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Eye Movements Induced by Stimulation of the Pontine Reticular Formation: Evidence for Integration in Oculomotor Pathways

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Ipsilateral horizontal eye movements were induced in monkeys at short latency by electrical stimulation of the paramedian zone of the pontine reticular formation (PPRF). Eye muscle potential changes occurred within 2.3–3 msec after PPRF stimulation. This is 0.5–1 msec longer than activation from MLF stimulation over monosynaptic pathways. Within limits the amplitude of the eye movements induced by PPRF stimulation was independent of eye position, the velocity was constant, and the amplitude and speed were linearly related to the frequency of stimulation. Depending on the strength, frequency, and duration of stimulation, eye movements similar to slow phases of nystagmus and pursuit movements, or saccades and quick phases of nystagmus could be induced by PPRF stimulation. In alert animals the eyes held the new positions of deviation for variable periods after stimulation. These periods of fixation were generally longer than several hundred milliseconds and were similar to naturally occurring positions of fixation. Previous studies have suggested that slow and rapid eye movements and positions of fixation in the horizontal plane are generated in the pontine reticular formation. The data are compatible with this hypothesis. Moreover, activity induced by the stimulating pulses appeared to have been mathematically integrated. It seems likely that one integration of neural activity in the visual-ocular or vestibulo-ocular reflex arcs probably takes place in the PPRF.

Introduction

It is known that one or more integrations of neural activity takes place in the vestibulo-ocular reflex arc (33, 37). However, the location of the various integrators is still unknown. The present study was initiated when it was observed that eye movements induced by stimulation of the paramedian zone of the pontine reticular formation (PPRF) were most often of constant velocity. Constant velocity movements suggest integration of

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neural activity, since at any time during the induced movements, the extent of deviation was proportional to the number of stimulating pulses which had been introduced to that moment. The present findings indicate that one integrator of neural activity responsible for eye movements in the horizontal plane is probably located in the PPRF.

Methods

Eleven juvenile rhesus monkeys were used in these experiments. Bipolar electrodes with a 0.5-mm tip separation were implanted in the PPRF under anesthesia using stereotaxic techniques. The PPRF occupies medial portions of nucleus reticularis magnocellularis of the pontine reticular formation in the monkey (21). It is shown in the cross-hatched area of Fig. 1A. Potential changes which preceded rapid eye movements were recorded through the PPRF electrodes used for stimulation (10). After electrolytic lesions were made through the PPRF electrodes (Fig. 1B), there was pa-

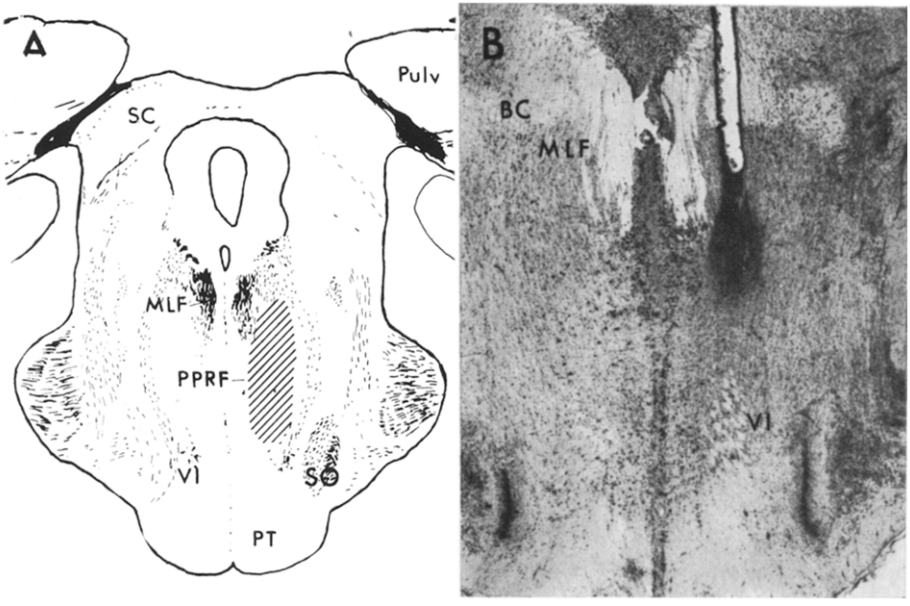

FIG. 1. A, Diagram of the brain stem in the P 0.5 vertical stereotaxic plane (35). The approximate location of the paramedian zone of the pontine reticular formation (PPRF) is cross-hatched. B, Left PPRF lesion in monkey 507 which produced conjugate paralysis of gaze to the left. Stimulation through the electrodes prior to lesion produced eye movements of the type described in this report. Cresyl violet stain. Pulv., pulvinar; SC, superior colliculus; MLF, median longitudinal fasciculus; VI, abducens nerve roots; PT, pyramidal tract; SO, superior olive; BC, brachium conjunctivum.

