four more naive females, the offspring of which are identified as the '25–48 h' offspring. After 24 h with these females each male was then returned to the initial cage containing the drinking water with 5% sucrose solution (with or without METH) and the cycle repeated. Each naive female was exposed to males for 6 consecutive days.

The neonatal (21-day) mortality of the offspring of the three groups of males is shown in Fig. 2. In 21 days, 13% of 132 offspring sired by control males died, whereas 56% of 100 offspring sired by high-dose METH males died (difference very significant: $\chi^2 = 47.08$, $P < 0.001$) and 34% of 100 progeny of low-dose METH males died (difference from controls significant: $\chi^2 = 13.59$, $P < 0.01$, and from high-dose of METH progeny: $\chi^2 = 8.91$, $P < 0.01$). The neonatal mortality of 244 offspring of males which had received METH 25–48 h before mating was only 25%. This did not differ significantly ($\chi^2 = 3.41$, $P > 0.05$) from the 21-day mortality of their controls (17%). Of the ten litters sired by control males only one had a death rate in excess of 30% (Fig. 3), whereas of the eight litters sired by the high-dose METH males, six litters lost 40% or more of the offspring born alive. The low-dose methadone litters had a smaller death rate than the high-dose METH offspring. These data demonstrate that the increased mortality of the METH-sired offspring is not simply a consequence of the deaths of the offspring of a small proportion of the males, but of an increased mortality in virtually all litters.

Pretreatment of male rats with METH before mating thus produces a significant increase in neonatal (21-day) mortality of the offspring of the METH-treated males and naive females when compared to control matings. Our data show a dose-response relationship for this phenomenon as well as evidence

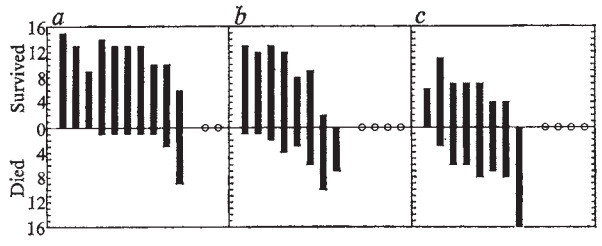

Fig. 3 Survival and death in each litter of offspring born to females mated to (*a*) controls and males receiving (*b*) low- and (*c*) high-dose METH 0–24 h before mating. The vertical black bars show the survival or death of the live offspring from each litter. ○, Females which did not deliver offspring.

that the lethal effect is seen primarily in offspring sired during the first 24 h following administration of METH to the male. Morphine produced a similar but less marked effect. An urgent problem in medicine is the fact that 1–3% of all infants born have one or more unexpected congenital anomalies which cannot be explained by classical teratology. Our preliminary results suggest that it is necessary to investigate not only the drugs which were administered to the mother before and during pregnancy, but also those drugs used by the father. This approach may contain the answers to some of the unexplained problems of childhood growth and development.

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1 Isbell, H., and Vogel, V. H., *Am. J. Psychiat.*, **105**, 909 (1949).
2 Dole, V. P., and Nyswander, M., *J. Am. med. Ass.*, **193**, 646–650 (1965).
3 Jaffe, J. H., *Proc. 5th natn. Conf. Meth. Treatment*, 1414–1421 (1973).
4 Smith, D. J., Heseltine, G. F. D., and Corson, J. A., *Life Sci.*, **10**, 1233–1242 (1971).
5 Smith, D. J., Joffe, J. M., and Heseltine, G. F. D., *Physiology and Behavior* (in the press).

Physiology of visual cells in mouse superior colliculus and correlation with somatosensory and auditory input

THE two main targets of the mammalian optic nerve fibres are the lateral geniculate body and the superior colliculus (optic tectum). From studies with various techniques, and in several mammalian species including the cat[1-5], monkey[6-9], rabbit[10-12], rat[13], and ground squirrel[14] three major functions of the superior colliculus have been described. In the superficial layers the visual input is processed in a specific way; in deep layers several sense modalities, chiefly visual, auditory and somatosensory, are brought together; stimulation of the tectum results in an orienting of the animal's eyes, head or body towards a location corresponding topographically to the part of the tectum stimulated.

Gordon[1] has shown that for a given location in the cat tectum there is a good correlation between the positions of visual receptive fields and the directions from which maximal auditory responses are evoked. She also found a correlation between preferred directions of stimulus movement in the two modalities. The agreement between visual and somatosensory cells was much looser, although visual receptive fields near the vertical midline were correlated with tactile fields on the face, and temporal visual fields, with tactile fields on the body or legs. She rarely observed responses from whiskers. Cats move their eyes and especially their heads extensively, however, and a very close relationship between retinotopic and somatosensory maps was perhaps not to be expected.

