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Neuroethology: A Meeting of Brain and Behavior

Meeting Report

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Introduction

On August 23–28, 1998, a diverse group of approximately 600 people interested in animal behavior and the nervous system gathered on the campus of the University of California at San Diego, in La Jolla, California, for the Fifth Congress of the International Society for Neuroethology. Continuing the spirit of previous congresses held in Tokyo (1987), Berlin (1989), Montreal (1992), and Cambridge (1995), local organizer Bill Kristan and other members of the planning committee, headed by Joachim Pflueger, combined plenary sessions, symposia, poster sessions, and social events, creating a program that encouraged lively and informal discussions. New forums for scientific exchange included a Young Investigator Award symposium, which allowed this year's four awardees to present their work to the entire congress, and informal ad hoc talks, a refreshing venue for material too current to have been included by the abstract deadline.

What exactly is neuroethology? The field emerged out of traditional ethology, or the study of animal behavior (usually in the animal's natural environment), which was championed by the likes of Lorenz, Tinbergen, and von Frisch. Neuroethology evolved when ethologists, in collaborations with physiologists and anatomists, delved into the neural bases of the behaviors they were studying. Assuming that a good working definition of a modern neuroethologist includes anyone who attended the recent meeting, the definition has expanded to encompass all those interested in understanding the link between brain and behavior, including those taking more traditional top-down approaches (i.e., study a natural behavior in detail and then try to uncover its neural underpinnings) and those taking more bottom-up approaches (identify an interesting neural phenomenon in a reduced preparation and then try to understand how it contributes to behavior).

In an effort to link neural events with behavior, neuroethologists often rely on experimental animals, both vertebrates and invertebrates, that are highly specialized to perform specific behaviors, such as electric fish (electrolocation), bats (echolocation), owls (sound localization), songbirds (vocal learning), and bees (navigation to food sources). Because these animals have evolved under selection pressures to perform particular behaviors very reliably (for example, owls hunt at night and can localize sound with extreme accuracy), they allow the experimenter to explore behavior in a quantitative fashion and to investigate a nervous system that is often highly differentiated to perform a specific function. Because neural mechanisms, especially at the cellular and small circuit level, have proven to be remarkably conserved throughout evolution (fish as well as primates have a vestibulo-ocular response [VOR], for example), it makes good sense to study highly specialized and often less complex nervous systems to learn general principles. At the same time, the difficulties with such animals can be substantial: the anatomy, physiology, and genetics are usually incompletely described compared with more "standard" laboratory animals such as mice and rats, and obtaining and breeding them is often challenging. As we highlight in this review, however, a careful analysis of natural behavior afforded in these "specialist" species can help to define the problems that more generalized brains need to solve, and can therefore serve as a strong guide for focusing cellular-level questions of broad interest.

Neuroethology has historically emphasized a comparative approach to understanding brain function, and the strength of this strategy was readily apparent from many of the presentations at the meeting. In addition, the emergence of new technologies, especially techniques for chronic recording and imaging in relatively intact nervous systems, are enabling researchers to understand the neural basis of behavior under natural conditions, which to many neuroethologists is a long-term goal.

The subject diversity of the meeting was enormous: what other meeting can boast a talk on in vivo imaging of dendritic calcium dynamics followed by one on elephant pheromones? In an attempt to convey the range of subjects discussed at the meeting and to capture the excitement of recent developments in neuroethology, we discuss several presentations, broadly organized by some general themes that emerged: sensitive periods and circuits for learning, synaptic plasticity in the adult CNS, and the reciprocal relationship between genes and social behavior. Furthermore, we highlight results obtained using novel tools, both man-made (multi-electrode recording arrays) and biological (cone snail toxins). Finally, we cover two special symposia, one honoring the Society's Young Investigators and one in memory of Walter Heiligenberg.

Sensitive Periods and Circuits for Learning

Sensitive and/or "critical" periods, which are very common in sensory system development, are also a key part of behavioral development. In some cases, the neural mechanisms underlying sensitive periods are becoming understood. Recent results show that critical periods are less "hard wired" and more experience dependent than had been previously believed. Furthermore, pathways involved in learning in the young animal may be involved in the maintenance of stable adult behaviors.

Human Language Learning

P. Kuhl (University of Washington, Seattle) demonstrated how very early language exposure leads to the formation of perceptual maps in human infants that then

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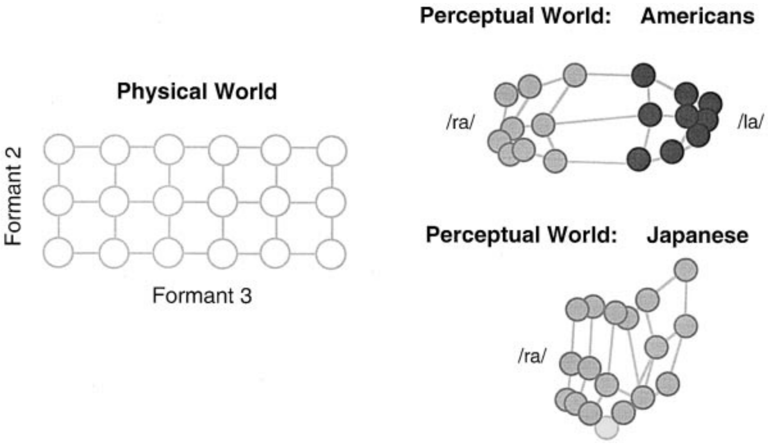

