Hormonal Control of Behavior: Amines and the Biasing of Behavioral Output in Lobsters

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Hormones and neurohormones act on the nervous system to produce important changes in behavior. Amine actions in the lobster nervous system and their possible relations to aggressive behavior in lobsters were studied in order to explore how such changes might come about.

MOST OF US ARE FAMILIAR WITH THE IDEA THAT CHEMICALS can influence our behavior. Materials we ingest or inject alter our mood, emotional state, and level of arousal; stimulants awaken us and make us anxious; depressants have opposite effects; and the drive for drugs of abuse can come to dominate our existence. We recognize further that chemicals normally secreted within our bodies can profoundly modify our behavior. For example, epinephrine (adrenaline) plays an important role in the classic "fight or flight" response, and gonadal hormones are essential to our sexual drives. But how and where do these substances act in our nervous systems to produce such dramatic changes in our behavior? These and related questions are addressed in this article, which is based on studies in which the lobster nervous system was used as a model.

Much has been written about the hormonal control of animal behavior (*1*). Indeed, although the ideas presented in this article have evolved from studies from my laboratory with lobsters, very similar notions have been presented before by other authors examining a wide variety of animal experimental systems (*1–5*). The main postulate of this article is that hormones and neurohormones interact with the nervous system (and other tissues of the body) to bias behavioral output toward highly adaptive stereotypical responses. Further, the substances capable of such influences probably do not have single sites or targets of action in the nervous system: rather, they modify the functioning of many (all?) parts of the nervous system concerned with the behavior in question. Such compounds, therefore, can influence large areas of the nervous system in a way that parallels the manner in which transmitters, acting through second messengers, alter the properties of individual nerve or muscle cells: they bring the system (a cell for a transmitter or a circuit for a hormone) from one stable state to a second new stable state that now shows a changed response to selective stimulation. This is done by the alteration or sensitization of a logical set of component pieces that together modify the output of the system. For example, certain transmitters, acting through second messengers and their biochemical cascades, cause covalent modification of a number of functionally related cellular proteins in target neurons. β-Adrenergic activation of cardiac muscle causes changes including those in membrane channels, carbohydrate metabolism, Ca^{2+} uptake and storage, and contractile proteins (*6*). The consequence of this set of changes (and of probable secondary changes resulting from the primary alterations) is that, for a period of several minutes after treatment with the biogenic amine, muscles contract more vigorously and relax faster in response to stimulation. The original state of the cell is reestablished by enzymes (phosphatases in this example) that restore the modified proteins to the levels of phosphorylation found before amine exposure. The change in the entire set of proteins is responsible for the altered response of the cell, and similar covalent modification of any individual protein of the set may come close to mimicking the response but cannot duplicate it. Similarly, when hormones or neurohormones modify behavioral output, the postulate is that the hormonal substances generate new behavioral patterns by changing the response properties of logically arranged sets of neurons ["assemblies," in a somewhat larger sense than those proposed by Hebb (*7*); for a clear statement of this idea see Menzel and Bicker (*2*); for similar ideas see Arnold (*3*), Dominick and Truman (*4*), and Pfaff and Modianos (*5*)].

This idea is expressed in greater detail in the following statements (Fig. 1). (i) Environmental signals (such as day-night cycle lengths, interactions with conspecifics or intruders, and proximity of food) act through sensory pathways to enhance the release of a hormone. (ii) The hormone may be released from glandular tissues or from specific sets of neurons and may function in isolation or in dynamic balance with other humoral substances. (iii) In either case, the hormone finds its receptors and sensitizes receptor-enriched territories within the nervous system that function together either to read out a new or different pattern of behavior or to enhance or diminish the effectiveness of an existing pattern. (iv) The territories may include sensory elements, groups of neurons in higher processing centers, and motor or hormonal output systems. The elements (neurons, muscles, and glands) in each of the sensitized areas may have functioned in other roles in the organism before exposure to hormone. (v) The sensitization process is a gain-setting mechanism,

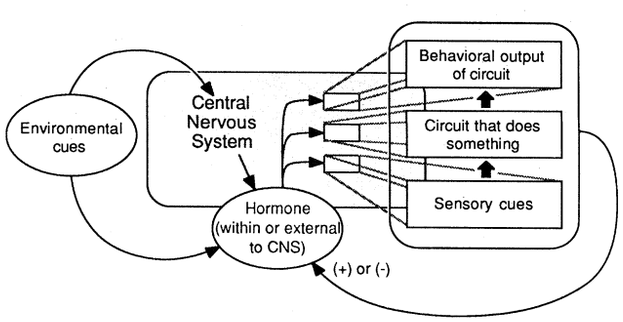

Fig. 1. Diagrammatic representation of hormonal sensitization of the response properties of sets of neurons (see text).