We have studied the superior colliculus in the mouse, a small compact animal with very little eye movement and relatively little head movement; a mouse rather turns its whole body towards an interesting object. The major part of the mouse's visual field is crossed by an elaborately developed somatosensory organ, the vibrissae. Whisker movement in the mouse is very rapid, but the excursions are small, so that the whiskers bear a relatively constant relationship to the visual field. One should therefore not be surprised to find a close topographical relationship between the tectal projections from retina and whiskers.

In our study, ten mice of the C57BL/6J strain were used. Throughout the experiment a mouse was kept under light anaesthesia (pentobarbital and chlorprothixene) and was neither paralysed nor artificially respirated. (For exact procedures, see Dräger[15].) The head was held fixed by means of a small metal block glued to the skull, thus leaving the ears free. Visual receptive fields were mapped on a translucent tangent screen placed at a distance of 10.5 cm from the mouse. Electrolytically polished tungsten electrodes were used for recording. Electrode tracks, most of which were perpendicular to the tectal surface, were marked by several small electrolytic lesions (2 μA for 2 s) and reconstructed histologically. A total of 323 recordings were made in 48 penetrations. Of these records, 145 were probably from tectal cells. The remaining 178 recordings, from unit clusters or poorly resolved units, were useful for purposes such as topographical mapping of the tectal surface.

Cells in the superficial layers had small visual receptive fields (average diameter 9°) whose locations in the visual field varied according to a topographical map similar to that described for other vertebrates[16]: the nasal visual field projected anteriorly and the upper visual field medially. These cells responded only to visual stimulation, with best responses to a slowly moving small spot of any shape. One-quarter of the cells preferred one direction of movement; for most cells the preferred direction was upward. Deeper in the tectum most visual cells had very different receptive-field properties, with large fields (20°–60°), sluggish and transient responses to small moving objects, little or no response to large stimuli, and often a directional selectivity with preference for upward movement. Characteristically these deeper-layer cells tended

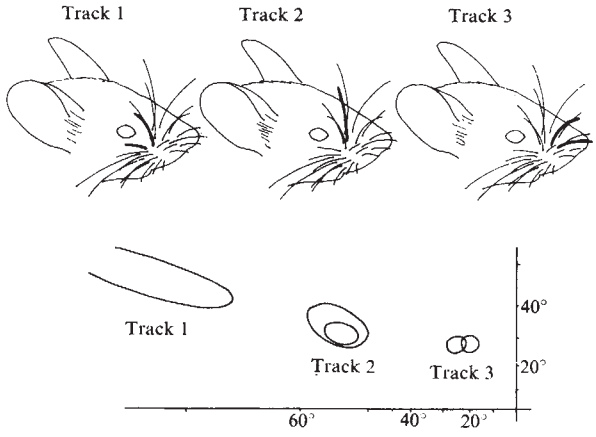

Fig. 1 Correlation between somatosensory and visual receptive fields recorded in three successive electrode penetrations. Lower part of diagram shows visual receptive fields recorded in superficial tectal layers and mapped on tangent screen. Mouse was facing the tangent screen at right angles, 10.5 cm behind it. Origin of coordinate axes marks intersection with the long axis of the mouse. Upper part of the diagram indicates whiskers giving strongest responses in the same electrode tracks at a deeper level; these whiskers are drawn as thicker lines.

to habituate if the same stimulus was repeated, but fired again if the spot or object was moved through a different part of the field. Similar visual receptive field properties in the superior colliculus have been described in other species[5,6,10,12,13].

At a slightly deeper level, in the stratum griseum mediale, cells responding to somatosensory or auditory stimulation were first encountered intermixed with visual cells, and with cells responding to two (or rarely to all three) modalities. Still deeper in the tectum, over a distance of several hundred μm, somatosensory or auditory modalities tended to take over completely until, in some penetrations, the electrode again entered an area of mixed responses. There was no segregation of somatosensory and auditory cells into sub-layers; cells responding to a given modality seemed rather to be arranged in clusters with some intermixing at the boundaries between clusters.

Somatosensory responses were obtained about twice as frequently as auditory. In most penetrations the tactile receptive fields were located on one or a few whiskers. Gently tapping one whisker evoked a short burst of spikes with little difference in response as the direction of hair deflection was varied.