Figure 1. The Perceptual Magnet Effect

For American listeners, acoustic space is perceived as "shrunk" near best instances of two consonants used in English and "stretched" at the boundaries between the two. Japanese listeners report no such "magnet effect" for American categories that are not shared in Japanese speech. Adapted from Kuhl (1998).

alters subsequent language development (reviewed by Kuhl, 1998). This experience-dependent perceptual mapping may regulate sensitive periods for both speech perception and production. Using a clever assay in which a infant is trained to turn her head toward a novel sound, Kuhl and her colleagues demonstrated that young infants can discriminate phonetic units used in every human language. By 10–12 months, however, the same children have become "culture bound," failing to discriminate between speech sounds not used to distinguish words in their native language, just as is the case for adult speakers. For example, Japanese adults cannot discriminate readily between "r" and "l" in English; e.g., "rake" and "lake" sound the same. A parallel transition also occurs in infant speech production, in that after the first year, utterances reflect a child's native language, whereas earlier utterances are more universal.

What is going on in an infant's brain during this transition? Kuhl presented convincing data that the process of listening to language leads to a "perceptual magnet effect," where exceptionally good representations of a phonetic category are formed, and these representations attract less good examples of that category toward them (Figure 1). For the young listener, therefore, acoustic space becomes effectively warped around good examples of categories, and in the process it becomes more difficult to hear differences between the representation at the center of the magnet and surrounding sounds. In the "r" and "l" example, native English speakers perceive the perceptual space around best instances of "r" or "l" as "shrunken," and the boundary between the two as "stretched"; in contrast, Japanese listeners exhibit no distortions around these sounds but do exhibit such distortions on other regions of acoustical space. Kuhl showed that the magnet effect is already present in 6 month olds, before children recognize word meanings or use much structured language. Furthermore, it exists for native language sounds only, thus demonstrating the role of language experience. This magnet effect accentuates contrasts used in the native language while deemphasizing those not used, a process which could assist word learning in a powerful way.

What does this have to do with critical periods? It is well known that it becomes difficult to learn an additional language later in one's life, and even more difficult to speak the new language without a native-language-specific accent. Kuhl suggested that the early critical period for learning a language effortlessly and without accent might not be defined only by a simple maturational process per se (for example, older brains have simply lost some cellular component necessary for learning) but rather that the duration of the critical period depends on learning itself; early language experience leads to perceptual magnet effects that alter the brain by creating an auditory perceptual filter through which all language must pass. New language learning is subsequently forced to take place on top of a sensory filter that is optimized for another language. What then determines when the filter in an infant becomes refractory to further modification, or "crystallized"? Kuhl suggested that new perceptual categories are added in very young infants because new input continues to revise the existing statistical distribution of categories. With continued experience, however, the representation of a particular vowel, for example, no longer changes significantly; perhaps it is this loss of change that causes the individual to become less sensitive to input, thereby closing the sensitive period.

Calibration of Auditory and Visual Maps in Owls

How might early sensory experience influence brain structure and function during sensitive periods in development? E. Knudsen (Stanford University) presented new findings on sensitive periods for experience-dependent shaping of auditory maps in the barn owl's brain, a system where detailed measurements can be extended to the cellular level. Using cues derived from the timing of auditory information arriving at the two ears, or interaural timing differences (ITDs), the owl's brain creates a map of auditory space, such that individual neurons become tuned for particular ITDs. In the optic tectum (equivalent to the superior colliculus of mammals), the auditory space map is in register with an analogous map of visual space; cells in a particular location fire best for ITDs that correspond to regions of visual space mapped at the same location. Knudsen's group has studied what happens to both the animal's sound localization ability, as evidenced by rapid and precise orienting head turns, and the tuning of the tectal cells, when the owl's visual experience is altered during development. An earlier finding was that when owls were fitted with prismatic spectacles to systematically displace the visual field, they compensated behaviorally when the prisms were attached at an early age, up until about day 70 after hatching. After 70 days, the "sensitive period," compensation was severely restricted. The cellular correlate of this adaptive behavior was that the auditory space map was shifted so that it stayed in register with the optically shifted visual map.

Knudsen described new experiments documenting that the age at which owls could compensate in response to prisms (and ITD values would shift adaptively in the optic tectum) was significantly extended, from ∼70 to ∼200 days, when owls lived in a rich environment, such as a large aviary (Brainard and Knudsen, 1998). Furthermore, the capacity for recovering normal sound localization following prism removal persisted well into adulthood in the enriched environment, whereas it was restricted to ∼200 days in an impoverished one. The sensitive period for these compensatory neural events, therefore, depends on many factors, including the quality of the sensory experience of the animal.

