periods varying from 16 hours, as recommended by Meister and Abendschein (*6*), to 5 hours, as recommended by Kun and Garcia-Hernandez (*7*). The clear supernatants were spotted, along with known standards of glutamic acid, alanine, and α-amino butyric acid, on strips of filter paper; developed in phenol and water in an atmosphere of ammonia; dried; and sprayed with ethanolic Ninhydrin.

α-Ketoglutaric and pyruvic acids were present in all the hydrolyzates examined (*8*). The derivatives of these keto acids appeared in three bands, the lowest one running parallel to known α-ketoglutaric acid hydrazone and the higher two running with the two bands of pyruvic acid derivatives (*3*).

In an attempt to explain the presence of α-ketoglutaric acid in the commercial hydrolyzates, the following experiment was made. Five grams of pyruvic acid and 5 g of glutamic acid were added to 150 ml of 10*N* HCl and refluxed for 14 hours, after which time the HCl was distilled off directly (*9*). The remaining semisolid mass was taken up in 100 ml of distilled water, and the solution was filtered. The acid-carbonyls present in the filtrate were isolated and identified by the methods described previously for the isolation and identification of the α-keto acids in the casein hydrolyzates examined.

α-Ketoglutaric acid was present in the filtrate from the acidified and heated pyruvate-glutamic mixture.

Franck and Knoke (*1*) found that during acid hydrolysis of casein the β-hydroxy α-amino acids serine and threonine gave rise to pyruvic and α-ketobutyric acids, respectively. They found, under the conditions of their experiment (6*N* HCl, 14 hours, 140°C), no other α-keto acids.

The logical precursor of the α-ketoglutaric acid found in the commercial casein hydrolyzates would be glutamic acid. The keto acid could arise under the rigorous conditions of hydrolysis (*9*) by the condensation of pyruvic acid initially coming from the degradation of serine, and the glutamic acid would be freed during hydrolysis. This condensation product, presumably a Schiff base, could be rearranged and split in such a manner as to yield α-ketoglutaric acid as one of the cleavage products.

These findings may be of interest in nutritional studies in which acid-hydrolyzed casein provides the source of amino acids in experimental media. If the cultures for which the media are prepared possess active transaminase systems, the fact that α-ketoglutaric and pyruvic acids are present initially in the media might (i) lead to misinterpretation of differences in the levels of amino acids before and after growth (that is, glutamic acid and alanine levels could be affected by transamination involving the α-keto acids present initially in the media); (ii) account in part for the differences in efficiency of casein hydrolyzate media and completely synthetic media in supporting bacterial growth.

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9 April 1959

Activation of Single Lateral Geniculate Cells by Stimulation of Either Optic Nerve

Abstract. The lateral geniculate nucleus is organized in such a way that, initially at least, information from the one eye is almost exclusively segregated from that from the other eye. Single-unit recording, however, confirms the histological evidence that bilateral integration does take place. A small number of cells (< 8.5 percent) receive afferents directly from both optic nerves and are discharged by stimulating either nerve (direct interaction). More common is delayed interaction, where the cells are discharged independently by either optic nerve but only after a relatively long latency. Indirect interaction effects also occur.

The lateral geniculate nucleus is a synaptic center on the direct path between retina and cerebral cortex. In the higher mammals the acquisition of binocular vision is associated with the development of a partial decussation of optic nerve fibers at the chiasma where fibers from both eyes now pass to each lateral geniculate nucleus. While these changes are taking place, distinct cellular laminae develop in the nucleus, but the fibers from each eye terminate in separate cell layers. Many studies have been made, particularly in the cat, regarding the possibility of binocular integration taking place in the lateral geniculate nucleus. Earlier histological (*1*) and electrophysiological (*2*) studies gave negative results (see *3*). Later, Bishop and Davis (*4*) provided clear evidence of some degree of binocular interaction. At that time this interaction was regarded as being due to extracellular flows of current from active cells affecting the excitability of resting cells in adjacent inactive layers. Recent work in this laboratory (*5–7*) indicates that this factor is probably of minor importance and that the existence in the geniculate of bilateral synaptic connections of varying complexity provides a basis for the small degree of binocular interaction that takes place at this level.

By studying the patterns of degenerating nerve terminals following section of one optic nerve in the cat, Hayhow (*5*) confirmed that each cell layer receives fibers from one eye only. He demonstrated, however, that the interlaminar regions which contain large cells (*nucleus interlaminaris centralis* and *nucleus interlaminaris medialis*) receive fibers from both eyes. This suggests that these regions may be concerned with the integration of information from the two eyes.

The technique of recording from single cells provides confirmation of the supposition that there are cells in the lateral geniculate nucleus which may be activated independently from either eye. Thus, Erulkar and Fillenz (*8*) have recorded from single units which responded to light flashes presented to either eye. Using glass micropipette electrodes filled with 3*M* KCl (direct-current resistance, 5 to 10 megohms) under Horsley-Clarke stereotaxic control, we have now recorded, extracellularly, in the region of the lateral geniculate nucleus, from about 270 postsynaptic units that have responded to electrical stimulation of the optic nerves. Of these, only 23 (8.5 percent) responded to stimulation of either optic nerve with a latency in each case of less than 10 msec. Final confirmation that binocular interaction occurs in the lateral geniculate requires, however, a clear demonstration that the recording sites were actually intrageniculate and that the units concerned were not fibers of passage on their way through the nucleus.

