Electrical Stimulation of the Paramedian Reticular Formation: II. Testing a Gaze Control Hypothesis.

266.3

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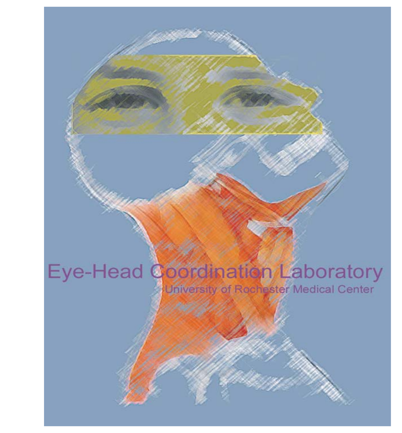

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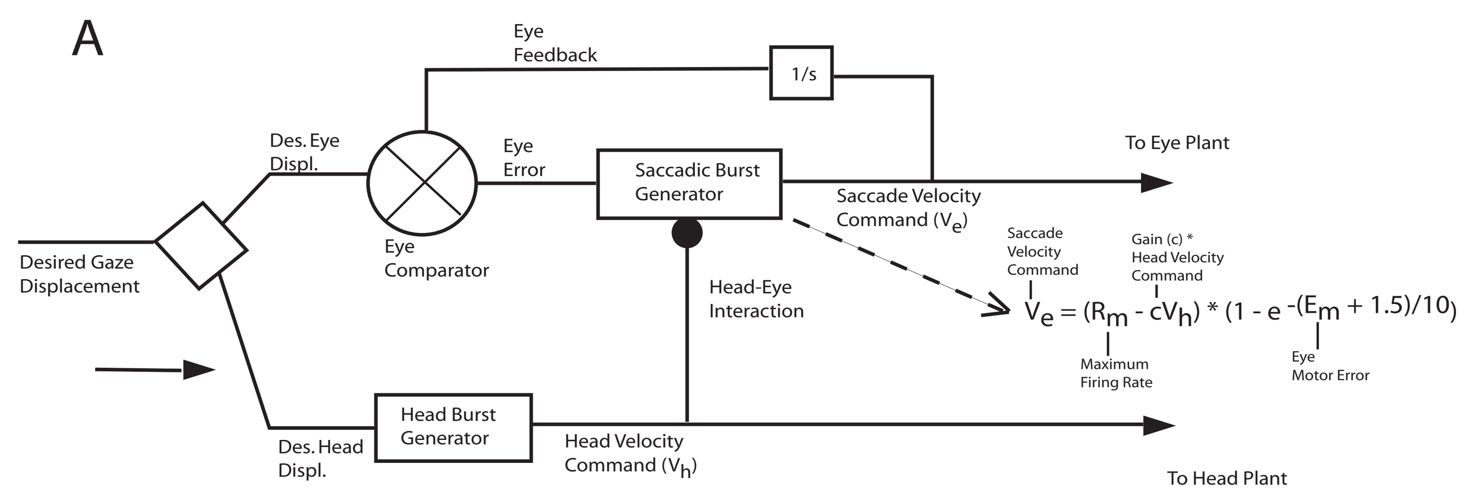
Introduction:

The Nucleus Reticularis Gigantocellularis (NRG) receives direct input from the Superior Colliculus and projects monosynaptically to motor neurons controlling dorsal neck muscles. The NRG is well placed to play a critical role in controlling head movements that make up a component of eye-head orienting movements. This assumption is confirmed by electrical stimulation of the NRG which (in the absence of ongoing movements) can evoke ipsilateral horizontal head rotations (see poster # 266.2).

Here we use electrical stimulation of the NRG during a visually-guided gaze shift in order to test the critical predictions of several gaze control models.