ralysis of conjugate gaze to the ipsilateral side (6, 13, 21). The location of the electrodes was determined in histological sections after animals were killed.

During testing monkeys were seated in a primate chair with arms and legs restrained and head held by a sponge-covered clamp. The brainstem was stimulated with trains of square waves delivered through the bipolar electrodes using currents of 0.05–0.3 ma. EMG's of eye muscles were recorded with concentric bipolar electrodes. Eye movements were recorded by electrooculography (EOG) using amplifiers with dc-coupling. The EOG was differentiated to determine angular eye velocity using an rc-coupled amplifier with a 0.002-sec time constant. Techniques used for inducing and recording eye movements have been described in detail (26). EMG's and EOG's were displayed on the screen of a storage oscilloscope.

In the succeeding figures an eye movement to the right is shown by an upward deviation of the EOG trace. The EOG was calibrated by showing the animal lights separated by 15 or 30° in a dimly lit room. Alternatively, the velocity of slow phases of optokinetic nystagmus (OKN) was used to calibrate the EOG. It was assumed that the eyes were moving at the velocity of a moving optokinetic drum at speeds up to 45°/sec (1).

Results

General Characteristics of PPRF-Induced Deviations. When the PPRF was electrically stimulated in the alert or anesthetized monkey, the eyes moved in the horizontal plane to the ipsilateral side. If the stimulating electrodes were centrally located in the PPRF, the induced movements were conjugate, and were of similar amplitude and velocity in both eyes. If the electrodes were dorsal to the PPRF, the median longitudinal fasciculus (Fig. 1, MLF) was stimulated, and the ipsilateral eye adducted instead of abducted (7, 9). If the electrodes were in ventral parts of the PPRF, the roots of the abducens nerve (Fig. 1, VI) were simultaneously activated, and the ipsilateral eye abducted faster and farther than the contralateral eye adducted.

Eye movements induced by PPRF stimulation were smooth and continuous and had a forced quality. The animal could not resist them, and they took precedence over all other eye movements. While PPRF-induced deviations were in progress, they were not interrupted by spontaneous eye movements in any direction. An example is shown in Fig. 2A. The stimulus began during a saccade to the left. It abruptly terminated the spontaneous saccade, and the eyes moved smoothly and continuously to the right for the duration of stimulation (horizontal bar). During prolonged PPRF stimulation the eyes deviated continuously until they were in full ipsilateral gaze.

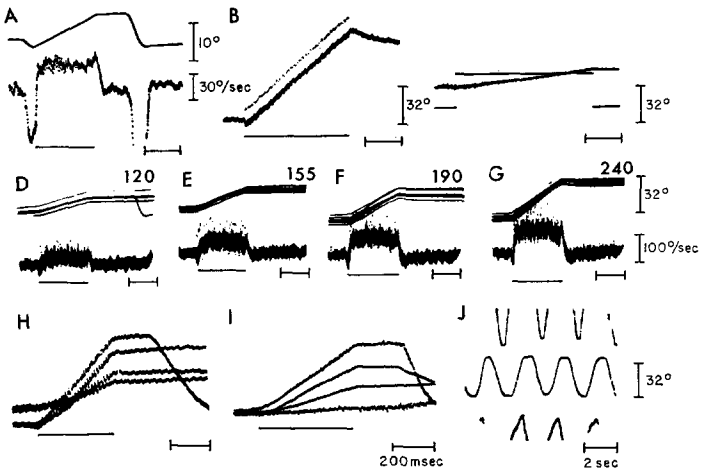

FIG. 2. Eye movements induced by PPRF stimulation. In A–G the top trace is the bitemporal DC–EOG. The bottom trace in A and D–G is the differentiated EOG showing eye velocity. The stimulus artifact is shown underneath. H. Series of constant velocity eye movements induced by stimulation frequencies of 100, 120, 155, and 200 Hz from bottom to top, respectively. I, Eye movements induced by stimulation at one frequency (200 Hz) with pulses of 0.01, 0.04, 0.07, and 0.10 msec duration from bottom to top, respectively. J. Sinusoidal eye movements induced by alternately changing the voltage of left and right PPRF stimuli. The top trace is the artifact of the left PPRF stimulus and the bottom trace of the right PPRF stimulus. The middle trace is the DC–EOG. The time markers are 100 msec in B and H, 200 msec in A, C–G, I, and 2 sec in J.