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biasing the output of the organism in set directions (for example, display male or female pattern of behavior, fight or flee, explore, search for food, or assume dominant or subordinate role). The biasing may take minutes to days to manifest itself and may last varying periods of time. (vi) What has changed is that the organism now responds to particular sensory stimuli with an altered output appropriate to the new situation. (vii) Genetic or environmental influences may produce a wide range of variation within individuals in the effectiveness of any particular hormonal gain-setting mechanism. Thus the control of output patterns in response to environmental stimuli may be highly effective in some cases, less effective in others, or completely ineffective in the absence of gain setters or their receptors. The latter case may not be incompatible with survival; it may only influence the competitiveness of the animal. (viii) The circuit itself may further enhance or diminish the release of the hormonal substance and thereby tend to maintain or turn off a gain-setting mechanism (see below).

Some of these points will be illustrated by the results of our studies on the role of biogenic amines in aggressive behavior in lobsters. A large literature, however, supports the belief that other substances that exert important behavioral effects in animals, such as steroid hormones and peptides, function in similar ways (*1, 3–5*).

Biogenic Amine-Containing Neurons in Vertebrate and Invertebrate Nervous Systems

In the vertebrate central nervous system, neurons containing norepinephrine, dopamine, and serotonin are concentrated for the most part in small clusters in discrete brainstem nuclei (*8*). Neurons using other transmitters often coexist with the amine-containing neurons in these nucleii. The aminergic cells are among the first categories of neurons to differentiate and to express their transmitter phenotype in the developing nervous system (*9*). The appearance of amines early in development has attracted considerable attention and has prompted much speculation on their possible functional roles (*9, 10*). Space will not allow presentation of this interesting work here, but it will be reviewed in a forthcoming publication (*11*). The fields of innervation of individual amine-containing neurons are enormous; processes of single cells traverse wide areas of the central nervous system, often ignoring the functional subdivisions that exist within regional and local boundaries (*8, 12*). For many years it was believed that similarly wide areas of the nervous system were involved in activating these cells. Recent studies of noradrenergic neurons in the locus ceruleus of the rat brain, however, suggest that a far more restricted innervation originating from two groups of medullary neurons may be the major synaptic input to the locus ceruleus cells (*13*). In some target areas, amine-containing neuron terminals have the morphological features of classical neurotransmitter endings, while in others the synaptic specializations typical of synaptic structures are absent (*14*). In either case, however, it is uncertain whether amines have highly restricted actions on targets in the immediate vicinity of their terminals or act like local hormones uniformly bathing small regions of neuropil close to their terminals. Amines also are found in the peripheral autonomic nervous system, in the general circulation, released for the most part from the adrenal medulla and from neurons of the autonomic nervous system (but also from other sites like mast cells), and in the cerebrospinal fluid possibly released from terminals ending on ventricular surfaces (*15*). The enigma of the amine neurons in the vertebrate nervous system is that despite compelling evidence of their importance (*8, 16*) little is known of how they function in behaving animals. In contrast, with invertebrates much progress has been made in relating amine function to behavior. While this review focuses on our work exploring the possible roles of serotonin and octopamine (the phenol analog of norepinephrine) in aggressive behavior in lobsters, it could equally well have focused on other elegant studies exploring the roles of the following: serotonin in swimming (*17*) and feeding (*18*) behavior in leeches; biogenic amines in learning in molluscan (*19*) and insect (*20*) systems; serotonin in feeding behavior in molluscan systems (*21*); octopamine in flight behavior of locusts and moths (*22*); or any of a further wide variety of interesting behaviors that have been defined at a cellular level in other invertebrate species (*3, 4, 23*).

In invertebrates, the segmental organization and relative simplicity of the central nervous system have allowed a precision in the definition of the systems of amine-containing neurons that has not yet been possible in vertebrate systems. Thus in several species of invertebrates all of the amine-containing neurons in the nervous system have been mapped (*24, 25*), unique cells and cellular