Hypotheses:



Critical Predictions:

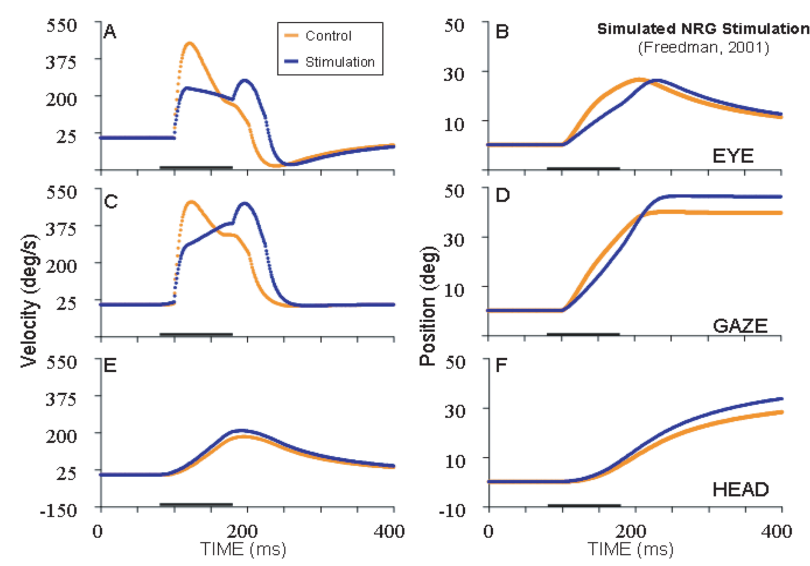
The model outlined in panel A makes two critical predictions based on artificial activation of the head command pathway during an ongoing gaze shift:

1) Saccade kinematics will be altered

- as a result of the hypothesized head-eye interaction (a signal proportional to head velocity reduces the gain of the saccadic burst generator) this hypothesis predicts that stimulation along the ipsilateral head command path will transiently reduce saccade velocity.

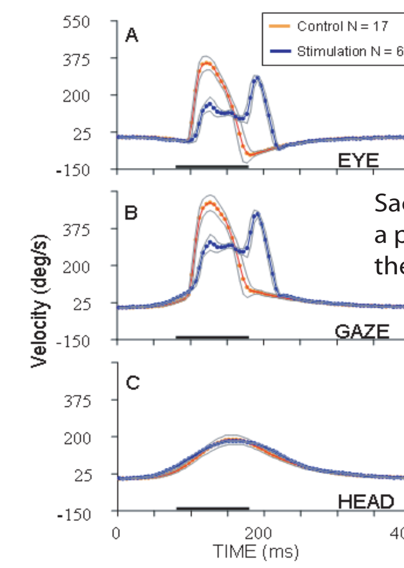
2) Gaze shifts will be HYPERMETRIC

- This hypothesis does not assume that gaze amplitude is under dynamic feedback control. As a result, there will be no compensation for the the increased head contribution resulting from stimulation of the ipsilateral head pathway. The resulting gaze shifts will be hypermetric.



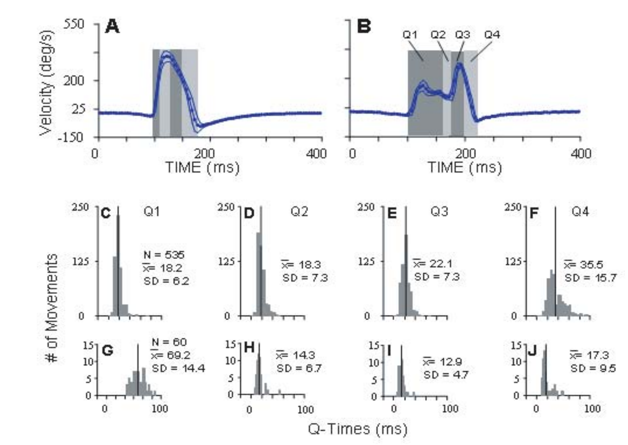
Results:

NRG Stimulation Alters the Kinematics of Ongoing Saccades.

