by acetylcholine and methacholine was unaffected by transection of the hypogastric nerves peripheral to the IMG or by the occlusion of the renal arteries and veins. These results suggest that the ganglionic depression by acetylcholine and methacholine was not due to activation of neurons in the IMG or to release of catecholamines from the adrenal medulla but to the activation of adrenergic inhibitory neurons in the pelvic plexus.

Thus, these experiments provide further evidence for the existence of an adrenergic inhibitory mechanism in vesical parasympathetic ganglia (*7*). We have shown that intraarterial administration of the cholinomimetic agents acetylcholine and methacholine can activate such a mechanism. These substances produced a biphasic depression of ganglionic transmission: an early depression, which was presumably a direct effect of the agents on ganglionic transmission, and a late depression, which was dependent upon the release of endogenous catecholamines. The late inhibition was blocked by both an α-adrenergic blocking agent and by atropine. We conclude therefore that the cholinomimetic substances activated the adrenergic inhibitory neurons via muscarinic receptors (Fig. 2B).

On the other hand, atropine did not block the ganglionic inhibition evoked by electrical stimulation of sympathetic pregaglionic fibers. This result indicates that the adrenergic inhibitory neurons are synaptically excited via nonmuscarinic receptors (Fig. 2B). By analogy with synaptic transmission in other peripheral ganglia, it seems likely that the latter receptors are of the nicotinic type. However, the injection of nicotinic stimulants did not produce adrenergic inhibition. Nevertheless, these substances might have activated the adrenergic inhibitory neurons, but the inhibition was undetectable because of the predominant excitatory action of nicotinic stimulants directly on the parasympathetic ganglia.

The direct effects of the cholinomimetic agents on transmission in bladder ganglia underscore the complexity of drug actions at ganglionic synapses (*2*). Acetylcholine and methacholine produced a direct (early) depression of transmission and then a late facilitation, both of which were blocked by atropine. Similar effects have been observed (*11*) in sympathetic ganglia after the administration of these agents, and there has been considerable speculation (*2, 3, 5*) about the physiological significance of these effects. The present observations raise the possibility that atropine-sensitive synaptic mechanisms may also be present in parasympathetic ganglia.

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Neuronal Correlates of Eye Movements in the Visual Cortex of the Cat

Abstract. *About 10 percent of the cells in the visual cortex of awake cats do not respond to stationary parallel stripes in any orientation or to stripes moving across the visual field in any direction at a moderate speed (up to 132 degrees per second), but these cells are either excited or inhibited during saccadic eye movements when the animal faces a patterned visual environment. Of nineteen such cells tested in total darkness, seven discharged in association with eye movements. For saccade-related discharges, the latency during retinal stimulation is typically shorter than the latency in total darkness.*

Psychologists and neurophysiologists alike are intrigued by the ability of the brain to distinguish between image motion on the retina brought about by object movement and by active movement of the eye. The most promising hypothesis for a mechanism which might allow the brain to differentiate between the two types of image motion was that of a corollary discharge (*1*) that somehow modifies the visual input during an eye movement. In studies of single units, neither in the visual cortex (*2*) nor in the frontal eye fields (*3*) have neurons been found whose discharge pattern before or during eye movements could be interpreted as a corollary discharge. Only in the superior colliculi (*4*) and in the lateral geniculate body (*5*) are neuronal responses typically related to eye movements. In area 17 of awake monkeys, some neurons in the visual cortex are excited or inhibited during rapid eye movements as well as during fast object movements (angular velocity as great as 900° sec^{-1}). But these neurons did not discharge in relation to eye movements during total darkness (*2*).

More than 300 neurons in the visual cortex of awake cats were studied and classified into four types according to their dominant response during image movements (*6*). These types were (i) units that responded continuously to stationary gratings (parallel stripes) of a certain orientation (24 percent); (ii) units that responded to stripes of an optimal orientation that were moving at right angles to that orientation at a moderate speed, 12° to 100° sec^{-1} (25 percent); (iii) units that could be driven only by undefinable movements, such as shadows of wiggling fingers on the uniformly illuminated projection screen (20 percent); and (iv) units that only showed a response during a saccadic eye movement while the cat was looking at a large contrast pattern, such as a checkerboard (10 percent). Some of the type iv neurons also fired in association with rapid eye movements during complete darkness. The remaining 21 percent of neurons were unclassifiable.

