Sympathetic denervation (postganglionic; see 'methods') after causing a transitory decrease had no significant effect on kallikrein concentration in the submandibular gland. Figure 1 shows that although there was an increase after 1 day, followed by a decrease after 2–4 days, it returned to normal and remained there 1 week after ganglionectomy. This temporary reduction in kallikrein content did not occur in 2 cats after preganglionic sympathectomy. 2 weeks after pre- and postganglionic sympathectomy there was no change in the number and appearance of the apical granules of the striated ducts, in the concentration of acid phosphatase and β- glucuronidase, nor in the weight of the gland. Also, there were no gross microscopic changes in the acinar or demilune cells.

Duct ligation: Ligation of the submandibular duct for 3–4 days caused a marked decrease in kallikrein content of the gland. In 2 such experiments the kallikrein concentration (esterase units per unit protein) fell to 3 and 4% of the contralateral control gland. Also, there was a complete disappearance of the apical granules in the striated ducts and characteristic dispersion and longitudinal arrangement of mitochondria (figure 2). The larger secretory granules of the acinar cells showed some degenerative features but these were very minor compared with the almost complete disappearance of the apical granules from the striated duct cells. Changes in appearance of demilune cell granules were not noteworthy.

Discussion. 2 main conclusions may be derived from these experiments in the cat: a) The synthesis or storage of kallikrein depends on an intact parasympathetic innervation. It is now well established that sympathetic nerve stimulation rather than parasympathetic strongly mobilizes the secretion of kallikrein in saliva[7,8,13]. In contrast, however, our results clearly demonstrate that kallikrein disappears almost completely from the gland after 1–2 weeks with parasympathetic denervation but that with sympathetic denervation the kallikrein concentration is normal at this time and remains so afterwards (figure 1). It must be concluded, therefore, that the parasympathetic nerve exerts some trophic or other action on the gland cells. We also noted that there was a substantial atrophy of the gland after parasympathectomy but not after sympathectomy. Figure 1 shows that 2–4 days after postganglionic sympathectomy there is a temporary reduction in the kallikrein content of the gland which then returns to normal. This temporary reduction is perhaps due to 'degeneration secretion'[17] since it did not occur after preganglionic sympathectomy which does not result in degeneration of the postganglionic axons. b) Our results support the view[7,8] that kallikrein is located in the striated duct cells of the cat's submandibular gland. They show that there is always a marked decrease in the number of apical secretory granules in these cells when there is a depletion of kallikrein irrespective of whether it is as a result of duct obstruction, parasympathetic denervation, or sympathetic nerve stimulation.

These studies do not establish the physiological role of salivary kallikrein but since they indicate that it is secreted into the ducts rather than into the interstitial fluid and circulation, they lend no support to the view that this enzyme is the regulator of functional hyperaemia in the gland[10]. The presence in the submandibular gland of known active macromolecules like kallikrein, renin, nerve growth factor, and of a new one like sialotonin[18], suggests that the physiological significance of the salivary glands may extend beyond those relatively simple functions which are generally assigned to them.

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Information processing along the course of a visual interneuron

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Summary. Locust ocellar retinal cells are innervated by giant second order cells, 2 mm long, which show discrete zones of integration along their course, including a major zone in the axonal length of the neuron. The complex synaptic arrangements which exist between higher-order afferent and efferent cells and these second order cells along their course suggests that transmission takes place by the electrotonic spread of slow potentials. The size and accessibility of these visual interneurons offers a unique preparation for examining mechanisms of graded synaptic transmission.

