How the oculomotor system repairs itself

A fairly common example of the brain repairing itself is the recovery from a sudden peripheral vestibular lesion. Spontaneous nystagmus and dizziness result. These symptoms diminish over the next two to three weeks and, in a few months, not a trace of the disorder remains. We take this compensation process for granted and little attention has been paid in neurophysiology to the brain mechanisms that must protect all our sensory-motor responses in the same way. Some part of the brain must sense it if our responses are no longer appropriate to the stimuli. We call this dysmetria. It not only detects dysmetria but sets about at once to correct it. To do this it must be able to strengthen some synaptic connections and weaken others until orthometria (absence of dysmetria) is re-established. Such a process is adaptive because it restores proper function; it is plastic because the changes in behavior are semipermanent and it is a primitive form of learning by the brain.

Much milder forms of adaptive repair are continually taking place every day and they need not be initiated by internal damage. Consider a person who starts wearing glasses with a fairly strong + spherical correction. They magnify everything by, say, 1.2x. First, he must learn that objects are not as big as they seem but he must also deal with an even more basic problem. When he turns his head to the left, say, at 100 degrees per second, his normal vestibulo-ocular reflex rotates his eyes in his head at 100 degrees per second to the right so that his visual axes make no net movement and the images of the environment remain stationary on his retina. This is normal behavior and the gain of the reflex (eye velocity/head velocity) is said to be 1.0. With spectacles that magnify by 1.2, the image of the world now moves at 120 degrees per second to the right (relative to the head) not 100 degrees per second. The eyes move too slowly, they do not compensate and, to the patient, the world appears to shift to his right at 20 degrees per second. This is called oscillopsia and it often leads to temporary discomfort and even nausea when a patient's prescription is changed. But in this case the dysmetria was caused by an external device not an internal injury. Since the end result is the same, namely oscillopsia (or vestibulo-ocular dysmetria) it is reasonable to suppose that the same adaptive repair mechanism that counteracted it when it was created by an internal lesion would also set about to “repair” this reflex when dysmetria was caused by glasses. If that happened, then the patient’s reflex should change so that...
its gain rose to 1.2. This hyperactivity would now rotate his eyes just fast enough to keep the image of the world (seen through his new glasses) stationary on his retina whenever he moved his head. And that is just what happens.

Gonshor and Melvill Jones were the first to realize this. They read about psychologists who wore reversing prisms which turned the whole visual world about backwards, left to right! These people could adapt so well to such prisms that they could even go mountain climbing while wearing them. Now when these people moved their head to the left, the image of the world went relatively to the left, not the right! If their eyes moved reflexively to the right as usual they would have gross oscillopsia. If their brains were to adapt, their vestibulo-ocular reflex would have to be rewired backwards and that is very nearly, in fact, what happens. The subjects in the experiments of Gonshor and Melvill Jones wore reversing prisms for many weeks. The gain of their reflex was tested in the dark every day by sinusoidal rotation. After only a few days, there were periods in each cycle when their eyes were moving in a direction opposite from normal. This was a rather startling finding since we often tend to think that the vestibulo-ocular reflex (the "three neuron arc") is a fairly simple, and therefore rigid, brain-stem reflex.

Four other studies have since confirmed this finding. Ito and collaborators in Tokyo have shown that the gain of the vestibulo-ocular reflex in the rabbit can be raised or lowered by visual stimuli that move in such a way as to augment or oppose the vestibular eye movements. I have put reversing prisms on cats chronically. After about a week the gain of their reflex dropped from about 0.90 to 0.10. The gain did not reverse but the reflex was at least very nearly extinguished. Miles and Fuller put telescope lenses, which magnify by 2x, chronically on monkeys. For them to see clearly during head movements, the gain of their reflex would have to increase to 2.0. It did. G. M. Gauthier and I (unpublished observations) repeating that experiment in man. After wearing these telescope glasses for five days, our subject's gain rose to about 1.5. By now there is no question that the gain of the vestibulo-ocular reflex is amazingly adaptive and reflects the working of an internal system whose function is to suppress dysmetria.

In 1972, Ito proposed that the part of the brain which was responsible was the vestibulocerebellum, chiefly the floccular-nodular lobes. This structure is ideally located for this purpose because it receives a direct projection from the canals and projects in turn, via Purkinje cells, onto the vestibular nucleus. Thus, part of the whole reflex actually runs through this part of the cerebellum as a parallel branch. Ito reasoned that the cerebellum could only know if it had adjusted the gain correctly if it could see the final result, that is, whether or not images slipped on the retina. In their laboratory, Maekawa and Simpson demonstrated a projection from the rabbit's retina to its vestibulocerebellum on climbing fibers which carried just the needed visual information. Thus, the vestibulocerebellum has all it needs to detect dysmetria and repair it by modifying the strengths of its intracerebellar synapses.

Such a delightful theory sounds too simple and mechanistic to be true but subsequent research seems to bear it out. Ito and co-workers showed that removal of the flocculus in the rabbit abolished the plastic control of gain by vision. I have shown that removal of the cat's vestibulocerebellum abolishes the effect of reversing prisms on the gain. Recently (unpublished observations), I have shown that removal of the vestibulocerebellum in the cat while it is still wearing prisms promptly abolishes the drop in gain caused by the prisms, which suggests that the adaptive modifications actually did take place in the cerebellum itself. Ghelarducci, Ito, and Yagi (personal communication) have recently shown that the discharge rate modulation...
of Purkinje cells undergoes appropriate plastic changes in the rabbit flocculus associated with plastic changes in gain. While there are many details left to be cleared up, and species differences to sort out, the theory that the vestibulocerebellum is the site of the adaptive learning in the vestibulo-ocular reflex seems to be borne out by experimental research.

The implications of this theory are far reaching. If the cerebellum acts like a motor repair shop for the gain of the vestibulo-ocular reflex, does it repair other aspects of the reflex? Is it instrumental in suppressing spontaneous nystagmus? Does it repair other types of oculomotor dysmetria such as saccadic dysmetria? If so, it is ironic to realize that one bi-product of cerebellar repair is to hide oculomotor disorders of slow onset from the neuro-ophthalmologist. When a disorder is finally manifest, it means either that it has become so bad that the cerebellum can no longer cover for it or else that the cerebellum itself has become involved. This raises the interesting question of how well the adult brain is able to repair damage to the repair shop itself and puts a completely new slant on interpreting the oculomotor abnormalities seen in patients with cerebellar lesions.

Finally, it is tempting to speculate whether motor learning and repair are not a generalized cerebellar function. Thus, at least many of the automatic reflexes and adjustments in the spinal control of righting and locomotion could also be under the repair supervision of transcerebellar pathways from and to the cord.

At any rate, the research on the adaptive control of the vestibulo-ocular reflex could become a major breakthrough in cerebellar physiology because it offers, for the first time, a specific, testable theory on a simple reflex which has an input that is easily controlled and an output that is easily measured. It is this simplicity which may act as the key to open the door to our understanding of more complex functions of the cerebellum.

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REFERENCES