In the first type (Fig. 4A), the main termination sites were in the superior rectus and the inferior oblique subdivisions of the oculomotor nucleus. However, major axonal branches recrossed the midline and terminated in identical motoneuron pools on the other side of the midbrain. The extent of synaptic terminations on the left and right sides were judged to be equal.

In the second type (Fig. 4B), major termination sites were in the trochlear nucleus, whose motoneurons innervate the superior oblique muscle, and in the inferior rectus subdivision of the oculomotor nucleus. Major axon branches crossed the midline with terminal arborizations in the same sites on the contralateral side (Fig. 3). The extent of terminal branching was nearly equal on both sides of the brain.

Termination loci for these two secondary vestibular neuron types are those predicted to underlie reciprocal excitatory-inhibitory innervation of motoneurons in flatfish vestibulo-ocular reflexes (Fig. 2). The first type may be a candidate for contracting both superior rectus and both inferior oblique muscles. Since vestibulo-ocular reflexes are thought to be organized in a push-pull fashion, we would expect relaxation of both superior obliques and both inferior recti at the same time. The second vestibular neuron type exhibits the appropriate termination pattern to mediate simultaneous inhibition of these muscles.

Our data show that an adaptive change in the vestibulo-ocular reflex system occurs in second-order vestibular neurons. In both the cat and the rabbit, excitatory and inhibitory horizontal canal neurons exclusively contact abducens or medial rectus motoneurons (*16*). To our knowledge, secondary vestibular neurons related to the horizontal canal have not previously been shown to terminate on vertical extraoculomotor neurons. Thus, the extensive axonal arborizations of flatfish horizontal canal neurons onto the oculomotor and trochlear nuclei seems to be a novel development initiated by the necessity to adjust eye movements to a new environmental situation. In this context, the next important problem to resolve is whether these cell types are newly born or whether they arise from existing vestibular cells through retraction of synaptic contacts and growth of new collaterals during metamorphosis. Thus, we cannot be certain that the adaptive change prompted during the flatfish metamorphosis is equivalent to adaptive plasticity occurring in response to an experimental perturbation. However, the discrete changes observed in some properties of vestibular neurons during adaptive plasticity (*17*), in conjunction with our findings, may point to a wider functional role for secondary vestibular neurons in this context. The alteration in flatfish secondary vestibular neuron morphology is an example of one way the vertebrate central nervous system has dealt with a situation requiring a large adaptive modification.

W. GRAF
Rockefeller University, New York 10021
R. BAKER
Department of Physiology and Biophysics, New York University Medical Center, New York 10016

