Dynamics of Abducens Nucleus Neuron Discharges During Disjunctive Saccades

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Introduction

To optimize visual perception, it is essential for foveated animals to precisely align their two visual axes on targets of interest. Therefore it is not surprising that the oculomotor system of these animals has developed sophisticated mechanisms to ensure the tight control of binocular positioning. More than a century ago, Hering (1868) proposed the elegant “theory of equal innervation” as a conceptual framework for the study of binocular control. When applied to eye movements between two immobile targets, for example, Hering’s theory suggests that two separate neural subsystems should exist that control different aspects of these movements (Fig. 1). On the one hand, a conjugate saccadic subsystem would rapidly yoke the eyes in a given direction to generate movements between targets located at a constant depth but at different horizontal eccentricities. On the other hand, a slow and separate vergence subsystem would rotate the eyes by the same angle but in opposite directions to generate eye movements between targets located at different depths but at constant eccentricities. To date, the neural basis of these two subsystems has been extensively studied in isolation. Under these conditions, neuronal circuitry that are involved in generating conjugate saccades (reviewed in Moschovakis et al. 1996; Scudder et al. 2002) or slow symmetric vergence shifts (reviewed in Gamlin 1999; Mays 1995a) have been well characterized.

However, during our normal daily activities these two subsystems do not always function in isolation: we generate simultaneous conjugate and vergence eye movements anytime we rapidly reorient our eyes between targets located at different eccentricities and depths. During such eye movements, termed disjunctive saccades, the two eyes rotate by different angles and with different trajectories. Accordingly, a question that naturally arises is: does Hering’s theory hold true during disjunctive saccades?

In fact, although Hering’s theory is attractive in its simplicity and in the anatomical and physiological correlates that support it during pure conjugate or vergence movements, it cannot account for a number of observations made during disjunctive saccades. For example, a number of studies have clearly demonstrated that the straightforward linear summation of the conjugate and vergence components of eye motion predicted by the theory of equal innervation does not occur during disjunctive saccades (human: Collewijn et al. 1995, 1997; Enright 1984; Erkelens et al. 1989; Kenyon et al. 1980; Ono et al. 1978; Oohira 1993; Zee et al. 1992; monkey: Maxwell and King 1992). Rather, it was shown that the vergence component of the movement is dramatically accelerated...
when compared with a control pure vergence shift, while the saccadic movement is slowed down in comparison to control conjugate saccades, suggesting central interactions between the conjugate and vergence neural pathways. We have recently furthered the evidence supporting the central coupling between the conjugate and vergence premotor circuitry by describing synchronized oscillations in the conjugate and transient vergence of conjugate saccades and gaze shifts (Sylvestre et al. 2002).

Recent reports have also indicated that some neural structures previously assumed to form the conjugate saccadic system do not carry purely conjugate information during disjunctive saccades. For example, electrical perturbations of the superior colliculus during disjunctive saccades were shown to modify both the conjugate and vergence trajectories (Chaturvedi and VanGisbergen 1999, 2000). Also, premotor saccadic burst neurons that are active only during saccadic eye movements (Sylvestre and Cullen 1999b; Zhou and King 1998) and nuclei prepositus/vestibular neurons (McConville et al. 1994; Zhou and King 1996) were found to preferentially encode the velocity and position of one of the two eyes (i.e., do not encode the conjugate eye position) during disjunctive saccades and disjunctive fixation, respectively. Thus these studies have provided convincing evidence that Hering’s law is violated at the premotor level during disjunctive saccades. It is likely that these neurophysiological observations represent the substrate for the saccadic facilitation of vergence, where the faster vergence velocities are supplied through the saccadic circuitry (see Sylvestre et al. 2002).

Although we are now beginning to better understand the premotor mechanisms of binocular control during disjunctive saccades, surprisingly nothing is known about the actual signals that are generated by extraocular motoneurons to drive these eye movements. To date, all of our knowledge on motor patterns during disjunctive movements was obtained during slow, nonsaccadic eye movements (Gamlin et al. 1989; Gamlin and Mays 1992; Keller 1973; Keller and Robinson 1972; King and Zhou 2000; King et al. 1994; Mays and Porter 1984; Zhou and King 1996, 1998). Most of these studies were conducted on neurons in the abducens nucleus (ABNs), which contains two subpopulations of neurons: motoneurons (AMN) that project to the ipsilateral lateral rectus and internuclear neurons (AIN) that project to medial rectus motoneurons (OMNs) in the contralateral oculomotor nucleus (see Fig. 1; Delgado-Garcia 1986a,b). It was found that nearly all ABNs, including identified AMNs and AINs (Gamlin et al. 1989), encode similar signals during slow vergence eye movements. When the eyes symmetrically converge (i.e., both eyes move nasally), the discharges of ABNs decrease, while they increase during divergence (i.e., both eyes move temporally). In contrast, OMNs that drive the medial rectus muscles increase their discharges when the eyes converge (Gamlin and Mays 1992; King et al. 1994; Mays and Porter 1984). Thus the discharge patterns of AMNs and OMNs during slow disjunctive eye movements are modulated appropriately to drive the eye muscles to which they project, but those of AINs are modulated inappropriately to drive the contralateral eye to which they project. These results, overall, are consistent with Hering’s theory of equal innervation (Mays 1998).

In the present study, our primary objective was to determine whether the signals carried by ABNs during disjunctive saccades are appropriate to drive the motion of the eye to which they project. Since AMNs ultimately drive the extraocular muscles of the ipsilateral eye, the conjugate and vergence-related premotor inputs that they receive during disjunctive saccades might be combined, on a neuron-by-neuron basis, to generate motor signals that are exclusively related to the movements of that eye. Alternatively, single neurons might encode mixed signals that get sorted out at the population level, such that the overall ABN drive to the ipsilateral eye is appropriate. Finally, the convergence of conjugate and vergence-related premotor signals on ABNs might be incomplete or inappropriately, such that the discharge patterns of AMNs would not account entirely for the movements of the ipsilateral eye. In this scheme, additional mechanisms at or downstream to the abducens nucleus, for example co-contraction of the agonist and antagonist muscles, would be required to fine tune the eye movements. A secondary goal of this study was to determine whether ABNs encode conjugate and vergence signals similarly during disjunctive saccades and disjunctive fixation. As we described above, there is evidence that the source of the vergence-related premotor signals differs in these two conditions. Consequently, there are no a priori reasons to assume that, for example, a neuron that encodes conjugate signals during disjunctive saccades will also encode conjugate signals during disjunctive fixation. Some of the results have been reported in abstract form (Sylvestre and Cullen 1999b).