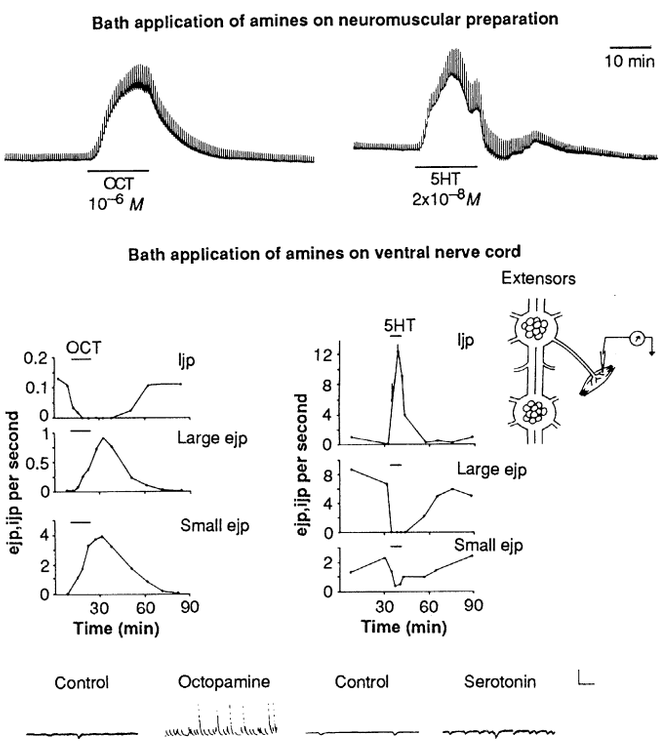

Fig. 2. The effects of bath-applied serotonin (5HT) and octopamine (OCT) on exoskeletal muscle preparations and on neurons of the ventral nerve cord. (**Top**) A recording of the actions of serotonin on basal and nerve-evoked muscle tension from the opener muscle of the dactyl of the walking leg. The short upward deflections are rapid contractions evoked by stimulating the excitatory nerve innervating this preparation (four pulses at 40 Hz). No opposition is seen in the actions of amines on exoskeletal muscle preparations. Both amines generate sustained contractions and enhance the nerve-evoked contractions. Note that serotonin is at least 50 times more effective and usually produces a much greater effect on nerve terminals (not shown here). (**Bottom**) The effect of bath-applied amines on motor neurons of the ventral nerve cord. These actions are monitored by recording from muscle fibers (postural extensors in this example) and noting changes in activity (see inset diagram). Octopamine enhances the firing of excitatory and diminishes the firing of inhibitory neurons innervating the preparation. This is shown on the lower left in an intracellular recording from a muscle fiber and is graphed on the upper left where the rates of firing of two excitatory and one inhibitory neuron are shown; ejp, excitatory junctional potential; ijp or Ijp, inhibitory junctional potential. On the right side of the figure the actions of serotonin are illustrated. Serotonin has opposite actions to octopamine: it enhances the firing of inhibitory and diminishes the firing of excitatory neurons innervating the preparation (see records on lower right and graphs on upper right; scale bars: 1 second, 1 mV except for octopamine, which is 2 mV). [The lower part of the figure is reprinted from Harris-Warrick and Kravitz (*34*) with permission, copyright 1984 the Society for Neuroscience]

structures have been described (see below), and in some cases the developmental origins of particular cells have been traced to the individual blast cells that are their progenitors (*26*). Like the vertebrate amine-containing neurons, the invertebrate cells have extensive arborizations, but the ganglionic subdivisions of the nervous system have in some cases allowed morphological subclasses of cells to be defined. These subclasses suggest that possible functional differences exist among a total population of aminergic neurons. For example, in the lobster nervous system, 120 serotonin-containing cells are found throughout the ventral nerve cord (*24*). In the thoracic and abdominal parts of the nerve cord, the serotonin-containing cells are grouped into three sets (together about 30 of the 120 cells) that differ in the location of their cell bodies and the directions their axons take to ascend or descend the nerve cord (see below). The best studied of these sets comprises seven pairs of neurons, one pair in each ganglion from the fifth thoracic (T5) through the sixth abdominal ganglia (A6). Two particularly large cells in this set are described below and are likely to be involved in the control of posture and its associated behaviors. The clear morphological subgrouping of serotonin-containing cells in lobsters and in other invertebrates should allow the functional role of each set of cells to be explored separately. Similar anatomical and functional subgroupings may exist within pools of amine neurons in the vertebrate central nervous system. However, the compact grouping of vertebrate cells into nuclei, combined with the very large arborizations of individual cells, has made it difficult to define the functional boundaries of single cells in other than global terms. For example, could one find cells concerned with motor function that might send processes to motor cortex, basal ganglia, cerebellum and spinal cord, or brainstem motoneuron pools but not to visual or olfactory cortex (*27*)?

The Lobster Model: Serotonin and Octopamine and Aggressive Behavior in Lobsters

When injected into freely moving lobsters, serotonin and octopamine generate stable and stereotypical postures that resemble those seen in dominant (serotonin) and subordinate (octopamine) lobsters (*28*). Serotonin injection caused animals to stand tall on the tips of their walking legs with their claws open in front of them and their abdomens loosely tucked downward; octopamine injection caused animals to stand low to the substrate with their claws and walking legs extended and pointing forward and with their abdomens hyperextended upward. The opposing postures result from serotonin-induced contraction of all the postural flexor muscles and octopamine-induced contraction of the postural extensors. Such actions could be due to the amines having opposing actions on peripheral exoskeletal muscles, or from amines acting differentially on neurons innervating these muscles within the ventral nerve cord.