References and Notes

1. A. F. Fuchs, in *Handbook of Behavioral Neurobiology*, A. L. Lowe and E. S. Luschei, Eds. (Plenum, New York, 1981), vol. 5, p. 303; F. A. Miles and S. G. Lisberger, *Annu. Rev. Neurosci.* **4**, 273 (1981); M. Ito, *ibid.* **5**, 275 (1982).
2. A. Gonshor and G. Melvill Jones, *Proc. Can. Fed. Biol. Soc.* **14**, 11 (1971).
3. D. Policanski, *Sci. Am.* **246**, 116 (May 1982).
4. G. Retzius, *Das Gehörorgan der Wirbelthiere: Morphologisch-Histologische Studien*, vol. 1, *Das Gehörorgan der Fische und Amphibien* (Samson & Wallin, Stockholm, 1881).
5. The eyes remain stationary in the world while the fish rotates around the eyes.
6. H. Schöne, *Biol. Jahresheft* **4**, 135 (1964); C. Platt, *J. Exp. Biol.* **59**, 491 (1973).
7. S. S. Easter, P. R. Johns, D. Heckenlively, *J. Comp. Physiol.* **92**, 23 (1975).
8. C. Platt, *Soc. Neurosci. Abstr.* **2**, 1532 (1976).
9. W. Graf, *Biol. Bull. (Woods Hole, Mass.)* **161**, 313 (1981); ______ and J. I. Simpson, in *Progress in Oculomotor Research*, W. Becker and A. Fuchs, Eds. (Elsevier, Amsterdam, 1981), p. 409.
10. J. Szentágothai, *J. Neurophysiol.* **13**, 395 (1950); M. Ito, N. Nisimaru, M. Yamamoto, *Exp. Brain Res.* **24**, 257 (1976); *ibid.*, p. 273.
11. R. R. Gacek, *Acta Oto-Laryngol. Suppl.* **254**, 1 (1969); C. Bell, *J. Comp. Neurol.* **195**, 391 (1981); G. E. Meredith and A. B. Butler, *ibid.*, in press.
12. R. R. Gacek, *Larnygoscope* **81**, 1559 (1971).
13. J. Szentágothai, *Arch. Psychiatr. Nervenkr.* **116**, 721 (1943).
14. Neurons receiving input from the left (lower) labyrinth were identified by their monosynaptic electrical responses to bipolar stimulation of individual ampullary nerves. Axons of identified cells were then injected in the medial longitudinal fasciculus at the midbrain level. After a survival time ranging from 8 to 12 hours, the fish were transcardially perfused with a solution of 1 percent paraformaldehyde and 1.25 percent glutaraldehyde in phosphate buffer (*p*H 7.4). The brains were later processed according to a diaminobenzidine acid–$CoCl_2$ method. Axonal trajectories and termination sites of secondary vestibular neurons were analyzed with a light microscope. Nine completely stained neurons were reconstructed displaying the characteristics of either of the two neuron classes outlined in Fig. 4.
15. W. Graf, R. A. McCrea, R. Baker, *Exp. Brain Res.*, in press. The three-neuron arc connectivity of the flatfish vertical vestibular systems would be substantially sufficient for the production of compensatory eye movements following a movement around the longitudinal axis of the animal. However, if movements were to occur in the earth horizontal plane, the above three-neuron arc would not be adequate.
16. R. Baker and S. M. Highstein, *J. Neurophysiol.* **41**, 1629 (1978); N. Ishizuka, H. Mannen, S.-I. Sasaki, H. Shimazu, *Neurosci. Lett.* **16**, 143 (1980); R. A. McCrea, K. Yoshida, C. Evinger, A. Berthoz, in *Progress in Oculomotor Research*, A. Fuchs and W. Becker, Eds. (Elsevier, Amsterdam, 1981), p. 379.
17. S. G. Lisberger and F. A. Miles, *J. Neurophysiol.* **43**, 1725 (1980); E. Keller and W. Precht, *ibid.* **42**, 896 (1979).
18. Supported by the Grass Foundation, the Deutsche Forschungsgemeinschaft (Gr 688/1) and NIH grant 13742.

15 February 1983; revised 30 March 1983

Adaptive Complexity of Interactions Between Feeding and Escape in Crayfish

Abstract. *If crayfish (*Procambarus clarkii*) are presented with food or threat stimuli, or both, their feeding behavior and escape from threat by tail flips show flexible patterns of interaction. If they are engaged in eating large, relatively immovable pieces of food, escape is inhibited, whereas if small pieces of food are being eaten, the probability of escape is enhanced. If escape occurs during a feeding bout, large pieces of food are usually released, but small ones are not. These observations suggest that the neural circuitry responsible for coordination of behavior in invertebrates may not be as simple as usually assumed.*

One of the major accomplishments of the nervous system is to select particular behavior patterns from various alternatives all of which may be somewhat appropriate to the conditions of the moment (*1*).

Because of the relative amenability of invertebrate nervous systems to circuit analysis, some investigators are using the marine gastropods *Pleurobranchaea* and *Aplysia* to study behavioral choice. It has been found that when these animals are stimulated to produce one behavior, such as feeding, other behaviors, such as righting or defensive withdrawal, are inhibited (*2*). Such observations suggest that relatively direct coordinating pathways might cross-connect the circuitry mediating different behaviors and provide a basis for behavioral coordination and choice.

However, our observations on the response of crayfish (*Procambarus clarkii*) to a conflict between feeding and escape indicate that control systems responsible for response selection in these animals are unexpectedly complex and sophisticated. As with *Aplysia* and *Pleurobranchaea*, feeding can lower the probability of escape from threats in crayfish, and escape can suppress feeding. But these interactions are not fixed. When crayfish are eating large pieces of food that they cannot move easily, feeding usually inhibits escape, but with small and portable pieces of food, feeding increases the probability of escape. Furthermore, when animals make escape responses, they usually release large pieces of food, thus terminating feeding, but they carry small pieces with them.

