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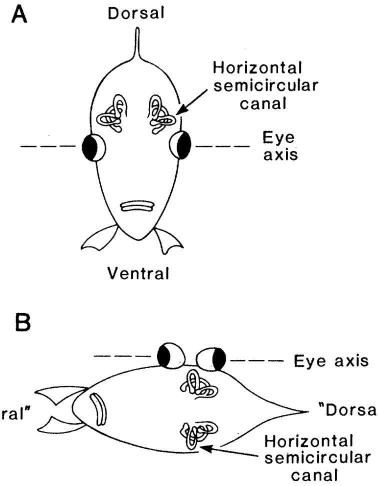
Adaptive Changes of the Vestibulo-Ocular Reflex in Flatfish Are Achieved by Reorganization of Central Nervous Pathways

Abstract. *Flatfish provide a natural model for the study of adaptive changes in the vestibulo-ocular reflex system. During metamorphosis their vestibular and oculomotor coordinate systems undergo a 90° relative displacement. As a result, during swimming movements different types of compensatory eye movements are produced before and after metamorphosis by the same vestibular stimulation. Intracellular staining of central nervous connections in the flatfish with horseradish peroxidase revealed that in postmetamorphic fish secondary horizontal semicircular canal neurons contact vertical eye muscle motoneuron pools on both sides of the brain via pathways that are absent in all other vertebrates studied.*

Adaptive plasticity of the vestibulo-ocular reflex has been the subject of numerous studies, but so far causal explanations of the phenomenon at a neuronal level have not been successful (*1*). In those experiments the normal vestibulo-oculomotor coordinates of a specimen were altered to induce a discrepancy between oculomotor commands and the visual feedback produced by the head movement eliciting the reflex (*2*). The flatfish species constitutes a natural experiment on adaptive changes because a 90° relative displacement of the vestibular and ocular coordinate systems takes place during metamorphosis (Fig. 1). In early larval stages, the flatfish are pelagic and their swimming movements are like those of other fish. In a later metamorphic stage, the body tilts 90° to one side as they become the bottom-adapted adult flatfish (*3*). During this period the eye which would have faced the sea bottom migrates around the dorsal aspect of the animal toward the upper pigmented side. No other aspects of the fish's symmetry change, including the labyrinths, which remain in their original positions (*4*). As a result, the lateral semicircular canals become orientated vertically, while the orientation of the optic axes remain constant with respect to the environment (Fig. 1B) (*5*). Thus the optic axes and the horizontal semicircular canals are finally arranged perpendicular to each other. Nevertheless, the flatfish has a functioning vestibulo-ocular reflex which appropriately stabilizes the animal's visual world during head movements (*6*).

The extent of changes necessary for adaptation of the vestibulo-ocular reflex can be seen in the compensatory eye movements occurring during swimming. In an upright fish, when the body moves in a horizontal plane the head rotates around a vertical axis, thereby stimulating the lateral (horizontal) semicircular canals. This stimulus causes compensatory horizontal eye movements with one eye moving backward and the other forward (*7*). Since the adult flatfish propels its body by use of the same swimming movements, the lateral semicircular canals are stimulated similarly even though the head movement now occurs in a vertical plane. The observed compensatory movements of the two eyes are now rotations approximately around the optic axes in the same direction at the same time with respect to the visual environment (Fig. 2) (*8*). Given a normal vesti-



