much as 1 log unit greater than spot 1.

The sizes of receptive fields of both units reveal that they integrate the activity of several cartridges and that they do so more extensively along the mediolateral axis of the eye. However, the complex temporal characteristics of both units indicate that more than simple summation of the retinular cell signals occurs in the first optic ganglion. The spatial and temporal characteristics of the discharge of the sustaining unit suggest that the sustained discharge reflects the excitatory influence of the retinular cells converging on a single cartridge while the off discharge reflects a rebound from inhibition (*13*) resulting from the excitation of neighboring cartridges along the mediolateral axis. The discharge characteristics of the on-off unit are not so easily explained. The receptive field organization of sustaining units is similar to that of eccentric cells in *Limulus* and of certain retinal ganglion cells (on center) in the vertebrate eye, for, like both, lateral inhibition can be demonstrated and antagonistic discharge (off) can be elicited by stimulation of the surround region of the receptive field (*14*). However, in contrast to the concentric receptive field organization of the eccentric and retinal ganglion cells that of the sustaining unit is not circularly symmetric.

The existence of centripetal discharges in the intermediate chiasma establishes that spike potentials are a mode of neural communication between the first and second optic ganglia; however, only two different types of units have been identified on the basis of their discharge behavior to various stimuli (spatial, temporal, spectral, polarization) (*15*), and at least six centripetal fibers, associated with each cartridge, have been identified anatomically (*4*, *16*). It would appear that either the units unaccounted for do not support impulse traffic, or they do and their discharge behaviors are either not sufficiently different from those of the on-off and sustaining units as to be distinguished with the types of stimuli available or their signals cannot be observed with the techniques used. The anatomical study of Trujillo-Cenóz (*16*) revealed two large fibers (3 to 4 μm) associated with each of the many bundles of fibers comprising the intermediate chiasma, and these fibers correspond to the axons of the type I monopolar cells of each cartridge. It is, therefore, possible that one large fiber of each pair is responsible for the on-off discharge while the other mediates the sustained discharge; however, it is difficult to account for the disparity in spike size between the two types of units. Furthermore, Autrum *et al.* (*6*) have recently recorded hyperpolarizing slow potentials without evidence of spikes from neurons in the first optic ganglion which they believe are monopolar cells. These observations are difficult to reconcile unless the micropipette renders the cell incapable of spike generation or unless spikes do not invade the cell body. The situation is further complicated by a recent report by Strausfeld and Braitenberg (*4*) that a type II monopolar cell associated with each cartridge sends collaterals to adjacent cartridges along the +Y and −X axes where they terminate on one of the type I monopolar cell processes, for the axis of interaction implied by this anatomical observation is roughly perpendicular to the axis of interaction manifested by the elliptical receptive fields of the on-off and sustaining units. Although the functional and structural correlates of the first optic ganglion remain unsettled, it is clear that profound transformations are made on the retinular cell signals.

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8. The outlines reflect only the relative shape and size of the receptive field of the on-off and sustaining units. A more absolute measure is given by the angular sensitivity which is the reciprocal of the stimulus intensity required to elicit a criterion response (one spike) as a function of the angular orientation of the stimulus relative to the receptive field center of the unit.
9. The separation, measured in degrees of arc, between points having half the maximum sensitivity and lying on an axis line of the receptive field is called the half-sensitivity angle along that axis. If the receptive field is circularly symmetric, then one half-sensitivity angle suffices.
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12. The pinched appearance of the on region is not particularly well reflected in the half-sensitivity angle values since these measurements were made at threshold. The effect is best observed in experiments to map the receptive field when the stimulus intensity is 2 to 3 log units above threshold.
13. Inhibition and off discharge are frequently associated; for example, see R. Granit, *Sensory Mechanisms of the Retina* (Oxford Univ. Press, London, 1947); C. A. G. Wiersma and T. Yamaguchi, *J. Exp. Biol.* **47**, 409 (1967); M. L. Wolbarsht, H. G. Wagner, E. F. MacNichol, Jr., in *The Visual System: Neurophysiology and Psychophysics*, R. Jung and H. Kornhuber, Eds. (Springer-Verlag, Berlin, 1961), p. 163; R. Granit, *Receptors and Sensory Perception* (Yale Univ. Press, New Haven, 1955). The strength of the off discharge or postinhibitory rebound depends greatly on the species and the level of the nervous system.
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Serum Dopamine-β-Hydroxylase: Decrease after Chemical Sympathectomy