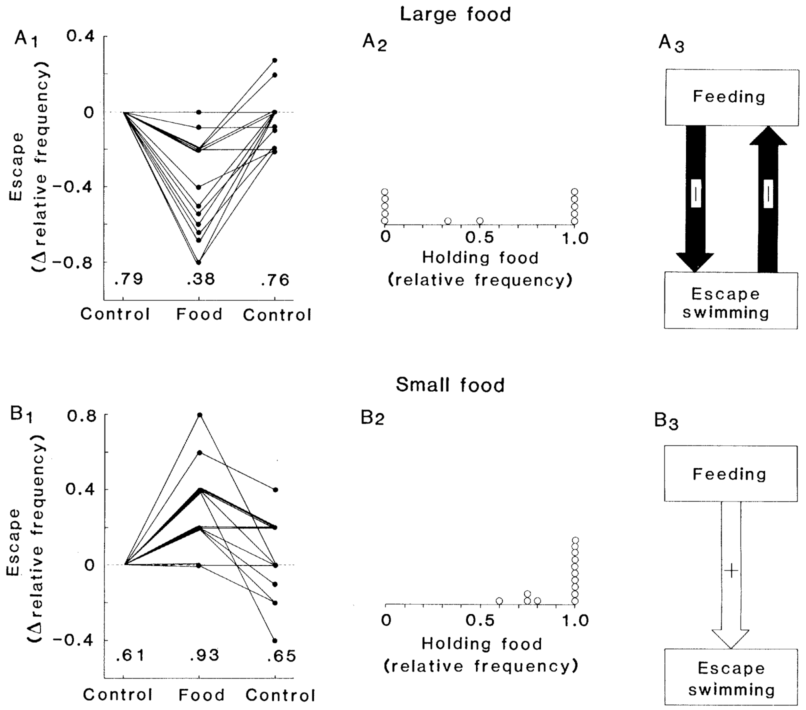

Fig. 1. Interactions of feeding and escape. (A) Large food trials. (A_1) Relative frequency of escape from threat on control trials and during consumption of large pieces of food (15 animals; between four and eights sets of three trials (triplets) were conducted per animal); ordinate values are differences from the first control trial. Results for each animal (points connected by lines) are plotted separately and superimposed, with mean relative frequencies of escape on each trial below. (A_2) Relative frequency of holding large pieces of food during tail-flip escape; points represent different animals; three animals that never flipped while holding food are not included. (A_3) Schematic representation of the interactions indicated by the results in (A_1) and (A_2). (B) Small food trials (14 animals; four to eight triplets per animal). Results are presented as described for (A).

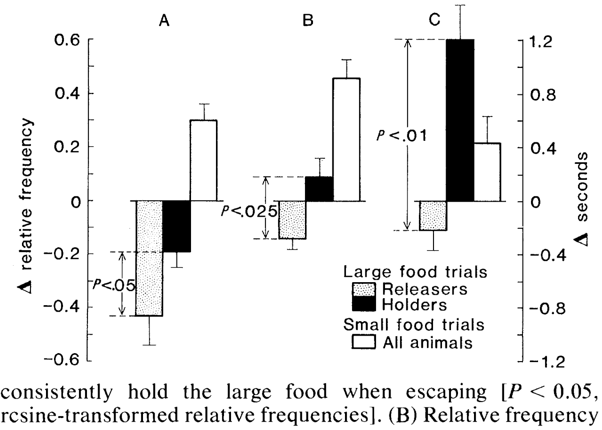

Fig. 2. Comparison of crayfish that hold and release food on large food trials. Bar graphs represent the differences between trials with food and the average of the two control trials for animals that consistently held large food when escaping and those that always released it. The corresponding differences for all animals on small food trials are shown for comparison. Error bars show standard errors of the means. (A) Relative frequency of escape is higher (that is, less depressed) for animals that consistently hold the large food when escaping [$P < 0.05$, $t(8) = 2.14$, one-tailed test on arcsine-transformed relative frequencies]. (B) Relative frequency of escape to visual stimulation before contact is greater for holders of food than releasers [$P < 0.025$, $t(8) = 2.35$, one-tailed test with arcsine-transformed relative frequencies]. Note that by this measure escape tendency of holders is greater than on control trials. (C) The duration of tail-flip bouts is longer among holders [$P < 0.01$ for the difference between holders and releasers; $t(7) = 4.39$, two-tailed test on log-transformed durations]. The prolongation of tail-flipping in animals carrying food (greater for large food than small) may reflect the attempt of animals to progress through the water carrying a load. The small reduction of tail-flip duration in releasers correlates with a tendency of escaping animals not to swim far away from large pieces of food.

