METHODS & DESIGNS

A smoke-mixing device for measuring nicotine preference

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A smoke-mixing device is described that allows individuals to select their preferred nicotine deliveries from cigarette smoke on a puff-by-puff basis. This methodology offers advantages over previous strategies to investigate the role of nicotine as a reinforcing constituent of tobacco.

Tobacco smoking is widely believed to be a form of nicotine dependence (Armitage, Hall, & Morrison, 1968; Jarvik, 1970; Russell, 1976), yet no definitive evidence has fully substantiated this conclusion. The present paper describes a new apparatus that can be used to directly test the nicotine hypothesis of cigarette smoking based on the premise that there is an optimal level of nicotine in tobacco smoke that the smoker seeks.

The need for this apparatus is exemplified by the problems encountered in previous studies of the role of nicotine in cigarette smoking. The main experimental approach has been to vary the nicotine delivery of cigarettes and determine whether smokers titrate, that is, adjust their manner of smoking to maintain a constant intake of nicotine. Studies have shown only partial regulation of nicotine intake (see Gritz, 1980, for a review). The titration paradigm can be criticized on several grounds, however. First, even assuming that nicotine is the main ingredient smokers seek, titration may not be observed. Alterations in nicotine deliveries affect the taste and enjoyment of smoking. Low-nicotine

cigarettes are usually disliked and discourage an individual from smoking as much as would be necessary to regulate nicotine intake. While attempting to compensate for a reduced nicotine yield by taking more puffs, the smoker may also have to ingest more aversive constituents in smoke. These factors tend to prevent complete titration. On the other hand, even when titration is observed, the interpretation is ambiguous. Russell (1979) has argued that titration would be predicted by assuming nicotine were solely aversive (and that smokers limited their intake so as not to exceed some aversive level). Titration is therefore not a rigorous test of the hypothesis that nicotine is positively reinforcing. In view of these practical and logical difficulties, it is not surprising that reductions in nicotine content often produce little or no change in the rate of tobacco self-administration (e.g., Griffiths, Henningfield, & Bigelow, 1982; Herning, Jones, Bachman, & Mines, 1981; Jarvik, Popek, Schneider, Baer-Weiss, & Gritz, 1978).

We have developed a very different approach to investigate nicotine's role in cigarette smoking, using a choice, or preference, paradigm. In this procedure, subjects utilize the smoke-mixing apparatus described below to adjust the nicotine concentration in cigarette smoke on a puff-by-puff basis, and they select an optimal level at a given time. Since the nicotine content is under the subject's control (by turning a knob), the rewarding and/or aversive properties of nicotine at a specific time can be inferred by the nicotine level

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chosen. The selection is performed by means of the smoke-mixing device shown in Figure 1. It consists of a two-barreled, glass cigarette holder, constructed from a three-way stopcock, that blends smoke from two sources: a high- and a low-nicotine cigarette, equivalent in other respects (e.g., tar delivery, carbon monoxide). For this purpose, we have employed the University of Kentucky Reference cigarettes: 2A1, .48 mg nicotine, 36.4 mg tar; 2R1, 2.45 mg nicotine, 36.8 mg tar, when smoked by the FTC method to a 23-mm butt. As in blending hot and cold water with a faucet, subjects may turn a knob and vary the ratio of smoke drawn from the two cigarettes and, hence, the nicotine concentration of the smoke inhaled. The mixing of smoke takes place within the modified Teflon stopcock, shown in detail in Figure 1. The center core of the stopcock was first drilled out, and then three slits were cut to allow the inside to communicate with the exterior. One of these slits, the largest (approximately 3 mm wide), connects to the mouthpiece and allows smoke to travel unimpeded into the smoker's mouth. The other two slits, located on the opposite side of the stopcock, are much narrower (approximately 1.2 mm wide). These two smaller slits are offset with respect to each other, so that when one is perfectly aligned with one channel of the cigarette holder, the other is not, and vice versa. Intermediate rotations of the stopcock cause partial alignment of each slit with the corresponding channel in varying degrees. At a given setting, some smoke is drawn through each side of the mixer. The precise ratio depends on the alignment of the slits, which is controlled in turn by the vernier knob operated by the subject. The overall draw resistance presented by both slits is negligible compared to that of a cigarette.

The flow of smoke through each side of the holder is measured by means of differential pressure transducers (Statham Model PM6TC $\pm$ 2.5-350), which sense the pressure difference across the restriction tube in each barrel. The diameter of this tube (1.6 mm) is sufficient to prevent accumulation of smoke residue and presents a small, fixed draw resistance. The use of differential

Figure 1. Diagram shows principle of operation of smoke mixer and system for monitoring smoke flow through each channel.

Figure 2. Calibration curves of flow measurement for mixer channels. Each point represents the mean of five determinations (standard deviations lie within the filled circles).

pressure measurements across a constant resistance is necessary so that variations in the length of the cigarette as it burns do not affect the relationship between flow and pressure measured by the transducer. This system is similar to those used previously in studies of smoking topography (Creighton, Noble, & Whewell, 1978; Rawbone, Murphy, Tate, & Kane, 1978). The output from the transducers leads to a polygraph to be recorded, and measuring the height of the puff profile on each channel yields the flow through that side. Calibration records were produced by independent determination of flows using a vacuum pump and Gilmont spherical float flow meters. Figure 2 shows transducer voltage plotted against flow for each channel of the mixer. Figure 3 shows how the relative mixture of smoke, and hence nicotine delivery, changes as the knob is turned. The estimate of nicotine delivery (Nic) of the smoke mixture is computed as follows:

Nic (mixture) =

$$\frac{\text{Flow (Side 1)Nic 1} + \text{Flow (Side 2)Nic 2}}{\text{Flow (Side 1) + Flow (Side 2)}}$$

Nic 1 and Nic 2 are the nicotine deliveries for the two types of cigarettes employed.