Abstract. *Dopamine-β-hydroxylase is an enzyme that is localized to catecholamine-containing vesicles in sympathetic nerves and the adrenal medulla, and is also found in the serum. Treatment of rats with 6-hydroxydopamine, a drug which destroys sympathetic nerve terminals, leads to a decrease in serum dopamine-β-hydroxylase activity. The decrease is not due to an effect on the adrenal medulla or to an increase in circulating inhibitor or inhibitors of enzyme. These data represent evidence that at least a portion of the circulating dopamine-β-hydroxylase activity arises from sympathetic nerve terminals.*

Dopamine-β-hydroxylase (DBH), the enzyme that catalyzes the conversion of dopamine to norepinephrine (*1*), is localized to the chromaffin granules in the adrenal medulla (*2*) and to the catecholamine-containing vesicles in

sympathetic nerves (*3*). This enzyme is released with catecholamines when the isolated perfused adrenal gland is stimulated with acetylcholine (*4*) and when the nerves to the isolated perfused spleen are stimulated (*5*).

A DBH activity in the serum of both man and experimental animals has been described (*6*). Serum DBH activity is similar to that of the adrenal enzyme as judged by cofactor requirements, oxygen requirement, K_m (Michaelis constant) for substrate, and response to cupric ions (*6*). When rats are stressed by means of forced immobilization, a procedure that increases catecholamine excretion (*7*), there is an increase in serum DBH activity, and the increase occurs even in the absence of the adrenal glands (*8*).

Our study was undertaken to determine the source of serum DBH activity. If this circulating enzyme is derived from the adrenal medulla, the sympathetic nerves, or both, it might prove to be an easily measured index of the activity of these tissues. 6-Hydroxydopamine (6-OHDA) causes a partial destruction of sympathetic nerve terminals (*9*), while not affecting the adrenal medulla. Serum DBH activity in the rat decreases after treatment with 6-OHDA, indicating that at least a portion of the serum DBH originates in sympathetic nerve terminals.

All animals used were male Sprague-Dawley rats (160 to 200 g) (from Hormone Assay Labs, Chicago). They were either normal or sham-operated, or they had been subjected to surgical removal of the adrenal medulla. The adequacy of adrenal demedullation was verified by examination of sections of the adrenal glands stained with hematoxylin and eosin.

6-Hydroxydopamine hydrobromide (Regis Chemical Company, Chicago, Illinois) was dissolved in 0.001*N* HCl within 15 minutes of injection, and each treated animal was injected intravenously by the tail vein with either 34 or 68 mg of 6-OHDA (calculated as base) per kilogram of body weight. This injection was followed by 0.5 ml of saline. Control animals received the same volume of HCl and saline intravenously. Animals were killed by decapitation; blood was collected (on ice) and centrifuged; serum was separated and was either assayed for DBH activity the same day or was immediately frozen for assay the next day (*10*).

Purified bovine adrenal DBH was prepared by a modification of the method of Geffen *et al.* (*11*). Catecholamines were assayed by methods previously described (*12*). Lactate dehydrogenase activity in the serum was determined as described by Kornberg (*13*) by measuring the oxidation of reduced nicotinamide adenine dinucleotide, with 20 μl of rat serum in each assay. The results were expressed as change in absorbance at 340 nm per minute per milliliter of serum. The DBH activity was measured by a sensitive enzymatic assay (*14*) modified for the determination of serum activity described in detail elsewhere (*6*). A unit of DBH activity represents 1 nmole of octopamine formed per milliliter of serum per 30 minutes of incubation.

Normal rats were given two injections of 6-OHDA 24 hours apart and were killed 72 hours after the first injection, a time at which adrenergic nerve terminals have been observed, in electron microscopic studies, to be degenerating after the doses of drug used (*9*). In repeated experiments, serum DBH activity was reduced 18 to 25 percent after this treatment (Fig. 1A). In no experiment was there a significant difference between the effects of the two doses of the drug which were used. As has been reported by other investigators, a 95 percent reduction in cardiac norepinephrine was found 3 days after the injection of 6-OHDA (*9*).