The capacity for adaptive changes in ITD tuning in the adult owl also depends on the specific type of experience that the owl had as a juvenile. For example, Knudsen showed data from experiments in which owls learned abnormal associations as juveniles by wearing prisms, and then the prisms were removed (Knudsen, 1998). When similar prisms were reattached at much later times (birds over a year old), owls were able to compensate for them rapidly. They did not, however, compensate for prisms that displaced the visual field differently from the original prisms (left versus right, for example), and control birds of the same age that had never experienced prisms as young birds did not compensate even with extended exposure. Previous data demonstrated that abnormal prism experience leads to new and specific anatomical rearrangements. Knudsen therefore speculated that the expanded capacity for change in the adult that had abnormal experience during a juvenile sensitive period derived from the continued presence of this additional anatomical projection. Furthermore, his group is starting to identify the source of the instructive signals for these compensatory neural events.

Songbird Vocal Learning

New findings about the developmental regulation of plasticity also came from presenters examining vocal learning in zebra finches. As adults, zebra finches sing a single stereotyped song that they learned as a juvenile. Song learning involves vocal motor practice that requires auditory feedback to match vocalizations to a memorized model. Following the practice phase, song then becomes stable or "crystallized," and the requirement for acute auditory feedback is sharply reduced. Pathways involved in juvenile song learning, however, continue to play a role in the maintenance of adult behaviors.

What pathways mediate song learning? Forebrain circuitry that controls song can be divided into two general streams. The direct motor pathway for song consists of HVc and its target nucleus, RA. Projection neurons from RA leave the forebrain and make synaptic contacts on motor neurons that control muscles for breathing and singing. An additional forebrain pathway originates in a separate subpopulation of HVc neurons and ends in RA, but it does so indirectly, in that it consists of at least three other nuclei in the forebrain and thalamus before connecting back to RA. This anterior forebrain pathway (AFP) has been a focus of research for understanding neural mechanisms underlying vocal learning, because lesions of this pathway in juvenile birds severely disrupt song learning, although similar lesions in adults have no effects on normal song, despite the fact that the pathway remains connected to RA throughout a bird's life. These data, together with the observation that cells in the AFP respond selectively to playback of conspecific song, have raised the possibility that the AFP contains a "template" of the tutor song and that this template somehow "instructs" the motor pathway during vocal learning, perhaps by providing some type of error signal about the quality of the song produced.

New experiments suggest that the role of the AFP extends into adult life, at least with respect to motor learning and the production of song. It had already been shown that adult song may not be as "crystallized" as had been suspected: removing auditory feedback in adult birds (by deafening) produced changes in the song on the order of a few weeks in zebra finches, and even faster in other birds. Now, A. Leonardo and M. Konishi (California Institute of Technology) have extended these observations using a clever computer-controlled feedback experiment to alter auditory feedback to adult birds. Specifically, they monitored a bird's vocalizations, and, every time the bird sang, played back a slightly delayed version of that song so that the normal auditory feedback from the bird's own song was contaminated by the altered song. Remarkably, the bird's song changed substantially, usually after a few months in this environment. Importantly, unlike deafening, this form of altered sensory experience is reversible: the birds eventually sang their original song again after the feedback was removed. Thus, the stable song of adult finches is actually actively maintained using auditory feedback. An important question that remains is whether the AFP plays a role in the "decrystallization" of song similar to the role that the AFP is hypothesized to play in the juvenile.

A. Doupe and colleagues (University of California, San Francisco) presented evidence that the AFP is also used in the maintenance of the adult song by auditory feedback. M. Brainard in Doupe's group showed that lesioning the nucleus LMAN, the output of the AFP, largely prevented the slow degradation of song quality following adult deafening. The AFP, therefore, can mediate vocal motor plasticity throughout the bird's life, not only during song learning but also in the adult, although this is most evident when the normal match between motor commands and the resulting sensory feedback is disrupted. Additionally, using chronic recording techniques, N. Hessler in Doupe's group showed that there is song-related activity in LMAN during singing, even in adult deafened animals, providing further evidence that the AFP may play a role in adults. Intriguingly, the amount of activity depends on the social context in which the bird sings. These findings parallel results from molecular studies showing heightened immediate-early gene (IEG) activity in the AFP during singing and changes in gene