The locust, Schistocerca gregaria, possesses 3 ocelli, 2 lateral and 1 median, each consisting of around 1000 visual cells lying beneath a common cuticular lens. Individual ocelli are innervated by 7 giant interneurons, 10 μm in diameter, and a number of smaller cells whose axons run out from the brain in an ocellar nerve approximately 2 mm long. 4 of the giant interneurons innervate both the median and 1 lateral ocellus. The interneurons are of the classical annelid/arthropod form with anatomically unipolar cell bodies, lying within the brain, whose neurites give rise to a T or a Y shaped axon terminating in dendritic arborisations. In the invertebrate nervous system the integration of information in electrotonic form is generally considered to be confined to the dendritic regions of the cell, the axon transmitting information from point to point usually by means of action potentials. Although presenting a conventional appearance in Golgi and cobalt stained material[1], serial thin sections and semi-thin sections show that the synaptic organisation of these large interneurons is unusual. 3 major zones of integration can be identified along their length, one of which comprises a major section of the axonal region of each fibre. Longitudinal sections through the ocellar tracts show that they resemble elongated neuropilar areas rather than fibre tracts.

The first integration zone, within the ocellus, consists of an extensive network of dendrites onto which the visual cells are highly convergent. The giant fibres are not equivalent in this region, those linking the ocelli synapse with the upper regions of the descending visual cell axons,

the remainder synapse with the terminal regions of the visual axons. The synapses between the visual cells and the second order cells are generally diadic in nature and there is an extensive arrangement of lateral and feedback synapses throughout the ocellar synaptic plexus[2]. The synaptic organisation of the plexus at this level has been compared with that seen in the vertebrate inner plexiform layer[3]. After leaving the ocellus the interneurons become ensheathed in glia for part of their length and are seldom found in synaptic contact.

In the proximal half of the ocellar nerve synapses can be found both between the giant axon profiles themselves and between giant axons and smaller blebbed dendritic processes (figure 1). In these associations the same giant interneurons can be both extensively pre- and postsynaptic (figure 2, a, b and d). Cobalt staining from the ventral nerve cord (VNC), and subsequent sectioning and intensification by the modified Timm technique, shows that descending VNC units give rise to large numbers of long, blebbed dendrites which enter the ocellar tracts and run out into the nerve. These dendrites ring the giant axon profiles over their course within the protocerebrum and the proximal part of the ocellar nerve (figures 1 and 2, c). The majority of the blebbed profiles seen in electron microscope observations arise from the dendritic

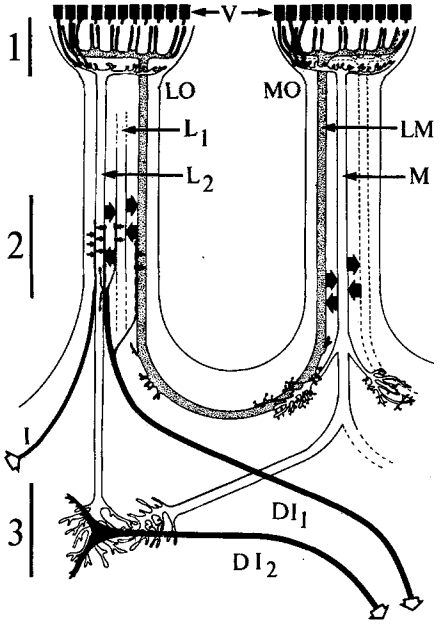

Fig. 1. A schematic diagram illustrating the stratification of the major synaptic zones along the course of the second order ocellar neurons in the lateral and median ocellus. For clarity only 3 complete second order fibres have been shown. Cell L_2, innervating the lateral ocellus, projects to the ipsilateral posterior slope neuropile where it has extensive dendritic fields. Cell M, from the median ocellus, forms similar dendritic fields in the posterior slope area in both halves of the brain. Cell LM, stippled, is 1 of the 2 fibres which innervate a lateral and median ocellar pair. These cells have no output outside the ocellar tracts. Synaptic zone 1 consists of contacts between visual cells and the repeated arborisations of second order cells in the ocellar cup. In zone 2 the giant axons are involved in both pre and postsynaptic contacts, making axoaxonic contact with each other, axodendritic contacts with afferent third order descending VNC units, DI_1, and dendroaxonic contacts with intrinsic brain interneurons, 1. Shortly beyond zone 2 in the median nerve 1 fibre, M, gives rise to 2 dendritic branches which turn back into the lateral ocellar tracts but stop short of zone 2. In zone 3 the giant fibres synapse dendrodendritically and dendroaxonically with descending VNC units, DI_2. LO, MO, lateral and median ocelli; V, visual cells.