**METHODS**

Two rhesus monkeys (*Macaca mulatta*) were prepared for chronic extracellular recording using the aseptic surgical procedures described...
saccades (–30°) were elicited by stepping the target between (Fuchs and Robinson 1966). Extracellular single unit activity was of both eyes were recorded using the magnetic search coil technique the duration of the experiment. The horizontal and vertical positions 3.5° screen located 55 cm away from the monkey’s eyes (isovergent, a system of two galvanometer controlled mirrors onto a cylindrical horizontal plane will be discussed in the present report. To elicit room for a juice reward. Only eye movements restricted to the Behavioral paradigms elsewhere (Sylvestre and Cullen 1999a). To briefly summarize, a stainless steel post that allowed the complete immobilization of the animal’s head was attached to the animal’s skull with stainless steel screws and dental acrylic. Two stainless steel recording chambers oriented stereotaxically toward the abducens nucleus on the right and left side of the brain stem, respectively, were also anchored in the implant. An eye coil (3 loops of Teflon coated stainless steel wire, 18–19 mm diam) was implanted in each eye (Judge et al. 1980) to allow recordings of binocular eye movements with the magnetic search coil technique (Fuchs and Robinson 1966). All procedures were approved by the McGill University Animal Care Committee and were in compliance with the guidelines of the Canadian Council on Animal Care.

Behavioral paradigms

Both monkeys were trained to follow a target light in a dimly lit room for a juice reward. Only eye movements restricted to the horizontal plane will be discussed in the present report. To elicit conjugate eye movements, a red HeNe laser target was projected via a system of two galvanometer controlled mirrors onto a cylindrical screen located 55 cm away from the monkey’s eyes (isovergent, ≈3.5° convergence). Ipsilateral and contralaterally directed conjugate saccades (≥5–30°) were elicited by stepping the target between horizontal positions in a predictable and an unpredictable sequence. In addition, smooth pursuit eye movements were obtained using a sinusoidally moving target (40°/s peak velocity; 0.5 Hz).

An array of 16 computer-controlled red light emitting diodes (LEDs; with intensities comparable to that of the laser target) were utilized to elicit different types of vergence eye movements. First, symmetric (pure) vergence eye movements were obtained using four LEDs (convergence angles: 17°, 12°, 8°, and 6°) and a laser target that were aligned with the monkey’s mid-sagittal plane. Second, disjunctive saccades were generated using a variety of paradigms. In a first configuration, the target jumped from one of the mid-sagittal LEDs described above to an eccentric laser target (i.e., right or left of the mid-sagittal plane). During this paradigm, monkeys made disjunctive saccades with conjugate components 5–30° in amplitude in both directions and converging or diverging vergence components with amplitudes 4–13°. Disjunctive saccades were also obtained using LEDs that were positioned in a configuration similar to the Müller paradigm (see Ramat et al. 1999 for examples). More specifically, four LEDs were aligned with the left eye at an angle of ≈45° to the right of the mid-sagittal plane, and four other LEDs were aligned with the right eye at an angle of ≈45° to the left of the mid-sagittal plane. This paradigm elicited disjunctive saccades during which the left or the right eye barely moved, respectively. Finally, to enrich the variety of disjunctive eye movements in our data set (and the monkey’s viewing experience), we also performed trials in which any of the LEDs and laser targets were randomly presented.

Data acquisition procedures

During the experiment, the head-restrained monkey was comfortably seated in a primate chair. The monkey’s head was restrained for the duration of the experiment. The horizontal and vertical positions of both eyes were recorded using the magnetic search coil technique (Fuchs and Robinson 1966). Extracellular single unit activity was recorded using enamel insulated tungsten microelectrodes (7–10 MΩ impedance, Frederick Haer; for details, see Sylvestre and Cullen 1999a). Targets, data acquisition, and on-line data displays were controlled using real-time experimentation system (REX), a QNX-based real-time acquisition system (Hayes et al. 1982).

The abducens nucleus was identified as previously described (Sylvestre and Cullen 1999a). Because of the invasiveness of implanting an electrode in the abducens nerve for antidromic activation (Delgado-Garcia et al. 1986a,b) and/or a recording electrode in the lateral rectus for spike triggered averaging (Fuchs et al. 1988), we elected to physiologically identify putative AMNs and AINs using an approach modified from Sylvestre and Cullen (1999a) (see also Broussard et al. 1995). Specifically, Fuchs et al. (1998) found that identified AINs and AMNs formed fairly distinct clusters when their eye velocity sensitivities during sinusoidal smooth pursuit were plotted as a function of their eye position thresholds (see Fig. 8 of Fuchs et al. 1988). In fact, only a small area of their scatter plot showed overlap of the two neuron types. This area of overlap can be easily defined using an upper border \( R = 2.0 - 0.033 \times \text{Threshold} \) and a lower border \( R = 1.4 - 0.033 \times \text{Threshold} \). Here, we obtained a similar scatter plot for the neurons in our sample and used the borders described above to separate putative AMNs from AINs. Neurons that were plotted above the top border and below the lower border were labeled as putative AINs and AMNs, respectively, while those that were plotted between the upper and lower borders could not be identified and were labeled as ABNs.

When a neuron was properly isolated, unit activity, horizontal and vertical positions of the right and left eyes, target position, and table velocity were recorded on a digital audio tape (DAT). The isolation of each unit was re-evaluated off-line during playback. An abducens neuron was considered to be adequately isolated only when individual action potential waveforms could be discriminated using a windowing circuit (BAK) during saccades (e.g., see Fig. 1 in Sylvestre and Cullen 1999a), during fixation and during smooth pursuit. Right eye, left eye, and target position signals were low-pass filtered at 250 Hz (analog 8-pole Bessel filter) and sampled at 1 kHz. Subsequent analysis was performed using custom algorithms (Matlab, The MathWorks).

Coordinate conventions

The eyes are referred to as either ipsilateral or contralateral based on their location relative to the recording site. Positive and negative values indicate eye positions that are to the right and left of the central position (i.e., straight ahead), respectively. Each eye was calibrated separately by having the monkey fixate monocularly (i.e., one eye masked) on a variety of targets at different eccentricities and depths.

The motion of the eyes is also reported in terms of conjugate and vergence coordinates

\[
\text{Conjugate} = \frac{(\text{Left Eye} + \text{Right Eye})}{2} \quad (1a)
\]

\[
\text{Vergence} = (\text{Left Eye} - \text{Right Eye}) \quad (1b)
\]

The left eye and right eye inputs to Eq. 1 could be either position or velocity signals. For the conjugate position signal \( (Eq. 1a) \), positive and negative values correspond to the right and left of the central plane, respectively. For the vergence position signal \( (Eq. 1b) \), larger positive values indicate greater angles of convergence. Note that vergence position signals are always positive, but that vergence velocity signals can be either positive (during convergence) or negative (during divergence).

Analysis of abducens neuron discharges

Before analysis, recorded eye position signals were digitally filtered with a 51st order finite-impulse-response (FIR) filter with a Hamming window, using a cutoff at 125 Hz. The position signals were digitally differentiated to produce eye velocity profiles. Zero-phase forward and reverse digital filtering was employed to prevent phase distortion. A spike density function in which a Gaussian function was convolved with the spike train (SD of 5 ms for saccades, 10 ms for smooth pursuit and fixation) was utilized to represent the neuronal discharges (Cullen and Guitton 1997; Cullen et al. 1996; Sylvestre and Cullen 1999a,b).

Horizontal saccades were defined as having vertical amplitudes
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<10% of their horizontal amplitudes. Conjugate saccades had changes in vergence angles <2.5°, and were directed either ipsilaterally ("ON" direction) or contralaterally ("OFF" direction) to the recording site. Disjunctive saccades during which both eyes moved either in the direction ipsilateral or contralateral to the recording site, and for which one eye moved at least twice more than the other (mean ∆vergence: 6.2 ± 1.3°), were selected for the analysis. Note that for each neuron analyzed, the numbers of converging and diverging disjunctive saccades were matched. Fixation periods were defined as time intervals having peak conjugate and vergence velocities <10°/s. All analyzed fixation intervals had conjugate positions ipsilateral to the neuron’s threshold.

