extracted three times with $CHCl_3$ (40 ml); the combined $CHCl_3$ fractions were reduced to about 12 ml under vacuum, and the residue was transferred to a separatory funnel and extracted three times with TA (20 ml); the resulting aqueous fraction was centrifuged to remove any emulsion, adjusted to *p*H 9, and extracted three times with $CHCl_3$ (60 ml); the $CHCl_3$ was removed under vacuum, and the residue was transferred in water (2 ml) to a carboxymethyl-cellulose column (1 cm by 5 cm); the column was rinsed with water (10 ml), and then the alkaloids were eluted with 4*M* NH_4Cl (15 ml); the eluate was extracted three times with $CHCl_3$ (15 ml), the combined $CHCl_3$ extracts were dehydrated with Na_2SO_4, and then the solvent was removed under vacuum. The residue was assayed for total ergot alkaloids with *p*-dimethylaminobenzaldehyde (PDAB), according to the procedure of L. E. Michelon and W. J. Kelleher [*Lloydia* **26**, 192 (1963)], except that it was dissolved in TA (0.5 ml) and treated first with PDAB (0.5 ml) and then, after 10 minutes, with $NaNO_2$ (0.1%, 0.1 ml). Ergonovine maleate was used as a standard.

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De Gustibus Non Est Disputandem: A Spiral Center for Taste in the Brain of the Teleost Fish, *Heterotis niloticus*

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The teleost fish, *Heterotis niloticus*, has elaborate paired, spiraled pharyngeal structures that aid in concentrating and swallowing food. These epibranchial organs are lined by an epithelium rich in taste buds. Both the taste buds and the muscles of the epibranchial organs are innervated by components of the vagal nerve. Horseradish peroxidase neuronal tracing experiments show that these nerve fibers are connected centrally to an enormous epibranchial portion of the vagal lobes—a special visceral sensory and motor region of the medulla. The epibranchial portion of the vagal lobe is among the most remarkable structures found in the brains of vertebrates, for it is itself a spiral.

A NUMBER OF SPECIES OF TELEOSTEan fishes have paired structures at the posterior end of the pharynx that function as accessory digestive organs aiding in both concentrating and swallowing food particles. These pharyngeal structures, generally known as epibranchial organs (*1*–*3*), are secondary upgrowths of the walls of the most posterior gill pouch and are intimately associated with the epibranchial portions of the fourth and fifth gill arches. Epibranchial organs occur in some members of four groups of teleosts: Osteoglossiformes (one species), Clupeiformes (many), Gonorynchiformes (possibly all), and Characiformes (some). On the basis of their distribution and their various morphologies, epibranchial organs are believed to have evolved independently in each of these major groups in relation to the repeated evolution of microphagous habits (*1*).