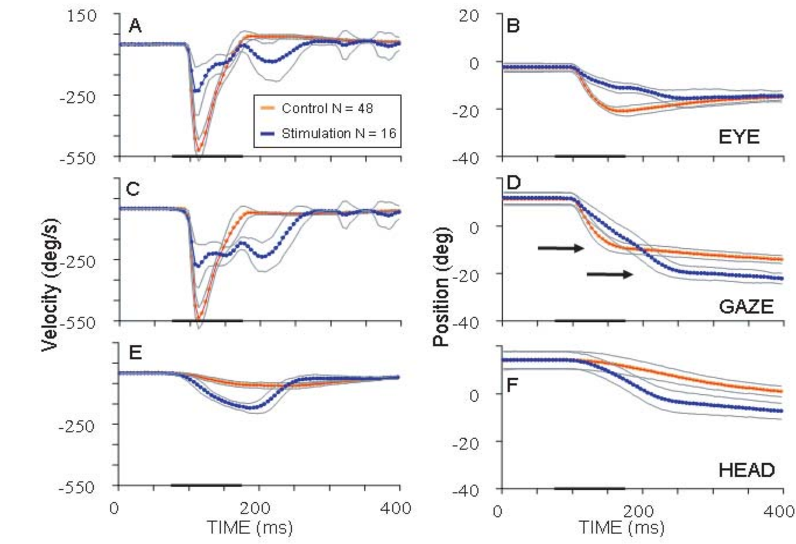


Saccade velocity is reduced during NRG stimulation, and a pronounced re-acceleration of the eyes is associated with the end of the stimulation train.

The change in saccade kinematics is quantified by calculating the time required to complete each 25% of the saccade. This quartile analysis is illustrated below. Data from one NRG stimulation site shows the dramatic changes in saccade kinematics during NRG stimulation. Statistically significant changes in kinematics were observed at all 24 sites at which data were collected - this includes over 75 unique stimulation conditions (site, location of flashed visual target, stimulation frequency, duration and current).

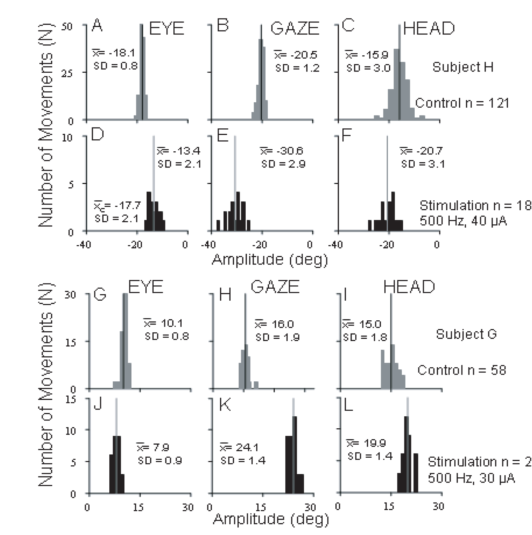


NRG stimulation produces HYPERMETRIC gaze shifts



In this example, the visual target was flashed at a location 20 deg to the left of the fixation location. Gaze shift amplitudes during control trials were 18 deg.

When the ipsilateral NRG was stimulated at the onset of the movement gaze shift amplitudes were much larger - 30 deg.