A total of 357 cortical neurons were recorded in 90 experiments on 20 unanesthetized, awake cats. The surgery

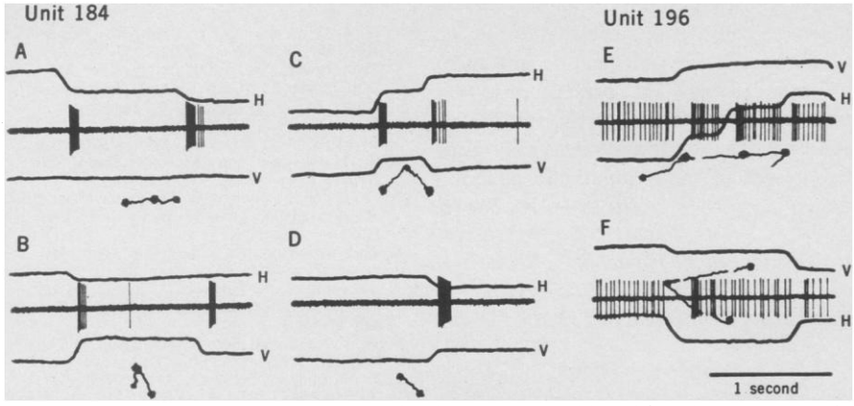


Fig. 1. Excitatory (A–D, unit 184) and inhibitory (E and F, unit 196) responses. The horizontal (H) and vertical (V) components of the EOG are given. Upward deflections of the H and V tracings represent motions of the eyes to the right and upward, respectively. Irregular tracings indicate eye direction in two-dimensional space. When the eyes were motionless the trace was also motionless and produced a large spot on the film. Records for each unit are not consecutive. Stimulation was by a checkerboard pattern.

was performed about 1 week prior to the first experiment. The skull was opened, a vertical cylinder was fixed with acrylic cement over the skull opening, two transverse tubes were embedded in the cement, and electrical contacts were similarly mounted. Silver–silver chloride electrodes were implanted subcutaneously at the outer canthi of the eyes for recording the electrooculogram (EOG) in the horizontal plane and above and below the left eye for recording in the vertical plane. During testing, the animal's head was held rigidly in the stereotaxic instrument by inserting two pairs of ear bars into the transverse tubes mounted on the skull. The unanesthetized animal was otherwise unrestrained, and its eyes were free to scan the entire visual field. Neuronal discharges were recorded from areas 17 and 18 with insulated stainless steel electrodes driven through the dura. Details of the preparation and the recording procedures have been described (*6*).

The routine test on each unit was as follows. (i) The maintained discharge rate was determined while the animal was looking at a rear-projection screen evenly illuminated at 61.4 cd/m^2. The screen was 72 cm from the animal and subtended 56° of the visual field horizontally and 48° vertically. (ii) The response to the onset and offset of diffuse light was observed. (iii) The response to stationary gratings was tested by showing light and dark stripes, rotated at various angles to determine the optimal orientation. (iv) If the unit was not sensitive to the stationary stimulus, it was then tested by moving stripes across the field. The direction of motion was varied in 22.5° increments from 0° (motion from left to right) to 337.5°. The velocity of the stripes was varied in increments of 12° sec^{-1} from 12° sec^{-1} to 132° sec^{-1}. Thus the angular velocities of target motion were less than the velocities of image motions during saccadic eye movements (*2*). (v) If the unit was sensitive to either stationary or moving stimuli, ocular dominance and binocular interaction were studied by comparing the effects of uniocular and binocular stimulation. (vi) If the unit fired in association with eye movements, the neuronal discharges and horizontal and vertical EOG's were recorded during stimulation with a checkerboard pattern of alternating light and dark rectangles, 3° by 2°. (vii) The firing of the unit was studied further in total darkness.

Of the 357 neurons tested, 39 clearly responded to spontaneous rapid eye movements (saccades) when a stationary pattern (stripes or checkerboard) was shown on the screen. These neurons showed no response to stationary gratings of any orientation when the eyes were not moving, and they did not show a consistent response to stripes moving at moderate speed (below 132° sec^{-1}). The maintained discharge rates of some of these neurons were slightly altered by illumination or during presentation of a pattern (for example, unit 248 in Fig. 3), but a well-defined on or off response was never seen when a diffuse light was switched on and off.

