Contribution of the Rostral Fastigial Nucleus to the Control of Orienting Gaze Shifts in the Head-Unrestrained Cat

DENIS PÉLISSON, LAURENT GOFFART, AND ALAIN GUILLAUME
Espace et Action, Institut National de la Santé et de la Recherche Médicale Unité 94, 69500 Bron, France

Pélisson, Denis, Laurent Goffart, and Alain Guillaume. Contribution of the rostral fastigial nucleus to the control of orienting gaze shifts in the head-unrestrained cat. J. Neurophysiol. 80: 1180–1196, 1998. The implication of the caudal part of the fastigial nucleus (cFN) in the control of saccadic shifts of the visual axis is now well established. In contrast a possible involvement of the rostral part of the fastigial nucleus (rFN) remains unknown. In the current study we investigated in the head-unrestrained cat the contribution of the rFN to the control of visually triggered saccadic gaze shifts by measuring the deficits after unilateral muscimol injection in the rFN. A typical gaze dysmetria was observed: gaze saccades directed toward the inactivated side were hypermetric, whereas those with an opposite direction were hypometric. For both movement directions, gaze dysmetria was proportional to target retinal eccentricity and could be described as a modified gain in the translation of visual signals into eye and head motor commands. Correction saccades were triggered when the target remained visible and reduced the gaze fixation error to 2.7 ± 1.3° (mean ± SD) on average. The hypermetria of ipsiversive gaze shifts resulted predominantly from a hypermetric response of the eyes, whereas the hypometria of contraversive gaze shifts resulted from hypometric responses of both eye and head. However, even in this latter case, the eye saccade was more affected than the motion of the head. As a consequence, for both directions of gaze shift the relative contributions of the eye and head to the overall gaze displacement were altered by muscimol injection. This was revealed by a decreased contribution of the head for ipsiversive gaze shifts and an increased head contribution for contraversive movements. These modifications were associated with slight changes in the delay between eye and head movement onsets. Inactivation of the rFN also affected the initiation of eye and head movements. Indeed, the latency of ipsiversive gaze and head movements decreased to 88 and 92% of normal, respectively, whereas the latency of contraversive ones increased to 149 and 145%. The deficits induced by rFN inactivation were then compared with those obtained after muscimol injection in the cFN of the same animals. Several deficits differed according to the site of injection within the fastigial nucleus (tonic orbital eye rotation, hypermetria of ipsiversive gaze shifts and fixation offset, relationship between dysmetria and latency of contraversive gaze shifts, postural deficit). In conclusion, the present study demonstrates that the rFN is involved in the initiation and the control of combined eye-head gaze shifts. In addition our findings support a functional distinction between the rFN and cFN for the control of orienting gaze shifts. This distinction is discussed with respect to the segregated fastigiofugal projections arising from the rFN and cFN.

INTRODUCTION

The cerebellum is classically known to contribute to the control of movement accuracy (for review see Ito 1984; Lewis and Zee 1993; Stein and Glickstein 1992; Thach et al. 1992). Lesions or dysfunctions of the cerebellum lead to a long-lasting dysmetria of movements of the limbs and/or of the eyes. Experiments with the use of anatomic, electrophysiological, and lesion techniques in animals delineated lobules VI–VII of the cerebellar vermis and the caudal part of the underlying fastigial nucleus (cFN) as the critical territories involved in the control of saccadic eye movements (Noda 1991).

Indeed these medioposterior cerebellar areas receive projections from many oculomotor- and visual-related structures in the brain stem (cat: Carpenter and Batton 1982; monkey: Carpenter and Batton 1982; Noda et al. 1990). Purkinje cells in vermal lobules VI and VII project to and monosynaptically inhibit cFN neurons (Courville and Diakiev 1976; Hirai et al. 1982; Noda et al. 1990), which in turn project to several oculomotor-related structures in the brain stem reticular formation (Carpenter and Batton 1982; Homma et al. 1995; Noda et al. 1990), to the superior colliculi (Hirai et al. 1982; May et al. 1990), and to the thalamic nuclei (Katoh and Deura 1993; Kyuhou and Kawagushi 1987; Stériade 1995). Saccade-related activities were recorded in both vermal lobules VI–VII and cFN (cat: Gruart and Delgado-Garcia 1994; monkey: Fuchs et al. 1993; Ohtsuka and Noda 1991b, 1995), and low-intensity electrical microstimulation of either lobules VI–VII or the cFN evokes saccadic eye movements (Cohen et al. 1965; Fujikado and Noda 1987; Noda et al. 1988). Finally, any acute dysfunction of the FN leads to dysmetric saccades in the head-fixed monkey (Ohtsuka et al. 1994; Ohtsuka and Noda 1991a; Robinson et al. 1993; Vilis and Hore 1981). This dysmetria, which resembles that reported in human cerebellar patients, was interpreted as a deficient modulatory action normally exerted by cFN during movement execution on the brain stem saccadic pulse generator (Ohtsuka and Noda 1995; Robinson et al. 1993). We recently investigated the deficits of saccadic shifts of gaze (eye + head) after cFN inactivation in the head-unrestrained cat; the type of gaze dysmetria that was observed led us to propose that cFN also contributes to the processes that specify movement metrics during the period that precedes movement onset (Goffart and Pélisson 1994, 1997, 1998; Goffart et al. 1998).