The dynamic eye position and velocity sensitivities of a neuron during saccades were estimating using linear optimization techniques that have been described in detail elsewhere (Sylvestre and Cullen 1999a). The rationale for using this technique as opposed to a more conventional metric-based analysis approach is described in the Appendix. The specific linear regression models utilized in this study are described in RESULTS. The goodness-of-fit of a given model to the data were quantified using the Variance-Adjusted-For (VAF = 1 - [var (mod - fr)/var (fr)], where mod represents the modeled firing rate and fr represents the actual firing rate). For the estimation of linear models (like those utilized in this report), the VAF is mathematically equivalent to the correlation coefficient R². A VAF value of 1 indicates a perfect fit to the data, and a value of 0 indicates a fit that is equivalent to a mean value. Note that the VAF can be utilized for the direct comparison of the goodness-of-fit of model estimations and predictions. The dynamic lead time of individual neurons (tL) was determined during conjugate saccades as described in Sylvestre and Cullen (1999a).

Statistical analysis of model parameters

In this study, the residuals of the multiple regression model utilized for the analysis of the discharge dynamics of ABNs during disjunctive saccades (see model Est-ic-all in RESULTS) were not always normally distributed. Therefore standard statistical tests could not be performed on the parameter estimates because the assumptions inherent to these tests were invalid. To compensate for this limitation, we estimated the probability distribution of the model parameters in Est-ic-all (and also Est-cv-all, see RESULTS) using a nonparametric bootstrap approach. This analysis method is described in Carpenter and Bithell (2000). It is particularly well suited for small samples with unknown probability distributions (Carpenter and Bithell 2000; Press et al. 1997; Richmond et al. 1987).

Briefly, the final model parameters in model Est-ic-all (see RESULTS) were estimated from an original data set of N (usually >40) disjunctive saccades (where ½ were divergent and ½ were convergent; both eyes moved in the "ON" direction). Then 1,999 “new data sets” of N saccades were obtained by randomly re-sampling with replacement from the original data set. Every new data set differed from the original due to saccade repetitions and omissions, and from the other new data sets due to the randomness of the re-sampling process. Preliminary tests conducted on 10 neurons selected randomly indicated that 1,999 re-samplings were sufficient to obtain stable distributions (i.e., yielded the same mean and SD as when using 2,999 or 3,999 re-samplings). The model parameters were then estimated on each of the new data sets.

Following the re-sampling process, 95% confidence intervals were computed for each model parameter (as well as for more complex statistics such as the VAF; Sokal and Rohlf 1995) using the parameter values obtained across the 1999 iterations (Bca method, Carpenter and Bithell 2000). Parameters with 95% confidence intervals that overlapped with zero were not statistically significant and were removed from the model (e.g., see Fig. 4). Parameters with 95% confidence intervals that overlapped with one another were statistically identical and were replaced by conjugate parameters in the model (e.g., see Fig. 7). Note that the parameters were removed one at a time, starting with the parameter(s) that showed the most overlap, and that the parameters of the reduced model were estimated after each removal. This approach prevented removing important parameters whose numerical values were biased by the inappropriate parameters included in the original model.

RESULTS

The discharge dynamics of 50 abducens nucleus neurons (36 from Monkey B, 14 from Monkey J) were analyzed during conjugate and disjunctive saccades. Our analysis approach was as follows: first, we assessed whether we could predict the discharge dynamics of individual neurons during disjunctive saccades based on their discharge properties during conjugate saccades; second, we directly estimated the sensitivity of individual neurons to the velocity and position of either the right/left eyes or the conjugate/vergence traces on the same data set of disjunctive saccades. Based on this analysis, the neurons were sorted in five categories according to the type of eye velocity–related signals that they encoded during disjunctive saccades: monocular with a preference for the ipsilateral eye, monocular with a preference for the contralateral eye, binocular with a preference for the ipsilateral eye, binocular with a preference for the contralateral eye, or conjugate (i.e., equally encoding the motion of both eyes). The eye velocity sensitivity was chosen as the criterion because velocity signals are dominant during saccades (Sylvestre and Cullen 1999a).

In the following sections, we begin by demonstrating our analysis approach on a typical monocular ABN that preferentially encoded movements of the ipsilateral eye. We then contrast the results with those of a typical conjugate ABN. Next, we describe in detail the distribution of our sample of neurons across the categories described above. We also characterize the responses of ABNs during off direction disjunctive saccades. Finally, we compare the discharge properties of individual ABNs during disjunctive saccades and conjugate fixation.

Example monocular ABN with ipsilateral eye preference

We first estimated a neuron’s sensitivity to eye movements during conjugate saccades. Recall that during these movements, the two eyes rotate by the same amplitude and move with highly comparable trajectories. The bias, conjugate eye position, and velocity sensitivities of the neurons were estimated using the following dynamic model, which we have previously shown provides an adequate description of ABN discharge dynamics during conjugate saccades (Sylvestre and Cullen 1999a)

\[ FR(t) = b_{cs} + k_{cs}C(t - t_\alpha) + r_{cs}C(t - t_\alpha) \] (model Est-CS)

where \( FR(t) \) is the neuron’s instantaneous firing rate, \( b_{cs}, k_{cs}, \) and \( r_{cs} \) are constants and represent the neuron’s firing rate at eye position zero, the neuron’s conjugate eye position, and eye velocity sensitivities, respectively (\( c_{cs} \) refers to conjugate saccades), \( C(t) \) and \( C(t) \) are instantaneous conjugate position and velocity, respectively, and \( t_\alpha \) is the neuron’s dynamic lead time.

The model fits obtained for a typical ABN, unit B72_2, are shown in Fig. 2 for two conjugate saccades. This first-order model of eye position provided a good fit of the neuron’s firing
We next determined whether the conjugate model estimated above could be utilized to predict the neuron's activity during disjunctive saccades. During converging disjunctive saccades, the contralateral eye moves more than the ipsilateral eye (e.g., Fig. 3A), while the ipsilateral eye moves more than the contralateral eye during diverging saccades (e.g., Fig. 3B). Note that during these movements, not only do the velocity profiles of the ipsilateral and contralateral eyes peak at different values, but often they also exhibit differences in their dynamics. Therefore a good fit from the conjugate predictions would indicate that the neuron equally encodes the motion of both eyes (i.e., encodes conjugate eye movements).

The first indication that unit B72_2 did not encode conjugate eye movements came from the poor conjugate predictions shown in the top row of Fig. 3 (Pred-CS; VAF\textsubscript{Pred-CS} = 0.45). Such low prediction VAFs were observed for all monocular units (e.g., mean VAF\textsubscript{Pred-CS} = 0.45 ± 0.20, for the monocular ipsilateral eye preference category; see Table 1). Another characteristic of monocular units was that the conjugate predictions tended to overshoot the firing rate when the preferred eye (in
this example the ipsilateral eye) moved less (Fig. 3A), and to undershoot the firing rate when the preferred eye moved more (Fig. 3B). Thus the conjugate-based prediction analysis suggested that unit B72_2 did not encode the conjugate movements of the eyes but rather that it exhibited a marked preference for the movements of the ipsilateral eye.