Although 6-OHDA in the concentrations used does not affect concentrations of catecholamine in the adrenal glands (*9*), animals in which the adrenal medulla had been removed were treated with two doses of drug to

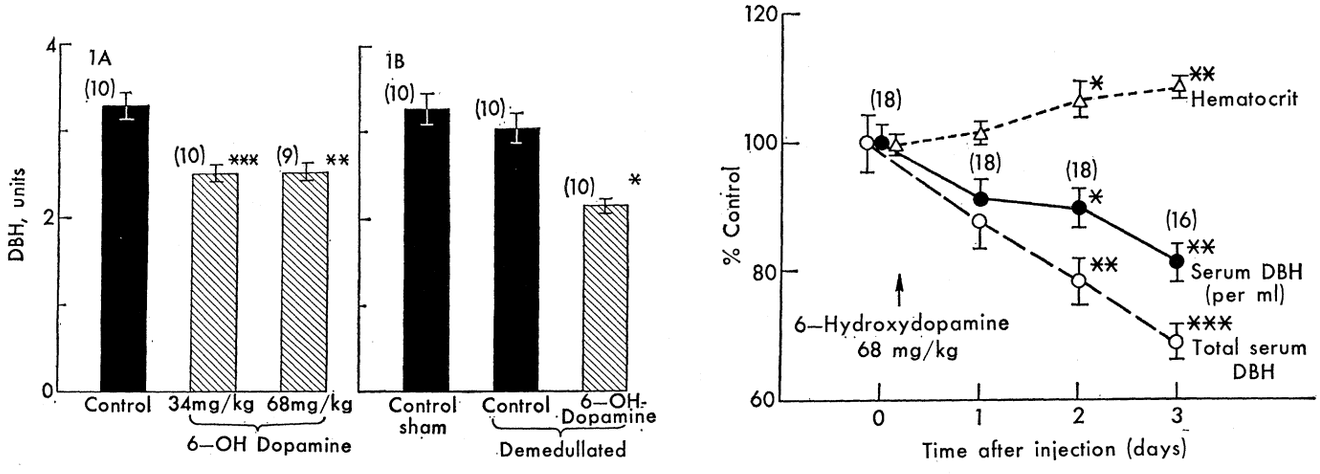

Fig. 1 (left). (A) Effect of two intravenous injections, 24 hours apart, of 6-hydroxydopamine (6-OHDA) of either 34 or 68 mg/kg on serum DBH activity 72 hours after the first injection. All serum samples were diluted with three volumes of water and assayed with 1 m*M* tyramine as substrate in the presence of 32 μM $CuSO_4$, with a 30-minute incubation period and internal standards of 40 ng of octopamine hydrochloride (*6, 8*). (B) Effect of two injections of 6-OHDA (68 mg/kg) on serum DBH activity on rats in which the adrenal medulla had been removed. The number of animals in each group is given in parentheses. * $P < .02$ compared with control. ** $P < .01$ compared with control. *** $P < .001$ compared with control. Fig. 2 (right). Relative values of serum DBH expressed both as total serum activity and activity per milliliter of serum are shown at 24, 48, and 72 hours after single intravenous injection of 68 mg of 6-OHDA per kilogram. Relative hematocrit values are also shown. The number of animals in each group is given in parentheses. * $P < .05$ compared with control. ** $P < .01$ compared with control. *** $P < .001$ compared with control.

rule out the possibility that the changes in serum DBH activity might be due to an effect on the adrenal medulla. The treatment resulted in a decrease of serum DBH activity of the same magnitude as that seen in normal rats (Fig. 1B). As in previous studies (*8*), no significant difference was found between serum DBH activity in sham-operated animals and that in the adrenal-demedullated animals 12 days after operation (Fig. 1B), demonstrating that the adrenal medulla is not necessary for the maintenance of serum DBH activity.

Inhibitors of DBH have been found in many tissues. These inhibitors are thought to act by binding to the copper in the enzyme molecule, and the effect of inhibitors can be blocked by addition of cupric ions to tissue homogenates (*15*). Cupric ions also increase the activity of serum DBH (*6*). Because of the possibility that the decrease in DBH activity after treatment with 6-OHDA might be due to an increase in serum inhibitor (or inhibitors), pooled rat serums from a control group and from a group of animals treated with two doses of 6-OHDA (68 mg/kg) were mixed with purified bovine adrenal DBH in the absence of cupric ion. Serums from the treated animals had shown a 25 percent decrease in DBH activity, but no increase in the inhibition of pure DBH was seen in its presence. Control serums inhibited purified DBH 48.3 ± 4.4 percent and that from treated animals inhibited 47.4 ± 2.3 percent.

