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HOW WE LOOK: STUDIES OF OCULOMOTOR-SYSTEM NEURAL CONNECTIONS

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ABSTRACT

The neural connections of the reticular formation (RF) with the vestibular nuclei (8V) and the ascending medial longitudinal fasciculus (MLF) were studied, because many neurons in these structures carry eye-movement and head-movement (vestibular) signals and are only one or two synaptic connections removed from eye motorneurons. We used stimulating electrodes placed in specific brainstem structures and a single-neuron recording microelectrode in anesthetized or decerebrate cats. Connections were determined when the neurons were excited either forwards (orthodromically) or backwards (antidromically) by a shock. Four classes of neurons were studied. One neuronal class in the pontine RF projects axons into the ascending ipsilateral MLF; these axons terminate in the midbrain. Some of these cells receive excitation from both vestibular nerves and are probably involved in the vestibulo-ocular reflex. Another class of RF neurons projects to either the ipsilateral or the contralateral 8V. A third class located amidst lateral-rectus motorneurons in the VIth nucleus projects into the contralateral ascending MLF and excites medial-rectus motorneurons for the contralateral eye so that the two eyes move horizontally in the same direction. A fourth class located in and just beneath the 8V receives monosynaptic input from the vestibular nerve and projects into the contralateral MLF. The possible roles for these neurons in controlling eye movements are discussed.

Abbreviations: MLF: medial longitudinal fasciculus; RF: reticular formation; 3: oculomotor (IIIrd cranial nerve) nucleus; 4: trochlear (IVth cranial nerve) nucleus; 6: abducens (VIth cranial nerve) nucleus; 8V: vestibular nuclear complex of the VIIIth cranial nerve.

INTRODUCTION

The oculomotor system is one of nature's most sophisticated control systems. It functions in the fixation of gaze upon visual objects and in the maintenance of steady retinal images during head and target movements. It thus beautifully complements and augments the capabilities of the visual system. There are five types of eye movements: fast, tracking, convergence upon near objects, image stabilization during movements of the visual surroundings, and image stabilization during head movements (vestibulo-ocular reflexes). We mainly will discuss the anatomical substrates for the last type, image stabilization during head movements. Motorneurons from the VIth cranial nerve nucleus (Fig. 1) control the lateral rectus muscle of the eye, motorneurons from the IVth nucleus control the superior rectus muscle, and motorneurons from the IIIrd nucleus control the other four extraocular muscles. Head rotations about all three axes of rotation are sensed by the semicircular canals, and head linear movements in all the three dimensions by the macula and saccule; the canals, macula and saccule are contained within the labyrinth (vestibule) of the inner ear. The vestibular signals travel along the VIIIth nerve to the 8V, a complex of four major and several minor clusters of neurons. The simplest pathway of a vestibulo-ocular reflex involves only one interneuron whose cell body is in the 8V. There are several projection varieties of this interneuron: ipsilateral or contralateral, excitatory or inhibitory axons to the IIIrd, IVth and VIth nuclei (Brodal, 1974; Cohen, 1974); some of these axons ascend within the fiber bundle called the MLF. Thus many MLF fibers originate in 8V. These pathways are important but insufficient by themselves to produce the complete vestibulo-ocular reflex. Additional neurons, some studied by the authors, are located in nearby parts of the brainstem (in the divisions called the midbrain, pons and medulla; Fig. 1) and in certain other structures. Some neurons located in the medial RF (the core of the brainstem) beneath the IIIrd, IVth, VIth and VIIIth cranial nerve nuclei are active only a few milliseconds preceding fast eye movements. Damage to this part of the RF will paralyze horizontal eye movements. Our electrophysiological experiments were done to characterize the types and interconnections of such neurons.

These experiments were conducted with living cats and measured the electrical responses of neurons and their interconnections, which are called synapses. (Anatomical techniques usually do not determine interconnections.) The neuronal action potential is an electrical pulse of about +100 mV amplitude and 0.5 msec duration which is actively propagated from the cell body down the axon to the terminal(s) without attenuation at a speed of 0.2 to 120 m/sec, depending