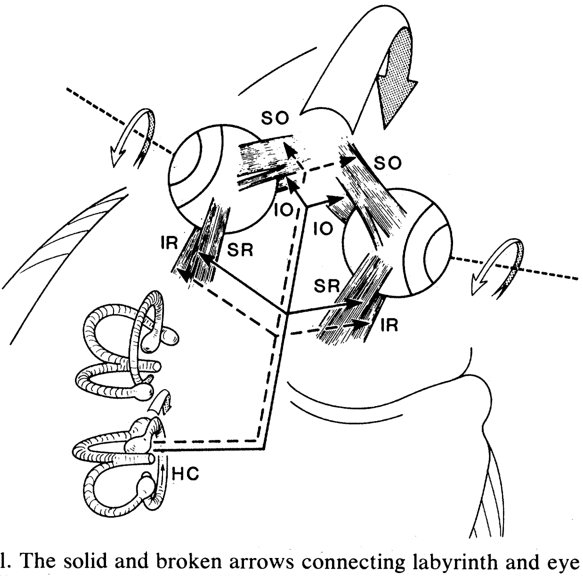


Fig. 1 (left). Spatial relationship of labyrinths and eye axes before metamorphosis (A) and in an adult flatfish (B). Fig. 2 (right). Extraocular muscle co-contractions required for the production of compensatory eye movements during a downward movement of the head. Backward rotations of the eyes (small arrows around the optic axes, which are symbolized by broken lines) would be produced by contractions of the superior rectus (*SR*) and inferior oblique (*IO*) muscles. The downward head movement (large arrow) eliciting these compensatory eye movements would activate the vertically oriented horizontal (lateral) semicircular canals (*HC*). The direction of canal displacement is shown by the small arrow above the left (lower) horizontal canal. Ampullopetal endolymph current is illustrated by the arrow inside the canal. The solid and broken arrows connecting labyrinth and eye muscles suggest the prospective excitatory and inhibitory connections required for an appropriately functioning vestibulo-ocular reflex. The horizontal canal pathways have to undergo a rearrangement leading to new extraocular motoneuron termination sites on both sides of the brain. Abbreviations: *IR*, inferior rectus; *SO*, superior oblique.

bulo-ocular reflex in the adult flatfish in the face of a 90° displacement in the vestibular and oculomotor coordinate systems, the question arises whether the sites of the adaptive changes are peripheral (that is, mechanical at the level of the eye), central (that is, neuronal reorganization), or a combination of both.

Specimens studied were right-sided winter flounders *Pseudopleuronectes americanus*. We first examined the gross anatomy and kinematic characteristics of the extraocular muscles by dissection and by photographing a corneal mark after electrically stimulating single eye muscles with bipolar electrodes. The actions of extraocular muscles resembled those of the lateral-eyed goldfish or rabbit (*9*). Therefore, a downward movement of the head should produce backward rotations of both eyes through bilateral activation of the superior rectus and inferior oblique muscles (Fig. 2). After confirming the mechanical role of these vertical eye muscles, we used the intracellular horseradish peroxidase (HRP) method to study the central distribution and individual morphology of extraocular motoneurons. No qualitative differences were found in any features when the flatfish was compared with lateral-eyed animals.

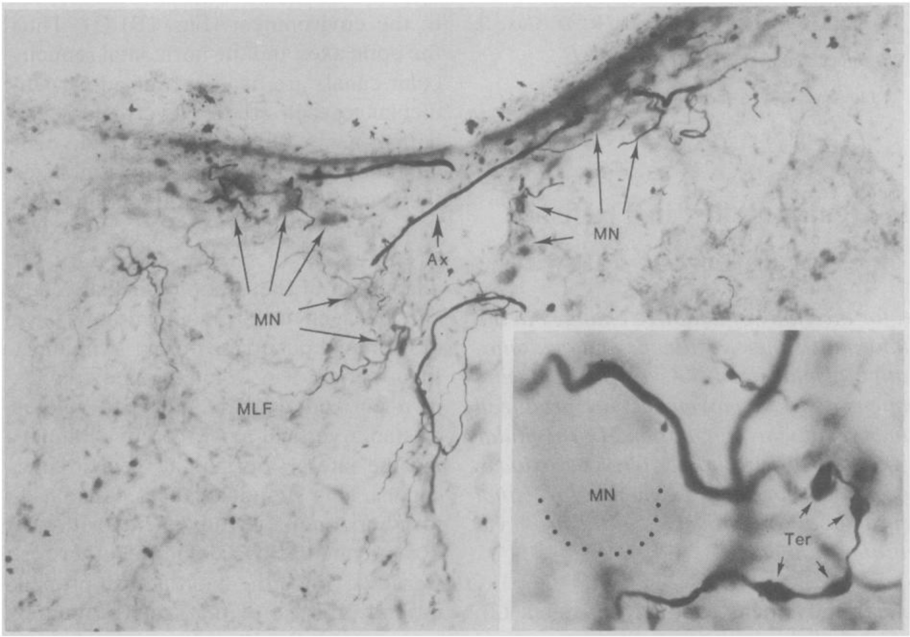


Fig. 3. Intracellular HRP in horizontal canal secondary vestibular neurons. Axon collaterals (*Ax*) are crossing the midline within the oculomotor nucleus at the level of inferior rectus motoneurons (*MN*). Coronal section, ×110; *MLF*, medial longitudinal fasciculus. (Inset) Terminals (*Ter*) (at high magnification, ×625) appear near the neuropil of oculomotor neurons (*MN*).