Nystagmus was not evoked by PPRF stimulation, and the induced eye movements were not different in light or in darkness. In some, but not all monkeys, pupillary dilatation accompanied stimulation. If animals were unrestrained, the head moved to the ipsilateral side, and the monkeys circled in that direction (42). Vertical eye movements were not induced by unilateral or by bilateral PPRF stimulation.

Constant Velocity Deviations. The most striking finding of this study is that when the PPRF was electrically stimulated, the induced ocular deviations were most often of constant velocity. This was true whether stimulation began during ongoing eye movements (Fig 2A) or during periods of fixation (Fig. 2B, C). The range over which the eyes moved with constant velocity was large, and the eye movements could last for relatively long periods of time. The eyes deviated about 65° in Fig. 2B, and the movement lasted for about 700 msec in Fig. 2C.

Eye movements induced by PPRF stimulation were regular in amplitude and reproducible if the same stimulus was repeated (Fig 2D–G). Neither amplitude nor velocity of the induced movements depended on the

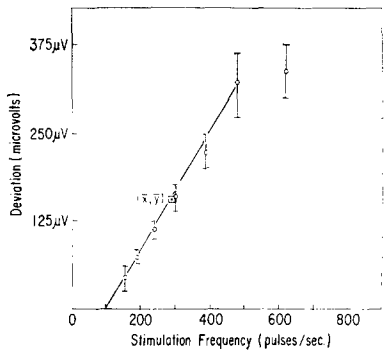

FIG. 3. Relationship between amplitude of deviation induced in the right eye by left PPRF stimulation (ordinate) and frequency of stimulation. The stimulus was a 200-msec train of pulses at the frequency shown on the abscissa. Each mean (open circles) was calculated from 20 samples. The vertical bars show the standard deviations. The induced eye movements were of constant velocity up to frequencies of 400 Hz and no deviations were induced at frequencies below 155 Hz. Within this range the means lay close to the straight line calculated by the least-squares estimate.

position of the eyes in the orbit over wide ranges. Within the range of constant-velocity eye movements, there was a linear relationship between amplitude of induced deviation and the frequency of stimulation (Fig. 3). In this range there was also a linear relationship between the maximum

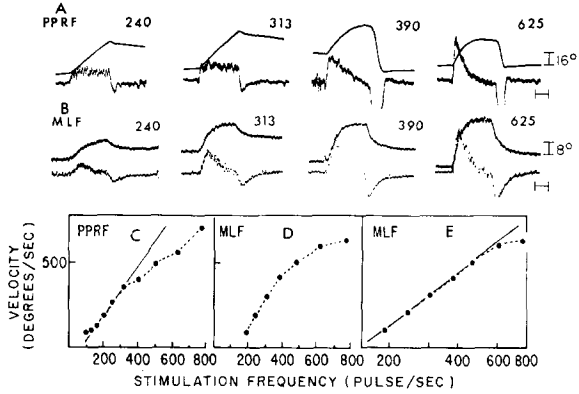

FIG. 4. A, Eye movements induced by right PPRF stimulaiton and B, by left MLF stimulation. The top trace in each series is the DC-EOG recorded across the left eye. The bottom trace is the differentiated EOG. The number above each set of traces is the stimulation frequency. The duration of stimulation is apparent in the velocity trace. Below are graphed mean maximum velocities induced by each frequency of stimulation. About five samples were used to derive each mean. C and D have linear scales and E a logarithmic scale on the abscissa. The ordinates are linear. The linear portion of the curves in C and E are marked by lines hand-drawn through the points. The time base is 100 msec in A and 50 msec in B.