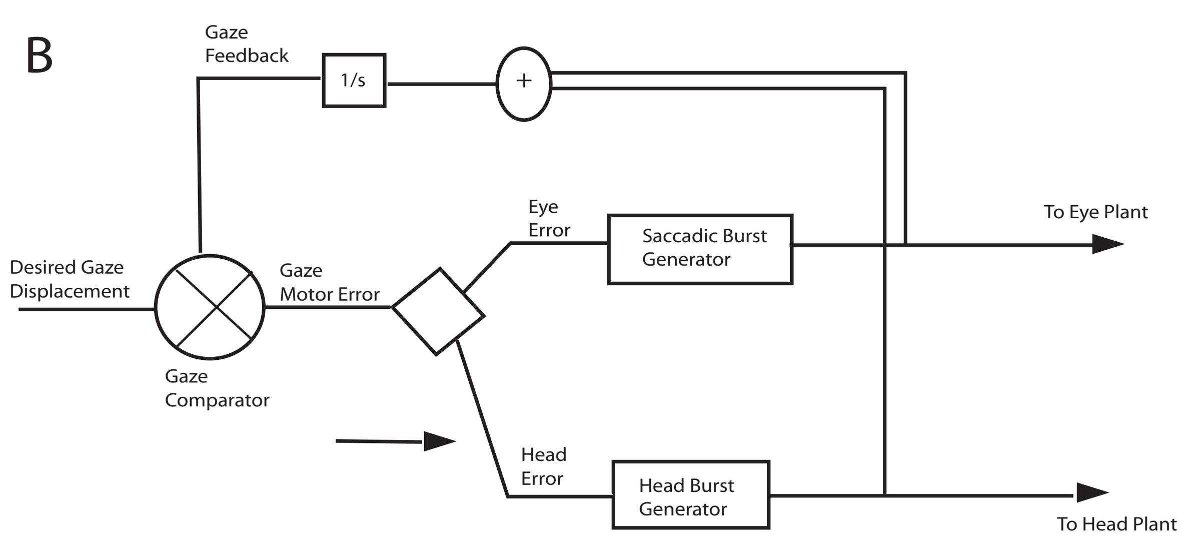


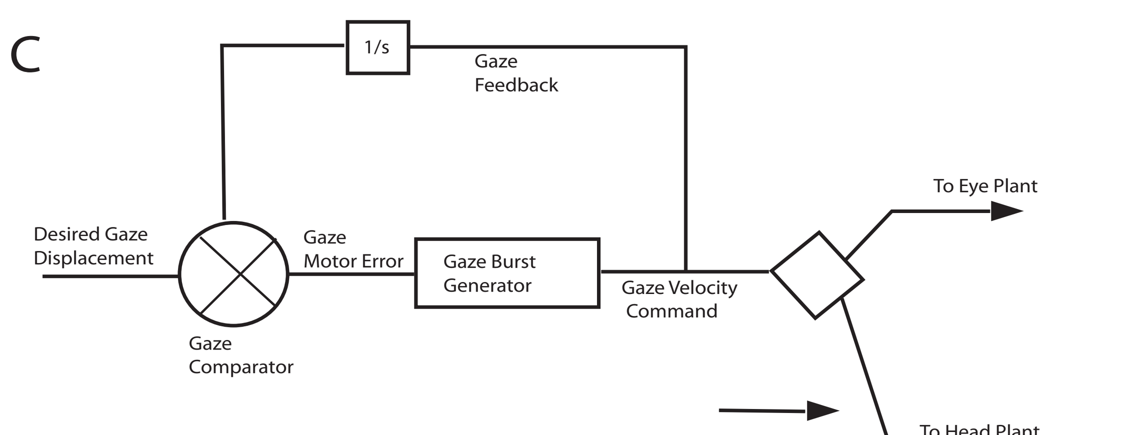
Examples from two stimulation sites comparing the amplitude of control saccades (gray) with the amplitudes of gaze, eye and head components of movements made during NRG stimulation (black).

In both examples gaze is ~150% HYPERMETRIC

Note that eye movement amplitudes are slightly smaller during NRG stimulation than during controls. This could be a result of the vestibulo-ocular reflex working to drive the eyes in the opposite direction. When VOR gain is calculated based on NRG stimulation without an ongoing movement (see Quessy and Freedman, 2002) the expected eye counter-rotation can be estimated for each site. When eye movements are corrected for this effect (X_C), they are not statistically different than control movements.

Similar results were observed for all 75 conditions tested. This includes 24 stimulation sites, 4 target locations, up to 3 stimulation frequencies and 3 stimulation durations.





Alternative Hypotheses:

Panel B illustrates a class of gaze control model which utilizes an estimate of gaze displacement as feedback to control gaze amplitude. In this particular scheme, downstream from the gaze comparator, the gaze signal is decomposed into separate eye and head signals. These separate signals serve as inputs to separate eye and head burst generator circuits. If the head command pathway were electrically stimulated near the onset of a visually-guided movement, this model predicts:

1) no difference on gaze shift amplitude - feedback control will produce normometric gaze shifts despite the artificially increased contribution of the head.

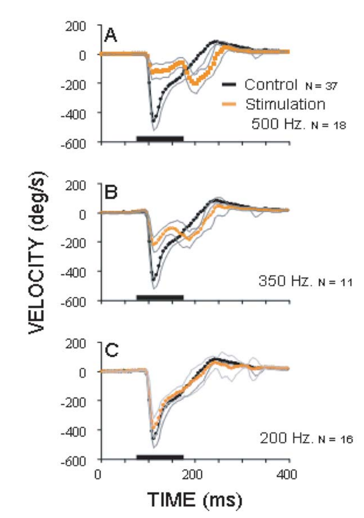
2) no difference in saccade kinematics - there is no explicit head-eye interaction within the dynamic portions of the model and so this model predicts no alteration of saccade kinematics during NRG stimulation.