Lobster exoskeletal muscles are innervated by excitatory neurons that use glutamate as a neurotransmitter (*29*) and inhibitory neurons that use γ-aminobutyric acid (GABA) (*30*). Quite early in our studies we (*31*), as well as other investigators (*32*), showed that amines could influence these muscles in dramatic ways, but there was no opposition of the type required to produce the distinct postures. Serotonin increased transmitter release from excitatory and inhibitory nerve terminals and caused muscles to undergo a long-lasting voltage- and Ca^{2+}-sensitive contracture and to generate Ca^{2+} action potentials. The latter were not seen before amine treatment. Octopamine also could increase release from excitatory nerves, but its effects were smaller. A nerve stimulus–dependent enhancement of transmitter release by octopamine has been seen in crayfish muscle, however (*33*). Like serotonin, octopamine caused contractures and action potentials to appear in muscle fibers. When flexor and extensor muscle pairs were examined, serotonin and octopamine generally caused facilitation of transmitter release and enhanced contractility in both types of muscle. While there were differences in the details of their actions from preparation to preparation, the generalization emerged that amines primed muscles to respond more vigorously for a sustained period of time (half times of 30 to 60 minutes), but there was no opposition in their actions (Fig. 2).

We next examined effects of amines on the ventral nerve cord and obtained an entirely different result. For these experiments, the tissue preparation was a dissected ventral nerve cord with the nerve roots still attached to postural flexor or extensor muscles. Because one can routinely identify individual neurons in central ganglia in these preparations, the interpretation of physiological experiments is greatly facilitated. When serotonin or octopamine was applied to individual ganglia, each amine evoked the readout of a motor program (*28, 34*). Serotonin enhanced the rates of firing of excitatory neurons to flexor muscles and of inhibitory neurons to extensor muscles while simultaneously diminishing the rates of firing of excitatory neurons to extensor muscles and inhibitory neurons to flexors. Serotonin, therefore, directed the readout of a motor program causing flexion of the postural muscles. Octopamine activated the opposite pattern: enhanced firing of excitors to extensors and inhibitors to flexors and diminished firing of excitors to flexors and inhibitors to extensors. The octopamine program dictated peripheral extension. Dozens of neurons in each ganglion (hundreds in the entire nerve cord) changed their firing patterns in a characteristic manner in response to each amine (Fig. 2).

When these two sets of results were combined (amines acting on central and peripheral tissues), we felt we had an adequate explanation of the postural alterations produced by injection of amines. Serotonin and octopamine directed the readout from the central nervous system of opposing motor programs onto peripheral substrates, the exoskeletal muscles, that responded more vigorously by virtue of aminergic "priming" of the muscles. There were clear parallels between the actions of amines on individual ganglia and the effects of stimulation of "command neurons" that had been described many years earlier by Wiersma and Kennedy and their colleagues (*35*). These workers reported that high-frequency firing of certain single axons (command neurons), which had been teased out of the ventral nerve cord by dissection, could cause the readout of motor programs similar to those activated by serotonin and octopamine. Our suggestion was that amines were interacting with command neuron circuits in some unknown way to yield opposing postures (*34*).

The next step was to find neurons in the lobster ventral nerve cord that contain serotonin and octopamine to test whether the firing of these cells mimicked the effects of bath-applied or injected amines. Serotonin and octopamine are found at high concentrations in two peripheral locations in the lobster nervous system and at lower concentrations throughout the ventral nerve cord (*36*). The peripheral locations are two neurosecretory sites, the pericardial organs at the distal ends of each of the second thoracic roots and the neurosecretory plexuses associated with groups of peripheral root neurons along each of the second roots. In these regions specialized neurosecretory terminals for each amine are found, and from these regions amines can be released by depolarization into the hemolymph bathing the roots. No aminergic nerve terminals end on lobster muscle fibers. Amines reach the muscles by circulation in the hemolymph from the peripheral release sites. The cell bodies of the amine neurons located in the central ganglia of the ventral nerve cord were mapped by means of immunocytochemical methods (*24*). Our data are far more complete for serotonin than for octopamine;