In comparison with the cFN as the following points suggest, there is no direct evidence for a contribution of the rostral part of the fastigial nucleus (rFN) to the control of saccadic gaze shifts. First, Robinson et al. (1993) mentioned in their cFN inactivation study in the head-fixed monkey that a control muscimol injection performed at an rFN site did not induce any dysmetria. Second, anatomic data suggest a rostrocaudal subdivision of the fastigial nucleus (FN) (Beitz 1982). Indeed, afferent and efferent connections are topographically organized along the rostrocaudal dimension of the nucleus. Corticonuclear projections arising from ver-
nal lobules I–V terminate in the rFN, whereas those arising from lobules VI–VIII terminate in the cFN (Courville and Diakiew 1976). On the efferent side, several oculomotor structures are contacted by neurons of either rFN or cFN. In the monkey the medial part of the nucleus reticularis gigantocellularis, the paramedian and lateral reticular nuclei, and the medial vestibular nucleus are predominantly contacted by rFN neurons (Batton et al. 1977; Noda et al. 1990), and in the cat a predominant rFN input is confirmed for the nucleus reticularis gigantocellularis, the paramedian reticular nucleus (Homma et al. 1995), and the ipsilateral nucleus prepositus hypoglossi (McCrea and Baker 1985). In both species, ascending fastigial projections to the superior colliculi and the thalamic nuclei arise exclusively from its caudal part (Batton et al. 1977; Hirai et al. 1982; Katoh and Deura 1993; Kyuhou and Kawaguchi 1987; May et al. 1990; Sté- ria- de 1995). Projections to the nucleus reticularis tegmenti pontis (Blanks 1988) and to the contralateral nucleus prepositus hypoglossi (McCrea and Baker 1985) also arise predominantly from cFN. However, this parallel organization of fastigial efferents cannot be generalized because some other structures are targeted by neurons located throughout the rostrocaudal extent of the FN. This was shown to be the case for the lateral and inferior vestibular nuclei (Batton et al. 1977; Homma et al. 1995), the nucleus reticularis gigantocellularis (Carpenter and Batton 1982), and the spinal cord (Matsushita and Hosoya 1978). Note that most of these latter fastigial projections terminate in structures that were proposed to contribute to head movement control (Co- wie and Robinson 1994; Drew and Rossignol 1990; Grantyn and Berthoz 1987; Isa and Sasaki 1988; Peterson 1977; Siegel and Tomaszewski 1983; Suzuki et al. 1989). Third, electrophysiological data also suggest a rostrocaudal organization of the FN as neuronal activities recorded in the rFN seem to differ from those recorded in the cFN. Indeed, electrophysiological studies in both cat (Gruart and Delgado- García 1994) and monkey (Büttnner et al. 1991; Ohtsuka and Noda 1991) did not find any saccade-related activity in the rostral half of the FN. Instead, these two studies described neuronal activities related to passive head rotation (see also Gardner and Fuchs 1975).

In summary, anatomic, electrophysiological, and inactivation data globally suggest a role of cFN in the control of head movements or posture. Moreover, some efferent projections (e.g., toward the paramedian reticular nucleus and the nucleus prepositus hypoglossi) suggest an additional role of the rFN in the control of eye movements and/or fixation. However, the distinct patterns of afferent and efferent connections and of electrophysiological properties for rFN and cFN predict qualitative differences in their respective contribution to the control of orienting gaze shifts.

To establish and understand the role of the rFN in the control of saccadic gaze shifts, we investigated in the head-free cat the effects of inactivating this area with the use of local injections of muscimol, on combined eye-head gaze shifts toward visual targets. In this paper, we report the deficits induced by injections in the rFN. In addition, because the experiments were performed under the same conditions as in our previous cFN inactivation study (Goffart and Pélisson 1994, 1997, 1998; Goffart et al. 1998), we compared the deficits related to rFN inactivation with those induced by cFN inactivation. Part of the data was published in abstract form (Pélisson et al. 1997).

**Methods**

The methods used were detailed in our previous papers (Goffart and Pélisson 1997, 1998) and will only be described briefly here.

**Animal preparation**

Three cats were prepared for the experiments under general anesthesia and aseptic conditions following the guidelines from the French Ministry of Agriculture (87/848) and from the European Community (86/609/EEC). Two coils were implanted for the recording of gaze and head position by the search-coil-in-magnetic-field technique (Robinson 1963). A recording chamber was stereotaxically implanted just over the cerebellum. Finally, a U-shaped plastic piece that served as a head-holding device and plugs soldered to the coils leads were fixed to the skull with cement. In one animal (cat L), a second recording chamber allowing access to the superior colliculus was implanted to perform other experiments.

**Experimental setups**

After recovery from surgery, each cat was placed in a hammock that gently restrained the body without constraint on natural movements of the head. The visual target was a spoon filled with a food puree (∼3° of visual angle), fitted with two infrared diodes that permitted continuous recording of its position (Urquizur and Pélisson 1992). The sudden presentation of this food target elicited a saccadic displacement of the cat’s gaze (eye-in-space), which was achieved by coordinated eye and head movements. These saccadic gaze shifts were recorded in two experimental setups. In the first one (‘‘screen setup’’), two animals (cats H and L) had to orient their gaze toward a target presented on either side of an opaque and planar screen situated 41 cm in front of them. Four different

![FIG. 1. Histological reconstruction of injection sites in the fastigial nucleus (FN; cat L). This parasagittal section through the cerebellum shows a marking lesion made at an injection site in the caudal part of the FN (cFN; arrow) and a site of injection in the rostral part of the FN (rFN; outlined circle) reconstructed from the electrolytical lesion. The size of the circle corresponds to the estimated area of muscimol diffusion (see Discussion).](https://i.imgur.com/3Q5Q5Q5.png)
screens were used to elicit gaze shifts toward targets located at \( \pm 15, \pm 19, \pm 27, \text{and } \pm 35^\circ \) with respect to the body sagittal plane. In the second setup ("hemicylindrical set-up"), a hemicylindrical panel was centered (41 cm radius) on the head of the animal (cat I). The target could appear in one of nine holes made in the panel, located at eye level and at eccentricities of 0, \( \pm 12, \pm 24, \pm 36, \text{or } \pm 48^\circ \) with respect to the animal's straight ahead gaze. For both setups, the animals were rewarded directly from the food target after eye- and head-orienting responses were completed. Although a fixation stimulus was usually present (a white knob at the center of the planar screen or an object presented in a hole of the hemicylindrical panel), the animals were not specifically reinforced for accurately fixating before target presentation. Note that the target was predominantly presented (90% of the trials) along the azimuth (i.e., in the horizontal plane that contained the animal’s head), which resulted in a majority of movements with a horizontal or near horizontal direction. For both setups and in about 90% of the trials, the ambient lights were turned off by an electronic shutter (5 ms response time) at the beginning of the gaze shift such that the orienting response was completed in darkness. In these trials, the lights were turned on again 2 s after target presentation.