As regards the latter point we now have satisfactory criteria (*9*) which enable us to distinguish between the responses from the region of the cell body (Fig. 1, *A*) and those from an axon (Fig. 1, *B*). In various ways the cell response can be fractionated into the separate components concerned in impulse generation (*9*). Twenty-three units responded to stimulation of either optic nerve with latencies of less than 10 msec.

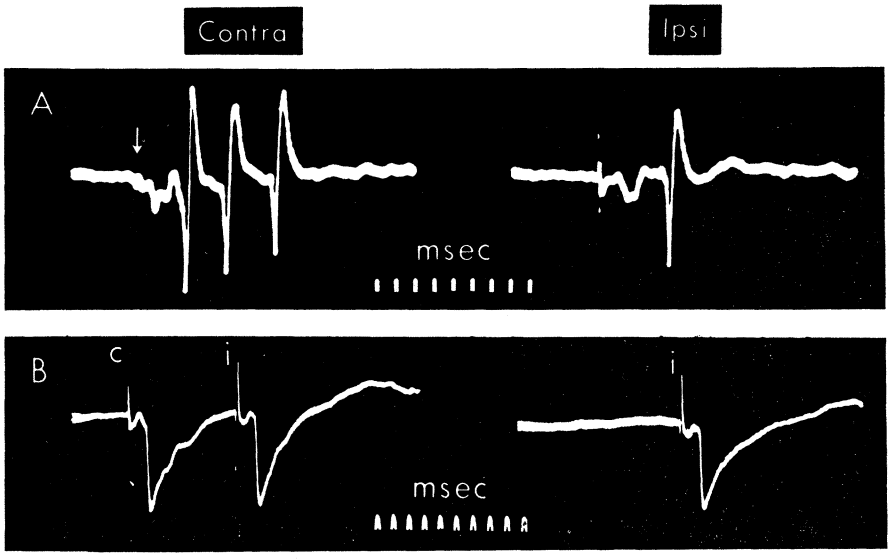

Fig. 1. (*A*) Extracellular responses from the vicinity of the cell body of a single lateral geniculate neuron following electrical stimulation of the contralateral and ipsilateral optic nerves, as indicated. The contralateral response shows repetitive firing. The arrow indicates the position of the stimulus artefact. (*B*) Extracellular responses from single postsynaptic geniculate axons following stimulation of the contralateral (*c*) and ipsilateral (*i*) optic nerves.

Responses from only four were clearly obtained in the vicinity of the cell body and responses from an additional three probably had a similar origin. Responses from the others were derived from postsynaptic axons.

With capillary microelectrodes we have not yet developed a satisfactory method for identifying histologically the site from which the records come, and we have had to rely both on measurements from macroscopic anatomical landmarks and on the general field potentials that result from the massed activity of the geniculate cells. We have, however, recorded identical unit responses with a steel microelectrode and confirmed the geniculate origin of these responses by the iron deposition (Prussian blue) method.

It has been possible to classify our interaction effects into three categories.

1) *Direct interaction.* The most debated aspect of binocular interaction at geniculate level concerns the possibility of direct interaction—that is, whether there are cells in the nucleus that are directly innervated and separately activated by optic nerve fibers from either eye. We consider that most of the 23 units probably fell into this category. However, the rigorous demonstration of direct interaction requires that the response be distinguished as coming from the vicinity of a cell body within the lateral geniculate nucleus (as discussed above) and with latencies to electrical stimulation of the optic nerves brief enough to exclude the possibility that an interneuron intervenes. The latter requirement restricts consideration to the rapidly-conducting group of fibers in the optic nerves. These fibers lead to the discharge of the corresponding geniculate neurons, with a latency of about 1.0 msec (*10*). The great majority of the geniculate cells normally have latencies to optic-nerve stimulation greater than 1.0 msec, so that one would not expect to find many cells in this category.

Of the 23 units only one (Fig. 1, *B*) responded with ipsilateral and contralateral latencies (1.2 msec in each case) less than 1.5 msec. This unit was, however, a postsynaptic axon. Another postsynaptic axon had ipsilateral and contralateral latencies of 1.3 and 1.7, respectively. Many of the units with slightly longer latencies may probably be included in the category of direct interaction if estimates of conduction velocity in presynaptic fibers made from measurements of threshold for stimulation are accepted. At least one of the responses in the latter group was obtained from the vicinity of the cell body. The latency of the geniculate response to photic stimulation of the retina is so long (*8*) that it would be difficult to establish direct interaction by means of light flashes.

2) *Delayed interaction.* The term *delayed interaction* may be used to refer to units which respond to stimulation of either optic nerve but only with a latency long enough to require the intervention of one or more interneurons. No doubt some of the 23 units referred to above fall into this category (short latency, delayed interaction). There are other units, however, which fire only after a latency of 100 to 300 msec (long latency, delayed interaction). We have not looked especially for units of this kind, and any observations we have made have been incidental to other studies. Nevertheless we have found 15 examples out of a total of 122 postsynaptic units recorded in eight experiments.

3) *Indirect interaction.* A geniculate cell may be discharged only by impulses in the one optic nerve, but it is commonly found that impulses in the other optic nerve may influence the firing pattern of that cell (see *8*). As yet we have not studied these indirect interaction effects to any extent.

It is clear that the lateral geniculate nucleus has a more complex function than to serve as a relay station. The direct exchange of information from the two eyes occurs here only to a limited extent, but, in the later stages of the visual process, after the visual messages have reached the cerebral cortex and other centers beyond the lateral geniculate nucleus, bilateral integration at geniculate level becomes much more widespread, possibly involving complex reverberating neuronal circuits. Recent histological studies and single-unit recording in our laboratory have demonstrated the presence of complex corticogeniculate connections.

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17 April 1959