The time course of the effect of a single injection of 6-OHDA on serum DBH activity was examined in two separate experiments. In each of these experiments serum DBH, expressed as activity per milliliter of serum was reduced significantly by 72 hours after the injection. The results of these experiments are shown in Fig. 2. Because rats treated with 6-OHDA develop diarrhea and become dehydrated, hematocrits were determined on blood from all animals. Hematocrits increased 10 percent during the 3 days after drug treatment (Fig. 2). Therefore, the magnitude of the change in serum DBH activity after treatment with 6-OHDA had been underestimated because of a reduction in total serum volume. It is possible to calculate relative values for total serum DBH activity if the assumption is made that red cell mass remains constant after drug treatment. With the use of the data presented in Fig. 2, a decrease in total serum DBH of 31 percent 3 days after a single injection of 6-OHDA was calculated. In these same experiments serum lactate dehydrogenase activity was determined in samples from control animals and from animals treated 72 hours earlier with 6-OHDA. Lactate dehydrogenase activity was increased in the treated animals from 2.13 ± 0.18 to 2.85 ± 0.21 (mean ± S.E.M., $P < .05$), demonstrating that the decrease of DBH after treatment with the drug was not a nonspecific phenomenon affecting all serum enzymes.

Because serum DBH activity still appeared to be decreasing 72 hours after 6-OHDA (Fig. 2), a long-term experiment was carried out. Rats were treated with 68 mg/kg twice within 24 hours and again with 68 mg/kg 1 week after the first injection. They were killed 2 weeks after the first injection, at a time that there is a continued depletion of norepinephrine in the heart and spleen (*9*). Two weeks after treatment was begun, serum DBH was reduced 20 percent in treated animals from 3.13 ± 0.31 to 2.49 ± 0.12 units (mean ± S.E.M., $P < .02$).

The "chemical sympathectomy" achieved with 6-OHDA, like the "immunosympathectomy" induced by anti-nerve growth factor (*16*), is only partial. The effects of 6-OHDA on norepinephrine stores vary greatly from organ to organ (*9*), and it has been reported that sympathetic nerves in rat mesenteric blood vessels are resistant to the effects of the drug (*9*). Even if most of the circulating DBH activity is derived from sympathetic nerve terminals, the incomplete nature of the sympathectomy achieved with 6-OHDA may explain the relatively small magnitude of the changes in serum enzyme activity found. Furthermore, that the vascular nerve terminals may be a major source of serum DBH is suggested by (i) immunofluorescent studies that have shown DBH to be present in nerves in the walls of blood vessels (*17*), (ii) evidence that vessels are a major source of the total norepinephrine excreted (*18*), and (iii) the resistance of vascular sympathetic nerve endings to destruction by 6-OHDA. It is also possible that only a portion of the serum enzyme activity is derived from sympathetic nerves, or that the decreases in activity in serum 3 days after drug were not larger because the circulating enzyme has a long half-life. This latter possibility is less likely as an explanation, however, because no further decrease in serum DBH was seen 2 weeks after treatment with 6-OHDA.

Our results demonstrate that a decrease in serum DBH activity occurs after a partial chemical sympathectomy. This finding is further evidence that the source of at least a portion of the serum DBH activity is the sympathetic nerve terminal, and that this easily measured, circulating enzyme activity might be useful as a measure of activity of the sympathetic nervous system both in normal physiologic responses and in certain disease states.

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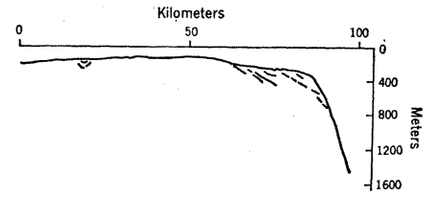

Fig. 2. Seismic cross section derived from records along line *G* of Fig. 1.

Orbitolina, a Cretaceous Larger Foraminifer, from Flemish Cap: Paleoceanographic Implications

Abstract. *The Tethyan larger foraminiferal genus* Orbitolina *has been found in the easternmost part of the western North Atlantic continental shelf at 46°30′N. All other known occurrences of the genus in North America are south of 33°N. The species is* Orbitolina conoidea *Gras; its abundance in a grain-supported limestone indicates a tropical neritic environment and precludes the influence of Arctic waters in the Flemish Cap region in Early or Middle Cretaceous times.*

Flemish Cap is the easternmost element of the Atlantic continental margin of North America. Although it is separated from the Grand Banks of Newfoundland to the west by the deep water channel of Flemish Pass, the water depth over the central part of the cap is less than 150 m (Fig. 1). Dipping sedimentary strata have been detected on the flanks of Flemish Cap. A fragment of fossiliferous limestone dredged from the southern slope of Flemish Cap (*X* in Fig. 1) contains abundant *Orbitolina conoidea* Gras, a Lower Cretaceous larger foraminifer of unquestionable Tethyan affinity.