**Muscimol injections**

The injections sites in rFN were defined with respect to sites in cFN where muscimol injections led to the gaze shifts deficits previously reported (Goffart and Pelisson 1994, 1997, 1998; Goffart et al. 1998). As previously described, the selection of these caudal injection sites was based on stereotaxic data and on the observation of deficits during inactivation (cat I) or on stereotaxic data confirmed electrophysiologically by recording from characteristic saccade-related activities in the alert, head-fixed animals (cats H and L). For each animal, at least one muscimol injection was first performed in each cFN. Then on other days, in all three animals injections were made 2 mm more rostral than these cFN sites on either the left or right side. Cats I and H received one injection in the left rFN (labeled I-L and H-L, respectively) and another in the right rFN (I-R and H-R, respectively), and cat L received one injection in the left rFN (L-L) and two injections in the right rFN (L-R1 and L-R2). In the three animals, injection sites were confirmed by histological reconstruction of electrolytic marks made a few days before killing (Fig. 1) (see also Fig. 1 of Goffart and Pelisson 1998).

**Behavioral tests**

After withdrawing the cannula, spontaneous eye movements were recorded both in the light and in the dark while the animal’s head was restrained. Then the head was freed and visually triggered gaze shifts were recorded within a 20- to 120-min interval after the onset of the injection. Postinjection recording sessions were separated from each other by \( \pm 3 \) days. A control recording session was performed the day preceding each injection to provide normative data about spontaneous eye movements (head fixed) and visually triggered gaze shifts (head unrestrained).

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**Fig. 2.** Relationships between orbital eye deviation and head angular deviation measured at the onset of orienting gaze responses. A: data were collected when the head-unrestrained animal (cat I) in the "hemicylindrical setup" was fixating various locations along the azimuth both before (\( \circ \), \( \circ \), \( \circ \), \( \circ \)) and during inactivation of the rFN (\( \bullet \), \( \bullet \)). Data shown in the other panels were collected in the "screen setup" in cats H (B) and L (C and D). Note that rFN inactivation induced a systematic contralateral rotation of the eyes in the orbit.
Data recording and analysis

Signals from eye and head coils were linearized (per equation in Judge et al. 1980) and scaled on-line by a custom-written computer program. Calibration parameters were established by a two-step procedure: the gain of each coil was measured before implantation by rotating the coil through known angles and after surgery the gain was checked and the DC-offset was measured in vivo by presenting the animal with an attractive target at different known positions in the visual field. The spatial resolution of the measurements of gaze and head angles was ±0.5°. The same computer program produced analog voltages proportional to the horizontal and vertical position of the spoon target relative to the animal's straight ahead gaze (Urquizar and Pélisson 1992). All six calibrated signals representing the horizontal and vertical positions of gaze, head, and target were sampled by a second PC computer (500 Hz, frequency), displayed and stored to disk for off-line analysis (DataWave software, Longmont, CO).

Gaze and head position waveforms were processed by PC software developed in our laboratory that includes conventional filtering (FIR filter, 70-Hz cutoff frequency) and differentiation algorithms and detects each saccadic gaze shift and head movement on the basis of a velocity threshold of 30°/s. Parameters of detected eye, head, and gaze movements were further processed and displayed by Statistica PC-based software (Statsoft). Statistical analyses included Student's t-tests and two-way, repeated measure analyses of variance (ANOVAs) with the experimental conditions (control vs. muscimol) and the movement directions (ipsiversive vs. contraversive) as factors. The effect of muscimol injection on the linear relationship between two parameters (e.g., gaze displacement amplitude vs. retinal error relationship) was tested by comparisons of linear regression parameters. Nonlinear relationships such as those linking head contribution to gaze displacement amplitude and maximum gaze velocity to gaze displacement amplitude (gaze main sequence) were analyzed after computing moving averages. Gaze shifts were sorted into 10° amplitude classes separately for each experimental session and for each movement direction relative to the inactivated rFN; the average value of head contribution (or maximum gaze velocity) was then computed in each class.

RESULTS

Muscimol inactivation of the rFN did not induce any ocular nystagmus in the head-fixed animal, either in light or in darkness. For some experiments a nauseous state and sickness could be observed after the end of the postinjection recording session. When these vegetative effects occurred during the recording session (cat H), recordings were suspended as soon as the first decline of motivation from the animal could be detected.

When the head was unrestrained, it appeared to be translated laterally toward the injected side by ~3 cm (as measured on video recordings) with respect to the body longitudinal axis for cats I and H. The third cat (L) showed either no detectable head translation (experiments L-R1 and L-R2) or a moderate one (1.7 cm in experiment L-L). No noticeable angular deviation or any tilt of the head was ever observed in any animal.

In all three animals the eyes were systematically rotated in the orbits away from the inactivated side. This is illustrated in Fig. 2 by plots of the horizontal angular position of the eyes as a function of the horizontal angular position of the head measured when the animals gazed at different locations. These relationships are shown for data collected before and after muscimol injection in the rFN. In all three cats (cat I tested in the hemicylindrical setup (Fig. 2A), and cats H (Fig. 2B) and L (Fig. 2C, D) tested in the screen setup], the relationships between eye angle and head angle indicate a shift of eye deviation after muscimol inactivation in a direction opposite to the injected side.

When examined outside the containment hammock after the end of the recording session, all three cats showed a severely impaired equilibrium and, because their forelimbs were displaced laterally away from the injected side, they systematically fell toward the injected side.

Gaze dysmetria

Visually triggered gaze shifts were investigated by presenting visual targets at different eccentricities along the azimuth situated at the level of the animals' head (see METHODS). We found that these saccadic gaze shifts were dysmetric after each muscimol injection and that the post-