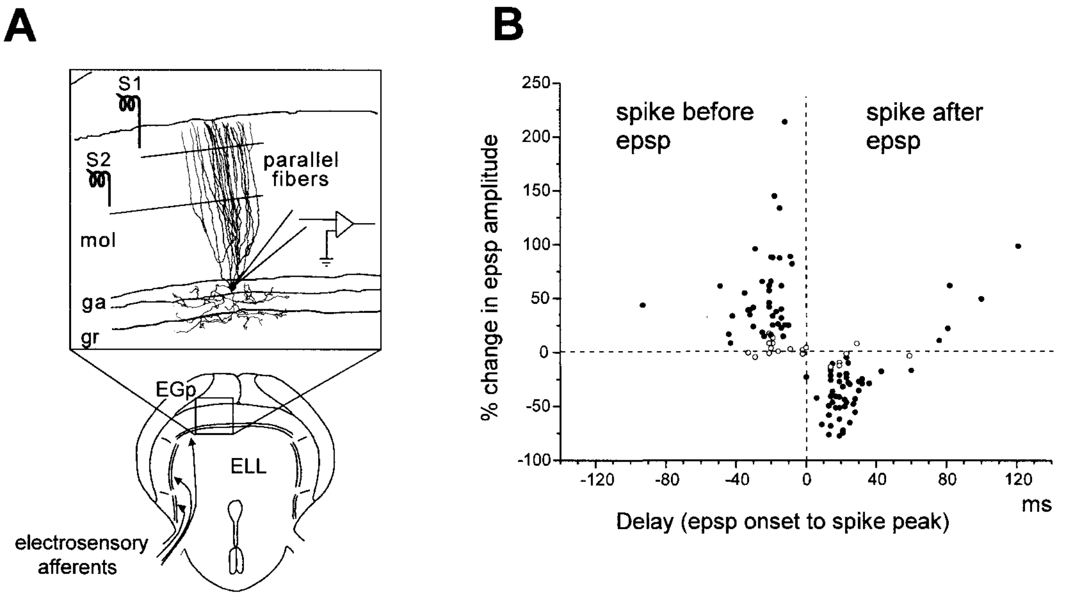

Figure 2. Synaptic Plasticity in a Cerebellum-like Structure of Electric Fish Depends on Temporal Order

(A) Cross-section of the ELL, with a reconstruction of a biocytin-filled Purkinje-like neuron, and schematic representations of the recording and stimulating electrodes. Abbreviations: EGp, eminentia granularis posterior; ga, gr, and mol, ganglionic, granular, and molecular layers of the electrosensory lobe, respectively.

(B) Whether the parallel fiber EPSP is depressed or augmented following pairing of parallel fiber stimulation with intracellular current injections depends critically on the delay between the EPSP and the action potential elicited from the current injection. Circles that are closed indicate significant changes; open circles are not significant. Adapted from Bell et al. (1997).

expression in the pathway depending on whether song is directed to a female (Jarvis et al., 1998). It remains to be determined exactly what role this activity in LMAN has in mediating changes in vocal output.

Synaptic Plasticity in the Mature CNS: Lessons from Electric Fish and In Vivo Imaging

Synaptic plasticity has been studied extensively in reduced preparations, where direct connections to the function of synaptic changes can be difficult to make. Two reports summarized here place synaptic plasticity in the context of behavior.

Electric Fish

C. Bell (Oregon Health Science University) described work that clearly demonstrated the strength of a neuroethological approach in elucidating synaptic mechanisms that underlie the nervous system's ability to predict (and then subtract) sensory input devoid of information content. Using in vivo and in vitro preparations, Bell's group studies a cerebellum-like structure in the medulla of electric fish, the electrosensory lobe (ELL) (Figure 2). Electric fish generate an electric organ discharge (EOD) that creates a weak electric field around themselves, which they monitor with specialized electroreceptors in their skin. Objects in the water distort the electric field, and the fish use this information to navigate (electrolocate). GABAergic Purkinje-like neurons in the ELL receive afferent information from electroreceptors onto their basal dendrites. Additionally, an efference copy, or "corollary discharge," of the command signal that generates the timing of the EOD arrives at the same cells via a parallel fiber input on the apical dendrites. Bell and colleagues have shown convincingly that the two signals, the reafferent information coming from the electroreceptors, and the corollary discharge signal originating centrally, interact on the Purkinje-like neurons in an "anti-Hebbian" manner: the Purkinje-like cells and their targets (the output cells of the ELL) use synaptic depression to ignore the component of the afferent response that is predictable, because it is linked to the ongoing EOD. Presumably, this subtraction allows more meaningful sensory input to stand out.

How is this subtraction mediated at the neural level? Using a brain slice preparation, Bell demonstrated plasticity at the parallel fiber synapse by temporally specific pairing of parallel fiber stimulation and intracellular current injection (to mimic afferent input onto basal dendrites) (Figure 2). When the intracellular current injection followed the excitatory postsynaptic potential (EPSP) evoked by stimulation of the parallel fiber pathway within 60 ms (which it turns out is approximately the duration of the parallel fiber EPSP), the EPSP amplitude was reliably and robustly depressed; functionally, this leads to a reduction of the excitatory drive to the cell at a specific delay. If the intracellular current injection either preceded the EPSP or followed it by more than 60 ms, however, the EPSP amplitude remained unchanged or was increased (Bell et al., 1997a); temporal order, therefore, is an important aspect of this anti-Hebbian plasticity. The plasticity was also input specific, and actively reversible, such that a depressed EPSP could be augmented simply by changing the delay between the evoked EPSP and the current injection during pairing. Interestingly, synaptic plasticity at the parallel fiber synapse requires that currents injected into the soma of the Purkinje-like cell generate an action potential (shown to be a sodium spike) and also requires NMDA receptor and calcium channel activity. Combined with previous in vivo evidence, Bell's work suggests that a back-propagated action potential originating from the basilar regions of the cell, where the sensory afferents terminate, is required for synaptic plasticity at the apical dendrites. Importantly, such plasticity is also present in the cerebellum-like structures of other fish where it has the same computational role of subtracting out predictable sensory input (reviewed by Bell et al., 1997b).

