## Effects of Noise on Plasma Renin Activity in Rats<sup>1</sup> (39867)

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Noise has been shown to induce a wide variety of nonauditory physiological effects (1-3), including persistent hypertension in laboratory animals (4-8). The present study was designed to determine whether acute noise can stimulate renin secretion in the unanesthetized rat.

Methods. All animals used were male Sprague-Dawley albino rats, 200-250 g. They were fed either standard Purina chow (containing 1% NaCl) or a sodium-free diet (Nutritional Biochemicals Corp.) and were housed individually in metal cages; the housing room was on a 6 AM to 6 PM lightdark cycle. The sodium-deprived rats received less than 0.5 mmole of NaCl per day; they were on the diet for 4-6 days prior to study and had reached stable balance. Experiments were performed in separate workrooms; the rats were conditioned to being moved in their cages from the housing room to the experimental sound box and remaining in the box (with the sound turned off) for 5 min on each of 3 days preceding the day of the actual experiment; the cages were then returned to the housing room and the animals were removed from the cages and handled briefly. The same six cages were placed in the box together each day and in the same position on the sound-box floor. The sound box was a sound-proofed wooden box with speakers built into its top.

On the experimental day, six rats were similarly placed in the box, the door was closed, and the sound was turned on at the desired frequency and intensity for 30 min; immediately thereafter, with the sound still on, the rat cages were removed one at a time and carried to the adjacent room, where the rats were decapitated, blood collection lasting 30 sec. Blood was collected into tubes containing 100  $\mu$ l of 7.5 g/dl

ammonium EDTA. Control animals were subjected to exactly the same sequence of events except that the sound was not turned on. All experiments with animals on the standard diet were performed from 8:30– 9:30 AM; controls and experiments were run on consecutive days (the order was rotated from experiment to experiment). The lowsodium animals were studied from 8:30– 10:30 AM, the longer time being made possible by the fact that a low-sodium diet eliminates most of the circadian rhythm for renin (personal observation).

Plasma renin activity (PRA) and plasma renin substrate (PRS) were determined by a modification (9) of the method of Haber *et al.* (10), which utilizes the generation of angiotension I during a standardized period of incubation and its measurement with the radioimmunoassay kits supplied by New England Nuclear.

All data are presented as means  $\pm$  one standard error (SEM). The analysis used to determine statistical significance between a set of noise levels and the control for that set was the multiple-comparison procedure of Dunnett (11). This method calculates the Student's t statistic in the usual way but then uses the Dunnett tables for P rather than the usual Student's t tables. This is necessary whenever a single group of animals is used as the control for multiple experimental doses (in this case, the multiple noise levels).

*Results*. Figures 1 to 3 summarize the effects of broadband<sup>2</sup> ("white-noise") and 2000-cps sounds on PRA in rats on the normal-sodium diet. Broadband noise caused a significant increase in PRA only

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<sup>&</sup>lt;sup>2</sup> Octive-band analysis of the broadband noise at 106 dB overall was as follows (all values expressed as dB-SPL): 61 dB at 0.065 kHz; 87 dB at 0.125 kHz; 89 dB at 0.5 kHz; 96 dB at 1 kHz; 101 dB at 2 and 4 kHz; 97 dB at 8 kHz; 82 dB at 16 kHz.



FIG. 1. Effect of broadband noise on plasma renin activity in rats on a normal diet.



FIG. 2. Effects of 2000-cps noise on plasma renin activity in rats on a normal diet.



FIG. 3. Effects of 115-dB noise on plasma renin activity in rats on a normal diet.

when the intensity was increased to 115 dB (Fig. 3); 2000-cps sounds failed to increase PRA at any intensity level studied.

Figure 4 demonstrates that the animals on a low-sodium diet have a greater PRA response to sound; a highly significant increase in response to broadband noise occurred at 100 dB (P < 0.01). The response to 90 dB was not statistically significant (P = 0.14).

Plasma renin substrate (PRS) was measured in all experiments and no differences were observed between any groups.

Discussion. These data demonstrate that intensities of noise well below the human pain threshold can acutely increase PRA in unanesthetized rats maintained on either a standard or a sodium-free diet; plasma renin substrate did not change, indicating that the PRA increase reflects increased plasma renin concentration. That sodium deprivation reduced the threshold for this effect is consistent with the fact that sodium deprivation enhances the renin-releasing effects of various stimuli (12).

Given the ability of noise to increase the activity of the sympathetic nervous system (13, 14), it is logical to postulate that the increased renin secretion is mediated by increases in circulating catecholamines or enhanced activity of the renal sympathetic nerves. This pathway has previously been shown to be involved in the renin response to other types of stress in the rat (9).

The finding that noise increases PRA may have implications for the pathophysiology of hypertension. Experimental hypertension has been produced in laboratory animals using either pure auditory stimuli (4–6) or mixed auditory-visual-vibratory stimuli (7, 8); the possible role of renin in these types of hypertension has not been investigated. Finally, it has been hypothesized that noise



FIG. 4. Effects of broadband noise on plasma renin activity in rats on a low-sodium diet.

may be a risk - factor for hypertension in people (2, 3, 14).

Summary. The effects of noise on plasma renin activity (PRA) were studied in unanesthetized rats. An intensity of 115 dB (broadband) was required to increase PRA in animals eating a normal diet; the threshold was only 90-100 dB for sodium-deprived rats. Stimuli at 2000 cps of up to 115 dB were ineffective in elevating PRA.

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- 1. Kryter, K. D., "The Effects of Noise on Man." Academic Press, New York (1970).
- Welch, B. L., and Welch, A. S. (Eds.), "Physiological Effects of Noise." Plenum, New York (1970).
- Falk, S. A., and Woods, N. F., N. Engl. J. Med. 289, 774 (1973).
- 4. Medoff, H. S., and Bongiovanni, A. M., Amer. J. Physiol. **143**, 300 (1945).

- 5. Yeakel, E. H., Shenkin, H. A., Rothballer, A. B., and McCenn, S. Mc., Amer. J. Physiol. **155**, 118 (1948).
- 6. Smirk, F. R., Brit. Med. J. I, 791 (1949).
- Hudak, W. J., and Buckley, J. P., J. Pharm. Sci. 50, 263 (1961).
- Rosecrans, J. A., Watzman, N., and Buckley, J. P., Biochem. Pharmacol. 15, 1707 (1965).
- Clamage, D. M., Sanford, C. S., Vander, A. J., and Mouw, D. R., Amer. J. Physiol. 231, 1290 (1976).
- Haber, E., Koerner, T., Page, L. P., Kliman, R., and Purnode, A., J. Clin. Endocrinol. Metab. 29, 1349 (1969).
- 11. Dunnett, C. W., Biometrics 20, 482 (1964).
- 12. Vander, A. J., Physiol. Rev. 47, 359 (1967).
- Ogle, C. W., and Lockett, M. F., J. Endocrinol. 42, 253 (1968).
- Arguelles, A. E., Martinez, M. A., Pucciarelli, E., and Disisto, M. V., *in* "Physiological Effects of Noise." Plenum, New York (1970).

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