The most striking feature was a very consistent relationship in any one electrode track between the location of visual receptive fields and that of somatosensory receptive fields. A series of three electrode tracks in one experiment is illustrated in Fig. 1. The axes in this illustration represent the horizon and the vertical midline of the mouse, drawn on the tangent screen so as to cross at the extended longitudinal axis of the mouse. Numbers on the axes mark degrees of eccentricity. Visual receptive fields in the three tracks are outlined on the screen. In the upper part of the figure, the whiskers giving the strongest responses from cells deeper in the tectum are drawn more heavily than the others. In the first track there was a clear correlation between temporal visual fields and posterior whiskers; moving nasally in the visual field in tracks 2 and 3 was accompanied by movement to more anterior whiskers. In other series of penetrations a similar correlation was seen between visual receptive-field positions and the whiskers that evoked the best responses at deeper levels in the tectum. If the visual receptive fields were progressively lower in a set of tracks, the whisker fields likewise moved down. By drawing the projections of the whiskers through the eye on to the tangent screen, we could show that for a given perpendicular penetration the visual receptive fields were crossed by just the whiskers that evoked maximal responses from the somatosensory cells deeper in the tectum. This correlation held not only for neighbouring visual and somatosensory cells, but also for single cells driven by both modalities.

In parts of the tectum in which visual receptive fields were far peripheral, and no whiskers lay in the way, somatosensory responses at deep levels were evoked from other parts of the body. Visual fields far down, where the mouse might see its own paw, were associated with tactile fields on the dorsum of the paw. Far temporal visual fields were correlated with somatosensory fields on the flank, shoulder and ear; here an upward movement in the visual field was paralleled by upward movement in the somatosensory map, from the flank to the tip of the ear.

Reactions to auditory stimulation were found less frequently than to tactile stimuli and they tended to be less well localised. Auditory responses could be evoked by complex sounds rich in high frequencies like clicks or crackling noises. Usually only sounds generated from a direction contralateral to the colliculus were effective in driving auditory cells. In eight out of thirteen cells the auditory receptive field in the horizontal plane was restricted to an angle of about 50°–150°, which included the visual and somatosensory receptive field of cells recorded simultaneously or in the close vicinity.

The mouse superior colliculus thus contains three topographical maps, superimposed and roughly in register, of the surroundings as observed through visual, somatosensory and auditory modalities. We assume that this system serves to orient the animal to an interesting stimulus whatever the sense modality.

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1 Gordon, B., *J. Neurophysiol.*, **36**, 157–178 (1973).
2 Sprague, J. M., and Meikle, T. H., *Expl Neurol.*, **11**, 115–146 (1965).
3 Stein, B. E., and Arigbede, M. O., *Expl Neurol.*, **36**, 179–196 (1972).
4 Sterling, P., and Wickelgren, B. G., *J. Neurophysiol.*, **32**, 1–15 (1969).
5 Straschill, M., and Hoffmann, K. P., *Brain Res.*, **13**, 274–283 (1969).
6 Cynader, M., and Berman, N., *J. Neurophysiol.*, **35**, 187–201 (1972).
7 Goldberg, M. E., and Wurtz, R. H., *J. Neurophysiol.*, **35**, 542–559 (1972).
8 Robinson, D. L., *Vision Res.*, **12**, 1795–1808 (1972).
9 Schiller, P. H., *Invest. Ophthal.*, **11**, 451–460 (1972).
10 Horn, G., and Hill, R. M., *Expl Neurol.*, **14**, 199–223 (1966).
11 Masland, R. H., Chow, K. L., and Stewart, D. L., *J. Neurophysiol.*, **34** 148–156 (1971).
12 Schaefer, K. P., *Brain Behav. Evol.*, **3**, 222–240 (1970).
13 Humphrey, N. K., *Expl Neurol.*, **20**, 312–340 (1968).
14 Michael, C. R., *Vision Res. Suppl.*, **3**, 299–308 (1971).
15 Dräger, U. C., *J. comp. Neurol.* (in the press).
16 Kruger, L., *Brain Behav. Evol.*, **3**, 169–177 (1970).

Conductance of channels opened by acetylcholine-like drugs in muscle end-plate

MOST recent views of the way in which acetylcholine (ACh) can cause ion channels to open postulate that the channel can exist only in one or other of two distinct conformations, open or shut[1–4]. In their simplest form, these theories predict that a channel, once it is open, will have the same conductance whichever drug caused it to open. We have estimated average single channel conductances for four cholinomimetic agonists, and find this prediction is not confirmed.

The mean single-channel conductance, and mean lifetime of the open state, have been estimated at the voltage-clamped end-plate of the frog (summer *Rana pipiens*) cutaneus pectoris muscle. Methods similar to those of Anderson and Stevens[5], were used with the addition of Normarski interference optics,