Imaging Somatosensory Cortex In Vivo

D. Tank (Bell Laboratories) highlighted the use of two-photon laser scanning microscopy to image action potential propagation in neocortical pyramidal neurons in rat barrel cortex. Tank, W. Denk, and colleagues are pursuing the question of whether back-propagation of action potentials from the cell body into dendrites is actively regulated and involved in synaptic plasticity.

Dendritic excitability was monitored using imaging of fluorescent calcium indicators, which can report the timing and spatial extent of action potentials. With the advent of two-photon laser scanning microscopy, this can now be done in vivo. Using two-photon excitation, optical penetration into cortex can reach 500 μm. This is possible because the longer wavelengths used are scattered less by tissue, and because the excitation is nonlinear: what light is scattered does not cause fluorescence. Phototoxicity is likewise confined to the focal point, and so two-photon imaging is less damaging than conventional methods. A final advantage is that because fluorescence only originates from the focal point, a detection pinhole is unnecessary, allowing for much greater light-gathering efficiency than confocal microscopy.

Tank showed preliminary data from layer 2/3 and layer 5 neurons in anesthetized adult rats obtained during simultaneous sharp microelectrode intracellular recording and calcium imaging (Helmchen et al., 1998, Soc. Neurosci., abstract). These experiments demonstrated that dendritic electrogenesis and calcium accumulations in apical dendrites can be altered by stimuli that change the animal's attentive state. Specifically, a strong pinch to the tail increased the number of sodium action potentials in layer 2/3 cells produced by whisker movement, with a concomitant increase in dendritic calcium accumulation. In addition, the amplitude and frequency of calcium transients associated with regenerative calcium spikes in the distal branches of layer 5 neuron apical dendrites showed significant enhancement.

This gating of back-propagation may be of significance in determining under what conditions synapses are modified. Yuste and Denk previously showed, in hippocampal pyramidal neurons, that delivery of a back-propagating action potential and a presynaptic input to the neuron together gives a larger calcium increase than the sum of the two signals acting separately. This supralinear summation represents a form of coincidence detection in the central nervous system, and plasticity is known to depend on calcium elevation. The in vivo results show that one of the signals necessary for this coincidence detection, the back-propagating spike, can be regulated by a tail pinch to the anesthetized rat, a stimulus that would undoubtedly capture the attention of an awake animal.

In the future, Tank hopes that genetically expressible fluorescent indicators, such as neuronally targeted calcium-sensitive green fluorescent protein (GFP), may allow optical recordings over long periods of time, and even from many neurons at once. Expression of the indicator by transgenic or viral transfection methods would also eliminate the need for microelectrode injection of dye and might even allow optical recording from awake animals.

Genes and Social Behavior

A key component of an animal's natural environment is the presence of other conspecifics; however, the obstacles in understanding the neural mechanisms mediating behaviors occurring between two (or more) animals are significant. Two strategies are outlined below, one using a genetically tractable organism to explore genetic influences on social behavior, and another exploring how complex social behaviors can influence gene expression within the brain.

An Innate Influence on the Social Behavior of **C. elegans**

C. Bargmann (University of California, San Francisco) described the work of postdoctoral fellow M. de Bono on the innate basis of social behavior. By examining the natural variation in feeding styles of the nematode *C. elegans*, de Bono has identified one nucleotide that causes a change in a single amino acid that confers a preference for different feeding patterns (de Bono and Bargmann, 1998). Naturally occurring *C. elegans* isolates display either solitary or social behavior as they dine on their bacterial substrates: solitary foragers disperse across an *E. coli* lawn to graze alone, while social feeders aggregate together to nosh in clumps. When taken off of food, dispersers and clumpers behave similarly, suggesting that the difference in dining style is a specific response to food, rather than simply a general difference in activity levels or odorant perception.

Bargmann outlined the forward genetics approach that resulted in the isolation and identification of *npr-1* (for *n*euro*p*eptide Y *r*eceptor), the single gene responsible for the degree of sociability between different strains. Impressively, the two naturally occurring alleles of *npr-1* in *C. elegans* differ by only one nucleotide (the solitary trait is dominant to the social one), and when DNA containing the relevant portion of the solitary allele was injected into a social mutagen-induced variant, it restored solitary behavior. Clues as to how and where *npr-1* might function include its homology to mammalian NPY receptors and its expression within *C. elegans* neurons. In mammals, NPY itself is a 36-amino-acid neuromodulator that can stimulate feeding and has anxiolytic properties in low doses. Thus, in worms, release of the *npr-1* ligand may be triggered by food and provide distinct types of neuromodulation depending upon the *npr-1* variant expressed.

A Social Influence on a Cichlid Nervous System

In contrast to a heritable and persistent social trait, R. Fernald (Stanford University) discussed how dynamic encounters between conspecifics influence a malleable social state and its associated neurobiology in an African cichlid fish, *Haplochromis burtoni*. Fernald's fieldwork within the shorepools of Lake Tanganyika in Africa had shown that the fish live in "lek-like" societies, in that 25% of the males control 90% of the territorial resources, including access to food and to gravid females. The social and reproductive status of males is plastic: if part of a territory is left vacant by removal of a dominant male (either through predation or experimenter intervention), a hitherto sidelined subordinate male can assume the dominant social state.