To directly quantify the sensitivity of individual ABNs during disjunctive saccades, we used the following two approaches. First, we described neuronal discharges as a function of the movements of each eye. This approach was motivated by recent studies of premotor neurons in the saccadic burst generator (Sylvestre and Cullen 1999b; Zhou and King 1998). Second, we utilized a conjugate/vergence based model to describe the activity of the same neurons during the same disjunctive saccades. This model structure follows from the proposal of Hering (1868) and is described in a subsequent section.

When applied to unit B72_2, the ipsilateral/contralateral eye movements-based approach first involved estimating the parameters of the following model on the sample of disjunctive saccades gathered for this neuron

\[
FR(t) = b_{DS} + k_{int}IE(t - \tau) + r_{DS}CE(t - \tau) + \ldots
\]

\[
\ldots r_{DS}tCE(t - \tau) + r_{DS}CE(t - \tau) \quad (\text{model Est-ic-all})
\]

where \(b_{DS}, k_{int}, r_{DS}, \) and \(r_{DS}tCE\) are the bias, ipsilateral eye position, contralateral eye position, ipsilateral eye velocity, and contralateral eye velocity sensitivities of the neuron, respectively (\(DS, I, \) and \(C\) refer to disjunctive saccades, ipsilateral eye, and contralateral eye, respectively; \(ie\) in the model name indicates the ipsilateral/contralateral eye-based approach), and \(IE(t), CE(t), IE(t),\) and \(CE(t)\) are instantaneous ipsilateral and contralateral eye positions and instantaneous ipsilateral and contralateral eye velocities, respectively. This model is the binocular expansion of Est-CS. Model fits obtained using Est-ic-all for unit B72_2 are shown in the second row of Fig. 3, A and B (thick black curve). Clearly, this model fit was far superior to the conjugate model predictions (VAF_{Est-ic-all} = 0.66 vs. VAF_{Pred-CS} = 0.45; mean VAF_{Est-ic-all} = 0.60 \pm 0.15 vs. mean VAF_{Pred-CS} = 0.45 \pm 0.20, for the monocular ipsilateral eye preference category, Table 1). Although this observation strongly supports the idea that unit B72_2 did not encode conjugate eye movements, it does not provide enough information to determine if it solely encoded the movements of one eye or a weighted mixture of both eyes’ movements.

To address this limitation, we estimated 95% confidence intervals for each of the model parameters in Est-ic-all using the bootstrap technique described in METHODS. Figure 4 shows the parameter estimates (vertical arrows) of Est-ic-all for unit B72_2 (left, eye velocity parameters; right, eye position parameters), as well as the bootstrap distributions (histograms) and the 95% confidence intervals (thick horizontal bars) for each parameter. Two important observations can be made from the 95% confidence intervals. First, for both the velocity and the position parameters, the parameter values estimated for the ipsilateral \(r_{DS}\) and \(k_{DS}\) and contralateral \(r_{DS}\) and \(k_{DS}\) eyes were statistically different (i.e., the confidence intervals did not overlap). This confirmed that unit B72_2 did not encode conjugate signals. Second, both the position and velocity parameters for the contralateral eye had confidence intervals that overlapped with zero (i.e., were not statistically different from 0). Therefore these parameters played no significant role in modeling the neuron’s discharge dynamics.

When the position and velocity terms relating to the contralateral eye \(r_{DS}\) and \(k_{DS}\) were removed from Est-ic-all and the remaining model parameters were estimated for this reduced model

\[
FR(t) = b_{DS} + k_{int}IE(t - \tau) + r_{DS}CE(t - \tau) \quad (\text{model Est-ic-red})
\]

the obtained fit was nearly identical to that of the full ipsilateral/contralateral eye-based model (Fig. 3, A and B, 2nd row, Est-ic-red, thick gray curves). Indeed, the goodness-of-fit of this reduced monocular model was the same as that of the full ipsilateral/contralateral eye-based model (VAF_{Est-ic-red} = VAF_{Pred-CS} = 0.66). The model parameters of Est-ic-red for unit B72_2 are shown in Table 2, in the monocular ipsilateral eye category. Note that the parameter values estimated for the “meaningless” eye were appropriately replaced by zeros. Also note that Est-ic-red will not be the same for all neurons (see Example conjugate ABN). Altogether, the prediction-based and estimation-based analyses clearly demonstrated that during disjunctive saccades, unit B72_2 encoded signals related to the motion of the ipsilateral eye only.

**Example conjugate ABN**

Figures 5–7 show the results of the same analysis of a typical conjugate ABN, unit B27_1. This neuron discharged a vigorous burst of action potentials during conjugate saccades that could be well described using Est-CS (Fig. 5; VAF_{Est-CS} = 0.69). However, in marked contrast to unit B72_2, the conjugate predictions of the neuron’s discharge during disjunctive saccades provided a fairly good fit to the data (Fig. 6, A and B, top rows, Pred-CS, thick black curve; VAF_{Pred-CS} = 0.54). This result, which was consistent across the category of conjugate ABNs (mean VAF_{Pred-CS} = 0.51 \pm 0.16; Table 1), provided strong indications that unit B27_1 encoded conjugate
## Parameter estimates during disjunctive saccades (sorted based on eye velocity sensitivities)

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<tr>
<th>Unit</th>
<th>Type</th>
<th>Parameter Estimates (Est&lt;sub&gt;rel&lt;/sub&gt;)</th>
<th>Monocular, ipsilateral eye preference (n = 17)</th>
<th>Binocular, ipsilateral eye preference (n = 10)</th>
<th>Binocular, contralateral eye preference (n = 3)</th>
<th>Conjugate (n = 15)</th>
<th>Population (N = 50)</th>
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* Ratio = [smaller parameter]/[larger parameter]; ipsilateral (i) or contralateral (c) eye. Italics numbers indicate averages ± SDs. Units: b, sp/s; k, (sp/s)/deg; r, (sp/s)/(deg/s). AMN, putative motoneuron; AIN, putative internuclear neuron; ABN, unidentified abducens neuron.
position and velocity signals and hence was equally sensitive to the motion of both eyes.

The estimation of Est-ic-all confirmed this conclusion. First, the goodness-of-fit provided by Est-ic-all was only marginally better than that provided by the conjugate predictions (Fig. 6, A and B, 2nd row, Est-ic-all, thick black curve; VAF_{Est-ic-all} = 0.57; mean VAF_{Est-ic-all} = 0.58 ± 0.11, for the conjugate category; Table 1). Second, as is shown in Fig. 7, for both the eye velocity (left) and eye position (right) sensitivities of the neuron, the estimated parameter values (vertical arrows) were very similar for the ipsilateral and contralateral eyes. Indeed, the bootstrap distributions (histograms) and the 95% confidence intervals (thick horizontal bars) overlapped for the ipsilateral and contralateral eye parameters (i.e., r_{i-DS} = r_{c-DS}, and k_{i-DS} = k_{c-DS}, at 95% confidence), but did not overlap with zero. It can be concluded from these results that unit B27_1 was equally sensitive to the position and velocity of the two eyes, and hence that it encoded conjugate signals during disjunctive saccades.