![Fig. 3](image-url) Time course of horizontal component of gaze shifts (cat I). These responses were elicited by presenting the visual target at the central location (along the animal's sagittal plane) in the hemicylindrical setup while the animal was fixating at various locations along the horizontal meridian. In the control session (A), gaze shifts converged onto the target. However, during inactivation of the left rFN (experiment I-L; B) or left cFN (C), leftward gaze shifts were hypermetric and rightward gaze shifts were hypometric. Whereas the hypometric error was proportional to the target retinal eccentricity in both cases, gaze hypermetric error was either proportional to or independent from target retinal eccentricity during inactivation of the rFN or cFN, respectively. B and C: i: horizontal displacement vectors of the gaze shifts. Note that target position is plotted relative to the head (target azimuth θ'; see text) and thus differs in the rFN inactivation condition (B: 4.18°) compared with the other conditions (A and C: 0°) because of the lateral translation of the head.
saccadic gaze error was largely confined to the horizontal dimension. Gaze shifts directed toward the injected side (ipsiversive responses) were hypermetric, whereas movements toward the opposite side (contraversive responses) were hypometric. To assess the consistency of these observations, for each gaze shift we measured the horizontal and vertical gaze error (horizontal and vertical distance from target to gaze at gaze-shift end). We then computed the average values for each control and muscimol session and separately for ipsiversive and contraversive gaze shifts before submitting the data to a two-way repeated measure ANOVA. The mean value \((n = 7\) experiments) of horizontal gaze error was \(-0.6^\circ\) (muscimol vs. control) for ipsiversive gaze shifts and \(-11.9^\circ\) versus \(-2.7^\circ\) for contraversive gaze shifts, whereas the corresponding values of vertical gaze error were \(-3.1^\circ\) versus \(-1.7^\circ\) and \(-2.6^\circ\) versus \(-1.3^\circ\), respectively. For horizontal gaze error, both the condition factor (control vs. muscimol) and the movement direction factor (ipsiversive vs. contraversive) reached statistical significance \([F(1,6) = 6.3, P < 0.05\) and \(F(1,6) = 68, P < 0.001,\) respectively]. In addition, a highly significant interaction \([F (12,6) = 516, P < 0.001]\) reflected an opposite sign for the error values of contraversive gaze shifts (hypometria) versus ipsiversive gaze shifts (hypermetria). In contrast for vertical gaze error, both factors and their interaction failed to reach statistical significance \([F (1,6) = 4.1, F (1,6) = 0.1,\) and \(F (12,6) = 0.0,\) respectively, all \(P > 0.05\)]. Note that the same two-way repeated measure ANOVA submitted to either the horizontal or vertical target eccentricity failed to reveal any significant effect \((P > 0.05)\), demonstrating that target eccentricities were equally balanced between control and muscimol conditions. Therefore this global analysis revealed specific increases of horizontal gaze errors during rFN inactivation. Thus all analyses presented in the rest of this paper were concentrated on the horizontal component of eye, head, and gaze displacements.

Figure 3 shows the time course of horizontal gaze displacements elicited by the presentation of the visual target straight ahead relative to the animal’s body. These responses were recorded in the hemicylindrical setup while the animal (\(cat I\)) was fixing at various locations along the horizontal meridian. During the control session (Fig. 3A), the final positions of all gaze shifts corresponded approximately to the target location. After muscimol injection in the left rFN (Fig. 3B), leftward gaze shifts were hypermetric and rightward gaze shifts were hypometric. Note that we took into account the lateral translation of the head observed after muscimol injection by plotting the target position relative to gaze shifts and \(\pm 11.9^\circ\) versus \(\pm 2.7^\circ\) for contraversive gaze shifts, whereas the corresponding values of vertical gaze error were \(\pm 3.1^\circ\) versus \(\pm 1.7^\circ\) and \(\pm 2.6^\circ\) versus \(\pm 1.3^\circ\), respectively. For horizontal gaze error, both the condition factor started from a location close to the target (trajectories labeled d and e in Fig. 3B) . When gaze started from a rightward and more eccentric position relative to the target, the subsequent ipsiversive gaze shift overshot the target by an amount that increased with initial gaze deviation \(14\) and \(11^\circ\) gaze error for responses labeled a and b initiated from \(47\) and \(34^\circ\), respectively). When gaze started from a leftward position, the subsequent contraversive gaze shift undershot the target by an amount that increased with initial gaze deviation as well \((\pm 11, \pm 13, \) and \(\pm 25^\circ\) gaze error for trajectories labeled g, h, and i, respectively). Thus whereas the sign of gaze dysmetria was related to the direction of the response with respect to the inactivated side, the size of gaze dysmetria was in both cases proportional to the retinal eccentricity of the target. This pattern of gaze dysmetria was also observed when the target was presented either in the ipsilesional or in the contralesional hemispace defined relative to the body sagittal plane. This is illustrated in Fig. 4 by representative

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**FIG. 4.** Time course of horizontal component of gaze shifts generated by \(cat L\) in the screen setup. Same conventions as in Fig. 3. Gaze shifts recorded during the control session are shown in A, whereas those recorded during inactivation of the right rFN (experiment L-R1) or right cFN are shown in B and C, respectively. No translation of the head was observed during any of these recording sessions. B and C: i: horizontal displacement vectors of the gaze shifts. Note that the pattern of hypermetria for ipsiversive gaze shifts differs between rFN and cFN inactivation experiments.
responses recorded from another animal in the screen setup after muscimol injection in the right rFN (experiment L-R1). No translation of the head was noted during this experiment. Like the previous one, this figure indicates that muscimol injection in the rFN (Fig. 4B) impaired both ipsiversive and contraversive gaze shifts and that in both cases gaze missed the target by an amount that increased with initial gaze deviation.

In the following quantitative analysis, which was performed separately for ipsiversive and contraversive gaze shifts, the responses to all targets were pooled. This analysis is illustrated in Fig. 5 by plotting the amplitude of horizontal gaze displacement as a function of the horizontal target eccentricity relative to gaze (horizontal retinal error) for experiments I-L (Fig. 5A) and L-R1 (Fig. 5B). To compute the horizontal retinal error we took into account the lateral translation of the head observed in cat I during the muscimol recording session by computing the target azimuth (α') relative to the shifted head position: α' = \arctg \left( \frac{\tan \alpha + (k \times \Delta/d)}{k \times \Delta/d \times \cos \alpha} \right)