the remainder of this section, therefore, focuses on serotonergic neurons. Of the approximately 120 cell bodies that stained for serotonin, at least one pair was found in each ganglion. In addition, elaborate arrays of stained processes were seen in the ganglionic neuropil regions, where synaptic contacts are made. One T-shaped neurite, seen in the subesophageal and in the T1 to T4 thoracic ganglia, was particularly intriguing. This neurite branched at a right angle from a nerve tract that ran the length of the ventral nerve cord and then divided, sending one branch to the central neuropil of the ganglion of origin and a second to the peripheral neurosecretory plexuses. Because we were looking for serotonergic cells that were likely to have both central and peripheral sites of action in postural control, we felt that if we could find the cells of origin of these branches we might have prime candidates for the postural control neurons. Although it was difficult to follow immunostained branches through complex neuropil regions, the results suggested that the two pairs of cells found in the T5 and in the A1 ganglia might be the neurons giving rise to those branches. Methods were worked out to identify these cells physiologically, and the identification was confirmed by a combination of intracellular dye injection and immunocytochemistry for serotonin (*37*). Identified cells then were injected with horseradish peroxidase (HRP) as an intracellular stain, and the morphological features were examined (Fig. 3, bottom) (*38*). We found that the cells in ganglion A1 were the origin of the T-shaped branches throughout the thoracic nervous system (in ganglia T4, T3, T2, T1, and the subesophageal ganglion). These cells, therefore, had extensive arborizations, as do vertebrate amine neurons, but the endings were highly repetitive in their location in each ganglion. Like the A1 cells, the T5 cells send their processes to peripheral neurosecretory plexuses and to locations in the ventral nerve cord, but by different routes from those of the A1 cells (*37*). By counting the numbers of serotonin-immunostaining axons supplying the peripheral neurosecretory regions, and comparing that information with the morphological features of the HRP-injected cells, we found that the T5 and A1 cells supplied all the axonal branches running to the neurosecretory regions. Hence these cells are the origin of circulating serotonin in the lobster and therefore are strong candidates to serve in postural control mechanisms. These cells also contain the pentapeptide proctolin, but little is known about how the amine and peptide interact to define the function of the neurons (*39*). The T5 and A1 cells are the largest members of a group of 14 cells found in pairs in ganglia T5 through A6 (Fig. 3).

Most of the studies exploring the physiological properties of serotonergic cells have been carried out with the A1 cells (*37, 40*). The cells show large action potentials with a characteristic undershoot and are spontaneously active, usually firing at a frequency of about 1 Hz. They appear to be neither electrically nor synaptically coupled to serotonin cells on the other side of the same ganglion or to those in the more anterior ganglion (T5). They receive sensory input from the periphery, but the modality of the input has not yet been identified. When depolarized with an intracellular electrode to fire at a high frequency, no effect on the output of the ganglion to either flexor or extensor muscles has been observed. The neurons are, however, wired into command-neuron circuits in ways suggesting a role in postural control: when flexor commands are activated the rate of firing of the cells increases (Fig. 4); when extensor commands are activated the rate of firing decreases. Even more striking is the observation that if the cell is hyperpolarized to prevent it from firing during flexor command neuron activation, then the output from the ganglion to motor neurons is modified. Activation of the serotonergic cell by the command neuron increases the rate of firing of certain of the neurons activated by the command circuit and decreases the rate of firing of others (Fig. 4). We are now in the process of identifying the units whose firing rates are altered by the serotonergic cell. At this point, however, it appears that the cell functions not as a control element but as a gain-setting element, enhancing the effectiveness of flexor commands (for schematic, see Fig. 5).

A next step in this work is to try to relate the function of the aminergic cells to aggressive behavior in lobsters. Two approaches, one developmental and the other behavioral, are being taken toward