Socially ascendant males undergo a behavioral and physiological transformation that is akin to the delayed onset of puberty. This blossoming includes heightened coloration, as well as increased aggressive behaviors, which take place within minutes. Changes that occur more slowly during this transformation include a peripheral increase in the size and mature state of the gonad, a central increase in the size of neurons within the hypothalamus that contain the reproductive regulatory peptide gonadotropin-releasing hormone (GnRH), and an increase in mRNA and protein levels of this peptide. When animals are forced to undergo the opposite change in social status, as when a dominant fish is deposed by a larger, more aggressive male, the loser displays a corresponding loss in GnRH neuronal soma and gonad size.

In terms of the reproductive axis, the correspondence between GnRH neuronal size, peptide levels, and gonadal readiness within the male makes sense. However, given that social dominance is not genetically prescribed, and that subordinate males cannot hope to reproduce, why should any male ever adopt the subordinate, nonreproductive path? Careful analysis by Fernald and postdoctoral fellow H. Hoffman have revealed two consequences of social status that may explain this question. First, the brighter colors and active behaviors of dominant, territorial males make them more susceptible to predation by birds, the cost associated with the flamboyance of reproductive opportunity. Second, the growth rate of subordinate males exceeds that of dominant ones, in effect constituting an intrinsic biological form of revolution. Thus, dominant males are at increased risk of both predator and conspecific attacks, which may explain why some animals bide their time and energies before stepping onto the reproductive stage.

Finally, changes in social status leave a molecular imprint on the GnRH neurons. When an individual assumes dominance for the first time, hypothalamic GnRH neurons enlarge within 1 week of their social transition. With a subsequent social demotion, however, the neurons shrink only part of the way back to the predominant size, and this reversion takes longer (3 weeks). Social influences therefore leave a lasting trace on the nervous system at many levels.

Simultaneous Recording from Multiple Neurons

The following two talks highlight the state-of-the-art use of multi-electrode arrays in collecting population activity from the nervous system. The first uses an in vitro retinal preparation to assess the information content available at early stages of sensory processing. The second uses a chronically implanted array to collect ensemble activity from the hippocampus of a freely behaving animal and then describes statistical models for decoding these higher level signals.

Extrapolation of Movement by the Retina

You're on the court, waiting to return the serve from your opponent. Here it comes, over the net, and so you prepare to meet the oncoming ball with your racket. The ball travels 2–3 m every 100 ms, yet, according to psychophysical experiments, it takes 70–100 ms for the signal from a flashed visual stimulus to make it to your visual cortex for you to become aware of it. How is it that you manage to insert your racket into the path of the ball before it has already passed you?

The biological machinery that supplies the answer to this apparent paradox of visual processing might reside in your retina, according to M. Meister (Harvard University). Postdoctoral fellow M. Berry made recordings from ganglion cells within a piece of rabbit retina, placed upon a planar multi-electrode array, while presenting either a flashed bar or a moving bar. Surprisingly, the continuously moving line induced a traveling wave of excitation whose peak occurred at, or slightly ahead of, the stimulus. In contrast, the flashed bar produced a brief burst of activity that peaked 70 ms *after* the flash, with a time course predicted by the rate of signal transduction. Thus, it appears that the retina itself is capable of extrapolating the movement of a continuously moving stimulus, and it somehow overcomes the limits otherwise imposed by signal transduction.

Meister presented evidence that the receptive field organization of photoreceptor inputs to ganglion cells coupled with a mechanism of rapid desensitization to strong stimuli, known as contrast gain control, enables a ganglion cell to anticipate a moving object. Basically, this works as follows: a ganglion cell has a large receptive field; it starts with high gain from the inputs of faraway photoreceptors, so that its firing rate rises rapidly when an object first invades the outer reaches of its receptive field. Then, only for objects that continue to move across the field and into the center, contrast gain control quickly suppresses firing. In this way, the peak firing rate is achieved for objects as they first enter the extreme outer edge of the field, much earlier in time than would have occurred for a stimulus that was flashed briefly within the center. Berry has developed a mathematical model that agrees very well with the observed physiological measurements, which includes both the known linear filtering properties of a cell's receptive field and a contrast gain control mechanism.

Place Cells in the Hippocampus

M. Wilson (Massachusetts Institute of Technology) and colleagues have been examining information encoding in the nervous system using multi-electrode arrays chronically implanted into rodents to record ensembles of cortical neurons during behavior. Wilson presented data gathered from a 12-electrode array placed into the CA1 region of the hippocampus in mice. Recordings were made as the mice moved from a familiar to a novel environment. When the animal occupies particular locations in a familiar environment, an assembly of CA1 cells (place cells) tends to fire together in such a way that the pattern of activity across the electrode array can be reliably "decoded" by the experimenter to predict where the mouse is in space. When the animal enters a novel space, excitatory and inhibitory cells that were formally active become quiescent. Meanwhile, previously quiet cells begin to fire, but do so in a less correlated fashion, making it difficult for the experimenter to decode the firing pattern to determine the location of the animal. After three passes into the environment, however, a more "mature" pattern of activity emerges as the responses become more like those for a familiar environment. This changing pattern of activity, therefore, represents an experience-dependent modification of a hippocampal circuit.

