

Table 1. Summary of noradrenaline concentration and T-maze performance data; S.E.M., standard error of mean.

Group	N	Noradrenaline, cortex and hippocampus (ng/g) (mean \pm S.E.M.)	T-maze, days to criterion	
			Median	Range
Control	7	291 \pm 15		
One-stage	3	269 \pm 19	11	8-16
Two-stage	4	308 \pm 20	10.5	6-13
One-stage total lesion	8	52 \pm 5	12.5	6-16
Two-stage lesion				
Partial	4	157 \pm 17	7	6-9
Total	3	65 \pm 16	7	5-9

with food reinforcement to habituate them to the general experimental situation. The animals were then given 12 trials each day in a T-maze in which entrance into an arm with an olfactory stimulus (1 percent amyl acetate solution) led to food reward (4). The criterion was 22 correct responses in 24 trials. Animals were again given free access to food upon reaching criterion, and behavioral testing ended with measurement of activity by means of an Animex meter (5) over a 90-minute period. Throughout the study each lesion group was tested concurrently with a nonlesion control group (3). The animals were killed by spinal stem were isolated for subsequent paraffin-embedding and staining with thionin, and the cortex and hippocampus were removed for noradrenaline assay (6).

The histological and chemical analyses (Table 1) demonstrated extensive destruction of the locus coeruleus in most animals. In the groups classified as having total lesions, only two animals had any identifiable locus coeruleus cells remaining. The reduction in cortical noradrenaline ranged from 67 to 90 percent in these animals. The one-stage bilateral lesions markedly debilitated the animals; ataxia, temporary aphagia, and urogenital disorders were observed (7). Postoperative recovery in the animals with bilateral two-stage lesions was both more rapid and more complete.

During the habituation trials, all animals increased their running speeds so as to complete the 120-cm runway within 5 seconds. The running speeds for the animals with lesions were consistently lower than those for the control animals; however, we attribute this to motor variables. Motor difficulties observed (7) in some animals in all the lesion groups may have restricted their maximum running speeds. Activity, as measured during the 90-minute test period, was positively correlated with

noradrenaline content (group with single-stage lesions and corresponding controls, $r = .82$; group with two-stage lesions and controls, $r = .67$). The motor disturbances and decreased activity in the animals with lesions may account for their slower speeds in the runway.

Running speed in the T-maze was not a limiting variable because the criterion was based on entrance into the goal arm rather than speed of traversal. There was no initial preference for the olfactory cue. The animals with bilateral single-stage lesions did not differ from their controls with respect to days to criterion (Table 1) [Mann-Whitney: $U = 11$, $P = .92$ (8)]. There were no significant differences for this measure for the group with total two-stage lesions, the group with partial two-stage lesions, and their controls [Kruskal-Wallis: $H_c = 2.13$, $P > .1$ (8)]. These results fail to demonstrate a learning deficit in a T-maze discrimination despite a substantial decrease in cortical noradrenaline caused by bilateral locus coeruleus lesions.

If the nucleus locus coeruleus is the substrate for a reinforcement system operative in appetitive learning, destruction of the nucleus should lead to deficits in any learning task with food reward. Since animals with complete bilateral lesions of the locus coeruleus

can learn a T-maze discrimination, we conclude that the structure is not an essential component of a common reinforcement system.