### Population distributions

The parameter values obtained for each ABN in our sample using Est-ic-red are shown in Table 2. Neurons are grouped in five categories according to the eye velocity-based criteria described below. Average parameter values (±SDs) are included for each category and for the entire sample. To quantify the “ocular-preference” of a given neuron, ratios of ipsilateral position and velocity signals estimated using Est-ic-red were comparable to those estimated during conjugate saccades ($P > 0.5$, paired t-test). Note that in Table 2, the parameter values for neurons with conjugate ocular preferences are represented as their monocular equivalent (see Eq. 2). Thus, when taken together, the prediction-based and estimation-based analyses clearly demonstrated that unit B27_1 encoded conjugate signals during disjunctive saccades.
and contralateral eye velocity (Ratio\textsubscript{vel}) and eye position (Ratio\textsubscript{pos}) parameters were calculated as follows using the parameter values from Table 2 (Est-ic-red)

\[
\text{Ratio} = (\text{smaller parameter value})/(\text{larger parameter value})
\]

To indicate which eye yielded the larger parameter (par.) value, each Ratio value is accompanied by an \(i\) or a \(c\), for the ipsilateral (ipsi.) or contralateral (contra.) eye, respectively.

The Ratio\textsubscript{vel} values were utilized to sort neurons in the categories shown in Tables 1 and 2, and can be interpreted as follows

- Monocular, ipsi. eye preference
  - contra. par. = 0
  - ipsi. par. = 0
- Monocular, contra. eye preference
  - ipsi. par. = 0
- Binocular, ipsi. eye preference
  - ipsi. par. > contra. par.
  - ipsi. par. \# contra. par. \# 0
- Binocular, contra. eye preference
  - contra. par. > ipsi. par.
  - ipsi. par. \# contra. par. \# 0
- Conjugate
  - ipsi. par. = contra. par. \# 0

Hence, monocular unit B72_2 shown in Figs. 2–4 had a Ratio\textsubscript{vel} = 0, while conjugate unit B27_1 shown in Figs. 5–7 had a Ratio\textsubscript{vel} = 1 (note that in this case, the \(i\) or \(c\) character was omitted because both parameters had equal values). This Ratio index was chosen because its interpretation is more intuitive than that of other indexes utilized in previous studies. For example, for the index utilized in the present study, values of 0.1 and 0.5i simply represent ratios of ipsilateral to contralateral eye parameters of 10:1 and 2:1, respectively. On the other hand, the same values of 0.1 and 0.5 for a common index \([\text{ipsi. eye \# contra. eye}] [\text{ipsi. eye \# contra. eye}];\) see for example Zhou and King 1998 \)

represent ratios of ipsilateral to contralateral eye parameters of 1.22:1 and 3:1, respectively.

A graphical summary of the Ratio values is presented in Fig. 8, where the distributions of Ratio\textsubscript{vel} (Fig. 8A) and Ratio\textsubscript{pos} (Fig. 8B) for our sample of neurons are shown. With respect to the eye velocity sensitivity of ABNs during disjunctive saccades, many ABNs in our sample (44%; light and dark red bars, Fig. 8A) exhibited monocular velocity sensitivities (i.e.,...
Ratio_{vel} = 0). Of these monocular ABNs, 73% preferred the ipsilateral eye (light red bars, Fig. 8A). Furthermore, 30% of the ABNs in our sample equally encoded the velocity of both eyes (i.e., conjugate, Ratio_{vel} = 1; blue bar, Fig. 8A). The remaining 26% of ABNs encoded the motion of both eyes (light and dark green bars, Fig. 8A), of which 77% favored the ipsilateral eye (light green bars, Fig. 8A). Only two neurons encoded opposite os directions for the two eyes (Ratio_{vel} < 0).

The distribution of Ratio_{pos} (Fig. 8B) was similar to that of Ratio_{vel}. Most neurons in our sample (70%) exhibited monocular preferences. Of these monocular ABNs, 63% preferred the position of the ipsilateral eye. In addition, 24% of all ABNs tested were equally sensitive to the position of both eyes. Only one neuron had a negative Ratio_{pos}. The main difference between the distributions of Ratio_{pos} and Ratio_{vel} was that slightly more units were binocular with respect to their velocity sensitivity than to their position sensitivity (24% vs. 6%, velocity and position sensitivities, respectively).

We conclude that during disjunctive saccades, our sample of ABNs is dominated by a subpopulation of neurons that monocularly encodes the motion of the ipsilateral eye (i.e., "monocular with ipsilateral eye preference"; Fig. 8) and by a second less pronounced subpopulation that encodes the conjugate motion of the eyes (i.e., "conjugate"; Fig. 8). As a result of this distribution, the average sensitivity to the velocity of the ipsilateral eye for our sample of ABNs was 1.5 times larger than that for the contralateral eye. The average eye position sensitivity of our sample of ABNs to the ipsilateral eye was also 1.5 times larger than that of the contralateral eye.

Coherence of the “preferred eye” for the position and velocity coefficients

For each neuron in our sample, our analysis approach identified a “preferred eye” (defined as the eye that yielded the largest parameter value) for both the position and the velocity sensitivities. Here, we asked whether the preferred eye for the position and velocity sensitivities of ABNs were matched on a neuron-by-neuron basis. To do so, we regrouped our data under three general categories: ipsilateral eye preference category (grouping the “monocular with ipsilateral eye preference” and “binocular with ipsilateral eye preference” cell types; Table 2), contralateral eye preference category (grouping the “monocular with contralateral eye preference” and “binocular with contralateral eye preference” cell types; Table 2), and conjugate category (Table 2). Hence, a total of nine permutations represent all the possible combinations of preferred eyes for the position and velocity sensitivities.

The fraction of neurons that fell within each of the nine possible categories are illustrated in Fig. 8C, where the x and y axes represent the three preferred eye categories for the position and velocity sensitivities, respectively, and the z axis represents the percentage of neurons that fell within each category. As is shown by the black columns, the majority of neurons (58%) exhibited coherence between their preferred eye for the position and velocity sensitivities (i.e., had the same preferred eye). Of those neurons, 62% preferred the ipsilateral eye, 17% preferred the contralateral eye, and 21% were conjugate. With the exception of noncoherent neurons that encoded ipsilateral position/conjugate velocity eye preferences and were equally numerous as those that exhibited conjugate coherence, no trend could be identified for the other categories of noncoherent neurons; they were approximately uniformly distributed over the remaining five combinations of preferred eyes (gray columns). Thus during disjunctive saccades, a majority of ABNs exhibited coherence in their preferred eye for the position and velocity sensitivities.