Panel C presents another alternative gaze control model. In this class of models, the decomposition of a gaze signal occurs only at the level of the eye and head plants: the control signals driving theseplants are identical. Under the test conditions this model predicts:

1) hypermetric gaze shifts - despite the gaze feedback loop, stimulation of the head command pathway in this scheme occurs below the branch point of the feedback loop. As a result this model predicts that there would be no compensation for the added head contribution.

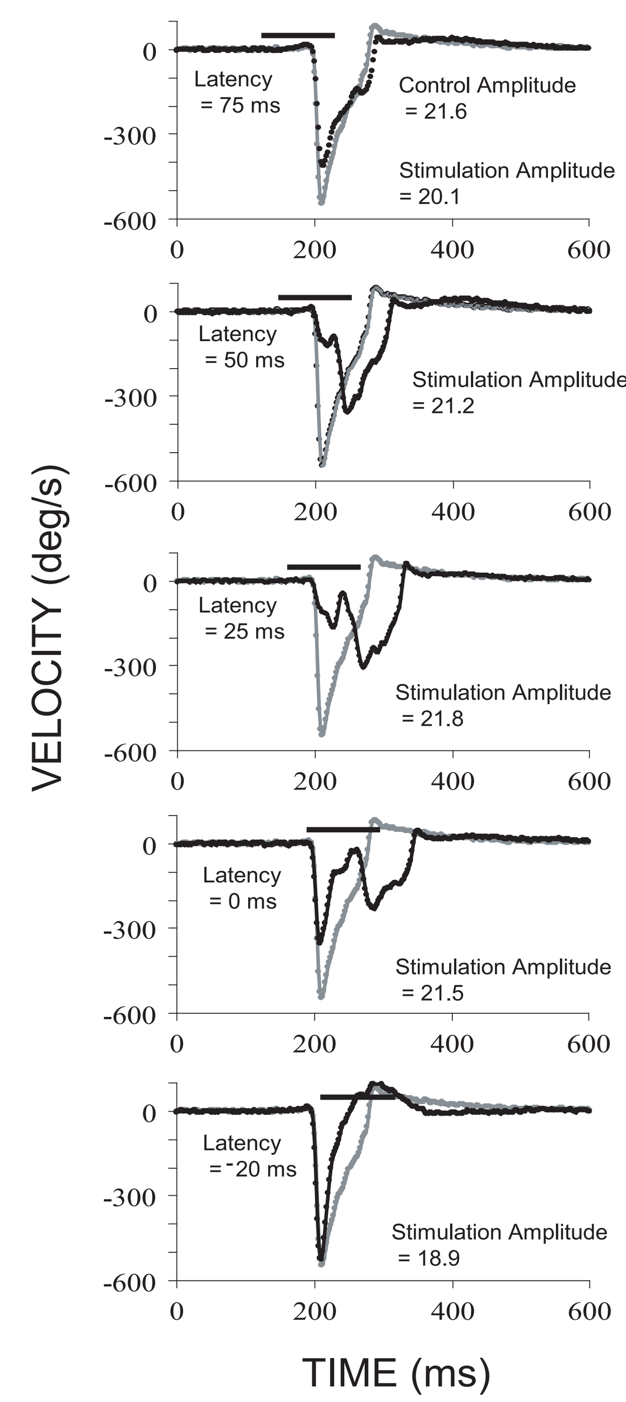
2) saccade kinematics will be unaffected by head pathway activation - there is no interaction between head and eye control circuitry (except perhaps via reflex mechanisms - a caveat which remains equally valid for all of the above hypotheses).