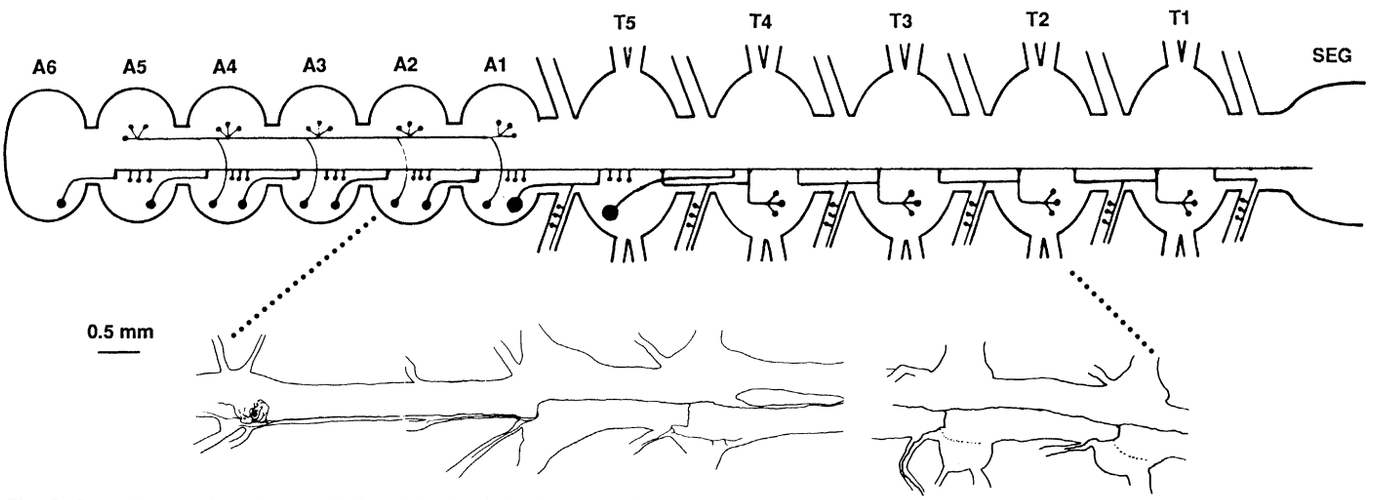

Fig. 3. Sets of serotonin-staining cells found in the abdominal part of the lobster nervous system. The abbreviations used in the figure are: SEG, subesophageal ganglion; T1 to T5, thoracic ganglia 1 through 5; and A1 to A6, abdominal ganglia 1 through 6. Two basic cell types formed into sets are observed (top). One set of cells (seven pairs, one in each ganglion from T5 to A6), which include the T5 and A1 neurons that are the focus of this review, send their major axonal projection forward in a lateral axon bundle. In the next anterior ganglion, these axons turn and join a medial axon bundle and ascend the nerve cord. In each anterior ganglion, the cells elaborate a characteristic axonal arbor. In the second set of cells (four pairs found in the A1 to A4 ganglia), the major axonal projection crosses the midline and descends the ventral nerve cord to the next posterior ganglion. The drawings are based on immunostained preparations and detailed morphological examinations have been carried out only on the T5 and A1 cells. A camera lucida drawing is presented (bottom) of an A1 cell that had been physiologically identified and then injected with horseradish peroxidase. The right and left parts of the drawing come from two different experiments, but these features have been seen repeatedly in A1 cells. Projections of the A1 cell are found in T1 and in the SEG but are not shown in this drawing. See (*37*) and text for details. [Reprinted from (*38*) with permission, copyright 1985 Plenum Press]

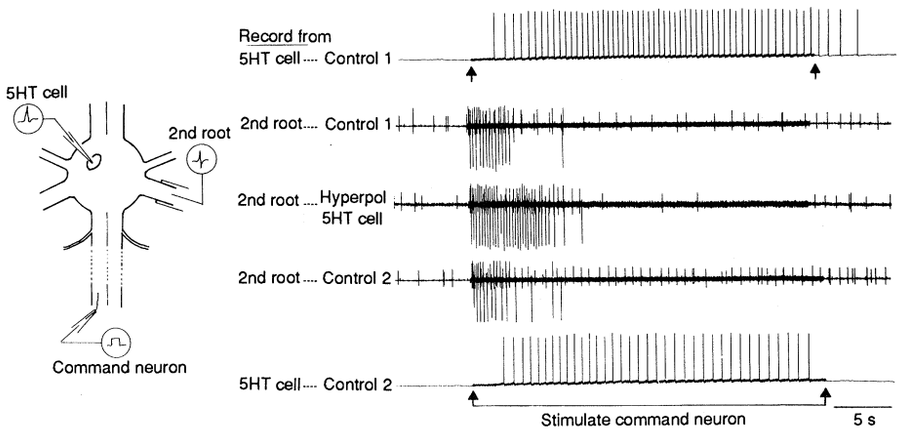

Fig. 4. Serotonin neuron action on the motor output triggered by activation of a command neuron. A command neuron was teased out of the ventral nerve cord, identified tentatively as a flexor command fiber, and stimulated at 70 Hz for 30-second time periods (see inset diagram). An intracellular electrode recorded activity from an A1 serotonin-containing neuron while a suction electrode monitored spike activity from the second root (this nerve root contains excitatory and inhibitory neurons innervating the extensor muscles). When the command neuron was stimulated, a train of action potentials was observed in the serotonin-containing cell (top record) and increased firing was seen in two neurons whose axons leave the nerve cord by way of the second root (second trace from top, note increased activity of units that show a large and a small spike). The command neuron was stimulated again, but this time the firing of the serotonin cell was blocked by hyperpolarizing the cell with the intracellular electrode. The same two units are activated by the command neuron, but the large-spike unit fires a greater number and the small-spike unit a lesser number of times in response to the command (middle trace). When the hyperpolarizing pulse is removed (lower two traces), firing the command neuron again activates the serotonin cell and the output of the second root resembles that seen in the first control period. This experiment was performed by Pokay Ma and is representative of other as yet unpublished experiments he has performed.

