-0.2°K for fixed humidity and -0.6°K for constant relative humidity. Hence the calculated bounds for average cloudiness are between -0.6° and 0.6°K ($\omega_s \leq 0.1$). For the present model a 10 percent stratospheric O_3 depletion yields a ΔT_s of ~ 0.01 at 35°N latitude. A comparison of calculated temperature differences assuming constant absolute humidity and constant relative humidity is given in Table 2.

If in the model the height of the maximum in the O_3 profile is arbitrarily decreased from 8.9 mbar (31.6 km) to 74 mbar (18 km) (by removing 50 mass percent of the O_3 from the former level and placing it in the latter level), ΔT_s (for $\omega_s = 0.1$) is +0.9°K. It is interesting that this arbitrary decrease in the height of the O_3 maximum yields a larger ΔT_s than complete stratospheric O_3 removal. This is in agreement with the results of Callis *et al.* (*12*) and Coakley (*13*).

To test the sensitivity of the results to the model cloud parameters, separate calculations of the steady-state temperature profiles were made for the cases of (i) no water clouds, (ii) no low-lying water clouds, and (iii) no high-lying water clouds. These results are shown in Table 4. A set of calculations was also performed for an 18-level atmospheric model; no essential difference was found between these and the calculations for nine levels.

The important new conclusions to be drawn from these calculations are that (i) with low-lying absorbing particles surface heating occurs when stratospheric O_3 is depleted (in contrast to the cooling calculated for stratospheric O_3 depletion with no absorbing particles) and (ii) surface albedo affects the amount of surface cooling or heating. For a sky with or without water clouds and with no suspended particles, the O_3 depletion produces less cooling with high surface albedos than with low surface albedos. With absorbing particles the O_3 depletion produces more heating with high surface albedos than with low surface albedos. Since the O_3 abundance, the surface albedo, and the effective albedo change with latitude, all effects must be considered simultaneously when considering O_3 effects at different latitudes. The surface temperature change when the O_3 is depleted, for average cloudiness at 35°N latitude, April, and a surface albedo of 0.6 or less, is between -0.6° and 0.9°K, while the effect is negligible for 10 percent O_3 removal. The sign of the surface temperature change is determined by the degree to which airborne particles affect the radiative balance. The final effect of O_3 depletion on the temperature must include all the physical details of the atmosphere, including (i) the photochemical balance, (ii) feedback due to changes in surface albedo and ice cover, (iii) feedback due to changes in cloud cover, and (iv) general circulation.

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Uterotrophic Effect of Delta-9-Tetrahydrocannabinol in Ovariectomized Rats

Abstract. *Chronic administration of delta-9-tetrahydrocannabinol, an active component of marihuana, has significant uterotrophic effects in ovariectomized rats as measured by the uterine weight gain bioassay for estrogens.*

The possibility that tetrahydrocannabinol (THC), one of the major active components of marihuana, may have estrogen-like activity has been raised by recent reports on heavy, chronic marihuana use in men (*1*) and THC administration in male rodents (*2*). However, other studies of similar concern in men (*3*) and male rodents (*4*) fail to support these findings.

Since the effects of marihuana use in women and THC administration in female rats are not well documented, the possibility that THC may have estrogen-like activity led us to examine the effects of THC in female rats, using the uterine weight gain and vaginal bioassays for estrogens. The data presented here demonstrate that delta-9-tetrahydrocannabinol (Δ^9-THC) has significant estrogenic activity, as measured by uterine weight gain in spayed rats.

Estrogens often elicit similar morphological and physiological responses in reproductive tissues of male and female rodents and human beings (*5–8*). Heavy, chronic marihuana use, estrogen, or THC administration has the following effects in men and male rodents. In men, heavy marihuana use is reported to elicit gynecomastia, oligospermia, and depression in plasma testosterone levels (*1*). Estrogen administration in men results in depressed testosterone levels, gynecomastia, antiandrogenic effects on secondary sex glands, and azoospermia (*5*). In male mice, chronic administration of THC induces complete arrest of spermatogenesis and regression of Leydig cell tissue and accessory sex glands (*2*). Chronic THC is found to increase adrenal weight, stimulate male breast development, and depress seminal vesicle weights and somatic growth in male rats (*2*). Depressed somatic growth, increased adrenal weight, and depressed seminal vesicle weights are also seen in estrogen-treated male rats (*6*). These findings lend further support to the possibility that heavy, chronic THC administration may have a direct or indirect estrogen-like activity.

