an apparent control of the amount of metabolite 4B found in the intestine. Administration of massive amounts of cholecalciferol does not increase the amount of metabolite 4B found in the intestine above approximately 0.2 I.U. (0.05 μg) per chick intestine (*4, 16*). In addition, it remains to be determined whether metabolite 4B is active in other cholecalciferol target tissues such as bone or whether it will be effective in alleviating any of the abnormalities in calcium metabolism discussed earlier. Until metabolite 4B is characterized and synthesized, these questions will probably remain unanswered.

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11. Fifteen hours after the intracardiac administration of a physiological dose of 10 I.U. of radioactive cholecalciferol to rachitic chicks, the bulk of the radioactivity in the plasma, liver, and intestine exists as three polar metabolites. These are designated metabolites 4A, 4B, and 4C on the basis of their chromatographic mobility on silicic acid columns. Metabolite 4A from both intestine and plasma has biological and chromatographic properties identical with 25-hydroxycholecalciferol (*4*), but it has not yet been chemically verified that metabolite 4A is 25-hydroxycholecalciferol. In the intestine the majority of the radioactivity is present in the form of metabolite 4B (*4*).
12. One international unit of cholecalciferol (vitamin D_3) is equal to 0.025 μg or 0.065 nmole. The minimum daily requirement for cholecalciferol in the chick is 10 to 20 I.U. (*13*).
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Superior Colliculus Cell Responses Related to Eye Movements in Awake Monkeys

Abstract. *Single cell responses were recorded from the superior colliculus of awake monkeys trained to move their eyes. A class of cells that discharged before eye movements was found in the intermediate and deep layers of the colliculus. The response of the cells was most vigorous before saccadic eye movements within a particular range of directions. These cells had no visual receptive fields, and visually guided eye movements were not necessary for their discharge, since they responded in total darkness before spontaneous eye movements and vestibular nystagmus.*

The superior colliculus has long been suspected to be associated with eye movements (*1*). Electrical and chemical stimulation experiments (*2*) have substantiated this point of view. Ablation of the superior colliculus has shown lasting effects on eye movements in some cases (*3*) but not in others (*4*). However, studies of single cells in the superior colliculus have dealt not with the effects of eye movements but with the determination of the visual receptive fields (*5*) or of proprioceptive input (*6*). We have now recorded responses of single cells in the superior colliculus of awake monkeys trained to make eye movements, and we have found neurons related specifically to eye movements rather than to any visual stimuli.

Rhesus monkeys (*Macaca mulatta*) were trained to look at a spot of light for periods of 1 to 3 seconds (*7*). The spot (width, 0.5 degree of arc) was projected on a tangent screen at a distance of 58 cm in front of the monkey. The spot could be held stationary or could be moved continuously with speeds ranging from 5 to 125 degrees of arc per second. This fixation point could also be made to jump instantaneously from one point to another by turning off the first spot as a second one at a different point came on. These methods could reproducibly elicit fixation, smooth pursuit eye movements, or saccadic eye movements.

During recording experiments the monkey's head was held rigidly according to the method developed by Evarts (*8*). Eye movements were measured by using vertical and horizontal electrooculograms (*7*), and lateral rectus electromyograms were obtained from ball electrodes implanted on the capsule overlying the lateral recti. The activity of single cells in the superior colliculus was recorded extracellularly using platinum-iridium microelectrodes insulated with glass that were positioned stereotaxically by a movable microdrive (*8*). The amplified signals from the neurons, electrooculograms, and electromyograms, together with information about the monkey's behavioral responses, were displayed on oscilloscopes and a penwriter and were stored on magnetic tape. At the end of the experiment, monkeys were killed, perfused with 0.95 percent saline and then 10 percent formalin, and 50-μm sections through the superior colliculus were stained alternately with Weil and cresyl violet stains.

We studied 332 cells in the superior colliculus of three monkeys. The anatomical location of 157 cells within the colliculus was determined histologically by proximity to electrolytic lesions made at the time of recording: 50 percent of the cells were in two of the upper layers of the superior colliculus (stratum opticum and stratum griseum superficiale), 40 percent in the intermediate layers (stratum griseum intermedium and stratum album intermedium), and 10 percent in the deep layers (stratum griseum profundum and stratum album profundum). The cells in the two upper layers had visual receptive fields, as has been reported previously (*5*). In the four deeper layers a variety of cell types were found, but in this report we consider only those cells related exclusively to eye movements. Of the histologically identified cells in the intermediate and deep layers, 20 percent were of this type; in the superficial layers, there were none. We studied 26 of these cells in detail.