Testing the alternative conjugate/vergence approach

In our second approach, we utilized a conjugate/vergence based model to describe the activity of the same neurons

\[ FR(t) = b_{2x} + k_{2x} C(t - t_0) + k_{2y} V(t - t_0) + \ldots \]

\[ \ldots r_{2y} C(t - t_0) + r_{2x} V(t - t_0) \] (model Est-ic-all)

where \( c_j \) and \( v_j \) refer to conjugate and vergence-related parameters, respectively, \( c_v \) in the model name indicates the conjugate/vergence based approach, and \( C(t) \), \( V(t) \), \( C(t) \), and \( V(t) \) are instantaneous conjugate and vergence eye positions and velocities, respectively. As for Est-ic-all, we estimated the parameters of this model on our entire data set of neuronal activities and computed bootstrap confidence intervals for all of the parameters. The latter were then used to reduce the model to its simplest form (Est-cv-red; note that this model can vary from neuron to neuron).

In its nonreduced form, Est-cv-all is mathematically equivalent to Est-ic-all. Accordingly, the VAF values obtained with both models were identical on a neuron-by-neuron basis. Furthermore, when the parameters of Est-cv-all were converted to those of Est-ic-all using the following relationships (shown for a neuron recorded to the left of the midline)

\[ k_{1x} = \frac{k_{2x} + k_{2y}}{2}, \quad k_{1y} = \frac{k_{2x} - k_{2y}}{2} \] (2a)

\[ r_{1x} = \frac{r_{2x} + r_{2y}}{2}, \quad r_{1y} = \frac{r_{2x} - r_{2y}}{2} \] (2b)

the parameters obtained with either model were all statistically identical (paired t-tests, \( P > 0.05 \)). However, because Est-ic-all and Est-cv-all are not always equivalent after one or more parameters have been removed and because the parameters in these models can take markedly different numerical values and have an inherent variability (i.e., have confidence intervals with nonnegligible widths), it was not possible to utilize Eq. 2 to derive Est-cv-red from Est-ic-red. Stated differently, we could not assume that if the bootstrap confidence intervals of the ipsilateral and contralateral eye parameters in Est-ic-all overlapped slightly (which we interpreted as conjugacy), the confidence interval of the vergence term in Est-cv-all would automatically overlap with zero. Hence, we properly evaluated Est-cv-red by independently computing bootstrap confidence intervals for the conjugate/vergence based model Est-cv-all on all the neurons in our sample.

Figure 9 shows the results of this conjugate/vergence analysis for our population of neurons. Note that to allow direct comparisons of these results with those described in the previous sections, we processed the parameters of Est-cv-red with Eq. 2 to obtain the equivalent parameter values in ipsilateral/contralateral eye coordinates, and then computed Ratio_{vel} and Ratio_{pos} indexes as described above. As illustrated in Fig. 9 by the axis labels between square brackets, a conjugate unit (ver-
those obtained with Est-cv-red (7 ± 11%). In contrast, for the remaining neurons, the VAF values obtained with Est-cv-red were only slightly larger than those obtained with Est-ic-red (2 ± 2%). Hence, for almost two-thirds of the neurons in our sample, model Est-ic-red provided markedly better goodness-of-fits than model Est-cv-red, while the latter model only provided marginally (if at all) better fits for the remaining neurons. Furthermore, and consistent with these results, the VAF values obtained with Est-ic-red were, on average, only 1% smaller than those obtained with Est-ic-all, while those obtained with Est-cv-red were 5% smaller than those obtained with Est-cv-all [recall that VAF(Est-ic-all) = VAF(Est-cv-all)]. Thus removing conjugate or vergence parameters from Est-cv-all (based on the bootstrap statistics) was far more detrimental to the goodness-of-fit than removing ipsilateral or contralateral eye parameters from Est-ic-all. We conclude that ipsilateral/contralateral eye based models were better suited for our analysis than conjugate/vergence based models.

Responses during off-direction disjunctive saccades

In good agreement with our previous findings (Sylvestre and Cullen 1999a), the majority of ABNs in our sample (82%) were driven into inhibitory cutoff (i.e., “paused”) during all off direction conjugate saccades. Similarly, most ABNs (64%) were also driven into inhibitory cutoff during all off direction disjunctive saccades. Whether the saccade was divergent or convergent did not affect the pausing behavior of these ABNs. Discharge patterns from a representative neuron in this category, unit J66_1, are shown in Fig. 10A during converging and diverging off-direction saccades. For the remaining ABNs, the amplitude of the conjugate movement appeared to be the main determinant of their pausing behaviors, since the neurons’ discharges were comparable during converging and diverging saccades. Of these neurons, the majority (67%) paused completely for disjunctive saccades with conjugate components >10°. In turn, 33% paused only for disjunctive saccades with conjugate amplitudes >20°. Figure 10B shows example disjunctive saccades from a neuron in this latter category (unit B76_1). Note that the neuron clearly paused for large amplitude converging and diverging saccades (right). Also note that, as for all neurons that did not always reach inhibitory cutoff, there was nevertheless a significant decrease in firing rate when the neuron did not pause. Thus the pausing behavior of ABNs is generally similar during conjugate and disjunctive saccades, with the exception that for movements of small amplitudes, slightly more ABNs pause during conjugate saccades.

Comparison of disjunctive saccades and disjunctive fixation

We next addressed whether individual ABNs retain the same preferred eye during disjunctive saccades and disjunctive fixation. For each neuron, we fitted its average firing rate as a function of the average ipsilateral and contralateral eye positions during intervals of disjunctive fixation. We next computed a Ratio_{pos} value for each neuron using the same procedure as defined above for calculating Ratio_{pos} during disjunctive saccades.

Figure 11A shows the distribution of Ratio_{pos} during disjunctive fixation. This distribution was similar to the distribution of Ratio_{pos} observed during disjunctive saccades (compare...
The main difference between the two distributions was that a greater proportion of ABNs encoded the position of both eyes during disjunctive fixation versus disjunctive saccades. As a consequence, during disjunctive fixation, fewer ABNs (48%) encoded the position of a single eye (of which 75% preferred the ipsilateral eye), while a comparable number of ABNs (26%) encoded the conjugate position of the eyes. Thus at the population level, ABNs generally encode the position of the two eyes in a similar manner during disjunctive saccades and disjunctive fixation.

For our sample of ABNs, the average sensitivity to the ipsilateral eye position during disjunctive fixation was 3.1 times larger than that of the contralateral eye. This ratio is larger than that observed during disjunctive saccades (1.5) because the parameter values estimated during fixation were larger than those estimated during disjunctive saccades. This result is consistent with our previous finding that the eye position sensitivities of ABNs decrease as the eye velocity increases (Sylvestre and Cullen 1999a). We attributed this observation to the changes in antagonist/agonist muscle interactions that occur at different eye velocities.

Putative motoneurons versus internuclear neurons

Figure 12 shows the relative distribution of preferred eye position and velocity sensitivities for the putative AMNs (abducens motoneurons) and AINs (internuclear neurons) in our sample. Note that eight neurons (labeled ABN in Table 2) could not be classified as AINs or AMNs using the identification criteria described in METHODS and were excluded from the following analysis. With respect to the eye position sensiti-
In this report, we provide the first characterization of abducens nucleus neuron discharges during disjunctive saccades. The analysis approach that we utilized allowed us, for each neuron, to reduce a generic ipsilateral/contralateral eye-based model of ABNs (AMNs; top row) and abducens internuclear neurons (AINs; bottom row). Conventions for red, blue, and green bars are as in Fig. 8.