Wilson then described similar experiments using mice that were genetically engineered to lack functional NMDA receptors in the CA1 pyramidal cells of the hippocampus. From brain slice work, it had already been shown that suspected cellular correlates of both short-term term and long-term memory are disrupted in these mice, and the mice perform poorly in a spatial search task compared with wild-type controls (Tsien et al., 1996). When the activity of CA1 pyramidal neurons was monitored in the chronically implanted knockout mice, place-related activity was still observed. However, there was a decrease in the spatial specificity of individual place fields compared with that seen in wild-type animals; the more diffuse and variable levels of activity resembled those of normal animals in a novel environment (McHugh et al., 1996). This decrease in covariance of the ensembles led to greater reconstruction errors by the experimenters in predicting the location of the mouse, suggesting that such coherence is the neural signature for recognition. Wilson and colleagues have used these types of studies to develop and test a statistical paradigm for quantitating the spatial information in ensemble place cell firing patterns (Brown et al., 1998).

Neuroethological Tools from Cone Snails

B. Olivera (University of Utah) delivered a fascinating talk summarizing the history of research on small peptide toxins produced by a genus of predatory marine cone snails (*Conus*) (Olivera, 1997). The work provides powerful tools for neuropharmacology and also has important implications for theories on the control and evolution of behavior. Cone snails, which use venom to hunt prey and escape from predators, produce a surprisingly complex cocktail of these poisons; an individual snail can make 50–200 small biologically active peptides (conotoxins), which it can deliver with a modified "tooth" that functions as a harpoon and hypodermic needle. The peptide cocktail is highly diverse, acting on a wide variety of peripheral and central neurotransmitter receptors.

At first glance, the strategy used by these cone snails seems inefficient, because their toxins often contain both agonists and antagonists for the same type of receptor. For example, the venom of one cone snail contains a peptide that prolongs sodium influx through voltage-gated sodium channels as well as a peptide that does the opposite by blocking sodium channels. Olivera detailed how close observation of the cone snail hunting strategy and an appreciation of the specificity of the peptides resolves this apparent paradox. For example, a number of snails use a strategy for hunting fish dubbed "hook-and-line," in which they poison a fish and then pull it toward their mouth. They maximize the chances of immobilizing and capturing the comparatively fast-moving fish by "harpooning" the fish and injecting a combination of toxin "cabals". The first, the "lightning-strike cabal" hyperexcites excitable tissues around the wound site. The peptide that keeps the sodium channels open is part of this potion, and in combination with other peptides that also increase excitability, the effect is to stun the fish almost instantaneously.

The peptide that blocks the sodium channel is part of the next stage in the attack, the "motor cabal," which contains a completely different set of toxins that act together in a coordinated fashion to block neuromuscular transmission, thus guaranteeing the immobilization of the fish. The dual-pronged attack can be effective, without the different toxins interfering with each other, because they selectively target distinct populations of sodium channels on different cells. Other peptides in the venom are similarly specific for distinct populations of voltage- and ligand-gated receptors, including G protein–coupled receptors. Furthermore, additional peptides enhance the potency of the response by more indirect means, including enhanced uptake of the channel-blocking toxins by blood vessels.

The exquisite selectivity of these toxins is of special interest to neurobiologists, because these toxins can bind selectively to particular isoforms of neurotransmitter receptors. Different ω-conotoxins, for example, can discriminate between distinct voltage-gated calcium channel subtypes by greater than 10^6-fold. The potential, therefore, for using these conotoxins for probing nervous system function appears enormous. As an example, Olivera described how a particular peptide (a specific NMDA receptor subtype antagonist), when injected into mice, causes distinct behavioral phenotypes depending on the age of the mouse (sleeping versus climbing, in young versus older mice), suggesting that developmental changes in the subtype composition of individual NMDA receptors mediate distinctly different behaviors. Olivera furthermore described how the incredible diversity of toxins might be generated (the peptides in any one species' venom are very different from those in any other) by a focal hypermutable region of the toxin-encoding gene, reminiscent of the hypervariable region of mammalian immunoglobulin genes.

Young Investigator Award Symposium

The society's choices for this year's Young Investigator Awards, B. Casasnovas (University of Bordeaux and CNRS), J. Lewis (University of Ottawa), G. T. Smith (University of Texas, Austin), and K. Catania (Vanderbilt University), for work in lobster, leech, electric fish, and mole, bespoke confidence in the strength of the comparative approach to nervous system structure and function. K. Catania's presentation exemplified this spirit as he is perhaps the sole investigator exploring the mechanosensory expertise of the star-nosed mole, *Condylura cristata*, a 50 g insectivore that is in peerless possession of 11 pairs of fleshy appendages that emanate from its snout (Figure 3). Catania studies the role of behavior in shaping mammalian brain development.