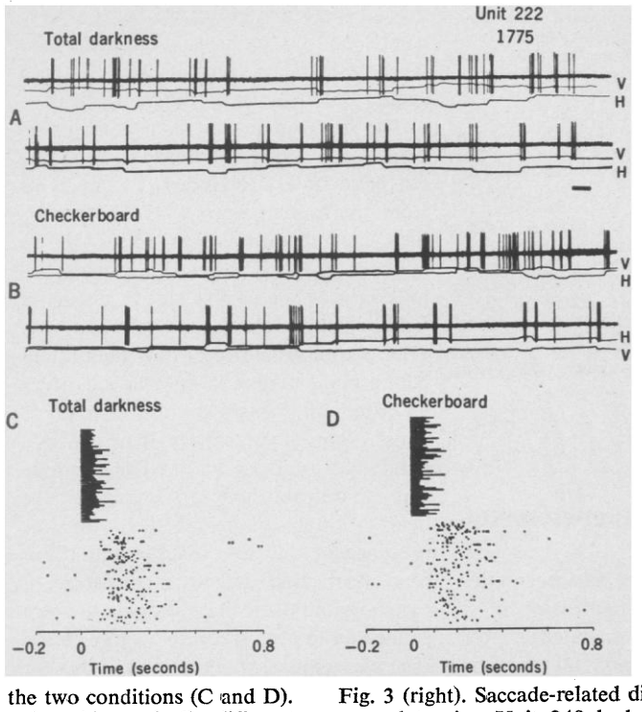
The responses to saccadic eye movements consisted of either a sudden burst of discharges (29 neurons) or a decrease in activity (10 neurons), during and after saccades. The latencies of the excitatory responses from the onset of saccades were between 20 and 100 msec in 22 units and greater than 100 msec in 7 units. Suppression always began shortly after the onset of a saccade and lasted for the duration of the saccade and sometimes longer.

One excited and one inhibited neuron are shown in Fig. 1. Unit 184 (A–D) was spontaneously quiet but fired vigorously after each saccade, regardless of the direction of the eye movement. In unit 196 (E and F), which showed a high maintained discharge rate, there was clear suppression of activity during saccades and a rebound discharge afterward. All other neurons that were inhibited by saccades showed a similarly high maintained discharge rate.

Nineteen neurons that were either excited or inhibited by saccades were tested while the animal was in total darkness. Saccade-related discharges were observed in seven excitatory cells. The latencies for saccade-related discharges during total darkness were 100 to 200 msec from the start of saccades; considerable variation in latencies was observed. Except for one neuron, the saccade-related discharge in the dark was always less brisk than that when the animal viewed a contrast pattern. The exceptional neuron also showed a long latency with the contrast pattern. In this neuron, the type of response and the latency were the same in both situations (Fig. 2). In the other six units, the latency of the saccade-related response was much shorter with a stimulus pattern (15 to 30 msec) than in total darkness. Two examples are shown in Fig. 3.

Neurons that responded to saccadic eye movements in darkness did not seem to be aggregated in columns, since neurons with other response patterns were always found in the same electrode tract. The approximate recording depth could be determined for some units and was in the lower half of the cortex.

An important question is whether the responses of the neurons described here can be interpreted as corollary discharges that help the brain to differentiate between object and eye movement. Let us first consider the saccade-related response when the animal is viewing a checkerboard or another contrast pattern. About 10 percent of the neurons tested responded to saccadic eye movement in any direction. This



