Thus the increase in acetylcholinesterase seems to be somewhat specific. The absence of increase in neurotubule protein is consistent with the earlier results[3], showing that protein synthesis is not required for initial elaboration of processes after removal of serum, implying that pre-existing neurotubule protein can be utilized.

We have observed, in agreement with the results of Seeds *et al.*[3], that transfer of neuroblastoma cells to serum-free medium induces most cells in the culture to elaborate axon-like processes. We also found that the latter processes are formed to the same extent if drugs which inhibit cellular DNA synthesis are added to the cells, even in the presence of serum. This indicates that serum *per se* does not inhibit the extension of axons directly, but probably acts by promoting cell growth and division which is antagonistic to morphological differentiation. For example, time lapse cinematography has shown that mitotic neuroblastoma cells withdraw their axon-like extensions completely (unpublished observations).

The fact that we observed a sizable induction of an enzyme involved in neural transmission accompanying the morphological differentiation suggests that a rather complex differentiation process may occur as a result of stopping cell proliferation. Not all enzymes involved with neural function were observed to increase, however. The drug studies suggest that there is *de novo* enzyme synthesis. It is conceivable that acetylcholinesterase is normally synthesized in the late G_1 phase of the cell cycle. Then the induction observed after removal of serum and addition of drugs could be accounted for by an arrest of the cells in late G1 and early S, and cholinesterase synthesis would continue for extended periods in these non-growing cells.

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JOSEPH R. KATES
RADENE WINTERTON
KURT SCHLESSINGER

Departments of Chemistry and Psychology,
University of Colorado,
Boulder, Colorado 80302

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1 Augusti-Tocco, G., and Sato, G., *Proc. US Nat. Acad. Sci.*, **64**, 311 (1969).
2 Schubert, D., Humphreys, S., Baroni, C., and Cohn, M., *Proc. US Nat. Acad. Sci.*, **64**, 316 (1969).
3 Seeds, N. W., Gilman, A. G., Amano, T., and Nierenberg, M. W., *Proc. US Nat. Acad. Sci.*, **66**, 160 (1970).
4 Eagle, H., *Science*, **122**, 501 (1955).
5 Ellman, J. L., Courtney, K. D., Andres, jun., V., and Featherstone, R. M., *Biochem. Pharmacol.*, **1**, 88 (1961).
6 Levitt, M., Gibb, J. W., Daly, J. W., Lipton, M., and Udenfriend, S., *Biochem. Pharmacol.*, **16**, 1313 (1967).
7 Potter, L. T., Glover, V. A. S., and Saelens, J. K., *J. Biol. Chem.*, **243**, 3864 (1968).
8 Borisy, G. G., and Taylor, E. W., *J. Cell. Biol.*, **34**, 525 (1967).

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Effects of LSD on Receptive Fields of Single Cells in the Lateral Geniculate Nucleus of the Cat

SMALL doses (~100 μg) of lysergic acid diethylamide (LSD) taken orally cause hallucinations and distortions of visual perception in man[1]. The latter effects suggest that LSD disturbs normal integrative functions in the visual pathways. It is known that transmission through the visual pathways is depressed by the drug, for small doses (15–30 μg/kg) given parenterally depress the response of the cat lateral geniculate nucleus (LGN) to shocks applied to the optic nerve[2,3]. Similar doses have no effect on the responses of the visual cortex to electrical stimulation of the optic radiation. These results

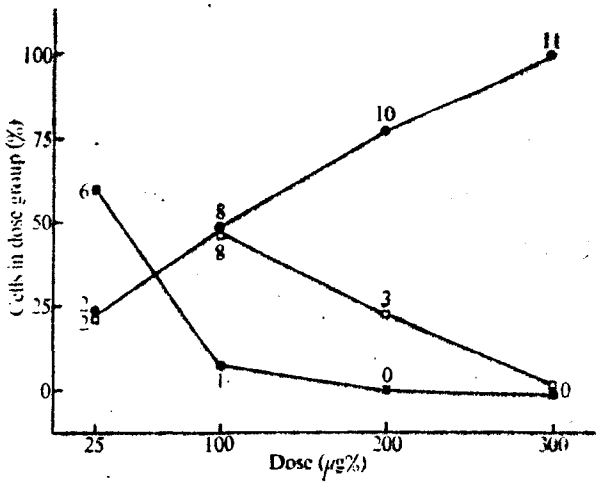

Fig. 1 Effects of LSD on spontaneous activity. Percentage of cells in which spontaneous activity was reduced by LSD (●); increased by LSD (□), and unchanged (■). The number of cells is shown beside each point. The number of cells of which activity was depressed is significantly greater for the higher doses (200 μg, $P<0.05$; 300 μg, $P<0.01$) than when the dose was 25 μg. Each cat weighed 3 kg.