arborisations of 6 identified afferent ocellar third order neurons which descend in the VNC, connecting the second order neurons with the thoracic motor centres. Some of the blebbed profiles seen in the proximal section of the nerve belong to smaller cells which have no other extensions outside the brain. A number of these intrinsic interneurons are presynaptic to the giant fibres (figure 2, b). Thus an extensive section of the axonal length of each giant interneuron participates in both input and output axodendritic synaptic contacts. Many of these are diadic in nature (figure 2, a and b).

Within the brain, over a limited region before the fibres turn under the protocerebral bridge, 1 unique interneuron develops dendritic branches bearing dendritic spines. Shortly before this point the giant cells become highly interactive and are repeatedly both pre- and postsynaptic to one another (figures 1 and 2, e). In these associations also the synapses are frequently diadic in nature. The type of organisation seen in the ocellar plexus thus is reflected within the axonal integration zone, with the characteristic bar synapse present, contacts generally diadic in nature and a good deal of reciprocal synapsing occurring. Beyond the protocerebral bridge all of the giant fibres, except the 4 which link the ocelli, project to the posterior slope of the protocerebrum. Here they arborise and form conventional dendritic fields which spread among the integrative segments and dendrites of interneurons descending into the VNC.

The presence of input synapses in the proximal half of the ocellar nerve does not accord with the view that the only function of the giant second order axons is that of transmission of information. The complex reciprocal interaction between giant second order neurons and other smaller profiles over nearly half their axonal length means that this must be considered an integration area rather than a discrete site of input to an axon with multiple spike-initiating zones[4]. It is therefore proposed that in the axonal synaptic regions the giant axons are not spiking and that only slow potentials are present. Interaction would then occur in a similar way to that found in other second order visual cells where slow potentials alone are effective in activating chemical synapses[5,6]. By comparison with arthropod systems in which information transmission occurs over some distance by means of slow potentials[7,8] it appears likely that the light-evoked hyperpolarisations recorded in the giant cells at the ocellar plexus[9] would spread electrotonically to the integration area. The large diameter of the axons indicates that the space constant would be long and that appreciable signal would remain over the distance involved. For the same reason any changes in membrane potential produced by input synapses to the giant axons would be expected to spread over a large area thereby increasing the integrative capacity of the system.

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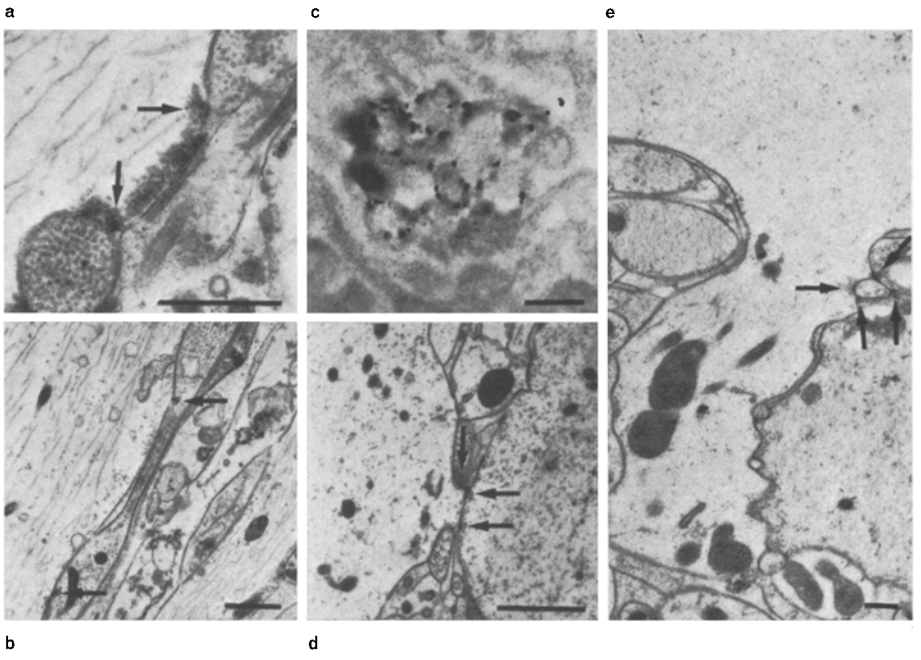