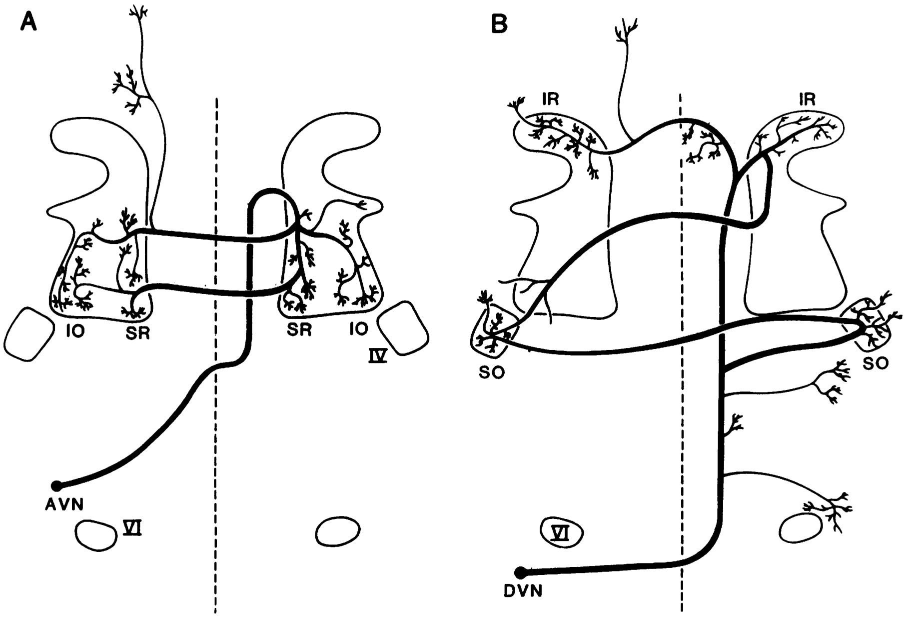


Fig. 4. Reconstruction of secondary vestibular neurons of the horizontal canal. (A) Type 1, prospective excitatory neuron. (B) Type 2, prospective inhibitory neuron. Abbreviations: *AVN*, anterior vestibular nucleus; *DVN*, descending vestibular nucleus; *SR*, oculomotor nucleus–superior rectus subdivision; *IO*, oculomotor nucleus–inferior oblique subdivision; *IR*, oculomotor nucleus–inferior rectus subdivision; *SO*, superior oblique motoneurons in trochlear nucleus; *IV*, trochlear nucleus; *VI*, abducens nucleus.

Since there were no apparent modifications at the final level of the oculomotor system (that is from motoneuron to eye muscle kinematics), the next most likely site for adaptive changes in the vestibulo-ocular reflex was the connectivity of the second-order vestibular neurons linked to the lateral (horizontal) semicircular canal system. The evidence suggests that the vestibulo-ocular reflex seems to depend largely on three-neuron arcs (*10*). The most direct neuronal network between the receptor (hair cells in semicircular canals) and the effector (extraocular muscles) consists of the primary vestibular afferent, the second-order vestibular neuron, and the extraocular motoneuron. Primary vestibular afferents from the semicircular canal ampullae project to separate secondary vestibular neuron groups located in the vestibular nuclei (*11*). The secondary vestibular neurons in turn project to specific oculomotoneuron pools (*12*), forming the principal vestibulo-ocular reflex connections (*13*). In all species studied to date, the lateral semicircular canal is linked agonistically to the ipsilateral medial rectus and the contralateral lateral rectus muscles. In the vertical vestibular system, the anterior canal can directly regulate the ipsilateral superior rectus and the contralateral inferior oblique, while the posterior canal connects to the ipsilateral superior oblique and the contralateral inferior rectus muscles. Inhibitory connections link the same muscles to the contralateral coplanar semicircular canals. We examined the morphology of secondary vestibular pathways of the flatfish with the intracellular HRP method (*14*), focusing on neurons linked to the lateral canal system. Principal vertical canal connections did not differ from those described for cats and rabbits (*15*). Neurons linked to the horizontal (lateral) canal system showed a dramatic reorganization in motoneuron connectivity (Fig. 3). Two types of horizontal secondary vestibular cells were found whose somata were located in the vestibular nuclear complex. Their axons crossed the midline before ascending in the medial longitudinal fasciculus.

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.

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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 in-