It is known that estrogenic compounds are implicated in endometrial carcinoma and breast cancer in women (*7, 9, 10*). In addition, administration of estrogen-like compounds during pregnancy induces vaginal cancer in human female offspring (*11*). In female rodents, estrogens also induce uterine, vaginal, and mammary cancer (*12*). Since oral administration of THC is now used as an antiemetic in patients receiving cancer chemotherapy (*13*), the similarities in human and rodent response to estrogen administration, as well as the possibility that marihuana (THC) may have estrogenic effects, were of interest.

Replacement therapy with estrogenic compounds is known to restore the reproductive tract of ovariectomized rats to the precastrate state (*8, 14*). Using the uterine weight response assay in a preliminary experiment, we found that the

uteri of spayed rats are sensitive to Δ^9-THC in doses ranging from 1 to 10 mg of THC per kilogram of body weight.

In the present experiment, we examined the effect of estradiol benzoate (EB) or Δ^9-THC or both in ovariectomized rats in the uterine weight gain and vaginal smear bioassays for estrogens (*8, 14*). Estrogen dosage was based on previous reports on the physiologic requirements for estrogen in spayed rats (*14*). The doses of THC were based on our preliminary studies. Delta-9-tetrahydrocannabinol was supplied by the National Institute on Drug Abuse.

At 75 days of age, female rats of the Charles River (CD) strain were weighed and either sham ovariectomized or bilaterally ovariectomized. The animals were grouped so that the average body weight of each group was between 184 and 189 g, and were treated as follows: group 1, sham-ovariectomized rats treated intraperitoneally with saline; groups 2 to 5, ovariectomized rats treated either with sesame oil intraperitoneally or subcutaneously, or with saline intraperitoneally or subcutaneously to serve as controls for injection trauma, vehicle, and route of vehicle administration; group 6, EB (2 μg/kg per day); groups 7 to 9, THC (1, 2.5, or 10 mg/kg per day, respectively); group 10, EB (2 μg/kg per day) plus THC (10 mg/kg per day). Treatment with 0.2 ml of the appropriate compound was begun on the day of operation and continued daily for 14 days. Estradiol benzoate and THC were administered in sesame oil according to common usage: estrogens administered subcutaneously (*8*), THC administered intraperitoneally (*15*). Daily vaginal smears were obtained according to the method described by Zarrow *et al.* (*8*), and the animals were weighed twice weekly. At the termination of the experiment, the animals were killed by guillotine, and the uterus and adrenals were removed, stripped of adhering fat and connective tissue, and weighed on a Mettler balance. Uterine and adrenal weights were calculated as milligrams of organ weight per 100 g of body weight. Significance of difference between groups was determined by Student's *t*-test. Vaginal smear slides were coded and read by two individuals.

Since uterine and adrenal weights of the ovariectomized controls (groups 2, 3, 4, and 5) did not differ significantly from each other, data were analyzed with combined control values. Table 1 and Fig. 1 show that EB had the expected action in ovariectomized rats: a uterotrophic effect as measured by increased uterine weights (*14*). All three doses of THC had significant uterotrophic effects. At the doses employed, neither estrogen alone nor THC alone caused an increase in adrenal weights, which has been seen by others when higher doses of either estrogen (*6*) or THC (*4*) are administered. However, when EB and THC are administered simultaneously, there is a significant increase in adrenal weight. Examination of vaginal smears demonstrated

Table 1. Effect of EB or THC or both on uterus and adrenal weights of ovariectomized rats. All animals were treated with the indicated compound or compounds for 14 days, starting on the day of operation. Uterine and adrenal weights, respectively, of control groups 2, 3, 4, and 5 were not significantly different when compared with one another. Therefore, values for these four groups combined (N = 21) were calculated: uterus, mean of combined controls ± standard error of the mean = 76.74 ± 2.82; adrenal, 25.07 ± 1.06. The P values (Student's t-test) are based on a comparison of means of experimental with combined control values. Abbreviations: i.p., intraperitoneal; s.c., subcutaneous.