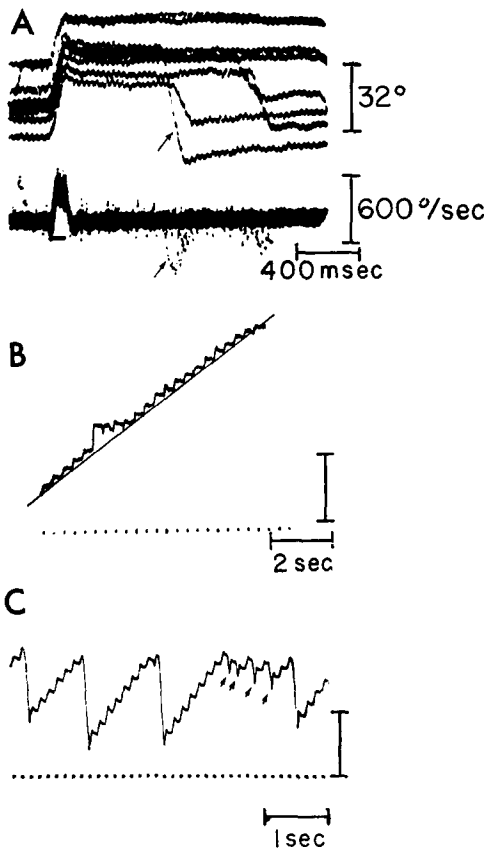

FIG. 5. A, Deviations and positions of fixation induced by right PPRF stimulation. The top traces are the bitemporal DC-EOG and the bottom traces, EOG velocity. The frequency of stimulation was 200 Hz and the duration of stimulation is shown by the horizontal bar under the velocity trace. At the onset of stimulation the eyes moved to the right and remained in the new position for extended periods of time after which spontaneous saccades frequently occurred in the opposite direction. A 30° saccade is marked by the upward arrow in the EOG and the velocity of this saccade by the upward arrow under the velocity trace. Note that the velocity of the induced movements was somewhat less than that of the 30° saccade, but was higher than that of other spontaneous saccades. B, C, Stepwise eye movements induced by right PPRF stimulation at a pulse train repetition rate of 5/sec in B and 10/sec in C. The duration of the pulse trains was 50 msec. The stimulus artifacts are shown under each trace. A straight line was drawn under the trace in B to emphasize the linear progression of the eyes from one side to the other during the induced movements. As the eyes reached lateral gaze in C, saccades which began after the end of the PPRF-induced movement returned the eyes to the opposite side. The arrows show saccades which were interrupted shortly after onset by the next PPRF-induced movement. The vertical bars in B and C represent 22° of deviation.

velocity of the induced movements and the frequency of stimulation (Fig. 4C). The maximum velocity of the movements could increase for stimulation frequencies over 300–400 Hz (Fig. 4C), but the changes were not linear.

The velocities of the movements in Fig. 2D–G varied between 30 and 100°/sec. This is similar to the velocities of pursuit eye movements and slow phases of nystagmus in the monkey (19, 26). Eye movements with velocities in the range of rapid eye movements, i.e., of saccades and quick phases of nystagmus, could also be induced by PPRF stimulation. In Fig. 2B the eyes were moving about 250°/sec and in Fig. 5A between 400 and 500°/sec. The velocity of the induced movements in Fig. 5A was greater than that of small spontaneous saccades which occurred several hundred milliseconds after stimulation, but was somewhat less than that of the larger fast saccade indicated by the upward arrows.

Eye movements in Fig. 2A–H were induced by holding current passage constant and changing stimulation frequency. Presumably the same number of elements were excited at different rates by the stimulating currents. If frequency was kept constant and current passage were changed, then all excited elements should be driven at the same rate, but their number should increase with each increase in the size of the current field. Changes in current field were produced by changing the duration of the stimulating pulses (28). This induced eye movements (Fig. 2I) which were similar to those evoked by changing frequency (Fig 2H). This implies that within limits the slope of constant velocity eye movements could be increased either by stimulating the same number of units at different rates or by increasing the number of elements which were excited.

Eye movements of inconstant velocity were also induced by PPRF stimulation (1) if frequencies or currents were changed during stimulation, (2) as the eyes reached lateral limits of gaze, or (3) if the frequencies of stimulation were above 300 or 400 Hz. An example of the first is shown in Fig. 2J. Sinusoidal eye movements of about 30° were induced at a frequency of about 0.4 Hz by simultaneously raising and lowering the voltage of pulses delivered through two PPRF electrodes, one on the right and one on the left side. Examples of nonlinear movements due to stimulation with higher frequencies are shown in Fig. 4A. Below 300 Hz the induced movements were of constant velocity. Above 313 Hz the deviations were concave, and the velocity fell at a constant rate during stimulation (390 Hz), or at a changing rate (625 Hz). All three types of movements shown in Fig. 4A occur during slow phases of OKN or caloric nystagmus (24, 26).