A

Cat I

Ipsiverive gaze shifts

- Control

- Muscimol

Contraversive gaze shifts

- Control

- Muscimol

B

Cat L

Ipsiverive gaze shifts

- Control

- Muscimol

Contraversive gaze shifts

- Control

- Muscimol

FIG. 5. Relationships between horizontal gaze amplitude and horizontal retinal error (experiments I-L and L-R1). Retinal error, corresponding to target eccentricity with respect to the cat’s visual axis, was corrected to take into account possible lateral translation of the animal’s head during inactivation of the rFN (see text). Positive and negative retinal error values correspond to targets located in the right and left hemifields, respectively. Positive and negative values of gaze amplitude refer to rightward and leftward gaze shifts, respectively. Regression lines are shown for control responses (○) and for responses recorded after muscimol injection in the rFN (●). For the control data, the regression equations were $y = 0.98x + 0.66 \quad (R^2 = 0.94, \text{significant correlation at } P < 0.001)$, $y = 0.96x - 3.01 \quad (R^2 = 0.94, \ P < 0.001)$, $y = 1.05x - 2.29 \quad (R^2 = 0.97, \ P < 0.001)$, and $y = 0.86x - 2.24 \quad (R^2 = 0.98, \ P < 0.001)$ for ipsiversive and contraversive gaze shifts in cats I and L, respectively. For the muscimol data, the regression analysis yielded the following equations: $y = 1.12x - 2.88 \quad (R^2 = 0.94, \ P < 0.001)$, $y = 0.55x - 1.93 \quad (R^2 = 0.76, \ P < 0.001)$, $y = 1.28x - 1.23 \quad (R^2 = 0.98, \ P < 0.001)$, and $y = 0.53x - 3.36 \quad (R^2 = 0.76, \ P < 0.001)$ for ipsiversive and contraversive gaze shifts in cats I and L, respectively.
contraversive gaze shifts (Fig. 5, bottom panels), their amplitudes were systematically reduced after muscimol injection, as seen in the reduced slope of the regression line. For each movement direction the effect of muscimol was tested by comparing the regression parameters obtained in all seven experiments with the control values (Student’s paired t-tests). The results revealed a statistically significant increase in the slope for ipsiversive movements [t (df = 6) = 3.6, P < 0.05] and a statistically significant decrease for contraversive movements [t (6) = 4.6, P < 0.01]. In contrast, the y-intercept did not differ significantly between the control and muscimol sessions either for ipsiversive gaze shifts [t (6) = 0.8, P > 0.05] or for contraversive gaze shifts [t (6) = 1.6, P > 0.05]. This last result allowed us to calculate for each gaze response the ratio of horizontal gaze amplitude to horizontal retinal error. Table 1 reports the mean values of this gain (G\(_{\text{gaze}}\)) obtained for all control and muscimol experiments. An increased gain of ipsiversive gaze shifts and a decreased gain of contraversive gaze shifts were systematically observed after muscimol inactivation of the rFN.

### Accuracy of gaze fixation

The data presented previously indicate that inactivation of the rFN led to consistent inaccuracies of primary saccadic gaze shifts. To further investigate this dysmetria, we tested the capability of the animals to compensate for this postsaccadic gaze error by generating correction saccades toward the visual target. This was done by selecting trials where the ambient light remained on (see METHODS) and by measuring the horizontal position of gaze during the period of sustained fixation that followed the last correction saccade. The results are illustrated in Fig. 6A for two rFN inactivation experiments performed with the hemicylindrical setup. The mean gaze position achieved during fixation of the three tested targets in the postinactivation session was shifted slightly relative to the control data in a direction ipsilateral to the injection side. Indeed, the y-intercept of the regression lines fitting the relationships between gaze and target position moderately increased during inactivation of the right rFN (1.9°) and decreased during inactivation of the left rFN (–3.7°) relative to the control value (–1.2°). These effects were quantified by extracting from each experiment the between-session (muscimol minus control) differences of y-intercept. The sign of the resulting values was related to the side of inactivated rFN, indicating a leftward or a rightward fixation offset for left or right rFN inactivation experiments, respectively. The absolute values of gaze fixation offset varied between experiments (Fig. 6C; rFN data) and on average were moderate (2.7 ± 1.3°, mean ± SD). Data from caudal injections are given for comparison in Fig. 6B and C (see Comparisons with cFN inactivation).

### Eye and head dysmetria

In the head-unrestrained cat, most gaze shifts (except when smaller than ~10°) are accompanied by a fast orienting movement of the head. We found that the amplitude of this head displacement was modified after each muscimol injection and that these changes paralleled the gaze dysmetria. Head movements directed toward the injected side were hypermetric, whereas those directed away from it were strongly hypometric. To quantify these changes in amplitude we calculated the amplitude ratio of horizontal head displacement to horizontal craniocentric error (target eccentricity relative to the initial head position). All trials with a craniocentric error <2° were excluded from analysis. The mean value of this gain (G\(_{\text{head}}\)) is tabulated for all control and muscimol experiments (Table 1). After rFN inactivation, an increased or reduced gain was observed for ipsiversive and contraversive head movements, respectively. These changes reached significance (P < 0.05) for six of seven experiments.

Because modifications in movement metrics related to rFN inactivation were observed for both gaze and head, we tested whether the head contributed to the gaze dysmetria.

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**Table 1. Gains in gaze shifts (G\(_{\text{gaze}}\)) and head movements (G\(_{\text{head}}\)) during inactivation of rostral fastigial nucleus**