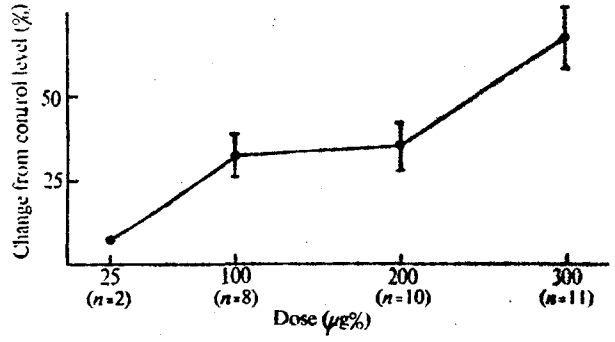

Fig. 2 Percentage reduction in mean spontaneous firing rate (ordinate) of cells depressed by LSD, in relation to dose (abscissa). Each point on the graph shows the average mean decrease in firing rate for each dose. The number of cells (n) in each dose level is given below the abscissa. The vertical bars show the standard errors. No standard error is shown for the 25 μg group because only two cells in this group were inhibited. Each cat weighed 3 kg.

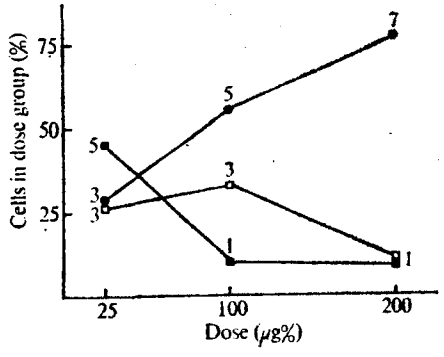

Fig. 3 Effects of LSD on the light-evoked responses of field centres of LGN cells. The number of cells is shown at each point. Symbols are as in Fig. 1. Each cat weighed 3 kg.

suggest a relatively selective influence of LSD on the LGN, which is known to be involved in the integration of signals passing to the visual cortex from the optic tract[4]. This function can be analysed by studying the receptive fields of single cells in the nucleus. We have therefore studied the effects of LSD on the spontaneous and evoked activity of cells in the LGN of cats, and present a brief account of some of our findings.

Sixteen adult cats (mean weight 2.7±0.33 (s.d.) kg) were used. Anaesthetic and surgical techniques were similar to those described earlier, as were the methods for recording from single

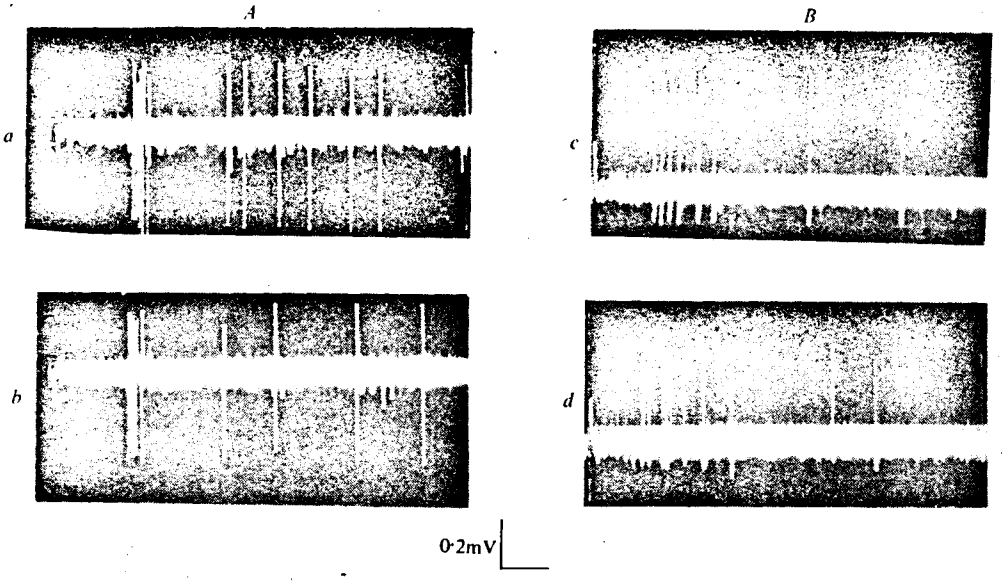

Fig. 4 Responses of two LGN units to light shone on the centres of their receptive fields. *A*, Cell with "on" centre, "off" surround. Centre responses before (*a*) and after (*b*) 100 μg of LSD had been administered. Analysis of the data for this cell showed that the centre responses were significantly ($P < 0.002$) smaller after the drug had been given than before. Trace triggered by onset of light. *B*, Cell with "off" centre, "on" surround. Centre responses before (*c*) and after (*d*) 100 μg of LSD. Responses significantly ($P < 0.002$) larger after injection than before. Responses *b* and *d* were recorded about 5 min after the injection of LSD. Time scale was 36 ms for *a* and *b* and 50 ms for *c* and *d*.