Comparison of Effects of PPRF and MLF Stimulation. When eye

muscle motor nerves are stimulated with constant frequencies, eye velocities and eye muscle contraction rates quickly reach some maximum value and then fall exponentially (Fig. 8 of Ref. 37, 5, 17, 20). This shows that when the same number of motor units are activated at a constant frequency, the induced deviations are not linear over any appreciable range.

The MLF contains axons which synapse directly on the cell bodies of oculomotor motoneurons (8, 38, 39) and strong adduction of the ipsilateral eye is induced when the MLF is electrically stimulated (7, 9). Ocular deviations induced by MLF stimulation were similar to those induced by VI nerve stimulation. They were concave (Fig. 4B), and their velocities were not constant, even for stimulus intensities just above threshold. As with motor nerve-induced deviations (37), the relationship between the frequency and maximum velocity of the MLF-induced deviations was exponential, being linear on semilogarithmic coordinates (Fig. 4E).

Fixation. When the PPRF stimulus ended, the eyes did not return immediately toward their initial position in the orbit. Instead they remained in the new position of deviation for periods of time which could extend for several seconds, but which were not shorter than several hundred milliseconds (Fig. 5A). Fixation occurred after every PPRF stimulus in the alert animal (Fig. 2A–I; 5A), except when the eyes were fully deviated in lateral gaze or after PPRF stimulation at high frequencies (Fig. 4A, 390 and 625 Hz).

Fixation occurred after fast (Fig. 5A) or slow (Fig. 2C, H) eye movements, and was produced even by brief pulse trains in the alert animal. This made it possible to move the eyes in stepwise fashion from one side of the orbit to the other by giving short trains of pulses repetitively (Fig. 5B, C). Even during relatively large excursions, the stepwise progression was usually linear. In Fig. 5B the eyes moved about 50° over 6 sec. The linear path of the individual steps in Fig. 5B and C indicate that the induced movements were approximately of the same size, and demonstrates that within limits of lateral gaze, the amplitude of the PPRF-induced deviations was not much affected by the position of the eyes in the orbit.

During stimulation in Fig. 5C, spontaneous saccades reset the eyes toward the opposite canthus as they moved far into lateral gaze. These spontaneous saccades were each interrupted by the next PPRF-induced movement. Toward the end of the trace in Fig. 5C, the onset of the return saccades was delayed. Then the amplitude of the return saccades was small because there was an immediate reversal of direction when the next PPRF deviation began (Fig. 5C, upward arrows). This emphasizes the powerful control which the PPRF exerts on the eyes.

Eye movements induced by recurrent pulse trains in the first part of Fig. 5C are similar to eye movements which occur during reading. During

reading there are short saccadic jumps between periods of fixation as the eyes scan across a line. At the end of a line, a larger saccade returns the eyes to the opposite side and the scanning movements begin again.

Characteristics of Eye Muscle Activity Induced by PPRF Stimulation. Eye muscles were strongly activated by PPRF stimuli. Above threshold, each shock to the PPRF induced a correspondng potential change in the ipsilateral lateral rectus and contralateral medial rectus muscles (Fig. 6A). Latency measurements were made on the contralateral medial rectus muscle rather than the ipsilateral lateral rectus because of the possibility of direct activation of abducens nerve fibers. The latency to activation of the contralateral medial rectus muscle was generally about 2.3–3 msec (Fig. 6A). The medial rectus muscle was activated in 1.8–2 msec by MLF stimulation, and the lateral rectus in 0.7–0.9 msec by VI nerve stimulation. Thus, the PPRF-induced activity was 1.6–2 msec longer than the nerve-induced activity, and 0.5–1 msec longer than the MLF-induced potentials. Since only one synapse is interposed between the MLF stimulating electrodes and eye muscle motoneurons (8, 38, 39), it would appear that the pathway from the PPRF contained at least one but not more than two synapses than did the MLF pathway.