Group	No. of rats	Treatment	Final body weight (g) (mean ± S.E.M.)	Uterine weight* (mean ± S.E.M.)	Adrenal weight* (mean ± S.E.M.)
		Sham-ovariectomized rats (controls)			
1	5	Saline i.p.	241 ± 5.38	368.55 ± 100.53	24.27 ± 1.16
		Ovariectomized rats (controls)			
2	6	Saline i.p.	253 ± 9.28	83.44 ± 6.34	26.04 ± 1.69
3	5	Sesame oil i.p.	266 ± 8.45	78.15 ± 5.53	23.57 ± 2.23
4	5	Saline s.c.	256 ± 11.03	75.37 ± 6.06	22.73 ± 2.98
5	5	Sesame oil s.c.	289 ± 6.99	68.67 ± 2.96	27.75 ± 1.22
		Ovariectomized rats (experimentals)			
6	7	2 μg/kg EB s.c.	231 ± 5.24	277.75 ± 16.69 †	27.47 ± 1.10 ‡
7	7	1 mg/kg THC i.p.	245 ± 4.51	98.89 ± 7.65 §	24.32 ± 1.51 ‡
8	7	2.5 mg/kg THC i.p.	243 ± 5.68	174.79 ± 20.91 †	24.42 ± 0.75 ‡
9	7	10 mg/kg THC i.p.	235 ± 4.09	118.61 ± 8.38 †	27.04 ± 1.88 ‡
10	6	2 μg EB + 10 mg THC	237 ± 6.20	248.83 ± 24.38 †	33.08 ± 2.37 §

*Expressed as milligrams of organ weight per 100 g of body weight. †$P < .001$. ‡Difference from controls not significant. §$P < .01$.

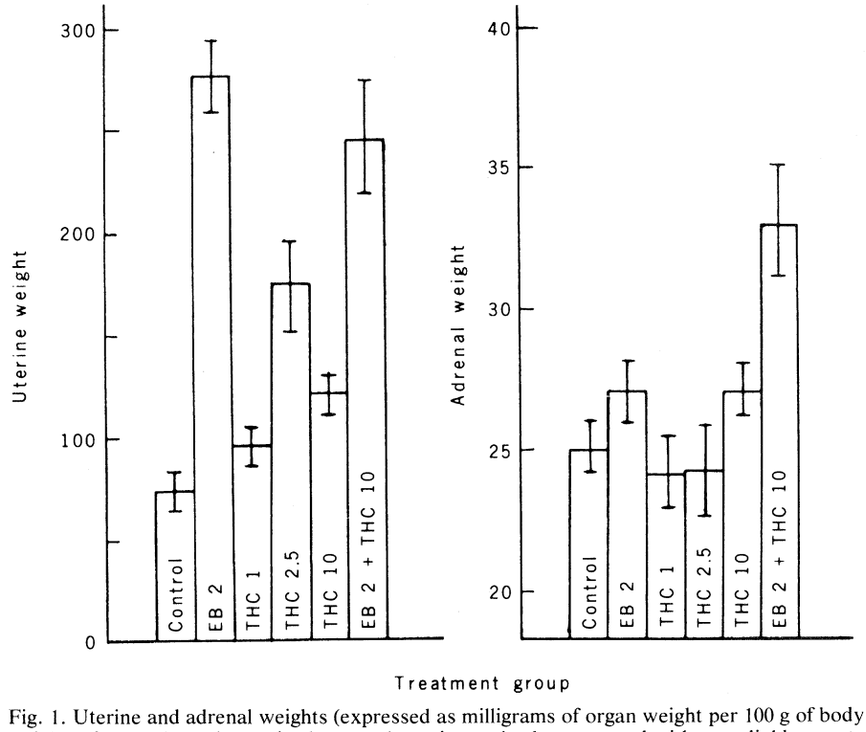

Fig. 1. Uterine and adrenal weights (expressed as milligrams of organ weight per 100 g of body weight) of control ovariectomized rats and ovariectomized rats treated with estradiol benzoate (EB) or delta-9-tetrahydrocannabinol (THC), or both. Uteri and adrenal weights of control ovariectomized groups 2 to 5 were not significantly different when compared to each other. Control values were based on combined ovariectomized controls. Uterus: combined control ± S.E.M. = 76.74 ± 2.82. Adrenal: combined control ± S.E.M. = 25.07 ± 1.06. EB 2 = 2 μg/kg per day; THC 1 = 1 mg/kg per day; THC 2.5 = 2.5 mg/kg per day; THC 10 = 10 mg/kg per day; EB 2 + THC 10 = 2 μg of EB + 10 mg of THC per kilogram per day. Each compound was administered for 14 days starting on the day of ovariectomy.

that sham-ovariectomized rats cycled normally; vaginal smears of ovariectomized rats treated with sesame oil or saline were typical of spayed rats: continuous diestrus. Ovariectomized rats treated with estrogen alone (group 6) and estrogen plus THC (group 10) showed vaginal estrus. Vaginal smears obtained from rats treated with THC alone (groups 7, 8, and 9) were not uniform; however, in general, the leukocyte counts were depressed and the epithelial cells, some of which were cornified, were increased over those of the controls. The data demonstrate that doses of Δ^9-THC which fall within the heavy, chronic ranges used in human (*3*) and animal (*2*) studies have estrogenic effects in ovariectomized rats as measured by uterine weight gain.