<table>
<thead>
<tr>
<th>Experiments</th>
<th>Conditions</th>
<th>G(_{\text{gaze}})</th>
<th>G(_{\text{head}})</th>
<th>G(_{\text{gaze}})</th>
<th>G(_{\text{head}})</th>
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<tbody>
<tr>
<td>I-L</td>
<td>Control</td>
<td>0.94 ± 0.17 (64)*</td>
<td>0.80 ± 0.22 (57)n.s.</td>
<td>0.82 ± 0.15 (59)*</td>
<td>0.82 ± 0.24 (54)*</td>
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<td></td>
<td>Muscimol</td>
<td>1.41 ± 0.43 (73)</td>
<td>0.87 ± 0.34 (65)</td>
<td>0.46 ± 0.13 (78)</td>
<td>0.63 ± 0.28 (56)</td>
</tr>
<tr>
<td>I-R</td>
<td>Control</td>
<td>0.71 ± 0.16 (68)*</td>
<td>0.67 ± 0.23 (47)*</td>
<td>0.75 ± 0.18 (64)*</td>
<td>0.65 ± 0.28 (44)n.s.</td>
</tr>
<tr>
<td></td>
<td>Muscimol</td>
<td>1.13 ± 0.41 (62)</td>
<td>1.29 ± 0.65 (44)</td>
<td>0.57 ± 0.17 (73)</td>
<td>0.56 ± 0.17 (63)</td>
</tr>
<tr>
<td>H-L</td>
<td>Control</td>
<td>1.06 ± 0.06 (44)*</td>
<td>0.98 ± 0.06 (43)†</td>
<td>1.06 ± 0.15 (49)*</td>
<td>0.96 ± 0.10 (47)*</td>
</tr>
<tr>
<td></td>
<td>Muscimol</td>
<td>1.18 ± 0.13 (18)</td>
<td>1.06 ± 0.16 (18)</td>
<td>0.71 ± 0.13 (22)</td>
<td>0.66 ± 0.12 (22)</td>
</tr>
<tr>
<td>H-R</td>
<td>Control</td>
<td>1.06 ± 0.12 (87)*</td>
<td>0.97 ± 0.11 (83)*</td>
<td>1.09 ± 0.14 (104)*</td>
<td>0.96 ± 0.07 (93)*</td>
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<tr>
<td></td>
<td>Muscimol</td>
<td>1.28 ± 0.19 (41)</td>
<td>1.27 ± 0.30 (40)</td>
<td>0.72 ± 0.09 (58)</td>
<td>0.70 ± 0.08 (58)</td>
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<td>L-L</td>
<td>Control</td>
<td>0.89 ± 0.12 (63)*</td>
<td>0.78 ± 0.25 (12)*</td>
<td>0.77 ± 0.17 (97)*</td>
<td>0.77 ± 0.09 (11)*</td>
</tr>
<tr>
<td></td>
<td>Muscimol</td>
<td>1.21 ± 0.37 (104)</td>
<td>1.59 ± 0.78 (55)</td>
<td>0.49 ± 0.13 (54)</td>
<td>0.40 ± 0.14 (41)</td>
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<tr>
<td>L-R1</td>
<td>Control</td>
<td>1.04 ± 0.26 (50)*</td>
<td>0.78 ± 0.19 (37)*</td>
<td>0.90 ± 0.10 (60)*</td>
<td>0.80 ± 0.19 (43)*</td>
</tr>
<tr>
<td></td>
<td>Muscimol</td>
<td>1.33 ± 0.21 (87)</td>
<td>1.46 ± 0.39 (38)</td>
<td>0.62 ± 0.13 (92)</td>
<td>0.67 ± 0.08 (34)</td>
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<tr>
<td>L-R2</td>
<td>Control</td>
<td>0.96 ± 0.17 (25)*</td>
<td>0.78 ± 0.17 (11)†</td>
<td>0.85 ± 0.11 (47)*</td>
<td>0.84 ± 0.13 (27)*</td>
</tr>
<tr>
<td></td>
<td>Muscimol</td>
<td>1.18 ± 0.32 (54)</td>
<td>1.04 ± 0.31 (20)</td>
<td>0.54 ± 0.18 (54)</td>
<td>0.65 ± 0.19 (57)</td>
</tr>
<tr>
<td>Means (N = 7)</td>
<td>Control</td>
<td>0.95 ± 0.13</td>
<td>0.82 ± 0.11</td>
<td>0.89 ± 0.13</td>
<td>0.83 ± 0.11</td>
</tr>
<tr>
<td></td>
<td>Muscimol</td>
<td>1.24 ± 0.10</td>
<td>1.23 ± 0.25</td>
<td>0.59 ± 0.10</td>
<td>0.61 ± 0.10</td>
</tr>
</tbody>
</table>

Values are mean ± SD with the number of observations in parentheses. Gain values were compared with a Student’s t-test between the control and muscimol conditions. The means computed on the seven experiments are indicated in the last row together with the mean percent changes between muscimol and control conditions. * P < 0.001; † P < 0.01; ‡ P < 0.05; n.s., P > 0.05.
The observation that gaze dysmetria increased with larger target eccentricities (see Figs. 3–5) suggests that the head might be responsible for increasing the gaze inaccuracy because head movements are also larger. If this is true the hypermetria of ipsiversive gaze shifts should be related to an increased displacement of the head during the gaze shift relative to control responses, whereas the contralateral hypometria should be related to a reduced head displacement during the gaze shift. To test this possibility, the amplitude of the horizontal head displacement during gaze shifts (or horizontal head contribution) produced before and after muscimol injection in the rFN is plotted as a function of horizontal retinal error in Fig. 7 (bottom panels) for experiments I-L (Fig. 7A) and L-R1 (Fig. 7B). Note that in both the control and the muscimol sessions the horizontal head contribution was negligible for small target eccentricities (<10°) and then increased linearly as a function of retinal error. As expected, the head contribution to the amplitude of ipsiversive gaze shifts increased during rFN inactivation. This modification of head contribution was proportional to target eccentricity, as indicated by an increase of the slope of the regression line fitting the relationship between both parameters (1.0 vs. 0.76 and 1.11 vs. 0.82 for each pair of muscimol and control relationships, respectively).

For contraversive gaze shifts, the head contribution was considerably reduced after rFN inactivation, and again a reduction of the slope of the regression line (0.37 vs. 0.61 and 0.44 vs. 0.66) indicated that this modification was related to target eccentricity. The dysmetria of ipsiversive (or contraversive) gaze shifts could result exclusively from an increased (or decreased) displacement of the head. However, the examination of Fig. 7 (top panels) shows that the eyes also strongly contributed to the dysmetria of gaze shifts, as indicated by the change in the amplitude of the ocular saccade for all target eccentricities in the ipsilateral and contralateral hemifields. To test the statistical significance of these modifications we selected for both cats I and L subsets of gaze shifts elicited by similar horizontal retinal errors in the control and muscimol conditions (mean horizontal retinal error = 30.2°, largest mean difference between control and muscimol conditions = 0.4°). Considering first ipsiversive responses the amplitude of the eye saccade was significantly increased after muscimol injection ($P < 0.001$ in both cats, mean increase = 6°), whereas the amplitude of the head
FIG. 7. Relationships between the horizontal amplitude of the eye saccade (top panels) or of the head contribution (bottom panels) and the horizontal retinal error for experiments I-L (A) and L-R1 (B) (same responses as in Fig. 5). Horizontal head contribution refers to the concurrent head displacement that was produced during gaze shift. Control data (○) and data collected after muscimol injection in the rFN (●) are shown superimposed for ipsiversive (leftward in cat I, rightward in cat L) and contraversive gaze shifts. Equations of linear fits (bottom panels) between the horizontal retinal error (x) and the amplitude of horizontal head contribution (y) are
\[
y = 0.76x - 7.38, \quad y = 0.61x - 6.71, \quad y = 0.82x - 6.46, \quad \text{and} \quad y = 0.66x - 4.74
\]
for ipsiversive and contraversive gaze shifts of cats I and L, respectively, recorded in the control session; and
\[
y = 1.00x - 12.30, \quad y = 0.37x - 4.73, \quad y = 1.11x - 9.02, \quad \text{and} \quad y = 0.44x - 1.64
\]
for ipsiversive and contraversive gaze shifts of cats I and L, respectively, recorded in the muscimol session.