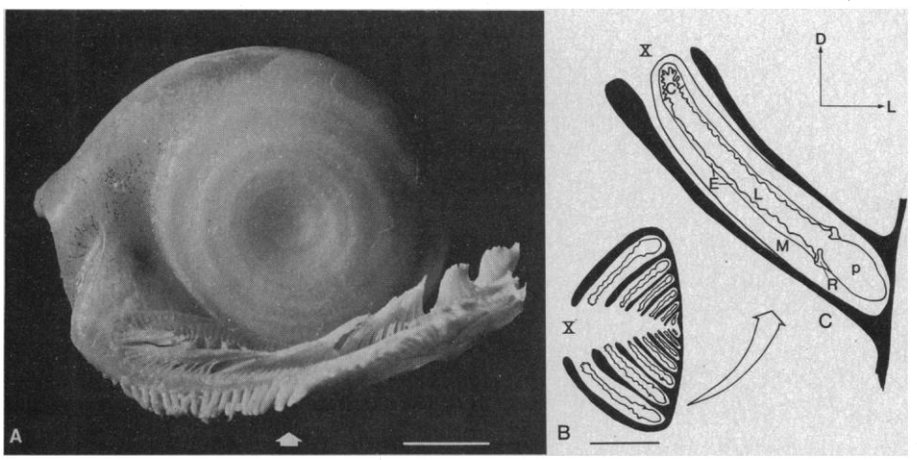

Fig. 1. Epibranchial organ of *Heterotis*. (A) Lateral view of right epibranchial organ and adjoining gill arch from a 27-cm specimen. Scale bar, 0.5 cm. (B) Line drawing of a transverse paraffin section through the epibranchial organ from a slightly smaller specimen. The white arrow in (A) indicates the level of this section. Scale bar, 0.5 cm. (C) Line drawing of a section through a single turn (enlarged) of the epibranchial organ shown in (B). In both (B) and (C) the cartilaginous capsule of the epibranchial organ is shown in solid black. Arrows in the upper right indicate dorsal and lateral directions for both (B) and (C). Abbreviations: C, central portion of the lumen; E, epithelium rich in taste buds and mucous glands; L, lumen; M, striated muscles; p, peripheral portion of lumen; R, modified gill rakers; X, portion of the vagal nerve that innervates the epibranchial organ.

Among the most elaborate of the known epibranchial organs are those of the freshwater African species, *Heterotis niloticus* (family Osteoglossidae). In *Heterotis*, each epibranchial organ consists of a flattened, blind tube that is coiled concentrically on itself, forming a spiral (Fig. 1). The number of turns of the spiral increases with the age and size of the fish, and organs with as many as seven complete revolutions have been reported in large specimens (*4*). Each epibranchial organ resembles a coiled snail shell and has the overall shape of a hemisphere with its convex surface facing medially. The right epibranchial organ forms a left-handed, or clockwise, spiral, and the left organ, a right-handed spiral.

The entire coiled tube is enclosed in a cartilaginous supporting capsule (Fig. 1). Peripherally, the lumen of the tube forms a trough or canal that opens posteriorly into the opercular cavity. This trough is bordered at either edge by a row of modified gill rakers that serve as a sieve or screen separating the peripheral trough from the remainder of the lumen of the tube. Centrally the lumen of the tube forms a small groove that is confluent with the buccal cavity near the esophageal opening. Between the peripheral trough and the central groove the lumen is walled on either side by striated muscles and lined by an epithelium containing many mucous glands and numerous taste buds (*4*).

In teleostean fishes, as in all vertebrate groups, taste buds are innervated by sensory components of the facial (VII), glossopharyngeal (IX), and vagal (X) cranial nerves. The gustatory fibers terminate centrally in the special visceral sensory region of the medulla, which in most teleosts consists of paired longitudinal columns of cells and neuropil that bulge somewhat into the fourth ventricle. In a few groups—notably

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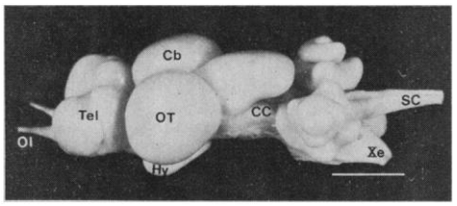

Fig. 2. Dorsolateral view of the brain of *Heterotis*. Note the paired, spiraled portions of the vagal lobe; they are innervated by a massive component of the vagal nerve that is connected peripherally to the epibranchial organ. Scale bar, 0.5 cm. Abbreviations: Cb, cerebellum; CC, cerebellar crest overlying the lateral line portion of medulla; Hy, hypothalmus; Ol, olfactory nerve; OT, optic tectum; SC, spinal cord; Tel, telencephalon; Xe, epibranchial portion of vagal nerve.

the cypriniforms, siluroids, and gadiforms—the special visceral sensory region is hypertrophied forming large dorsal bulges known as the facial and vagal lobes (*5*). The branchial muscles of the gill arches and their derivatives are innervated by motoneurons forming a column of cells near the visceral sensory column and sending their axons out via the trigeminal (V), facial (VII), glossopharyngeal (IX), and vagal (X) nerves.