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References and Notes

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2. G. M. Anlezark, T. J. Crow, A. P. Greenway, *Science* **181**, 682 (1973).
3. Coordinates were P 1.8, L 1.4, and V 6.7; the interparietal bone was made horizontal, and (0, 0, 0) was the intersection of the midline with a line extrapolated through the lateral lambdoid suture at the surface of the skull. Lesions were made by passing 1 ma of current for 10, 15, or 20 seconds between the tip of the electrode and a rectal cathode. In the two-stage group, lesions were made 1 week apart. Controls for the one-stage group were anesthetized and an incision was made over the skull; those for the two-stage group had no surgical treatment.
4. The apparatus is described by C. J. Long and J. T. Tapp [*J. Comp. Physiol. Psychol.* **72**, 435 (1970)]. The position of the olfactory cue varied according to a schedule of sequences [B. J. Fellows, *Psychol. Bull.* **67**, 87 (1967)].
5. J. Maj, B. Durek, W. Palider, *J. Pharm. Pharmacol.* **23**, 979 (1971).
6. A. Bertler, A. Carlsson, E. Rosengren, *Acta Physiol. Scand.* **44**, 273 (1958).
7. Seven of the initial 14 animals with one-stage lesions died before the completion of behavioral testing; none of the group with two-stage lesions died in this period. Those surviving animals in the one-stage group continued to lose weight for a median of 5 days after surgery (for the two-stage group: 4.5 days after the first lesion and 3 days after the second). An initial nystagmus and continued excessive tearing were also observed. Five animals were ataxic at the start of training (three in the two-stage group). Two surviving animals broke or loosened one of their upper incisors (four in the two-stage group). Urogenital disturbances, including bleeding from the penis, incontinence, and infection, were observed in 8 of the initial 14 animals in the one-stage group (none in the two-stage group).
8. S. Siegel, *Nonparametric Statistics* (McGraw-Hill, New York, 1956), pp. 116-127, 184-193.
9. We thank C. Kellogg, J. S. Schwartzbaum, and G. J. Thomas for their comments. Supported by NSF grant GB 38384 and PHS grant NS 10777.

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Chlorine Compounds and Stratospheric Ozone

The potentially serious impact of man-made chlorofluoromethanes (CF_xCl_y) on stratospheric O_3 is now documented in the scientific literature (1-3). In our recent report (2) we showed that the potential size of this atmospheric perturbation is large, so large that chemical control of the stratosphere will eventually pass to the chlorine oxides (ClO_x) that arise from CF_xCl_y usage. According to our calculations, the ClO_x sink for stratospheric O_3 can be ex-

pected to dominate natural sinks for O_3 by 1985 or 1990. This time dependence is striking. Time scales of decades arise from our current knowledge of atmospheric mixing rates, and from the present belief (1-3) that the only significant mechanism by which nature can break apart CF_2Cl_2 and CFCl_3 is by stratospheric photodissociation brought about by ultraviolet radiation.

One purpose of this technical comment is to facilitate the readers' efforts

to verify our calculations (2). Several statistics and definitions require clarification, and one minor error should be noted by those who desire to check our work exactly. The CF_xCl_y mixing ratio shown for the year 2005 in figure 2 of (2) does not result from a steady model 2 emission rate of $2 \times 10^7 \text{ cm}^{-2} \text{ sec}^{-1}$ at ground as the text implies. In fact, the text should read " 5×10^7 " on page 1166, column 1, line 46. Also we erroneously used a doubling time of 2.64 years in our computer computations, not 3.5 years as we stated. Consequently, we projected the total CF_xCl_y flux at ground level to be $5.2 \times 10^7 \text{ cm}^{-2} \text{ sec}^{-1}$ in late 1975 instead of the proper value, $4.2 \times 10^7 \text{ cm}^{-2} \text{ sec}^{-1}$. We have repeated our calculations for model 3 with the proper 3.5-year doubling time, a 5.05-year e-folding time. Although model 3 is more strongly affected than models 1 and 2, we find with these corrections only small changes in the model 3 results: the column O_3 destruction rate peaks around 1990, as before, at a value of about $1.55 \times 10^{31} \text{ molecule sec}^{-1}$ integrated over the globe. In our report (2) we showed a peak value (figure 1) of about $1.81 \times 10^{31} \text{ molecule sec}^{-1}$.

It should be noted that our presumed present stratospheric CIX (total concentration of gaseous chlorine compounds including Cl, ClO, and HCl) background accounts for more than half of the model 3 O_3 destruction rate and that stratospheric CIX concentrations are not well known (4). On the other hand, we must emphasize that uncertainties in the present CIX background do not affect the conclusions of our report (2). It is extremely important to learn present CIX values. Otherwise, future CIX increases will be impossible to document, whether due to chlorine release from CF_xCl_y , CIX injection by volcanoes, or HCl from the proposed Space Shuttle system (5).