cells and plotting receptive fields[5]. In all experiments, background luminance was 4 cd m^{-2}. After the field of an LGN cell had been plotted, a spot of light was focused on the centre of the field. The spot, which lasted 0.5 s and was 1.5 to 2 log units brighter than background luminance, was presented twenty times at 5 s intervals. The surround region of the field was similarly stimulated, but by an annulus of light. These responses and also the spontaneous activity of the cell were recorded on magnetic tape (control data). A dose of LSD (hydrogen tartrate salt), dissolved in 0.5 ml. of normal saline, was then injected through a cannula in the saphenous vein. The dose was 25, 100, 200, or 300 μg, each approximating to 10, 40, 80 and 120 μg/kg. Immediately after the injection the spontaneous activity and then the responses (experimental data) of the centre and surround of the field were recorded. Control and experimental data were compared. The period (3 min) in which spontaneous activity was recorded was broken down into epochs of 10 s. The number of spikes in each epoch was counted. Control and experimental counts were compared using the Mann–Whitney *U* test (two-tailed) and were considered significantly different if $P < 0.05$. The number of spikes present in the 0.5 s after the onset ("on" responses) or offset ("off" responses) of the light was counted for each set of twenty stimuli. Data for control and experimental responses were compared as described for spontaneous activity. Fifty cells were studied and data on field plots were obtained from twenty-nine of them. All statistical tests are two-tailed except where stated.

LSD affected spontaneous activity in a dose-dependent manner within a few seconds of the injection (Fig. 1). The percentage of cells of which spontaneous activity was reduced increased with the dose. The mean reduction in firing rate, expressed as a percentage of the mean control value, was greatest (68.3 ± 8.8 s.e.) with the largest dose (Fig. 2): the depression of activity was greater ($P < 0.05$) for this dose than for doses of 100 or 200 μg, for which the percentage changes do not differ significantly.

Not all the effects observed were depressive (Fig. 1). The spontaneous activity of eight out of seventeen cells was increased after injection of 100 μg of LSD, but was not increased in any of the eleven cells in the 300 μg sample. This difference was significant ($P < 0.01$). The facilitatory effect of the 100 μg dose was often considerable and amounted to a mean percentage increase in firing rate of 65.1 ± 21.4 (s.e.), compared with the pre-injection rate.

The effects on spontaneous activity of $\geqslant 200$ μg of LSD suggested that such doses would depress the evoked discharges to photic stimulation, an expectation which is supported by the data in Fig. 3. This graph is derived from a study of the centre responses of twenty-nine cells. When 25 μg of LSD was given, the responses of only three out of a sample of eleven cells were reduced. When 200 μg was given, the responses of seven out of nine cells were reduced. These proportions were significantly ($P < 0.05$, 1 tailed) different. An example of a unit of which centre response was depressed is shown in Fig. 4 *a* and *b*.

With all three doses used in the experiments on which Fig. 3 is based, the responses of some cells to centre (and also to surround) stimulation were significantly increased. Data for a unit with a centre response which was increased are shown in Fig. 4 *c* and *d*. Doses of $\leqslant 100$ μg were less depressive than a dose of 200 μg.

In fourteen out of twenty-six cells the responses to centre and surround stimulation were both affected by LSD in the same direction (that is the responses were either both decreased or both increased). In the other twelve cells the effects on the centre and surround responses were not in the same direction. There was no consistent relationship between field type ("on" centre or "off" centre) and the influence of LSD. Mixed effects of the drug on the centre/surround organization were more common when doses of $\leqslant 100$ μg were given than when the dose was 200 μg. Thus the centres and surrounds of seven of the nine cells in the group receiving 200 μg of LSD were affected in the same way (all depressed), whereas the centres and surrounds of only two of the eleven cells in the group receiving 25 μg were similarly affected. These proportions are significantly different ($P < 0.02$).

In doses of $\geqslant 200$ μg, LSD tends to depress the spontaneous and evoked activity of cells in the LGN, a result which is consistent with the observation that very large (1 mg/kg) doses of LSD given to unanaesthetized cats cause blindness, which is reversible[3]. Lower doses affect the organization of the receptive fields in the LGN in a complex way. Frequently, there is a change in the normal balance of centre/surround antagonism. This antagonism is thought to be an important mechanism for sensory contrast[6,7], and is almost certainly connected with pattern discrimination in the visual cortex[8]: so interference with the normal balance of this antagonism is likely to influence these functions. It is interesting that the lower doses used in these experiments were in the same range as that which, in man, is known to result in complex visual disturbances.

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JENNIFER M. MCKAY
GABRIEL HORN

Department of Anatomy,
University of Cambridge.

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