In *Heterotis*, the taste buds and striated muscles of the epibranchial organ are innervated by sensory and motor components of an extremely large branch of the vagus nerve. These nerve fibers are connected to a specialized, caudal portion of the vagal lobe. This "epibranchial" portion of the vagal lobe is not only very large, constituting about 15 percent of the entire brain in *Heterotis* (*6*), but is also among the most remarkable structures found in the central nervous system of any vertebrate. The epibranchial portion of the vagal lobe is itself a spiraled structure (Fig. 2) (*7*), forming a left-handed spiral on the right side of the brain and a right-handed spiral on the left side. The base of each spiral is continuous rostrally with the ordinary vagal lobe, and the axis of each spiral points slightly rostrolaterally. The dorsal surface of the epibranchial portion of the vagal lobe is the ependymal layer to which is apposed a subependymal, periventricular layer of small, granule cells. Deep to these cells lies a region of neuropil, and deep to it, a collection of large, multipolar cells. The central core of the spiral contains afferent and efferent fibers (Fig. 3).

To demonstrate the central connections of the fibers innervating the taste buds and the muscles of the epibranchial organ, horseradish peroxidase (HRP) was applied to restricted portions of the organ in a number of separate experiments, and the distribution of HRP-labeled fibers, terminals, and cell bodies was analyzed (*8*). Labeled fibers were seen in the large epibranchial branch of the vagal nerve and labeled sensory neurons were seen in the large ganglion associated with that branch. The central processes of these sensory neurons were traced into the epibranchial portion of the vagal lobe, where they terminate in the neuropil layer. Deep to, and apparently in register with, these afferent terminals were a number of retrogradely labeled multipolar motoneurons. This arrangement suggests that the sensory input from the taste buds may be used to guide the manipulation of food carried out by the muscles of the epibranchial organ. A similar suggestion concerning the palatal organ in cyprinids has been made by Finger (*9*). The HRP experiments demonstrate that in *Heterotis* the spiraled epibranchial organ maps onto the spiraled portion of the vagal lobe: base to base and apex to apex.

Like the epibranchial organ, the spiraled epibranchial vagal lobe displays an increased size and a greater number of turns in older and larger specimens (*10*). This continuous growth appears to make it possible for the epibranchial portion of the vagal lobe to provide a continuously expanding sensory region in the brain on which the continuously increasing number of sensory fibers carrying information from the taste buds can terminate. The best known spiraled end organ—the mammalian cochlea—does not project on to a spiraled central structure, nor do the central projections of the cochlea suggest its shape. Perhaps this is because the spiraled form of the cochlea develops before it is connected to the brain and both the cochlea and its nuclei are of determinate growth.

Although a number of other teleosts possess epibranchial organs, none of them are closely related to *Heterotis* and in none of them is the structure of the organ similar to that of *Heterotis*. In the few species that have been examined the vagal lobes are relatively pedestrian (*11*). Thus, even though other specialized "epibranchial" vagal lobes may be discovered in the future, the remarkable, spiraled gustatory region of the brain of *Heterotis* may well be unique.