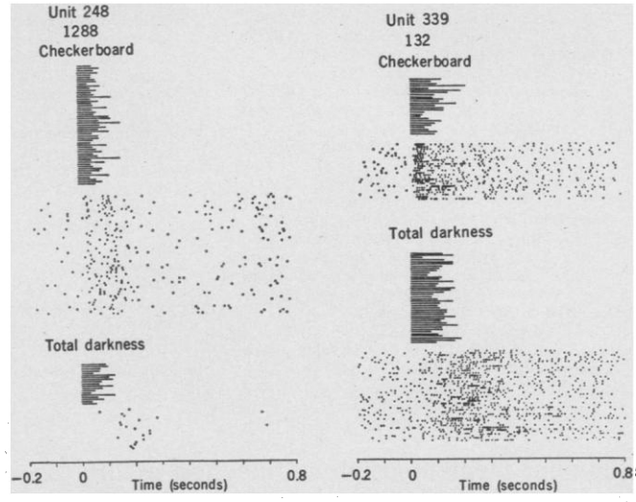


Fig. 2 (left). Saccade-related discharges of an excitatory unit in total darkness (A and C) and during exposure to a checkerboard pattern (B and D). The scale for A and B is 1 second. In C and D, horizontal bars represent duration of eye movements from time 0, while the rows of dots underneath represent single neuronal discharges. Note the long latencies for saccade-related discharges during vision (D) and the similarity of latencies in the two conditions (C and D). Fig. 3 (right). Saccade-related discharges, in the presence and absence of patterned stimulation, of two units with markedly different response latencies. Unit 248 had a very low rate of maintained discharge, an inconsistent and weak saccade-related response during vision, and a still weaker but reliable response in the dark. The maintained discharge rate was elevated during presentation of the checkerboard pattern. Unit 339 had high maintained activity, a brisk saccade-related response with short latency during vision, and a weaker saccade-related response with long latency in the dark.

group of cells were insensitive to the moderate velocities of target movement that we used (between 12° and 132° sec^{-1}). For these neurons, discharges are associated with the relatively high velocities of retinal motion during saccades in the presence of a patterned stimulus. Therefore, the discharges may be attributable to fast retinal motion, as was shown for some neurons in the monkey's visual cortex (*2*). It is possible that our units would also have responded to high-velocity target motions comparable to the velocities of saccadic movements, as did the units studied by Wurtz (*2*). Nevertheless, it seems doubtful that responses to high-velocity retinal motions like those associated with saccadic movements are useful for the perception of visual objects. In human perception, objects at such high angular velocity evoke only a blur, and the environment is not perceived during voluntary saccades or the fast (saccadic) phase of nystagmus.

Neurons in the visual cortex which we recorded during target motion did not respond to image motions with velocities greater than 100° sec^{-1} (*6*). Furthermore, the neurons that responded during saccadic eye movements were unaffected by direction of eye movement (and hence of image motion), whereas neurons that responded to more moderate target motions were highly specific in their directional sensitivity. Therefore, neurons that function in perception are not functioning during saccades. This explains satisfactorily the phenomenon of central inhibition and suppression (*7*).

The functional significance of the saccade-related responses can only be suggested. These responses may suppress responses of other neurons during saccades, or they may register that a saccade is taking or has taken place and may thus bring about resetting of the visual field after a saccadic eye movement. In this sense, responses of neurons in the visual cortex during saccadic eye movements can be considered a second kind of corollary discharge, one that occurs during any high-velocity motion—caused by eye, head, or body movement—of open eyes. In this context it should be noted that psychophysical experiments on humans have shown that fast image motion without saccadic eye movements has an effect on perception similar to the suppressive effect of saccades themselves (*8*). These experiments support our suggestion that cortical discharges of both retinal and oculomotor origin may be involved in the saccadic suppression effect.

The discharges produced by eye movements in total darkness may be related to the eye movements themselves and may be of oculomotor origin. A nonspecific effect due to general arousal seems unlikely, since arousal stimuli influence a much larger population of neurons in the visual cortex (*9*). Vestibular and auditory effects can be excluded by our experimental arrangement. Neurons that show a saccade-related discharge in the dark constitute a very small proportion of the neuronal population of the visual cortex (probably less than 5 percent). For these neurons, the discharge is only loosely related to the saccade; this is shown by the long latency and large variation of discharges. Because its latency is much longer than that of the saccade-related discharge during vision, the saccade-related discharge in the dark seems a poor candidate for a corollary discharge. But it may bring about a sufficient increase of noise in the cortical network to cause an effective increase of the perceptual threshold during saccades (*7, 10*).