Discrete eye muscles potential changes could be induced by PPRF stimulation at rates close to or in excess of the fusion rates of the fastest mus-

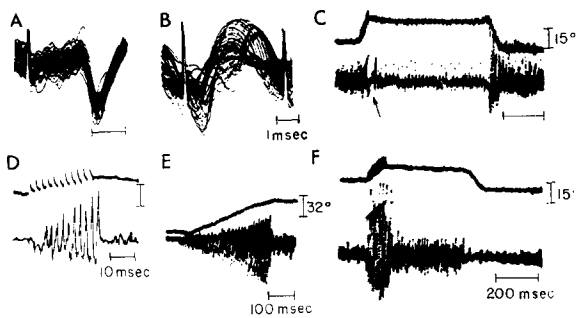

FIG. 6. EMG potential changes induced by right PPRF stimulation in left medial rectus muscle (A, B, D–F) and right medial rectus muscle (C). The top trace in C–F is the EOG. Each PPRF stimulus induced a discrete potential change whether the repetition rate was 1/sec (A), 250/sec (B), or 400/sec (D). There was a steady increase in the amplitude of the induced eye muscle potentials (D, E) as the stimulus continued. Activity in the right medial rectus muscle was inhibited during PPRF stimulation (C, upward arrow). Activity in both the agonist (F) and antagoist (C) during and after movement was similar to that which occurred during spontaneously occurring saccades and periods of fixation. The amplitude and velocity of the PPRF-induced eye movements in C and F were also similar to that of the spontaneous saccades which occurred after fixation. The time base is 1 msec in A and 200 msec in C and F.

cle fibers (Fig. 6B, D)(2, 5, 17, 20). A salient characteristic of eye muscle potentials during constant velocity movements was the progressive increase in amplitude as the stimulus continued (Fig. 6B, D, E). Associated with activation of agonists (Fig. 6F), there was inhibition of activity in antagonists (Fig. 6C, upward arrows).

Fixation produced by PPRF stimuli (Fig. 6C, F) was similar to that which occurs naturally. The level of activity in agonists was higher when the eyes were fixed in the deviated position than before stimulation, but was less in either position of fixation than during the rapid movement itself (Fig. 6F). Conversely, activity in antagonists was strongly inhibited during induced rapid movements and was less during periods of fixation farther into the off-direction of that muscle (Fig. 6C).

Effects of Alertness. When animals were lightly anesthetized with pentobarbital (Fig. 7A) or were drowsy (Fig. 7B), it was still possible to induce eye movements of constant velocity by PPRF stimulation. The slope and amplitude of these deviations was less than those of eye movements induced when animals were alert. Drowsiness or anesthesia had a striking effect on fixation which followed PPRF-induced eye movements. When animals were not alert, fixation was usually inconstant or was abbreviated (Fig. 7C, D).

Eye Movements Induced by Stimulation of Other Parts of the Nervous System. Horizontal eye movements are induced by stimulation of many parts of the central nervous system. These include the vestibular nerves and nuclei (14, 15, 40), the cerebellum (11, 18), the mesencephalic reticular formation (MRF)(6), and the cerebral cortex (18, 34, 41). There are a number of differences between these eye movements and the PPRF-

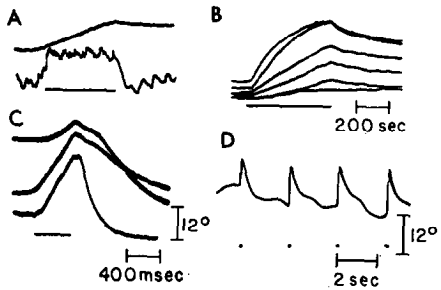

FIG. 7. Eye movements induced by PPRF stimulation when drowsy (B–D) or lightly anesthetized (A). A, Top trace, EOG, second trace, EOG velocity. The constant-velocity eye movements was induced by PPRF stimulation at 400 Hz. The animal had received 10 mg/kg pentobarbital. B, Eye movements induced by PPRF stimulation at frequencies of 100, 150, 200, 250, 400, and 500 from bottom to top, respectively. C, D, When animals were drowsy, the eyes failed to maintain the new position of deviation after the end of stimulation. The time base for A, shown under B, is 40 msec.