Fig. 2. *a* A giant interneuron is presynaptic to 2 small blebs. 2 divergent diadic synapses are arrowed. The blebs are packed with synaptic vesicles and are themselves presynaptic as well as postsynaptic structures. A transverse section taken at the base of the median ocellar nerve. Bar 0.25 μm indicates magnification. – *b* A number of long blebbed dendrites are presynaptic to giant interneurons which are themselves presynaptic to other small profiles in the same area. 2 divergent diads are arrowed. A longitudinal section from the median ocellar nerve proximal to the brain. Bar 0.5 μm. – *c* A 10 μm wax section through the lateral ocellar tract showing profiles filled by cobalt diffusion from the ventral nerve cord and treated by the modified Timm technique. Long, blebbed dendrites ring the giant interneurons over a considerable length. Thick sections indicate that a number of intrinsic interneurons terminate in a similar way in this region. Bar 10 μm. – *d* 2 giant interneurons are directly apposed over a short length of their membrane, 1 is postsynaptic to the other and also postsynaptic to a smaller profile. In this area a large interneuron may be both pre- and postsynaptic. Input or output synapses are usually grouped together in discrete areas a few microns apart. Here also synapses are usually diadic and divergent. Transverse section of the lateral ocellar nerve in the pars intercerebralis. Bar 1 μm. – *e* The giant interneurons give off very short, stubby collaterals which wrap around other giant second order cells. Small dendrites from third order cells interdigitate repeatedly between them. Synaptic arrangements are generally complex, diadic and reciprocal, black arrows. A transverse section in the brain anterior to the protocerebral bridge. Bar 0.25 μm.

Integration by means of slow potentials in second order cells is a common feature of visual sensory neuropile[10]. In the insect compound eye the large monopolar cells of the lamina only respond to retinal stimulation with graded hyperpolarisations[5,11]. A unique feature in the ocellar system is the size of the second order cells and the distances involved and the fact that the ocellar neuropilar area has become extended over the axonal length of the fibre. A contributory factor here may be the fact that the lateral and median ocelli are linked in pairs by 2 large axons. The axonal integration area described may thus in effect form a common neuropile area for each pair of ocelli. Information processing along visual interneurons of this size and accessibility offers a most promising preparation for examining mechanisms of graded synaptic transmission.

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Modification of the action of pentagastrin on acid secretion by botulinum toxin[1]

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Summary. I.v. botulinum toxin after 60–90 min abolished the dose-response relationship between pentagastrin and gastric acid secretion in anesthetized rats and guinea-pigs. The toxin reduced but did not abolish the acid stimulatory effect of histamine. As expected, the acid response to vagal stimulation was abolished and that to methacholine in rats was unaltered by the toxin.

Vizi et al.[3] have provided evidence that pentagastrin(PG) does not act directly to stimulate guinea-pig intestinal muscle, but via a cholinergic intermediary mechanism. We have found[4,5] that after morphine sulphate or hemicholinium administration to conscious Heidenhain pouch dogs a positive dose-response relationship between i.v. pentagastrin and gastric acid secretion is no longer obtainable. Morphine depresses acetylcholine release at cholinergic neuroeffector sites[6] and hemicholinium interferes with acetylcholine synthesis[7]. This suggests that the action of PG on gastric secretion also requires cholinergic mediation.

Material and methods. As a final test of this hypothesis we have measured PG-stimulated gastric secretion in anesthetized (chloralose) guinea-pigs and rats before and after botulinum toxin. In each animal after anesthesia