In: *Psychology of Learning and Motivation,* edited by G. Bower and J. T. Spence. New York: Academic Press, 1970, pp. 1–83.
7. Ritchie, J. M. Central nervous stimulants. II. The xanthines. In: *The Pharmacological Basis of Therapeutics,* edited by G. Goodman and A. Gilman. New York: McMillan, 1970, pp. 358–370.
8. Rozin, P. and J. W. Kalat. Specific hungers and poison avoidance as adaptive specializations of learning. *Psychol. Rev.* **78:** 459–486, 1971.
9. Segall, J. J. Coffee and myocardial infarction. *Lancet* **1:** 46, 1973.
10. Siegel, S. *Nonparametric Statistics for the Behavioral Sciences.* New York: McGraw-Hill, 1956, p. 166.
11. Weiss, B. and V. G. Laties. Enhancement of human performance by caffeine and the amphetamines. *Pharmac. Rev.* **14:** 1–33, 1962.