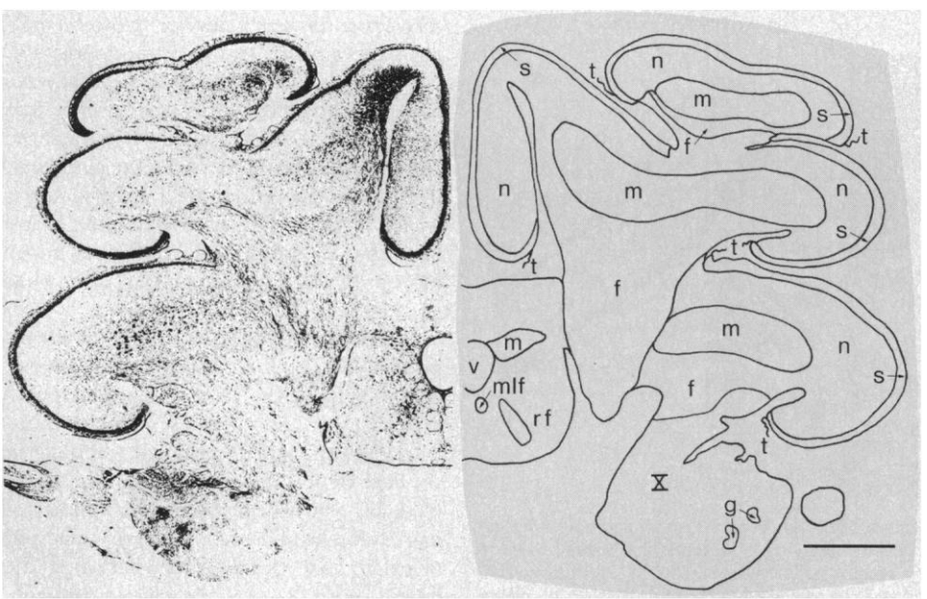

Fig. 3. Transverse section through the epibranchial portion of the vagal lobe in *Heterotis*. Photomicrograph (left) of a paraffin section stained with cresyl violet. Line drawing (right) indicating some of the structures present. Scale bar, 1 mm. Abbreviations: f, fiber layer; g, clusters of ganglion cells of vagal nerve; m, motoneuron layer; mlf, medial longitudinal fasciculus; n, neuropil region; rf, reticular formation; s, subependymal layer of granule cells; t, tela choroidea; v, fourth ventricle; X, vagal nerve.

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have not been adequately described or illustrated nor have their internal structure and connections been examined. Dorn's paper seems to have been virtually lost in the literature. I happened across it myself only after having independently discovered the vagal lobes of *Heterotis*. I have seen it cited only once [W. Harder, *Anatomy of Fishes*, part I, *Text* (Schweizerbart'sche, Stuttgart, 1975), p. 377.
8. Specimens were anesthetized with MS-222. Horseradish peroxidase (Boehringer-Mannheim), on the tip of a minuten insect pin, was applied to a small localized region of an epibranchial organ. After surviving 4 to 10 days, the animals were killed and their brains and epibranchial organs removed and processed to demonstrate the distribution of HRP with either tetramethylbenzidine or Hanker-Yates reagent as the chromogen [M.-M. Mesulam, *J. Histochem. Cytochem.* **26**, 106 (1978); J. S. Hanker, P. E. Yates, C. B. Metz, A. Rustioni, *Histochem. J.* **9**, 789 (1977)].
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12. I thank R. P. Vari for aid in obtaining preserved specimens of *H. niloticus* from the fish collection of the National Museum of Natural History; G. Meola for aid in obtaining live specimens of *Heterotis*; J. P. O'Reilly and A. Kinkler for histological assistance; G. E. Meredith for translating portions of d'Aubenton's paper from French into English; O. Rodbell for photographic assistance; W. M. Saidel for advice on photography, loan of photographic equipment, helpful discussions, and comments on the manuscript; C. A. McCormick for helpful discussions and comments on the manuscript; and T. E. Finger for comments on the manuscript. Some of the material in this report was presented at the 1982 meeting of the J. B. Johnston Club. Supported by NSF research grant BNS 18844.

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Molecular Analysis of the t(2;14) Translocation of Childhood Chronic Lymphocytic Leukemia

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Two rare cases of chronic lymphocytic leukemia (CLL) in children have been studied; both are associated with a previously undescribed chromosomal translocation [t(2;14)(p13;q32)]. In one patient the translocation was reciprocal and the breakpoint on chromosome 14 occurred just 5′ of the $C_{\gamma 2}$ region on the productive immunoglobulin heavy-chain allele. The breakpoint on chromosome 2 does not involve the κ locus but lies within an uncharacterized region that coincides with the position of a constitutive fragile site that occurs within normal lymphocytes. Data on the second patient are consistent with these findings and suggest that these cases represent a rare but distinct subgroup of CLL's with a specific cytogenetic change.

MALIGNANCIES ARE OFTEN ASSOciated with specific chromosomal translocations which are now thought to represent a discrete step in tumor development (*1*). Chronic lymphocytic leukemia (CLL) is the most prevalent form of leukemia in Western countries, but cytogenetic abnormalities associated with the disease are variable (*2*). Approximately half of all CLL's exhibit a normal karyotype. The most frequent cytogenetic change observed is trisomy 12. Translocations involving 14q32, which are common in Burkitt's and follicular lymphomas (*3*), are found in only 10 percent of CLL tumors.