The change in discharge rate of each cell preceded the eye movement, as is

shown in Fig. 1A. During this recording the animal was fixating a point that suddenly jumped 20 degrees of arc from left to right. An increase in rate of cell discharge precedes the resulting eye movement. The discharge of the same cell during successive similar eye movements is shown in Fig. 1B. The arrow indicates when the eye movement occurs. The cell discharge rate increases about 120 msec before the start of the eye movement, but with a very irregular time of onset; the end of the burst is well synchronized with the eye movement. Figure 1C shows the same cell discharges with the trace triggered on the stimulus jump rather than on the eye movement. The cell discharge pattern is related more precisely to the eye movement than to the stimulus movement.

For all the cells included in this study some portion of the burst of cell discharges preceded the eye movement. However, the interval between the neuronal response and the eye movement differed from cell to cell and within the response of a given cell (Fig. 1B). This interval ranges from 10 to 150 msec, with over half of the cells initiating their response 40 to 85 msec before the electromyogram burst associated with the eye movement. The discharge of roughly one-third of the cells ended before, one-third with, and one-third after the end of the movement. Some cells, like that of Fig. 1, ended their response well synchronized with the eye movements; some began their response time-locked to the eye movements; and some cells clearly increased their discharge rate before the eye movement but with no regular latency.

Each cell had a particular direction of eye movement associated with its most vigorous rate of discharge; the opposite direction of eye movement was associated either with no change in the firing rate or with a decrease. Thus, for the cell in Fig. 2A (the same cell as in Fig. 1), a horizontal eye movement from left to right (shown by a downward deflection of the electrooculogram) is preceded by a burst of cell activity, whereas the movement in the opposite direction is accompanied by a pause in the cell discharge. The optimal direction of eye movement was flanked on both sides by a range of eye movement directions that were associated with less vigorous responses. The entire range of eye movement directions varied from cell to cell from 50 to 135 degrees. The optimal direction of

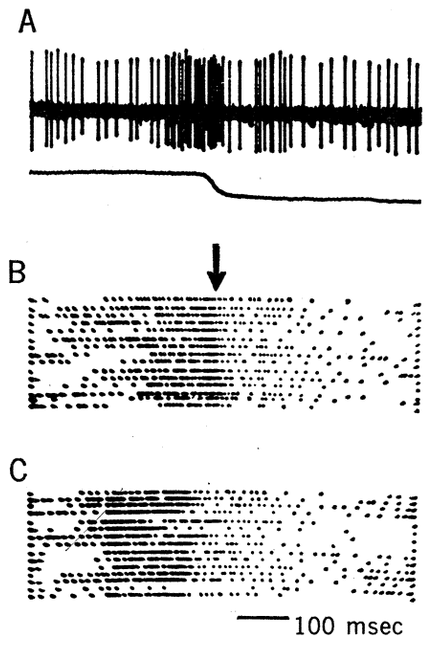

Fig. 1. Cell discharge associated with eye movement. (A) The rate of cell discharge increases before the eye moves from left to right through 20 degrees of arc (indicated by the deflection of the electrooculogram in the lower trace). (B and C) Each discharge of the same cell is indicated by a dot produced by intensifying the beam of an oscilloscope. A dot also indicates the beginning and end of each line. Successive lines are associated with successive eye movements. In (B), the start of each line is time-locked to the eye movement; each line begins 400 msec before the left-to-right eye movement, which occurs at the arrow in the middle of the line. In (C), each line is time-locked to the jump of the fixation point stimulus rather than to the eye movement. Each line starts at the time of the stimulus jump; the cell discharges and eye movements are the same set shown in (B).

eye movement in a given cell was to the side contralateral to the colliculus under study, or up or down in the vertical meridian. However, since the range of eye movement direction was as great as 135 degrees, some cells gave suboptimal responses for directions of eye movements toward the ipsilateral side.

Although the cell response depended on the direction of eye movement, it did not depend on the absolute position of the eye at the beginning or end of the eye movement. We could detect no difference in discharge pattern during comparable eye movements initiated from widely separated points on the tangent screen (which extended 30 degrees on either side of the midline).

All of the cells responded briskly before saccades but poorly, if at all, with slow pursuit movements. The cell responses may also vary with the amplitude of the eye movement. For example, one cell gave similar responses for saccades from 15 to 40 degrees of arc long in the optimal direction. Another did not respond with movements longer than 25 degrees of arc, although it gave maximal responses for movements from 5 to 20 degrees of arc long in the optimal direction.