NRG Stimulation effects on Saccade Kinematics Depend upon the frequency of Stimulation

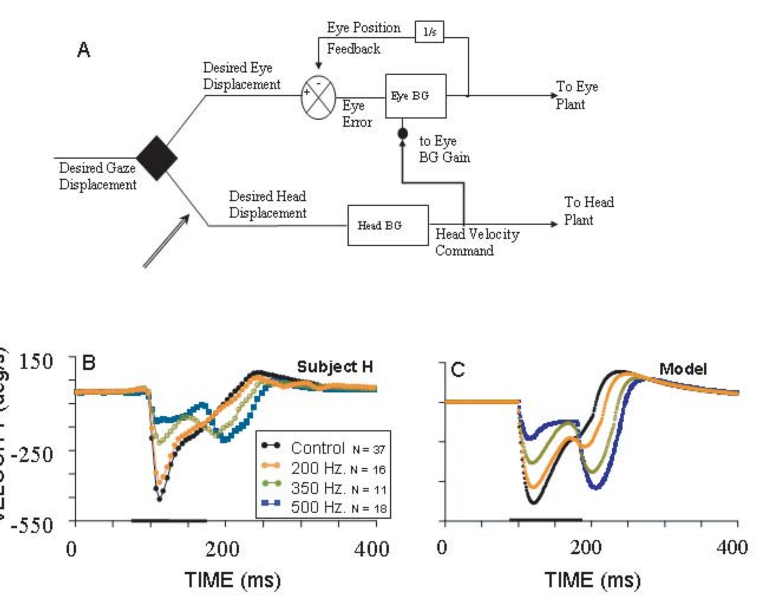


Saccade velocity is plotted as a function of time for control movements (black) and for movements made during NRG stimulation (orange). Three different stimulation frequencies were used at this site. When 500 Hz trains were used, saccade velocity increases to ~ 100 deg/s but no further during the stimulation train. At the end of the train, velocity increased dramatically. During 350 Hz trains, saccade velocity increased but this initial was much lower than peak velocities during control movements. Saccade velocity declined as the stimulation continued, and then a pronounced second velocity peak occurred in association with the end of the stimulation train. Minor, but statistically significant effects on velocity were observed at this site when 200 Hz trains were used.

Saccade Kinematics Depend on the Timing of NRG Stimulation Relative to the Onset of the Saccade:



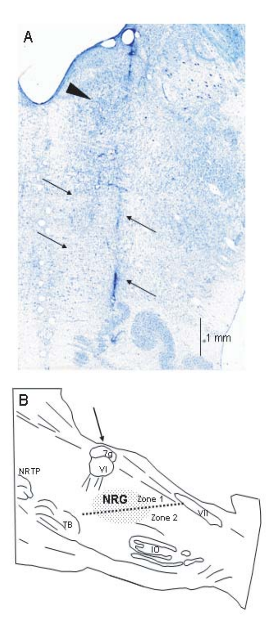
The timing of the onset of the NRG stimulation relative to the onset of the visually-guided movement was a critical factor affecting the kinematics of saccades. In the panels to the left, velocity a control movement is plotted in gray. Superimposed in each panel is the velocity saccade observed during NRG stimulation. In the upper panel stimulation began 75 ms before saccade onset. In subsequent panels the time from stimulation onset to movement onset decreased to 50, 25, 0 ms and finally in the bottom panel stimulation followed movement onset by 20 ms.



Comparison of the effects ofNRG stimulation using different frequencies on the kinematics of ongoing saccades, and the predictions of the Freedman (2001) model in response to simulated electrical stimulation along the head command pathway.

The upper panel shows the critical features of the model. In panel B, mean sacade velocities are plotted as function of time for four sets of movements: control movement - no stimulation (black); NRG stimulation using 200 Hz (orange), 350 Hz (green) and 500 Hz (blue) trains [100 ms and 30 uA].

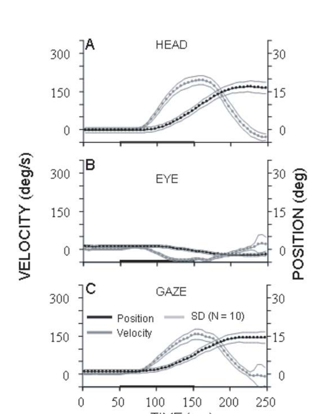
In panel C, simulated control (black) and NRG stimulation at different frequencies are plotted as functions of time.