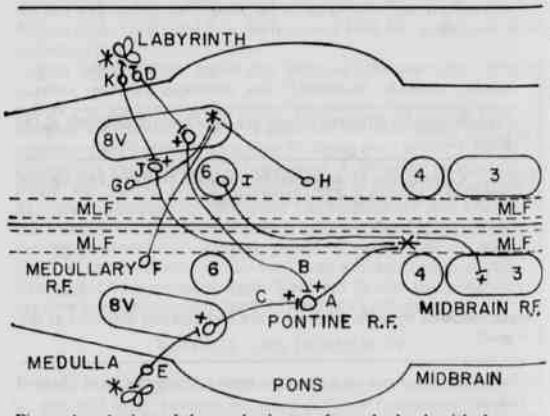

Figure 1. A view of the cat brainstem from the back with the cerebellum removed. The spinal cord is to the left. The motorneurons to the eye muscles originate in cranial nuclei III, IV and VI. The VIIIth nerve connects the labyrinth to the vestibular nuclei (8V). Abbreviations and the neuronal types A-K are described in the text. Asterisks indicate locations of stimulating electrodes.

on the size and type of axon. The longest axons exceed 1m, although the ones studied in these experiments are only approximately 1 cm long. The nervous system transmits information over axons as a series of action potentials.

MATERIALS AND METHODS

The action potential was detected as a weak −0.05 to −2 mV pulse by an extracellularly-located microelectrode placed within 0.1 mm of the cell body. (Because axons produce miniscule extracellular pulses, they are normally undetectable.) An electrical shock to the axon initiated an action potential, which traveled antidromically (backwards) to the cell body, where it was detected by the recording microelectrode. An antidromic pulse always occurred with the same time delay following the shock, because axons conduct at a fixed velocity; the antidromic pulse always occurred at and above the threshold shock strength (the all-or-none rule). The antidromic neurons which were detected followed four shocks at 300 to 1600 shocks/sec (synapses will not usually operate this rapidly). These antidromicity tests proved that the detected cell body projected its axon near the stimulating electrode.

Synapses between neurons were detected by electrically stimulating the presynaptic neurons to produce action potentials in them. These action potentials traveled foward (orthodromically) to the axon terminals, which then released a neurotransmitter chemical into the synaptic cleft. The chemical diffused across the cleft, bound with receptor molecules in the membrance of the postsynaptic neuron, and opened ionic channels. The subsequent flow of ions excited (or, for some synapses, inhibited) an action potential, which was detected by the micropipette (recording electrode). Because of fluctuations in the amount of transmitter released, a post-synaptic action potential sometimes did not occur or occurred at various latencies (e.g., between 0.5 and 3 msec); a synaptically-excited pulse thus easily could be distinguished from the constant-latency antidromic pulse.

Cats were used because they are inexpensive but still make relatively human-like eye movements. In some experiments the cat was anesthetized with pentobarbital. Because this anesthetic depresses synaptic activity, in other experiments an unanesthetized, decerebrated cat was used (short-acting ether anesthesia was used before decerebration). Although this unconscious cat did not make eye movements, neurons could be excited either antidromically or orthodromically to determine connections. The animal's life functions were maintained for the 12-24 hr experiments. After removal of part of the top of the skull and the cerebellum, the brainstem was exposed (the view was similar to that of Fig. 1) so that the electrodes could be inserted visually with micromanipulators. Stimulating electrodes were thin wires, insulated except for the tips. Electrode and neuronal locations were verified after experiments through histological procedures. The referenced papers give further details of methods.

Action potentials were recorded by a glass micropipette with a 10 μm tip diameter and filled with electrically-conductive 4 M NaCl solution. A wire inserted into the micropipette connected it to an amplifier. Signals were displayed upon an oscilloscope and photographed, as shown in our referenced papers. Shocks of 0.1 msec duration and ≤ 50 μA strength were given to the MLF at 1 mm posterior to the IVth nucleus, where many types of MLF axons pass. The 50 μA shock was strong enough to initiate an antidromic action potential in most MLF axons, but in few surrounding axons. The action potential traveled antidromically to the cell body, where it was detected by the micropipette. In other experiments antidromic action potentials were excited by shocks to the 8V. In various experiments stimulating electrodes also were placed into the labyrinth to excite the VIIIth nerve for testing orthodromic inputs.