There are two main sources of error to be considered in this measurement. The first is random variations in nicotine delivery between puffs from cigarettes of a given type. This error includes variations in nicotine concentration accompanying changes in the rate of puffing or volume of puffs (Creighton & Lewis, 1978). The magnitude of this error is probably less than $\pm 10\%$ in the range of puff parameters commonly encountered; however, observed puff volumes and interpuff intervals could be used in a retrospective analysis to improve the estimates of per-puff nicotine deliveries. The second

Figure 3. Proportion of smoke obtained from left channel of mixer at different knob settings. Each point represents the mean of five determinations (standard deviations lie within the filled circles).

source of error is the systematic increase in the concentration of smoke products across puffs from a single cigarette due to the rod filtration effect (Russell, Sutton, Feyerabend, & Cole, 1978; Wiley & Wickham, 1974; Young, Robinson, & Rickert, 1981). This factor can be corrected for it is known precisely how nicotine deliveries vary across the length of the particular cigarettes employed, and it can be minimized by restricting smoking to the distal halves of the cigarettes used. The burn rates of the two types of University of Kentucky research cigarettes are very similar over a wide range of mixture settings, so that the lengths and relative contributions of each cigarette to total nicotine delivery remain nearly constant across the length of the cigarettes.

We have tested the smoke mixer with several cigarette smokers and have found that they quickly learn to operate it to find a preferred nicotine setting. Some subjects keep the mixture setting adjustment constant after finding a preferred setting; others show steadily increasing or decreasing values across a session. Mean nicotine preference seems to be substantially elevated after a period of smoking deprivation. We are currently exploring in detail the variations in nicotine preference resulting from smoking abstinence and satiation. Nicotine preference can be assessed by this method with the smoke-mixer methodology, unconfounded by variations in puffing rate, other constituents in smoke, or sensorimotor and social aspects of the habit. Although we are primarily interested in nicotine preference, any constituent of smoke may be varied systematically

with the present device, if cigarettes are available with high and low yields for that particular component.

REFERENCES

- ARMITAGE, A. K., HALL, G. H., & MORRISON, C. F. Pharmacological basis for the tobacco smoking habit. *Nature*, 1968, 217, 331-334.
- CREIGHTON, D. E., & LEWIS, P. H. The effect of smoking pattern on smoke deliveries. In R. E. Thornton (Ed.), *Smoking behaviour: Physiological and psychological influences*. Edinburgh: Churchill Livingstone, 1978.
- CREIGHTON, D. E., NOBLE, M. J., & WHEWELL, R. T. Instruments to measure, record and duplicate human smoking patterns. In R. E. Thornton (Ed.), *Smoking behaviour: Physiological and psychological influences*. Edinburgh: Churchill Livingstone, 1978.
- GRIFFITHS, R. R., HENNINGFIELD, J. E., & BIGELOW, G. E. Human cigarette smoking: Manipulation of number of puffs per bout, interbout interval and nicotine dose. *Journal of Pharmacology and Experimental Therapeutics*, 1982, 220, 256-265.
- GRITZ, E. R. Smoking behavior and tobacco abuse. In N. K. Mello (Ed.), *Advances in substance abuse*. Greenwich: JAI Press, 1980.
- HERNING, R. I., JONES, R. T., BACHMAN, J., & MINES, A. H. Puff volume increases when low-nicotine cigarettes are smoked. *British Medical Journal*, 1981, 283, 187-189.
- JARVIK, M. E. The role of nicotine in the smoking habit. In W. A. Hunt (Ed.), *Learning mechanisms in smoking*. Chicago: Aldine, 1970.
- JARVIK, M. E., POPEK, P., SCHNEIDER, N. G., BAER-WEISS, V., & GRITZ, E. R. Can cigarette size and nicotine content influence smoking and puffing rates? *Psychopharmacology*, 1978, 58, 303-306.
- RAWBONE, R. G., MURPHY, K., TATE, M. E., & KANE, S. J. The analysis of smoking parameters: Inhalation and absorption of tobacco smoke in studies of human smoking behaviour. In R. E. Thornton (Ed.), *Smoking behaviour: Physiological and psychological influences*. Edinburgh: Churchill Livingstone, 1978.
- RUSSELL, M. A. H. Tobacco smoking and nicotine dependence. In R. J. Gibbins, Y. Israel, H. Kalant, R. E. Popham, W. Schmidt, & R. G. Smart (Eds.), *Research advances in alcohol and drug problems* (Vol. 3). New York: Wiley, 1976.
- RUSSELL, M. A. H. Tobacco dependence: Is nicotine rewarding or aversive? In N. A. Krasnegor (Ed.), *Cigarette smoking as a dependence process* [NIDA Monograph No. 23, DHEW Publication No. (ADM) 79-800]. Washington, D.C.: U.S. Government Printing Office, 1979.
- RUSSELL, M. A. H., SUTTON, S. R., FEYERABEND, C., & COLE, P. V. Addiction Research Unit nicotine titration studies. In R. E. Thornton (Ed.), *Smoking behaviour: Physiological and psychological influences*. Edinburgh: Churchill Livingstone, 1978.
- WILEY, R. M., & WICKHAM, J. E. The fabrication and application of a puff-by-puff smoking machine. *Tobacco Science*, 1974, 18, 67-69.
- YOUNG, J. C., ROBINSON, J. D., & RICKERT, W. S. A study of chemical deliveries as a function of cigarette butt length. *Beitrag zur Tabakforschung International*, 1981, 11, 87-95.

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