induced deviations: (1) Extrapontine stimulation in alert animals generally evokes saccades (Fig. 8A) or nystagmus (Fig. 8 B, C), but not smooth eye movements of constant velocity. Only if animals are drowsy, are deviations usually smooth and continuous (Fig. 8C; 15, 37). (2) PPRF-induced deviations were very regular and were not much affected by eye position. Movements induced from other parts of the nervous system were usually more variable in amplitude (Compare Fig. 8A with Fig. 2D–G) and tended to decrease as the eyes moved farther into lateral gaze (Fig. 8B, C). (3) The latency of eye movements induced by MRF (Fig. 8B, C), cerebellar (Fig. 8A), or cerebral stimulation (34) was generally greater than 10–15 msec and was longer than that of PPRF-induced deviations (Fig. 6A). The shortest latency of potential changes in horizontal eye muscles induced by cerebellar stimulation in cat was 5 msec (11), several milliseconds longer than by PPRF activation. Latencies of eye muscle potential changes from vestibular nerve and PPRF stimulation are roughly similar (2.8–3 msec) (14), and are about 0.5–1 msec longer than the shortest activation from vestibular nucleus stimulation (3, 4, 31, 32). Vestibular nucleus neurons activate and inhibit eye muscle motor neurons monosynaptically via the MLF (23, 31, 38, 39) and vestibular commissural fibers (4, 32).

Discussion

Findings which suggest that neural activity generated by the stimulating pulses was integrated include the following: (1) Step increases in frequency induced ramp-like eye movements over wide ranges of deviation

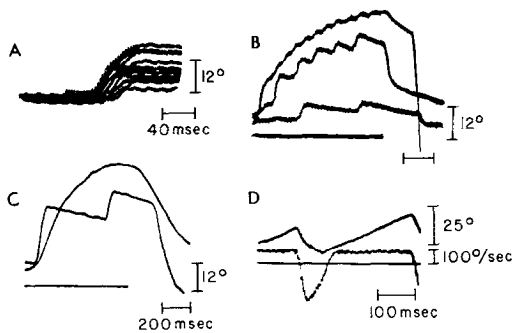

FIG. 8. A, Superimposed traces of saccadic eye movements to the right induced by stimulation of the right fastigial nucleus. Note the variation in the size of the movements induced from the same original eye position. B, Nystagmoid eye movements to right induced by left MRF stimulation. The stimulation frequencies were 100, 150, and 200 from bottom to top, respectively. C, Eye movements to the left induced by left MRF stimulation at a frequency of 200 Hz with the animal alert (bottom trace) and drowsy (top trace). D, Constant velocity slow phases of caloric nystagmus. The time base is 200 msec in B.

and stimulation. Within limits the size and speed of the movements were independent of eye position. (2) For movements of constant velocity, there was a linear relationship between amplitude of deviation and frequency of stimulation, as well as between frequency of stimulation and velocity of induced deviations. (3) At the end of the induced eye movements the new positions of fixation were held for prolonged periods of time in alert animals.

Some integration occurs almost every time there is an electrical, chemical, or mechanical transduction of neural activity. However, it is unusual to find a neural network which mimics a physical integrator so closely. It is particularly surprising that a pair of stimulating electrodes thrust into neural tissue can produce such precise effects in a coordinated system. However, constant velocity eye movements were obtained in all animals that were studied, and we would conclude that the paucisynaptic neural organization which lay between the stimulating electrodes and the eye muscle motoneurons was capable of producing a true integration of afferent impulses. It seems likely that this or a similar integrator is utilized in producing constant velocity eye movements during pursuit movements and slow phases of optokinetic or vestibular nystagmus.

Three categories of oculomotor activity were stimulated or induced when the PPRF was stimulated: positions of fixation, slow eye movements, and rapid eye movements. These data support the hypothesis that slow and rapid eye movements and positions of fixation in the horizontal plane are generated by neurons or neural pathways which lie in the PPRF (9, 10, 13, 21).

The latency of PPRF-induced deviations was shorter than of eye movements induced by stimulation of other parts of the cerebrum or cerebellum. This suggests that the PPRF lies distal to these structures in oculomotor pathways. Findings after lesions are in accord with this. Cerebral lesions cause gaze preference and changes in OKN (6, 25, 30) but do not abolish vestibular nystagmus. Cerebellar lesions also do not severely impair conjugate horizontal gaze (1, 12). In contrast, after unilateral PPRF lesions there is conjugate paralysis of horizontal gaze to the ipsilateral side, and after bilateral PPRF lesions there is total paralysis of horizontal eye movements (6, 21). After PPRF lesions it is not possible to drive the eyes into the ipsilateral hemifield by stimulation of other parts of the nervous system (13, 43). It seems likely that the bulk of visual–oculomotor and cerebellar–oculomotor pathways go through the PPRF before reaching eye muscle motor nuclei.