RESULTS

Four neuronal categories were studied:

1. **Reticulo-MLF neurons** (type A in Fig. 1) have cell bodies (circle) located in the medial pointine RF and project an axon (line) into the contralateral ascending MLF (Remmel et al., 1978). They also have been observed in anatomical studies (Graybiel, 1977; Cohen, 1974), which indicate that the axons terminate in the midbrain. They might function to coordinate horizontal and vertical eye movements. Most reticulo-MLF neurons receive excitatory (+) synaptic inputs from vestibulo-reticular neurons from both sides (types B and C), which in turn receive excitatory synaptic inputs from VIIIth-nerve fibers (types D and E; Remmel et al., 1979b). Thus a functional VIIIth nerve-vestibular nucleus (synapse), reticular (synapse), MLF pathway appears to exist. Additional interneurons also might contribute. This pathway might transmit head-movement information to the midbrain for controlling eye movements.
2. **Reticulo-vestibular neurons** were observed by shocking the 8V to antidromically excite RF cells (Remmel et al., 1977). They come in (at least) three kinds which are crossed (type F) or uncrossed (type G) from the medulla or uncrossed from the pons (type H). Anatomists (Hoddevik et al., 1974) also have observed them. These neurons might transmit eye- or body-movement signals from the RF to the 8V, where such signals have been detected.
3. **Abducens interneurons** (type I) with cell bodies amidst VIth-nucleus (abducens) motorneurons project their axons up the opposite MLF to terminate upon medial-rectus motorneurons in the IIIrd nucleus (Remmel et al., 1978). These neurons, first clearly demonstrated anatomically (Graybiel and Hartwieg, 1974), carry signals similar to those of lateral-rectus motorneurons and excite medial-rectus motorneurons for the opposite eye (Baker and Berthoz, 1977) to move the two eyes horizontally.
4. **Reticular neurons receiving excitatory monosynaptic input from the VIIIth nerve** and projecting an axon up the opposite MLF (type J) were detected for about 1 mm beneath the traditional anatomical boundary of the vestibular nuclei. Some of them receive monosynaptic excitatory input from VIIIth-nerve neurons (type K). Because these "RF" cells appeared very similar to the 8V cells immediately above them, the vestibular nuclei seem to be effectively larger than previously thought.

DISCUSSION

These studies demonstrated several new types of brainstem neurons and synaptic interconnections. It is impossible here to discuss the many other important neurons and interconnections described by others during the last decade (see Baker and Berthoz, 1977; Brodal, 1974; Cohen, 1974). Neuron by neuron and synapse by synapse, the amazing brain is being understood. Experiments are in preparation to record the behavior of the above neurons during eye movements in alert cats. Although almost all types of neuronal behaviors which the bioengineer might expect to find already have been observed in alert monkeys and cats (Baker and Berthoz, 1977; Cohen, 1974), unfortunately these behaviorally-defined neurons cannot usually be matched with the anatomically-defined types. The puzzle's pieces cannot yet be assembled, but the major outlines of the picture of the oculomotor system will become apparent during the next decades.

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BAKER, R. and A. BERTHOZ, eds. 1977. Control of gaze by brain stem neurons. Development in neuroscience. Vol. 1, Elsevier/North-Holland, Amsterdam.

BRODAL, A. 1974. Anatomy of the vestibular nuclei and their connections. Pp. 239-352, *In* Handbook of sensory physiology, Vol. 6 (Part 1) (H. H. Kornhuber, ed.). Springer-Verlag, Berlin.

COHEN, B. 1974. The vestibulo-ocular reflex arc. Pp. 477-540, *In* Handbook of sensory physiology, Vol. 6 (Part 1) (H. H. Kornhuber, ed.). Springer-Verlag, Berlin.

GRAYBIEL, A. M. 1977. Direct and indirect preoculomotor pathways of the brainstem: An autoradiographic study of the pontine reticular formation in the cat. J. Comp. Neurol. 175:37-78.

GRAYBIEL, A. M. and E. A. HARTWIEG. 1974. Some afferent connections of the oculomotor complex in the cat: An experimental study with tracer techniques. Brain Res. 81:543-551.

HODDEVIK, G. H., A. BRODAL and F. WALBERG. 1975. The reticulovestibular projection in the cat. An experimental study with silver impregnation methods. Brian Res. 94:383-399.

REMMEL, R. S., J. POLA and R. D. SKINNER. 1978. Pontomedullary reticular projections into the region of the ascending medial longitudinal fasciculus in cat. Exp. Brain Res. 32:31-37.

REMMEL, R. S. and R. D. SKINNER. 1979a. Monosynaptic vestibular nerve input to vestibular and adjacent reticular neurons projecting into the ascending medial longitudinal fasciculus. Exp. Neurol. 66:200-204.

REMMEL, R. S. and R. D. SKINNER. 1979b. Ascending vestibulo-reticulo-MLF pathway in cat. Neurosci. Abst. 5:804, abst. 2714.

REMMEL, R. S., R. D. SKINNER, D. B. YELVINGTON and L. SADIKIN. 1977. Cat reticular neurons projecting to the region of the medial vestibular nucleus. Neurosci. Letters 6:223-229.