Fig. 12. Distribution of eye position (left) and eye velocity (right) sensitivities of putative abducens motoneurons (AMNs; top row) and abducens internuclear neurons (AINs; bottom row). Conventions for red, blue, and green bars are as in Fig. 8.

**DISCUSSION**

In this report, we provide the first characterization of abducens nucleus neuron discharges during disjunctive saccades. The analysis approach that we utilized allowed us, for each neuron, to reduce a generic ipsilateral/contralateral eye-based model of ABNs (AMNs; top row) and abducens internuclear neurons (AINs; bottom row). Conventions for red, blue, and green bars are as in Fig. 8.

![Diagram](image)

During conjugate saccades, there is good evidence that negligible co-contraction occurs (i.e., simultaneous contraction of the agonist and antagonist muscles for a given eye; Fuchs and Luschei 1970; Robinson 1970; Schiller 1970). Therefore, the movement of an abducting eye reflects accurately the motor command carried by AMNs to the lateral rectus of that eye, as the medial rectus only provides passive resistance to the movement. However, we found that during disjunctive saccades the discharge dynamics of ABNs, on a neuron-by-neuron basis, did not exclusively reflect the motion of the ipsilateral eye. The question therefore arises as to whether ABNs, at the population level, encode signals that are sufficient to control the movements of the ipsilateral eye.

To address this question, we performed a simple simulation of the population drive to the lateral rectus of the ipsilateral eye (in this case, the right eye) that would have been generated during a conjugate and a disjunctive saccade. First, we selected a typical conjugate saccade from our data set (Fig. 13A, #1). Next, we utilized the dynamic models estimated on the actual data to reconstruct the firing rate that each neuron in our sample would have had during this saccade (FR, FR, n = 50). To determine whether we could predict the activity of our population of neurons during both conjugate and disjunctive saccades based on the sensitivity of each neuron to ipsilateral and contralateral eye movement, model Est-ic-red (Table 2) was selected for this analysis. The resulting N firing rates were averaged to provide an estimate of the population drive during this particular conjugate saccade (Fig. 13A, #3, solid curve). We then performed a comparable simulation using a hypothetical disjunctive saccade for which the right eye’s motion was identical to that of the conjugate saccade in #1, but the left eye’s motion was markedly reduced (Fig. 13A, #2). If one assumes that the agonist drive alone shapes the motion of the right eye during all saccades, then the two population drives produced in our simulation should be identical since the movement of the right eye was the same for both saccades. Indeed, as is illustrated in #3 of Fig. 13A, the population drives generated in both cases were quite similar. Thus the population drive generated by ABNs can, by itself, account for most of the ipsilateral eye movement during disjunctive saccades. Note that identical conclusions were drawn when we repeated this exercise using the parameter values obtained from the conjugate vergence-based analysis (Est-cv-red).

Although the population drive computed above could provide most of the drive necessary to move the ipsilateral eye, the area under the population drive during the disjunctive saccade was nevertheless approximately 15% smaller than that computed for the conjugate saccade (Fig. 13A, #3, gray shaded area; see legend). This is not surprising given that a significant percentage (66%) of the neurons in our sample were sensitive to the contralateral eye, which in our simulation moved less during the disjunctive saccade. To account for these apparently inappropriate signals at the level of ABNs, it is important to note that a number of simplifications were made.

**Implications for the motor drive to the agonist lateral rectus**

During conjugate saccades, there is good evidence that negligible co-contraction occurs (i.e., simultaneous contraction of the agonist and antagonist muscles for a given eye; Fuchs and Luschei 1970; Robinson 1970; Schiller 1970). Therefore, the movement of an abducting eye reflects accurately the motor command carried by AMNs to the lateral rectus of that eye, as the medial rectus only provides passive resistance to the movement. However, we found that during disjunctive saccades the discharge dynamics of ABNs, on a neuron-by-neuron basis, did not exclusively reflect the motion of the ipsilateral eye. The question therefore arises as to whether ABNs, at the population level, encode signals that are sufficient to control the movements of the ipsilateral eye.

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AMNs, while those that encoded the motion of the contralateral eye or the conjugate eye motion were AINs (Fig. 13B, #1). Based on this scenario, the motor drive sent to the lateral rectus during all saccades would be appropriate to move the ipsilateral eye, without further inputs required to the oculomotor plant. However, when we repeated the simulation shown in Fig. 13A using only the putative AMNs in our sample (see Table 2), our conclusions remained unchanged: the population discharge was still markedly smaller (approximately 18% decrease in total area) during the disjunctive saccade. We also observed experimentally that the physiological properties of putative AMNs and AINs during disjunctive saccades did not differ significantly. The small nonsignificant differences that we measured still could not account for the results of our simulation. For example, more AMNs encoded conjugate signals than AINs (Fig. 12), while the opposite might be expected. Thus, although we cannot completely rule out that the discharge properties of AMNs and AINs are selectively tuned to the motion of the eye to which they project, we argue that this mechanism plays a minor role during disjunctive saccades.

It is also conceivable that a sampling bias is responsible for the apparently inappropriate signals at the level of ABNs described above. Recent studies have identified two morphologically distinct classes of abducens neurons that appear to serve different physiological roles (Büttner-Ennever et al. 2001, 2002). The first class is composed of neurons with large somas distributed throughout the nucleus and that are divided into motoneurons that innervate twitch fibers (Büttner-Ennever et al. 2001) and internuclear neurons that project to the contralateral oculomotor nucleus (Destombes et al. 1979; McCrea et al. 1986; Spencer and Sterling 1977; Steiger and Büttner-Ennever 1978). The discharge properties of these neurons are consistent with them mediating all types of eye movements (Delgado-Garcia et al. 1986a,b; Fuchs et al. 1988; Mays and Porter 1984). In contrast, the second class is formed of small to medium-size motoneurons located in a shell-like structure around the medial edge of the abducens nucleus (Büttner-Ennever et al. 2001, 2002). These peri-abducens motoneurons innervate nontwitch muscle fibers whose function remains ill defined and receive premotor signals from the neural integrator, the smooth pursuit, and the vergence premotor areas, but not from the premotor saccadic burst neurons (Büttner-Ennever et al. 2001, 2002). Thus, given that 1) we were more likely to sample the activity of large neurons with our single unit recording techniques and 2) all of the neurons in our sample discharged in relation to saccadic eye movements, we conclude that our sample contained few if any of the smaller neurons of the nucleus shell. Whether the smaller neurons contribute to offset the observed discrepancy during disjunctive saccades remains to be determined.

Selective weighting of AMNs at the level of the lateral rectus could also be utilized to further “monocularize” the signals carried to this muscle (Fig. 13B, #2). For example, units that better encode the motion of the ipsilateral eye could make more efficient synapses, while units that better encode the movements of the contralateral eye would make weaker synapses. This proposed mechanism is consistent with the results of our simulation, where the population drive of ABNs during the disjunctive saccade was too small to generate the movement of the right eye (Fig. 13A, #3). Selectively increasing the weight of the motoneurons that are better tuned to the move-
ment of the ipsilateral eye could compensate for this deficit. We conclude that the selective weighting of AMN projections is most certainly a predominant mechanism during disjunctive saccades. Another way to increase the population drive during disjunctive saccades would be to have neurons in the abducens nucleus that are more sensitive to the vergence than to the conjugate eye movements. However, our sample of ABNs did not contain any neurons with such properties. In fact, only two neurons in our sample had vergence sensitivities more than one-half their conjugate sensitivities (see asterisk in Fig. 8).