Contribution of the eye saccade and head movement to the amplitude of gaze shifts

The saccadic component of the eye and the contribution of the head to the gaze shift are illustrated in Fig. 8 for the same experiments as in Figs. 5 and 7. We first consider the gaze shifts directed toward the injected side. For those ipsiversive gaze shifts exceeding 15° in amplitude, muscimol injection in the rFN led to an increased amplitude of the saccade of the eye in the orbit (Fig. 8, top panels). Consequently, the amplitude of the head contribution decreased slightly (P < 0.05 and P > 0.05 in cats I and L, respectively, mean decrease = 4°). For gaze shifts away from the injected side, an opposite pattern of modifications was observed. For contraversive gaze shifts larger than 10° in amplitude, muscimol injection in the rFN led to an increased amplitude of the eye saccade (Fig. 8, bottom panels). As described previously in relation to Fig. 7, we tested the statistical significance of these modifications on a subset of gaze shifts that achieved a comparable amplitude in the muscimol and control conditions (mean horizontal gaze displacement = 30.9°, largest mean difference between control and muscimol conditions = 0.6°). We found that the amplitude of the eye saccade significantly increased after muscimol injection (P < 0.001 in both cats, mean increase = 3.3°), whereas the amplitude of the head contribution decreased slightly (P > 0.05 and P < 0.05 in cats I and L, respectively, mean decrease = 3.1°). For gaze shifts away from the injected side, an opposite pattern of modifications was observed. For contraversive gaze shifts larger than ~10° the amplitude of the eye saccade (Fig. 8, top panels) tended to be reduced after muscimol injection, whereas the amplitude of the head component increased (Fig. 8, bottom panels). Again, comparisons between subsets of gaze shifts with matched amplitudes (mean horizontal gaze displacement = 29.1°, largest mean difference between control and muscimol condi-
GAZE SHIFTS DURING INACTIVATION OF rFN

FIG. 8. Relationships between the horizontal amplitude of the eye saccade or head contribution and the horizontal gaze displacement. Relationships linking eye saccade and head contribution to gaze-shift amplitude are plotted in top and bottom panels, respectively, for the movements recorded in experiments I-L (A) and L-R1 (B) (same responses as in Figs. 5 and 7).

The consistency of these observations was tested by a global analysis performed on the seven experiments (see METHODS). For each experimental session and each movement direction relative to the inactivated rFN, gaze shifts were sorted into 10° amplitude classes, and the amplitude of the horizontal head contribution was averaged within each class. Next, for each class the mean head contribution calculated in the control condition was subtracted from that calculated in the muscimol session. For the sake of comparison similar calculations were performed on data collected in the same animals during inactivation of the cFN (see Comparisons with cFN inactivation). The resulting data are shown in Fig. 9. Although the scatter of the data is substantial, the contribution of the head during inactivation increased on average for contraversive gaze shifts and decreased for ipsiversive gaze shifts. This resulted in a regression with a quite small, although statistically significant, slope for inactivation of either rFN (slope = −0.074, R² = 0.41, P < 0.001) or cFN (slope = −0.048, R² = 0.12, P < 0.01).

Eye and head latency

To investigate the effect of rFN inactivation on the initiation of eye and head movements, we measured the latency of gaze (or eye) and head movements from the time of target presentation. Figure 10 summarizes for all seven experiments the median latency computed separately for ipsiversive and contraversive movements. Considering first gaze

FIG. 9. Between-session differences (muscimol minus control) of head contribution computed in each 10° class of gaze-shift amplitude. Mean data from all 7 rFN inactivation experiments are shown by closed circles, and cFN data are shown for comparison (open circles). Negative and positive values of gaze-shift amplitude correspond to ipsiversive and contraversive responses, respectively. See text for regression analyses. Ipsi, ipsiversive; contra, contraversive.
FIG. 10. Summary of rFN inactivation effects on the latency of gaze shifts and head movements (all experiments). Median latencies of gaze shifts (A and B) and of head movements (C and D) recorded during the control sessions are shown by hatched columns; those recorded during the rFN inactivation sessions are shown by filled columns. Error bar represents the upper quartile value. Ipsiversive movements are shown in A and C; contraversive movements are shown in B and D. Latencies observed after each muscimol injection were compared with corresponding control data with the use of the Mann-Whitney U test (n.s., difference not statistically significant; * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$).

Latency data (Fig. 10, A and B), the time to initiate contraversive gaze shifts significantly increased after rFN inactivation for all seven experiments (mean change = 121 ms). In contrast, the time to initiate ipsiversive gaze shifts was shortened by 26 ms on the average: a statistically significant decrease was observed in five experiments and a slight but significant increase was observed in the remaining two experiments (cat H). These changes in gaze latency were associated with parallel changes in the latency of head movements (Fig. 10, C and D). In addition, the average modifications of head latency (increase of 110 ms and decrease of 16 ms for contraversive and ipsiversive movements, respectively) were comparable with those of gaze latency.

In most experiments, the above changes in head contribution to ipsiversive and contraversive gaze displacements were not associated with significant ($P > 0.05$) changes in the delay between the onset of gaze movement and the onset of head movement (gaze minus head latency). However, a significant trend emerged across all seven experiments: on average the eyes started earlier relative to the head for ipsiversive gaze shifts [average difference = 12.8 ms, Student’s paired test: $t(6) = 2.7, P < 0.05$] and later for contraversive gaze shifts [average difference = 8.4 ms, $t(6) = 2.5, P < 0.05$].

### Interaction between latency and metrics of gaze shifts

In previous sections we showed that inactivation of the rFN consistently modified both the accuracy and the latency of visually triggered gaze shifts. We consider now whether these changes in the metrics and in the initiation of gaze shifts were related to each other. To this aim we investigated the relationship between the gain (horizontal gaze amplitude/horizontal retinal error ratio) and the latency of gaze shifts separately for ipsiversive and contraversive responses. Examples of such relationships are presented in Fig. 11 for experiment L-R1. Two observations can be made. First, the effect of rFN inactivation on gaze gain is seen as a shift of the muscimol data toward higher or lower gain values for ipsiversive and contraversive gaze shifts, respectively. Second, a regression analysis of the relationship between the latency and gain of gaze shifts did not reach a statistically significant level (see equations in the legend to Fig. 11). The same regression analysis performed for all experiments revealed a statistically significant negative correlation only for some experimental sessions: 4 of 14 for ipsiversive movements (2 control and 2 pharmacological sessions) and 6 of 14 for contraversive movements (3 control and 3 pharmacological sessions). There was no statistically significant
regression in all other cases. Therefore it appears that on average rFN inactivation modified independently the gain and the latency of gaze shifts.