Male and female crayfish, 7 to 8 cm (rostrum to telson) in length, were held in group tanks, where they were fed about 0.6 g of brine shrimp per week. One week before the start of the experiment, they were placed in individual 10- or 20-gallon aquariums and fed only during experimental trials. A fish net was the threat stimulus, and animals were repeatedly chased and captured with it for several days before the start of the experiment. During testing the fish net was moved toward the crayfish from in front at about 2.5 cm per second until the animal escaped or the rostrum, or sometimes the legs, were lightly touched. Escape refers only to tail flips (*3*). "Small food" refers to pieces about one-third the size of crayfish and "large" to pieces about three times their size. At the end of food test trials, the food was taken away from the animal. Tests were conducted in sets of three trials (triplets) with 5 minutes between trials. The first and third trials were control trials for assessing the probability of escape from a threat in the absence of feeding. Conditions for the second trial were the same except that a piece of liver was placed in the middle of the tank, and the threat stimulus was not presented until the animal had been eating for 30 seconds (*4*). Between 8 and 16 triplets were conducted per animal, half with large and half with small food presented in irregular order; a few animals received only one size of food. Triplets were separated by at least 1 hour and not more than four per day were conducted with an animal.

In large food tests the average probability of escape on the control trials was 0.77 and that on the food trials was 0.38 ($N = 15$) (Fig. 1A). Probabilities of escape for individual animals, calculated as differences from the probability of escape on the first control trial (Fig. $1A_1$), showed that the probability of escape during feeding was quite consistently reduced [$P < 0.001$, $t(14) = 5.59$, two-tailed test on arcsine-transformed proportions]. Although probability of escape was reduced during large food trials, most animals did sometimes escape while feeding. About half of these reliably released the food, but the rest sometimes or always maintained their hold on it while executing tail flips (Fig. $1A_2$). Thus, feeding on large food and escape are mutually inhibitory, though neither behavior completely precludes the other (Fig. $1A_3$).

The results from small food tests were quite different (Fig. 1B). The average probability of escape was 0.63 for the control trials and 0.93 for food trials ($N = 14$). This increase during the food trials, like the decrease during large food trials, was quite consistent for all animals (Fig. $1B_1$) [$P < 0.001$, $t(13) = 5.83$, two-tailed test on arcsine-transformed proportions]. In contrast to the results for large food trials, animals that escaped while feeding on small food almost always carried the food with them (Fig. $1B_2$). Thus feeding on small food facilitates escape, and escape does not terminate feeding by forcing release of the food (Fig. $1B_3$).

These results make adaptive sense. If food is large, feeding and successful escape are incompatible. In cases where the animal apparently chooses to escape, feeding is commonly, but not always, terminated. However, on other occasions, the animal apparently chooses not to escape and to continue feeding despite possible danger; thus the probability of escape is lowered. With small food, escape and feeding (or at least retention of the food) are compatible; hence, they are not mutually inhibitory. Furthermore, because an animal in possession of food is a ready target for attack by conspecifics, it may be adaptive for the excitability of escape to increase. Indeed, Hagiwara and Wine (*5*) have independently reported that possession of food greatly increased the likelihood that crayfish would escape from conspecifics.

The only aspect of the results that did not seem adaptive was the tendency of some animals to hold the large pieces of food while flipping. Since small pieces of food are generally held while flipping, we considered the possibility that some animals might perceive the large food as small enough to carry. We, therefore, examined the results from animals that consistently held the large pieces of food while flipping to determine whether, as with animals eating small pieces of food, escape was facilitated or at least inhibited less than in other animals. We found that although the probability of escape from threats during feeding was diminished among the consistent holders of food, it was diminished less than that among animals that consistently released the large food (Fig. 2A). And if instead of examining the overall probability of escape, one examines the probability with which the approach of the fish net triggered an escape response (that is, the probability that escape occurred before the net reached the animal), then escape tendency was slightly facilitated in holders of large food (Fig. 2B), as it was in animals eating small food. Whether animals that held the large food while tail-flipping were actually "trying" to carry the food obviously cannot be determined. But as might be expected, if holders were trying to move the large pieces of food, bouts of tail-flipping of holders during large food trials were exceptionally long (Fig. 2C), and in a number of cases the food was dragged several body lengths.

Thus, the pattern of interactions of feeding and escape behavior in the crayfish are not fixed but depend on food size and perhaps on the animal's "judgment" of the food's portability. Such complex interactions, although common in vertebrates, are not expected in the crayfish. The results argue against simple models in which command neurons or pattern generation neurons for one behavior rather directly cause excitation or inhibition of circuitry mediating other behaviors (*2*). The complexity that we describe suggests that study of behavioral integration in invertebrates may provide more insight than might have been expected into the sophisticated vertebrate nervous system.