Finally, co-contraction of the medial and lateral recti of a given eye could also occur during disjunctive saccades (Fig. 13B, #3). This mechanism, however, would impede the movement of the eye during the saccade (i.e., it would compete with the agonist muscle in a push-pull manner). As a result, co-contraction would not compensate for the lack of agonist drive illustrated in Fig. 13A, but rather would accentuate it. Moreover, our experimental results suggest that there is negligible co-contraction during most disjunctive saccades (Fig. 10). For example, during saccades, the OMNs that control the medial rectus of the right eye (i.e., the antagonist muscle of that eye) receive strong inputs from the AINs on the left side of the brain stem. Because our analysis demonstrated that virtually all of these left AINs would pause completely during most large amplitude disjunctive saccades to the right (i.e., their off-direction is to the right), we can infer that the majority of OMNs are disfacilitated during these movements, and that minimal co-contraction occurs. This conclusion might differ for smaller amplitude disjunctive saccades, since approximately one-third of ABNs do not pause completely during these movements (e.g., Fig. 10B). As a consequence, OMNs would be less disfacilitated, and the medial rectus of the right eye would actively contract to oppose the drive from the abducens nucleus to the lateral rectus of this same eye. Recall, however, that co-contraction of the medial and lateral recti would be counter-productive to the ongoing eye movement.

**Implications for the motor drive to the agonist medial rectus**

Another implication of our results is that the signals sent by AINs to the OMNs that drive the movement of the contralateral eye (re the recording side) do not encode the monocular position and velocity of that eye. Such an observation has also been made on identifications and velocity of that eye. Such an observation has also been noted (the recording side) do not encode the monocular position and velocity of that eye. Furthermore, our sample of ABNs did not contain any neurons with such properties. In fact, only two neurons in our sample had vergence sensitivities more than one-half their conjugate sensitivities (see asterisk in Fig. 8).

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**Implications for the premotor drive to the abducens nucleus**

During conjugate saccades, most of the premotor drive that is related to the velocity of the eyes originates from the saccadic burst neurons, while the drive related to the position of the eyes comes from neurons in the neural integrator (reviewed by Moschovakis et al. 1996). What remains to be elucidated is the source of the vergence signals carried by ABNs during disjunctive saccades. On the one hand, previous studies have suggested that during disjunctive eye movements, both saccadic burst neurons (Sylvestre and Cullen 1999b; Zhou and King 1998) and neurons in the prepositus hypoglossi/vestibular nuclei (McConvil et al. 1994; Zhou and King 1996) carry signals related to the movements of both eyes, and often to the motion of a single eye. Furthermore, in all of these structures, neurons that preferred either the ipsilateral or the contralateral eye were found. These neural pathways could therefore provide ABNs with drives that are consistent with our finding that a large proportion of ABNs encode signals related to the motion of a single eye. On the other hand, neither the vergence-related neurons near the IIIrd nucleus, nor any other identified pure vergence-related neurons, project to the abducens nucleus (Gamlin 1999). Furthermore, if premotor neurons encoding vergence movements were to drive ABN discharges together with premotor neurons encoding conjugate movements, as proposed by Hering’s theory, then one would expect ABNs with properties ranging from pure conjugate to pure vergence sensitivities to be found. However, although we recorded ABNs that encoded the conjugate movements of the eyes, we never encountered any neuron that solely encoded vergence movements (see Figs. 8 and 11). In light of these results, we propose that the saccadic burst neurons and the neurons in the neural integrator provide the binocular information that is required to generate the discharge patterns that we recorded in the abducens nucleus during disjunctive saccades. Another striking result was that individual ABNs generally encoded the position of the same eye(s) during disjunctive saccades and disjunctive fixation (i.e., exhibited good coherence). In the neural integrator, neurons that encode the position of either eye can be found (McConvil et al. 1994; Zhou and King 1996). Hence, our finding strongly suggests that the eye position-related signal on any given ABN originate from the same premotor neurons in the neural integrator during disjunctive saccades and disjunctive fixation. An interesting implication of this proposal is that premotor neurons in the neural integrator should encode the motion of the same eye during disjunctive saccades and disjunctive fixation. Indeed, preliminary results indicate that prepositus hypoglossi neurons do generally encode the position of the same eye(s) during disjunctive saccades and disjunctive fixation (unpublished observations).

**General conclusions**

The primary objective of this study was to determine whether the signals carried by ABNs during disjunctive sac-
cades are appropriate to drive the motion of the eye to which they project. We found that although individual ABNs can encode the motion of both eyes to various degrees (ranging from monocular with a preference for either eye to conjugate), the population drive of ABNs still accounts for most (approximately 85%) of the movements of the ipsilateral eye. We propose that the selective weighting of the AMN projections to the lateral rectus fine tunes the motion of the ipsilateral eye by compensating for the differences in discharge properties that were observed among individual neurons. The organized tuning of AMNs versus AMNs, or the co-contraction of the medial and lateral recti, likely play minor roles during disjunctive saccades. The second goal of this study was to determine whether ABNs encode conjugate and vergence signals similarly during disjunctive saccades and disjunctive fixation. Indeed, we found that individual ABNs generally encode similar eye position-related signals during these two conditions. This result suggests that the premotor structures responsible for these signals are the same in both conditions.

A P P E N D I X

Classically, saccade-related bursting activity in the brain stem has been characterized using metric-based relationships, like the number of spikes in a burst (NOS) versus the amplitude of the corresponding eye movement (∆E). The primary assumption inherent to such a “NOS-based analysis” is that the NOS is proportional to the ∆E during a saccade

\[ \text{NOS} \propto \Delta E, \text{which implies that } fFR \propto fE, \text{and therefore that } FR \propto E. \]  

However, during saccades, the most simplified description of ABN discharge dynamics is \( FR(t) = b + kE(t) + rE(t) \), and not \( FR(t) = b + rE(t) \) (Sylvestre and Cullen 1999a). It is therefore clear that the assumption described in Eq. A1 is false under these conditions (i.e. \( FR \neq E \)), which invalidates the use of a NOS-based analysis for ABNs during saccades.

To further emphasize the potential risks of using a NOS-based analysis on ABN discharges, we re-analyzed our dataset of disjunctive saccades using the following model

\[ \text{NOS} = b + nE_\Delta E + nE_\Delta CE \]  

where \( \Delta E \) and \( \Delta CE \) are the changes in ipsilateral and contralateral eye positions, respectively. A particularly striking result was obtained with this analysis for our example monocular ABN, unit B72_2 (see Figs. 5–7). It is obvious from the raw data in Fig. 6 (and from the dynamic analysis) that this neuron did not encode the conjugate motion of the eyes. Nevertheless, the NOS-based analysis yielded the conclusion that \( nE_\Delta E \) (at 95% confidence), suggesting that unit B72_2 encoded conjugate eye movements. Similar misleading conclusions were obtained for many other neurons. This example complements that of our previous studies (Cullen and Guittion 1997a,b; Cullen et al. 2001) in demonstrating that NOS-based analyses often yield misleading results.

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