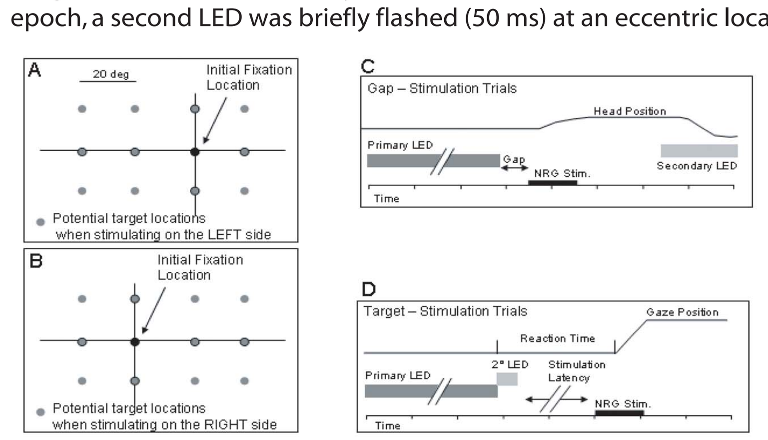
Methods:

The rostral-caudal and dorso-ventral extent of abducens nuclei were identified physiologically based on single unit activity and electrical stimulation in 3 hemispheres of 2 rhesus monkeys. NRG was localized within the region extending 2 mm caudally from the center of the Abd, and from 2.5 - 4 mm ventral to the ventral boundary of the Abd. The panel to the left shows a Nissl stain of the brainstem including an electrode track and lesions made at the end of stimulation in one of the two subjects. Below is a schematic diagram illustrating the region of the NRG.

When the NRG was stimulated (in the absence of ongoing movements) horizontal head movements were evoked. An example of head movements evoked at one site is shown in the panel to the right. The amplitude and velocity of evoked head movements depended on the parameters. In addition the gain of eye counter-rotation (B) during evoked head movements was quite low. Details of head movement metrics and kinematics, and effects of parameters of stimulation are given in the previous poster - Quessy and Freedman (266.2)



Task: In the preceding poster, head movements were evoked by stimulating the NRG just after a n initial fixation LED was extinguished. In that case, no eccentric targets were illuminated and stimulation occurred well before a voluntary movement could be initiated. In order to test the predictions of the alternative gaze control hypotheses outlined above, it was necessary to stimulate near the beginning of a visually-guided gaze shift. Subjects sat in a custom primate chair that restricted movements of the hips and shoulders to < +/- 5 deg, but permitted unrestricted movements of the head. During the "target-stimulation" trials, subjects had to fixate an initial LED for a randomly varied interval. At the end of this epoch, a second LED was briefly flashed (50 ms) at an eccentric location. After a reaction time the subjects initiated a gaze shift to the location of this flashed target. NRG stimulation was triggered by the computer with a latency which was set to approximate the reaction time of the subject. "target-stimulation" trials were randomly interleaved with "gap-stimulation "trials as well as control trials which were identical to the target-stimulation task except the no stimulation was delivered, and movements were made to the remembered locations of the briefly flashed targets.



Summary:

In order to test the differential predictions of several alternative gaze control models, we stimulated in the NRG near the onset of visually-guided, head-unrestrained gaze shifts. Data were collected from two subjects at more than 24 sites using several sets of stimulation parameters and locations for visual targets. At all sites and under all conditions the results consistently showed the following:

1) Electrical stimulation of the NRG altered the kinematics of ongoing visually-guided gaze shifts in a manner consistent with transient reductions in saccade burst generator gain.

2) Gaze shifts were HYPERMETRIC when the ipsilateral NRG was stimulated near the onset of a gaze shift. The degree of hypermetria depended upon the amplitude of the stimulation-induced head movement and the location of the target. Gaze shifts having amplitude 150% larger than control amplitudes were observed

These data are consistent with the predictions of the Freedman (2001) hypothesis which proposed that a copy of the head velocity command reduces the gain of the saccadic burst generator.

In addition, the observation that gaze shifts are hypermetric may be inconsistent with models which assume that gaze amplitude is under feedback control.