The rayed snout is used by the mole to locate food sources in its muddy subterranean habitat, where it has

Figure 3. Sensory and CNS Specializations of the Star-Nosed Mole

The star-nosed mole, *Condylura cristata*, a small insectivore, explores the world with 11 pairs of fleshy rays covered with specialized mechanoreceptors. One pair of rays has a special behavioral role and a corresponding enhanced representation in the cortex. Photograph courtesy of Ken Catania.

little use for eyesight. This seemingly bizarre mechanosensory appendage is indicative of an extreme behavioral bias and corresponding sensory specialization. Slow-motion video monitoring of the mole's foraging behavior shows the mole deploying its 11 pairs of fleshy rays to first discover and then probe potential food items with as many as ten different touches per second. Exploration by a single central pair of nasal rays, the eleventh, is an obligate step in this behavior. Although the eleventh pair is smaller than the other rays, and contains fewer Eimer's organs (the arrays of mechanoreceptors which initiate touch transduction), the intense behavioral focus suggested that there might be a corresponding internal bias to the sensory representation of this region. Sure enough, Catania has uncovered a virtual mechanosensory fovea: cytochrome oxidase staining of the mole's snout representation in somatosensory cortex has revealed a stripe for each of the 11 rays (similar to the correspondence between whiskers and barrel fields in rodent cortex), with a disproportionate area devoted to the eleventh pair. The cortical bias evident in the "molunculus" does not correspond to the peripheral innervation densities: the 11th ray actually contains the fewest Eimer's organs; instead, the cortical bias correlates with the behavior, i.e., the highest number of touches per nose part (Catania and Kaas, 1997).

This relationship suggests a role for behavior in shaping the cortex in an experience-dependent manner. Alternatively, an early emergence of the cortical bias, prior to sensory exploration, would be indicative of an "experience-expectant" mode of development. Catania's most recent work on neonatal moles (only four litters so far have been raised in captivity) reveals that the fleshy appendages begin as swellings and that, similar to the retinal fovea, the eleventh ray develops first, which could indicate an earlier level of activity. However, while the physiological pattern of activation is unknown, the anatomical pattern of innervation appears to be intact prenatally. Behaviorally, the neonatal mole likely uses its rays for nursing, and even at this early developmental time, there may be preferential use of the eleventh pair. Given the beautifully mapped anatomical relationships between the Eimer's organ sensory endings and the somatosensory cortex—indeed, the mole possesses not one or two but three orderly maps of the snout—this system holds much promise for ferreting out the emergence of behavioral influences on sensory processing.

The Walter Heiligenberg Memorial Lecture: Exquisite Navigational Skills of an Ant

R. Wehner (University of Zurich) delivered the first Walter Heiligenberg Memorial Lecture, established to honor Walter Heiligenberg, who was president-elect of the Society for Neuroethology at the time of his tragic death in an airline accident in September of 1994. Heiligenberg's wonderfully creative approach to characterizing the behavior and neural underpinning of a natural behavior of electric fish (the jamming avoidance response) epitomized the neuroethological approach (Heiligenberg, 1991) and inspired large numbers of researchers in the field.

Wehner chronicled his group's 20-year work on the navigational skills of the desert ant *Cataglyphis*, which are under strong selective pressure because the desert heat ensures that failure to return to the nest quickly after a foraging trip will result in death (Wehner et al., 1992). Remarkably, even though *Cataglyphis* strays in a wandering path far from the nest ($>$200 m, or the equivalent of 50 km/30 miles on a human scale), it returns on a direct path with extreme accuracy, accomplishing this feat with a compound eye system that relays information about polarized light to its tiny (0.1 mg) brain.

Wehner and his team have revealed strategies that *Cataglyphis* uses to navigate by making careful behavioral measurements in the field, followed by testing hypotheses under laboratory conditions. Furthermore, they design computer models and build robots based on principles derived from the ant studies and then test the robots (and thus the hypotheses) in extremely clever field experiments. They have discovered that the ants, using specialized photoreceptors in the visual system, derive compass information by analyzing the pattern of polarized light in the sky that arises due to scattering of sunlight in the atmosphere. The ants derive information about how far they have wandered, "odometer information," by a variety of cues, including self-induced motion across the eye and proprioceptive information from the legs, which they then integrate to navigate by dead-reckoning. Ingenious experiments demonstrate how the ants, employing strategies similar to those used by honeybees, can also use local terrestrial landmarks for navigational cues (Collett et al., 1998).

What parts of the nervous system mediate this navigational behavior? Wehner's team is making progress on this front with a variety of approaches. For example, by training the ants and then manipulating their sensory cues by alternately covering one eye, his team demonstrated that interocular transfer of certain types of information does not occur (Wehner and Mueller, 1985). Ants thus solve the complicated task of navigating by distributing the problem among specialized and interconnected modules, and it is the interaction of these modules that enables complex behavior.

Conclusions

By using a neuroethological approach of focusing on cellular and molecular events necessary to perform the job that the nervous system evolved to do, i.e., process relevant sensory stimuli and generate appropriate behavior, investigators are making progress in understanding the complexity readily apparent in even the simplest nervous systems. A special pleasure in attending these meetings is that practitioners of this approach display an unsuppressed enthusiasm for the animals with which they work, perhaps acquired from years of field work or simply an inherent enjoyment in understanding the diversity of animal adaptations; their enthusiasm is refreshing and contagious. We look forward to the next neuroethology conference in Bonn, Germany, in 2001.

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