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Magnetoencephalography: Detection of the Brain's Electrical Activity with a Superconducting Magnetometer

Abstract. *Measurements of the brain's magnetic field, called magnetoencephalograms (MEG's), have been taken with a superconducting magnetometer in a heavily shielded room. This magnetometer has been adjusted to a much higher sensitivity than was previously attainable, and as a result MEG's can, for the first time, be taken directly, without noise averaging. MEG's are shown, simultaneously with the electroencephalogram (EEG), of the alpha rhythm of a normal subject and of the slow waves from an abnormal subject. The normal MEG shows the alpha rhythm, as does the EEG, when the subject's eyes are closed; however, this MEG also shows that higher detector sensitivity, by a factor of 3, would be necessary in order to clearly show the smaller brain events when the eyes are open. The abnormal MEG, including a measurement of the direct-current component, suggests that the MEG may yield some information which is new and different from that provided by the EEG.*

Masses of excitable tissue, such as the heart and other organs, generate ion currents within the body. These currents, which produce a weak magnetic field around the body, were first detected about a decade ago. The techniques of detection have now been improved, and a new range of high sensitivity has now been reached. I have been using this new sensitivity to look around the human head for magnetic fields which are produced by electrical activity of the brain. Earlier measurement of the brain's magnetic field, because of the equipment used, was far less sensitive than the new arrangement and required cumbersome noise-averaging. I now report the first results of measuring the brain's magnetic field at the new, high sensitivity. My recordings show that the brain's magnetic field can now be detected in a simple and direct way. Also, I suggest that some of this magnetic data may contain information different from that found in the electroencephalogram (EEG). Measurements of the brain's magnetic field are of interest because of the possibility of obtaining such new brain information, unavailable to the EEG.

There are at least three different ways in which measurements of the brain's magnetic field can reveal information which is either unavailable or very difficult to obtain with the EEG. The first way is the measurement of d-c (direct current) generated in the brain. Although the brain's d-c varies with the normal and abnormal states of the brain (*1*), it cannot reliably be measured with the EEG because of the steady polarizing voltages developed by the junction of the electrodes and the scalp; however, measurements of the magnetic field from d-c currents in the brain can be reliable since there is no surface contact. The second way is to show, for some special neural events, that zero current is flowing in the head even though there is a nonzero EEG of these events. There are some generator distributions (*2*) which produce zero current everywhere in the head but nonzero voltages on the scalp; unless electrodes can be placed inside the head, only magnetic measurements can reveal these special distributions because the magnetic field will everywhere be zero. The third way is to show, for some special neural events, that there is a nonzero current in the head even though there is a uniform voltage everywhere on the scalp (*3*). In this case there will be a zero EEG of these events but a nonzero magnetic field.

The first measurement of a magnetic field from living currents was of the magnetic field produced by currents from the human heart (*4*). The heart's field, at maximum, was found to be about 5×10^{-7} gauss. This was one-millionth of the earth's steady magnetic field which is about 0.5 gauss; it was also one-thousandth of the fluctuating background magnetic field in an urban environment, which is about 5×10^{-4} gauss, root mean square (r.m.s.), in a bandwidth of 0 to 40 hz. The problem was therefore how to measure the heart's weak magnetic field in the presence of the large background. This first effort used detectors consisting of two large coils on the chest which were connected in opposition to largely cancel the background fluctuations. Another scheme for detecting the heart's field was a single, compact coil situated in a magnetically shielded room to reduce the background (*5*). This system was used for the other, earlier brain measurement (*6*). The brain's magnetic field amplitude, due to alpha rhythm, was found to be about 1×10^{-9} gauss at a distance of 5 cm from the scalp, or hundreds of times weaker than the heart's field. Elaborate noise-averaging was required to extract the brain signal from the intrinsic noise of the detecting coil, which was some 30 times greater than the small signal from the brain.

Recently, a more heavily shielded room was constructed at the Massachusetts Institute of Technology and a newly developed superconducting quantum interference device (SQUID) magnetometer was installed in the room. First measurements with this system (*7*) showed the heart's magnetic field with more clarity and sensitivity than was previously possible. The intrinsic magnetometer noise, which limited the sensitivity, was 1×10^{-9} gauss (r.m.s., per root cycle) during those first measurements; the frequency response was from d-c up to 500 hz. This ability to measure d-c, not possible with the previous coil detectors, was used in the next experiment with this system, which consisted of searching for d-c currents during heart injury (*8*). Simultaneously with these and other exploratory experiments, an effort was made to reduce the magnetometer noise (*9*). By redesigning several internal components, and by thinning the noise-producing silver