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Binocular Vision: Two Possible Central Interactions Between Signals from Two Eyes

Abstract. *Both foveae of light-adapted subjects were stimulated at the same time with monocularly presented lights of increasing or decreasing luminance. Combinations judged just detectable violated predictions of the energy summation and the probability summation hypotheses of binocular interaction. Rather, the results can be explained by independent central neural mechanisms that signal the sum or the difference of stimuli to two eyes.*

We have studied the interactions of signals from two eyes in human psychophysical experiments. Our binocular stimuli comprised pairs of simultaneous monocular luminance changes of 100-msec duration or less. The changes (of energy denoted E_L and E_R for left and right eyes, respectively) were either increments (E_L or E_R positive) or decrements (E_L or E_R negative). For a wide range of positive and negative values of E_L and E_R binocular thresholds seemed to obey the relation

$$E_L^2 + E_R^2 + 2KE_LE_R = 1 \qquad (1)$$

where K expresses the relative strengths of the mechanisms. This result is inconsistent with two theories of binocular interaction, the theories of energy summation and of probability summation (*1*). Rather, it supports the theory that two independent mechanisms, one that sums signals from two eyes and one that computes a difference, provide information to a more central decision center. Binocular neurons monitored in neurophysiological investigations appear to sum signals from two eyes and, often, to compute the difference of the signals from two eyes (*2*). Cells like these may be the neural substrate for the behavior we have observed in humans.

One line of research relevant to the study of the interaction of signals from two eyes concerns the comparison of monocular and binocular visual thresholds (*3*). The many studies designed to make this comparison provide an equivocal picture (*4–7*), but differences in reported data can be explained by the range of uncertainty inherent in psychophysical measurement (*8*). Moreover, comparing monocular with binocular thresholds unnecessarily restricts the investigation. We studied binocular stimuli whose monocular components were combinations of positive and negative luminance changes. We could thus test the various theories in circumstances under which their predictions differed (*9, 10*).

Light-adapted subjects fixated foveal targets of 10 minutes of arc in diameter (Monsanto 5047) in a mirror haploscope that allowed independent control of the stimuli to two eyes (*11*). The targets were continuously illuminated at levels judged by the subject to be equally bright. Stimuli were square pulse luminance changes

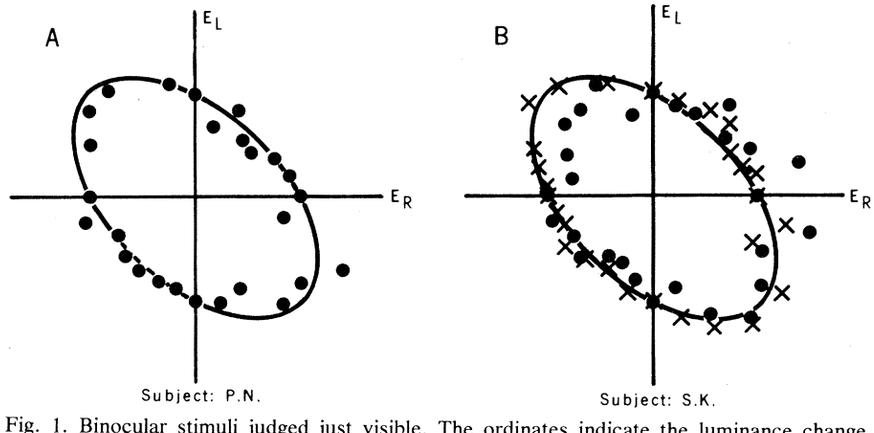

Fig. 1. Binocular stimuli judged just visible. The ordinates indicate the luminance change energy to left eye (E_L), and the abscissas indicate the luminance change energy to right eye (E_R). For both axes, the positive coordinates refer to luminance increments, and the negative coordinates refer to luminance decrements. Closed circles represent the data from two series of 28 stimuli, adjusted to be just visible by two subjects; crosses represent the median data from seven runs of subject S.K. Ellipse is fit by eye to the data on the constraint that it intersect axes the same distance from origin. For both subjects, decrements yielded 20 to 30 percent lesser threshold. This difference between the detectability of increment and decrement is well known (*21*). We chose to ignore it rather than to incorporate an additional parameter in our model to account for it. Accordingly, data points in a given quadrant have been normalized so that axis points always fall the same distance from the origin.