For every cell the response depended on the direction and speed of the eye movement; it was not a sensory re-

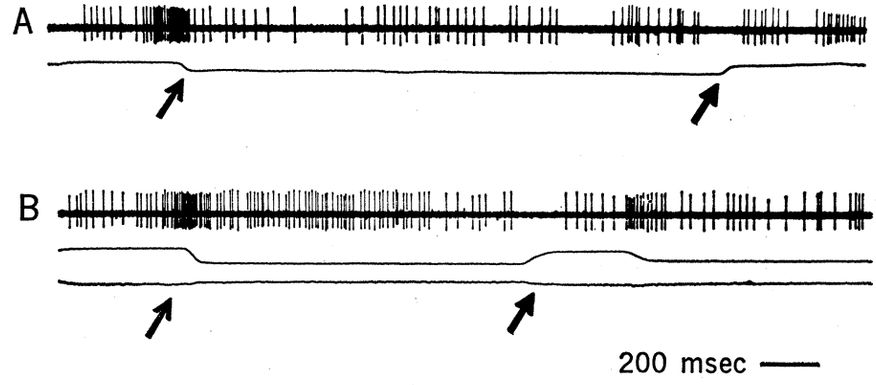

Fig. 2. Relation of cell discharge to direction of eye movement (A) and to stimulus guidance of eye movement (B) for the same cell as in Fig. 1. In (A), the rate of cell discharge increases with a rightward eye movement (left arrow at the downward deflection of the horizontal electrooculogram) but decreases with eye movement in the opposite direction (leftward eye movement with upward deflection at the right arrow). In (B), eye movements occur with no visual stimulus guidance in total darkness. The rate of cell discharge again increases before a rightward spontaneous eye movement (left arrow) and decreases before leftward eye movement (right arrow). Middle trace is horizontal electrooculogram; lower is vertical. Note that in both (A) and (B) the background rate of cell discharge fluctuates in the absence of any eye movements.

sponse to the visual stimulus that evoked the movement. In Fig. 2A the eye movements are in response to the change in position of the fixation point; thus, they are visually guided eye movements. In Fig. 2B the animal was in total darkness, yet the spontaneous eye movements of proper direction and distance are associated with similar cell responses. These cells also responded with the eye movements of caloric nystagmus, induced by irrigating the animal's ear canal with cold water, in light or total darkness (*9*). No visual receptive field could be found for any of these cells, with stationary or moving stimuli, during fixation or during eye movements; nor could any cell be affected by tactile or acoustic stimuli. Finally, these cells cannot receive proprioceptive input from stretch receptors because their response precedes the contraction of the eye muscles, as indicated by the electromyogram.

One possible function of these cells is that of upper motor neurons, which transfer movement commands to the lower motor neurons of the extraocular motor system. Neurons in the oculomotor and abducens nuclei discharge tonically to maintain the eye at a given position and phasically to move the eye during both saccade and smooth pursuit (*10*). In contrast, movement neurons of the superior colliculus respond best before saccades, poorly before smooth pursuit movements, and have no component of their response related to the static position of the eye at the beginning or end of the eye movement. The oculomotor neurons also discharge 4 to 10 msec before a saccade, but the superior colliculus cell discharge precedes the movement by up to 150 msec. The superior colliculus is not known to send many fibers directly to the extraocular motor nuclei (*11*). Thus any role that the superior colliculus neurons might have in the initiation or guidance of eye movements seems likely to be exerted through intermediate centers.

Alternatively, the superior colliculus cells could be transmitting a corollary discharge from the oculomotor system back to sensory systems. In this case the discharge of these neurons before each eye movement would not drive lower motor neurons but instead would send an "efferent copy" of the motor event to other regions of the brain, indicating that an eye movement was going to occur (*12*). An interaction between sensory input and corollary discharge has been reported for cells in the superior colliculus of the rabbit, since these cells are reported to respond differently to a visual stimulus when the head is moved passively or actively (*13*). In the monkey the response of neurons in the frontal eye fields of cerebral cortex has been suggested to serve as a corollary discharge for eye movement (*14*). These cortical neurons discharge almost exclusively after the eye movement and thus could not be involved in the initiation of eye movement. The superior colliculus neurons, on the other hand, always start to discharge before the eye movement and thus could be logically related either to the initiation of eye movement or to a discharge corollary to eye movement.

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Computer-Based Interviewing System Dealing with Nonverbal Behavior as well as Keyboard Responses

Abstract. *A digital computer has been programmed to conduct a medical interview while simultaneously monitoring the heart rate and keyboard response latency of the respondent for each question frame. The program can branch to new frames contingent upon the heart rate and response latency values, as well as the keyboard responses, and thus alter the course of the interview on the basis of this nonverbal information. The program is presented as a technique for studying the use of nonverbal respondent behavior in automated, clinical interviews.*

The use of digital computers to interview patients about their medical histories has been reported (*1, 2*). In direct interface with the patient and programmed to present new question frames contingent upon responses to current ones, the computer can model the physician in obtaining history data in detail and in exerting control over the interviewing process. Detail is obtained by the computer with branching, after affirmative responses, to questions designed to qualify the abnormalities indicated. The computer controls the interviewing process and increases the likelihood of satisfactory