KIRSTIE L. BELLMAN*
FRANKLIN B. KRASNE
Department of Psychology and
Brain Research Institute, University of
California, Los Angeles 90024

References and Notes

1. The assumption that animals select responses from a set of alternatives is a convenient simplification. In some instances this assumption may be misleading, because many behavior patterns can probably be so altered by the context of their occurrence that they cannot be identified as fixed, selectable entities, clearly different from other entities [see, for example, J. Szentagothai and M. A. Arbib, *Neurosci. Res. Program Bull. 12* (1974); J. C. Fentress, *Behav. Brain Sci.* **4**, 623 (1981); K. L. Bellman, doctoral thesis, University of California, San Diego (1979).
2. W. J. Davis, G. J. Mpitsos, J. M. Pinneo, *J. Comp. Physiol.* **90**, 207 (1974); *ibid.*, p. 225; M. P. Kovac and W. J. Davis, *Science* **198**, 632 (1977); *J. Neurophysiol.* **43**, 469 (1980); E. R. Kandel, *Behavioral Biology of Aplysia* (Freeman, San Francisco, 1979), chapter 9.
3. Stimuli of the kind used here generally elicit tail flips that are not mediated by the crayfish giant fibers [J. J. Wine and F. B. Krasne, *J. Exp. Biol.* **56**, 1 (1972)].
4. If an animal did not begin consuming food within 20 minutes, the experimental trial and its corresponding control trials were discarded; this happened on only four out of more than 150 triplets.
5. G. Hagiwara and J. J. Wine, personal communication.

* Present address: School of Dentistry, University of California, Los Angeles 90024.

2 June 1982; revised 2 May 1983

Down's Syndrome in Adults: Brain Metabolism

Abstract. *The cerebral metabolic rate for glucose, as measured with positron emission tomography and fluorine-18–labeled 2-deoxy-D-glucose, was significantly higher in four healthy young subjects with trisomy 21 syndrome (Down's syndrome) than the mean rate in healthy young controls. The rate of cerebral glucose utilization in the frontal lobe of a 51-year-old subject with Down's syndrome was significantly lower than the rate in the young subjects with this syndrome, but approximated the rate in middle-aged controls. Thus glucose utilization by the brain appears to be excessive in young adults with Down's syndrome but may decline with age in some brain regions.*

At least 150 developmental abnormalities and diseases may affect the human brain at an early age and cause mental retardation. Of these, Down's syndrome (DS) is the most common abnormality with an established etiology. Brains of young adult DS subjects show no consistent abnormalities, aside from a subnormal weight and a relatively simple convolutional pattern (*1–3*), but brains of DS subjects older than 35 years show senile plaques, neurofibrillary tangles, granulovacuolar neuronal degeneration, and reduced activities of choline acetyltransferase and acetylcholinesterase (*3–4*). These pathological changes occur in the same regions of the brain as the changes associated with Alzheimer's dementia. Although older DS subjects are frequently demented, the exact incidence of dementia in DS and its correlation with neuropathology have not been determined (*3, 5*).

Brain oxidative metabolism, which is coupled to neuronal activity, has been examined in individuals with DS; in subjects aged 32 to 49 years, cerebral blood flow and oxygen consumption rates did not differ significantly from their respective values in age-matched controls (*6*). In a study of halothane-anesthetized DS subjects (mean age, 29 years), the cerebral arteriovenous oxygen difference was greater, blood flow was reduced, and oxygen consumption was unchanged, compared to corresponding values in age-matched controls (*7*).

It now is possible to measure regional and overall cerebral metabolic rates for glucose ($rCMR_{glc}$ and CMR_{glc}, respectively) with positron emission tomography (PET) and ^{18}F-labeled 2-deoxy-D-glucose (^{18}F-DG) (*8, 9*). Because brain glucose utilization might provide information about the functional disturbance in DS, we measured glucose utilization with PET in healthy young and middle-aged DS subjects, as well as in healthy age-matched controls (*10*).

Healthy male volunteers, ten aged 21 to 33 years (mean, 27.5) and eight aged 45 to 55 years (mean, 49.1), were screened for the absence of primary or secondary brain disease or for conditions that might contribute to brain dysfunction (for example, hypertension, cardio-