The limestone was dredged from a depth of approximately 1480 m during a cruise of the C.S.S. *Hudson* in 1967 (*1*). The dredge haul consisted mainly of large angular slabs of limestone and well-rounded cobbles and pebbles of granite and gneiss. On the southern slope of Flemish Cap, limestone has been recovered in quantity only in dredge hauls from depths greater than 270 m (*2*), where seismic profiler results and bottom photographs indicate outcrops of layered rocks. The ubiquitous occurrence of well-rounded specimens of igneous rocks indicates an ice-rafted origin for this fraction of the samples.

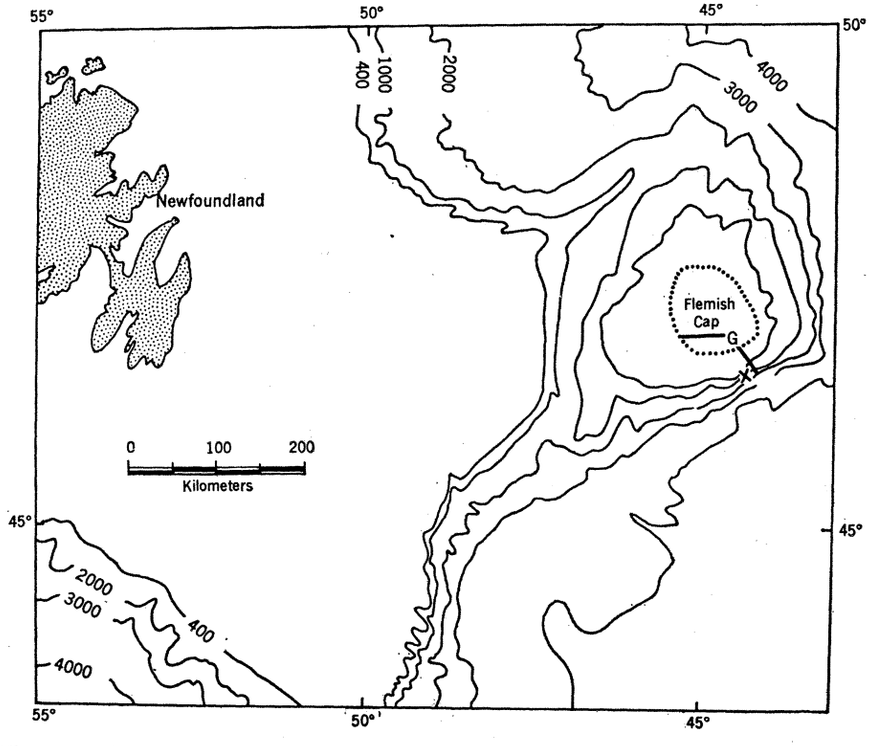

Fig. 1. Bathymetric map of the Flemish Cap area; isobaths are in meters. Letter *X* indicates sample location. Line *G* denotes the location of the seismic cross section in Fig. 2.

Seismic profiling was conducted over Flemish Cap in 1969 from C.S.S. *Hudson* and C.N.A.V. *Sackville* (*2*); a single-channel recording system was used, in conjunction with an air-gun energy source. The seismic profiler results show that the top of Flemish Cap is a smooth erosional surface, with a central area of seismically "hard" basement encircled by a zone of outward-dipping strata. The inferred extent of the central basement area is indicated by the dotted line in Fig. 1. One of the seismic profiler traverses, line *G* (Figs. 1 and 2), is in the vicinity of our sample station. A seismic cross section derived from the records along this line is shown in Fig. 2. The bottom profile is smooth, except for a minor step at the contact between the truncated strata and the basement media. Truncation of the layered rocks is also obvious on the slope of Flemish Cap.

The thin sections illustrated in this report (Fig. 3) were cut from a fossiliferous limestone specimen, which measured approximately 10 by 7 by 1.5 cm. This grain-supported limestone is extremely rich in specimens of the larger foraminifer *Orbitolina conoidea* Gras (*3*). In the thin sections examined, the density of tests is often about 40 per square centimeter. The form is generally conical. The very distinct marginal zone is about 0.04 mm thick. The radial zone is narrow and, at base, does not generally cover more than one-third of the diameter. The thick central reticulate zone includes a small amount of fine detrital particles. Calcite eyes are not seen. The megalospheric embryonic apparatus is apical and is surrounded by a number of periembryonic chambers. Because of the random orientation of the specimens of *O. conoidea* in the rock sections, few measurements could