Also our reference 11 in (2) presents 1973 CF_2Cl_2 and CFCl_3 production statistics as current. These quantities, $4.5 \times 10^8 \text{ kg}$ and $2.7 \times 10^8 \text{ kg}$, respectively, are DuPont's estimates of the 1973 annual global production. Presumably, the 1974 figures are larger.

The three paragraphs immediately above should assist others in repeating our calculations. Because of the potential seriousness of this problem, such checks are desirable. Similar reexamination of Crutzen's recent assessment of the expected O_3 depletion (3) are also to be encouraged. The sensitivity of model calculations to parameters such as the characterization of atmospheric transport through eddy diffusion coefficients, chemical reaction rates, and assumed background concentrations of certain species (for example, OH) must be ascertained. Researchers must reexamine stratospheric photochemical schemes for completeness: Have important gas-phase or heterogeneous reactions been overlooked? The search for alternative natural sinks (6) for CF_xCl_y should continue as we indicated (2) in reference 10. Researchers should also investigate the atmospheric fate of the fluorine atoms released from CF_xCl_y . No direct effect on stratospheric O_3 is expected (1-3), but reactions involving fluorine atoms may disrupt natural cycles of hydrogen-containing species and they may present possibilities for monitoring the CF_xCl_y effect.

Perhaps more important, atmospheric measurements of background gaseous concentrations are needed for OH, atomic oxygen, the nitrogen oxides, and the chlorine oxides, and, obviously, continued monitoring of O_3 is necessary. Short of observing O_3 decreases directly, the most telling measurement would be of ClO, its present abundance and its rate of increase. To assess the impact of HCl from the Space Shuttle, stratospheric OH data would also be useful.

Stratospheric profiles of CF_2Cl_2 , CFCl_3 , and CCl_4 are also needed immediately. As all these studies are formulated and completed, the appropriate industrial and governmental bodies may decide intelligently on questions of the regulation and control of CF_xCl_y production.

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2. R. J. Cicerone, R. S. Stolarski, S. Walters, *Science* **185**, 1165 (1974).
3. P. J. Crutzen, *Geophys. Res. Lett.* **1**, 205 (1974).
4. C. B. Farmer [*Can. J. Chem.* **52**, 1544 (1974)] has presented data from infrared measurements which implied an upper limit on the HCl mixing ratio (volume to volume) of 2×10^{-10} in the lower stratosphere. There is reason to believe that HCl is the dominant CIX species in the lower stratosphere. Later C. B. Farmer (paper presented at the 3rd Conference on the Climatic Impact Assessment Program, Cambridge, Mass., 27 February 1974) presented lower stratospheric infrared data which implied an HCl mixing ratio of 8×10^{-10} but noted that overlapping CH_4 bands confound data interpretation. Improved instrumentation may be needed to obtain reliable stratospheric CIX data.
5. Each Space Shuttle launch will deposit 5×10^4 to 10^5 kg of HCl in the stratosphere ["Environmental Statement for the Space Shuttle Program" (NASA, Washington, D.C., July 1972)]. At the projected launch rate of 50 shuttles per year, we calculate that the globally averaged HCl input rate is at least 100 times smaller than the corresponding chlorine injection rate due to continued CF_xCl_y usage at the 1973 levels.
6. P. S. Liss and P. G. Slater [*Nature (Lond.)* **247**, 181 (1974)] have established that the flux of CFCl_3 from the atmosphere to the ocean is about 2 percent of the industrial production rate.
7. We thank Dr. S. C. Liu for his extremely careful reading of our report (2), and for several helpful discussions on how to assist other readers. We acknowledge similar assistance from Prof. D. D. Davis. This research was supported by NASA grant NGR 23-005-616 and by the Climatic Impact Assessment Program, Department of Transportation, through NSF grant GA-43326.

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