From the vestibular system, the PPRF is by-passed by direct ascending and commissural pathways to eye muscle motor nuclei, but the PPRF does receive heavy projections from the vestibular nuclei (27, 29, 38). There

are few changes in OKN or spontaneous saccades after vestibular nuclei lesions (16), and even strong vestibular stimuli are unable to drive the eyes into the ipsilateral hemifield after PPRF lesions (13). This shows that the multisynaptic vestibulo-ocular pathways are very powerful and most probably go through the PPRF.

The course and extent of pathways between the PPRF and the abducens and oculomotor nuclei on both sides is not clear at present, but such projections must be relatively direct and profuse. This is suggested by the latency of the PPRF-induced eye muscle activity and by the powerful nature of the control which the PPRF exerts on horizontal eye movers. It is possible that the stimulating electrodes had directly activated axons which end on eye muscle motoneurons. However, there was simultaneous excitation and inhibition after PPRF stimulation (Fig. 6C, F), and an intermediate neuron or neurons is probably required to produce this coordinated pattern. It seems more probable that a neuron or chain of neurons in the PPRF had been directly or synaptically activated by stimulation, and in turn had activated eye muscle motoneurons, but this remains to be proven.

The finding that positions of fixation induced by PPRF stimulation were similar to those which occur naturally is of considerable interest. It suggests that fixation could be induced solely by local activity in the pons. Westheimer (44) has recently emphasized that eye movements and not positions of fixation are represented in most parts of the nervous system. If the postulate that the PPRF represents a supranuclear final common pathway for conjugate horizontal gaze is correct, then it would be sufficient for pre-PPRF structures, such as the cerebral cortex, the vestibular nuclei, or the cerebellum, to produce new positions of fixation merely by transmitting to the PPRF the activity necessary to move the eyes to a new position in the orbit. Once the eyes moved, they would be maintained in this position by the same "hold" mechanism which fixed the eyes after PPRF stimulation. The close relationship of the pontine reticular formation to alerting and rapid eye movements has been noted (22). The present findings suggest that fixation might also be a very sensitive index of drowsiness.

It is possible to make some tentative speculations from the findings about the nature of the activity reaching the PPRF and the eye muscle motor nuclei. Eye movements of constant velocity commonly occur under natural conditions. The data suggest that these deviations could be produced by constant rates of activity in a fixed number of elements in pre-PPRF pathways.

Only two variables could have affected contractions in eye muscles, the frequency of firing in motoneurons and the size of the active population. There is little quantitative information about how neural populations change during excitation, because of the difficulty in measuring the activity

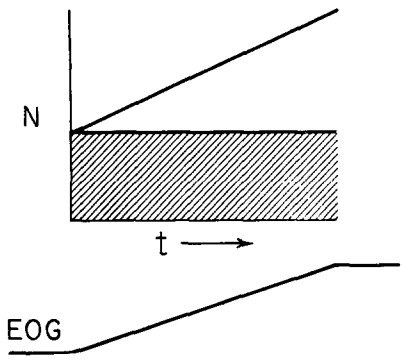

FIG. 9. Diagrammatic representation of how an equivalent population (N) of eye muscle motor units would change to produce a constant velocity eye movement if their firing frequency was constant. The cross-hatched area represents the N active at the beginning of eye movement and t represents time. The EOG is shown below.

of many units simultaneously. Potential changes in activated muscles were largely synchronous during PPRF stimulation (Fig. 6A, B, D). Therefore, it seemed likely that most fibers were being driven at the frequency of stimulation, although some could have been activated at some subharmonic. From this it is inferred that it was mainly the population of activated elements which was altered. Using constants obtained in previous studies on eye muscle activity induced by motor nerve stimulation (37) and assuming all motor units in the eye muscle to be equivalent, eye movements of constant velocity would be produced by a linear increase in the size of the active pool of motoneurons from most eye positions (Fig. 9). However, there are significant differences between individual muscle fibers (2) and the "plant" is also nonlinear (33, 36). For a linear eye movement to be induced by constant rates of activation, it would require that progressively stronger motor units be brought into activity as a movement progressed farther into the on-direction. This has been demonstrated, during slow and rapid eye movements (45), but makes a quantitative evaluation of how the neural population changes during various types of eye movement much more complicated.

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