this goal. When lobsters hatch, the first-stage larvae that are released do not look or behave like lobsters. First-stage larvae do not have large claws, walking legs, or swimmerets and have a simplified tail structure. They are top dwellers and filter feeders that mostly float in the water, but they can propel themselves by movements of swimming appendages or by vigorous tail flips. Over the next 2 to 4 weeks, depending on water temperature, the animals undergo three further molts (shedding of the exoskeleton) to form fourth-stage larvae, which resemble miniature lobsters. The initial part of the fourth larval stage is spent near the surface of the water but now the animals sweep around the tank propelled mostly by their swimmerets in a fully extended posture that resembles the "octopamine-posture" of older animals. They visit and rest on the bottom more and more frequently as this stage progresses and eventually settle down, begin to dig burrows, and start the solitary existence of a young lobster. It is not until the fifth or sixth stage that one observes the agonistic behavior that we have been studying. One approach, therefore, toward linking amine (or peptide) neurons to behavior is to examine the morphological and physiological properties of amine and peptide systems during late embryonic and early larval life to try to correlate functional changes in these systems with the emergence of aspects of behavior. Thus far, immunocytochemical analyses have shown that serotonin-staining neurons appear early in development (before midway through embryonic life) and that the cells and their processes resemble the adult neurons in their morphological features in these early developmental stages (*37, 41*). A different pattern is seen, however, with octopamine and with the peptide proctolin. These substances are found in embryonic lobsters in only very few of the neurons that ultimately will contain them. All of the early expressing cells are in the anterior (visceral) part of the nervous system. Almost all the other cells destined to contain these substances begin to express them during the transition from first through fourth larval stages. Of particular interest are the observations that the T5 and A1 cells express their serotonin phenotype by halfway through embryonic development but do not express the peptide proctolin until larval stages, some months later in normal development in the wild (*39*). Although these are preliminary studies, they demonstrate that interesting changes occur in the levels of neurohormones at a time when dramatic changes take place in behavior.

Finally the linkage to aggressive behavior: if two lobsters are placed together in a confined space, they "fight" (engage in agonistic encounters) (*42*). At the beginning of an agonistic encounter, juvenile animals approach each other in postures resembling those displayed by serotonin-injected animals. They then begin a series of encounter-specific behaviors, including antenna whipping, claw locking, pushing and shoving, and eventually tail-flipping to escape. At the end of several days one animal (invariably the larger) emerges as dominant, and the other becomes the subordinate. The dominant lobster stands in an elevated posture, typical of dominant animals of virtually all species, moving around the tank on the tips of its walking legs in a stance that resembles the "serotonin-posture." The subordinate animal crouches low to the substrate with its claws, walking legs, and abdomen extended, hides in corners of the tank, and backs away or tail-flips to escape the advancing dominant animal. The posture of the subordinate animal resembles that assumed by octopamine-injected animals. These postures are maintained for as long as the two animals are housed together, or until one of the animals molts. It will be of interest to determine whether changes in the properties of the amine-containing neurons have important roles in these behaviors.

Our studies have shown, therefore, that particular amine-containing neurons, acting at multiple levels in the nervous system, change the properties of a postural control system and bias its output (Fig. 5). The serotonin-containing neurons alter the output of command circuits and prime a more vigorous response in exoskeletal muscles. We have not yet explored the sensory side of this story but would not be surprised to find modifications in the sensitivity of sensory neurons that activate the postural control elements or the serotonergic cells. Indeed, Pasztor and Bush (*43*) have reported aminergic modulation of the sensitivity of oval organ stretch receptor cells in the lobster. The actions of amines in this lobster circuitry thus bear a close resemblance to the so-called "activational" component of the actions of steroids in both vertebrate and invertebrate systems (*2, 5*).

General Observations on the Cellular and Circuit Actions of Amines

It is widely accepted that biogenic amines can function in either short- or long-term ways at the membrane level. Recently, however, a body of literature has emerged suggesting that amines act at the transcriptional level as well (*44*). Thus amines may act at three levels and in three different time frames on target neurons: (i) to open ion channels directly (time frame of tens or hundreds of milliseconds); (ii) to affect ion channels and cell metabolism through second

messengers (minutes to hours); and (iii) to function at the transcriptional level either through second messengers or by as yet undiscovered routes (many hours to days or permanent). If amines do act at the level of the genome, then, like steroids (*45*), amines may play far more extensive and wide-ranging roles in the regulation of synaptic function and behavior than previously suspected. Perhaps these generalizations can be taken one step further. Can most, or all, transmitters, neurohormones, and hormones act at multiple levels? In particular, can these agents influence targets at the transcriptional level? A growing literature of recent papers supports this suggestion (*44, 46*). When investigators explore hormone or transmitter actions on target tissues, experiments usually are performed over short periods of time and under conditions in which contributions from other active substances or from endogenous sources of the material under examination have been eliminated. But this is not the natural state of affairs of neurons in the brain or indeed of cells in any tissue in the body. Neurons, muscles, glands, and sensory elements are bathed continually by a wide variety of humoral elements. The state of a cell at any point in time must be the result of the activities of these myriad influences. Perhaps no two neurons in the nervous system ever are identical in their transmitter content, receptor level, or general metabolic state. In immunocytochemical studies of neurotransmitters, wide ranges of intensities of staining are observed in apparently functionally homogeneous pools of cells. Such variations may only reflect events at particular instants in the life history of individual cells.