CLL is found almost exclusively in the middle-aged to elderly adult population (*4*). However, two children (L.H. and A.S.) were recently diagnosed as having a B-cell leukemia closely resembling CLL (*5*). The tumor cells of both patients display a previously undescribed chromosomal translocation with breakpoints occurring in band 13 on the short arm of chromosome 2 and band 32 on the long arm of chromosome 14 [t(2;14)(p13;q32)] (Fig. 1).

The proximity of the t(2;14) breakpoints to the mapped position of the immunoglobulin heavy chain (IgH) and immunoglobulin κ chain (Igκ) loci (*6*), and the involvement of these genes in the translocations of other B-cell malignancies, suggested that Ig genes or their associated sequences may have played a role in the generation of the t(2;14) translocation.

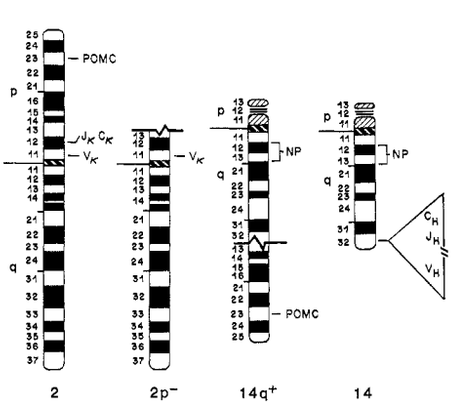

Fig. 1. Tumor chromosomes 2, 2p−, 14q+, and 14. A diagramatic representation of the translocated chromosomes is compared with that of the normal alleles. The breakpoints for both patients were found to be at 2p13 and 14q32 (*5*). The p and q denote the short and long arm, respectively, for each chromosome. Chromosomal structure is as presented in ISCN (*10*). The location of the genes for POMC, NP (*11*), and the immunoglobulin heavy- and light-chain gene segments are shown (*6*). The added material on the 14q+ is derived from the short arm of chromosome 2 (leaving a 2p−), but it could not be determined by cytogenetic analysis whether or not the translocation was reciprocal (that is, whether or not a small portion of chromosome 14 resides on the 2p−). Fibroblasts from patient L.H. displayed a normal karyotype and could not be induced to express any constitutional fragile sites (*12*).

The specific involvement of Ig sequences was determined by isolating the tumor chromosomes of interest from patient L.H. within separate somatic cell hybrids. These cell lines were then analyzed by several methods for the presence of specific genes (Fig. 1 and Table 1). Heterohybrid 4-D2 had the untranslocated tumor chromosome 14. It retains one of two tumor Ig joining region (J_H) alleles (Fig. 2A), $C_{\alpha 1}$ and $C_{\alpha 2}$ (Fig. 2B), as well as the more centromeric marker for chromosome 14, nucleoside phosphorylase (NP), but lacks any of the genes located on chromosome 2 (Table 1). The hybrid 8-D5.IB5 has the other J_H allele, as well as C_μ (Fig. 2A), C_δ (Table 1), and $C_{\alpha 1}$ (Fig. 2B), but does not have the more centromeric $C_{\alpha 2}$ segment or the gene for NP (Table 1). In addition, this hybrid bears one of the tumor κ alleles but lacks the POMC gene (pro-opiomelanocortin) from the distal end of the short arm of chromosome 2. Therefore, 8-D5.IB5 has retained the tumor 2p− chromosome. The complementary set of loci corresponding to the tumor 14q+ chromosome are found within the heterohybrid 12-B3 (Table 1). These results establish that the breakpoint on chromosome 14 has occurred between $C_{\alpha 1}$ and $C_{\alpha 2}$. They also show that the translocation was reciprocal, since the more distal IgH genes of one allele are located on the tumor 2p− chromosome. The presence of a single rearranged C_μ allele in LH, and the absence of C_μ and C_δ in 4-D2, reveals that the untranslocated tumor chromosome 14 has undergone a recombination event within the IgH locus resulting in the loss of these gene segments. The tumor cells of patient A.S. also had a single rearranged C_μ gene segment (Fig. 2A), suggesting that a similar event had occurred in

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