Neuronal circuits too may be extremely flexible (*47*). Many types of changes are intrinsic to the machinery of synaptic terminals. Frequency coding of transmitter release (facilitation, tetanic and posttetanic potentiation, and depression) varies greatly between individual neurons. This type of variability may allow much use-dependent alteration in the functioning of sets of neurons. When one superimposes on these intrinsic elements of flexibility the possibility of hormonal modification of transmitter release or of target responsiveness, then the capacity of even small sets of neurons to produce a wide range of processing and output becomes great. A particularly elegant example of this comes from recent work on the stomatogastric ganglion in the lobster (*47*). This small group of neurons linked together in a well-defined circuit gives completely different physiological outputs in response to the application of different hormones. It is as if the intrinsic circuit is a skeleton that can be molded by neurohormones to deliver different outputs in response to physiological needs. Perhaps the stomatogastric ganglion represents, in microcosm, what this article is concerned about at the level of entire organisms.

Summary

In this article I have used our studies in the lobster nervous system to illustrate how neurohormonal substances might influence the behavior of an animal. These substances appear to act as gain-setting devices, biasing the behavior of animals toward specific stereotypical responses when the animals are presented with particular types of sensory stimulation. The biasing takes place by actions of the hormonal substances at multiple levels both in the nervous system and in effector organs, possibly modifying the input, processing, and output of specific subsets of neurons to enhance the probability of a certain outcome. Such biasing of output increases the likelihood that the animal will respond appropriately to a new or changed set of conditions.

I have described only one of the many fascinating systems by which investigators are attempting to link events taking place in the nervous system to behavior. One only has to pay attention to animals in the wild to realize that the subtleties of animal behavior extend far beyond the wildest imagination of the higher vertebrate chauvinists among us. There is a rich frontier for present and future generations of investigators to explore in this field that offers the fascination of attempting to unravel the complexity of behavior and that, incidentally, will allow us to think more creatively and accurately about the problem of greatest interest to us all—understanding the human condition.

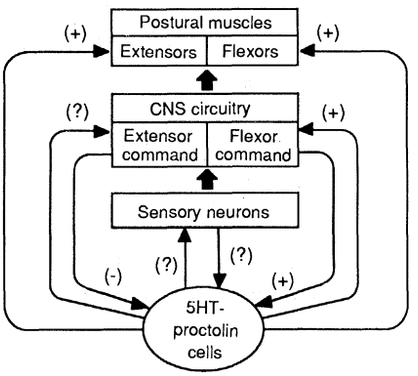

Fig. 5. Diagrammatic representation of the interactions of the T5 and A1 serotonin-proctolin–containing cells with exoskeletal muscles, central command circuits, and sensory elements (+, enhanced activity; −, diminished activity; CNS, central nervous system). See text for details.

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Research Articles

Soft X-ray Images of the Solar Corona with a Normal-Incidence Cassegrain Multilayer Telescope

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High-resolution images of the sun in the soft x-ray to extreme ultraviolet (EUV) regime have been obtained with normal-incidence Cassegrain multilayer telescopes operated from a sounding rocket in space. The inherent energy-selective property of multilayer-coated optics allowed distinct groups of emission lines to be isolated in the solar corona and the transition region. The Cassegrain telescopes provided images in bands centered at 173 and 256 angstroms. The bandpass centered at 173 angstroms is dominated by emission from the ions Fe IX and Fe X. This emission is from coronal plasma in the temperature range 0.8×10^6 to 1.4×10^6 K. The images have angular resolution of about 1.0 to 1.5 arc seconds, and show no degradation because of x-ray scattering. Many features of coronal structure, including magnetically confined loops of hot plasma, coronal plumes, polar coronal holes, faint structures on the size scale of supergranulation and smaller, and features due to overlying cool prominences are visible in the images. The density structure of polar plumes, which are thought to contribute to the solar wind, has been derived from the observations out to 1.7 solar radii.

THE STUDY OF THE SOLAR ATMOSPHERE IS COMPLICATED IN that the sizes of the fundamental structures that control the important physical processes are below the resolution limit possible with instruments now available for all wavelengths. This problem is a consequence generally of the dominant influence of the solar magnetic field, which is characterized by structure on the scale of 70 kilometers (0.1 arc second as viewed from Earth) or less (*1*). The problem has been especially acute for soft x-ray observations because the available techniques could not provide observations with both high spatial and high spectral resolution simultaneously.

Most solar x-ray observations have been made with grazing-incidence optical systems (*2*). These systems, which were first developed 40 years ago (*3, 4*), have been used successfully to observe the solar corona (*5*) and to study cosmic x-ray sources (*6*). Grazing-incidence optics can provide high-quality images, but they have no inherent ability to resolve spectral features. Consequently, images obtained with grazing-incidence optics and thin filters are of low to moderate spectral resolution, and they cannot be used to isolate

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