Gaze main sequence relationships

The dynamic characteristics of the gaze shifts were examined for each experiment. In Fig. 12, the maximum gaze velocity versus amplitude relationships are plotted for experiments I-L (Fig. 12A) and L-R1 (Fig. 12B; same data as in Figs. 5, 7, and 8). A slight slowing of ipsiversive gaze movements was noticed. This reduced velocity was especially apparent for large responses, i.e., with amplitude reaching 40°. For contraversive gaze shifts, a reduction of speed was also observed for some responses.

Gaze main sequences were then analyzed quantitatively. First, we computed moving averages as described in METHODS: the averaged value of maximum gaze velocity was computed within each class of gaze displacement amplitude.

![FIG. 12. Main sequence relationships in experiments I-L (A) and L-R1 (B) (same responses as in Figs. 5, 7, and 8). Maximum velocity of each saccadic gaze shift plotted vs. respective amplitude of horizontal displacement. Open circles, data from the control session; filled circles, data recorded during muscimol inactivation. C: summary of gaze maximum velocity changes during rFN inactivation (all experiments). The between-condition (muscimol minus control) difference of gaze vectorial maximum velocity is plotted against gaze-shift amplitude for several 10° amplitude classes (negative values correspond to muscimol-induced reductions in gaze velocity). Each set of empty circles connected by thin lines corresponds to a single experiment relationship, and the overall relationship (all 7 experiments pooled) is shown by filled triangles linked by a thick line. Note that data points in each amplitude bin were computed with a minimum number of 3 control and 3 rFN inactivated gaze shifts. Negative and positive amplitude values correspond to ipsiversive and contraversive responses, respectively.](https://www.jneurosci.org/content/19/13/5504/F12.large.jpg)

FIG. 11. Relationships between gain and latency of gaze shifts recorded before (○) and after muscimol injection (●) in the right rFN of cat L (experiment L-R1). Equations of regression lines in A (ipsiversive gaze shifts) are $y = -0.206 \times 10^{-3}x + 1.1$ and $y = -0.047 \times 10^{-3}x + 1.3$ for control and muscimol data (both nonsignificant at 0.05 level); equations of regression lines in B (contraversive gaze shifts) are $y = -0.043 \times 10^{-3}x + 0.9$ and $y = -0.161 \times 10^{-3}x + 0.68$ for control and muscimol data (both nonsignificant at 0.05 level).
of maximum gaze velocity to decrease during rFN inactivation. As previously reported in [Stu-initiation and gaze-shift metrics. As previously reported in interpretation of our findings first requires considering the lim-

These differences are plotted in Fig. 12 as a function of gaze-shift amplitude (bin centers). Besides a large variability among the seven experiments (note that the largest velocity reductions were observed for the 2 experiments performed in cat H), the grand means computed over all experiments were negative for all but one bin, indicating a tendency of maximum gaze velocity to decrease during rFN inactivation. Then, for each of the three bins providing enough data (10, 20, and 30°), the averaged maximum gaze velocity was submitted to a two-way repeated measure ANOVA with the experimental conditions (control vs. muscimol) and the movement directions (ipsiversive vs. contraversive) as factors. In all three ANOVAs, both factors and their interaction failed to reach statistical significance ($P > 0.05$). In summary, given the large between-experiment variability, the trend of a reduced velocity during inactivation of the rFN did not reach statistical significance within the amplitude range tested (5–35°).

Comparisons with cFN inactivation

In this last section we compare the deficits found in the current study with the deficits induced by inactivation of the cFN. To this aim we selected from a pool of previously published cFN inactivation experiments (Goffart and Pelisson 1997, 1998; Goffart et al. 1998) seven experiments that are directly comparable—with regard to experimental subjects, inactivated side, and amount of muscimol injected—with rFN experiments reported in this article.

Inactivation of either rFN or cFN led to hypermetric ipsiversive gaze shifts and hypometric contraversive gaze shifts. Whereas the contraversive hypometria was very similar for both inactivated sites within the FN, the ipsiversive hypermetria was qualitatively different between the cFN and rFN experiments and was related to either a bias or an increased gain, respectively (compare Figs. 3B and 4B with Figs. 3C and 4C). This difference was confirmed by a larger change of the $y$-intercept of the gaze amplitude versus retinal error relationship (Fig. 5) during cFN inactivation than that during rFN inactivation [8.5 ± 2.5° vs. 2.8 ± 2.6°, Student’s paired $t$-test, $t (6) = 4.3$, $P < 0.01$]. A second difference that distinguished rostral from caudal inactivation was related to the fixation of a permanently visible target. Indeed, a large ipsilesional gaze fixation offset was systematically observed after inactivation of the cFN (Fig. 6B) (for details see Goffart and Pélisson 1998). In addition, as shown in Fig. 6, gaze fixation errors observed during inactivation of the cFN (5.8 ± 1.5°) were larger than those observed during inactivation of the rFN (2.7 ± 1.3°) [paired $t$-test, $t (6) = 4.9$, $P < 0.01$]. A third difference between rostral and caudal inactivation concerned the relationship between gaze-shift initiation and gaze-shift metrics. As previously reported (Goffart and Pélisson 1997), the gain of contraversive gaze shifts decreased as the latency increased after muscimol injection in the cFN, whereas no consistent effect of rFN inactivation on gain vs. latency relationships was noted.

The following last three comparisons between the effect of cFN or rFN inactivation revealed either no or very slight differences. First, it was found that the modifications in gaze latency did not depend on the site of inactivation within the FN. Second, regarding gaze-shift dynamic, in both cases inactivation led to a moderate decrease of gaze velocity that failed to reach statistical significance in the 5–35° tested range of gaze-shift amplitude. Third, regarding eye-head coordination, we found a quite moderate change in head contribution to the gaze shift when either the cFN (Goffart et al. 1988) or rFN was inactivated. This change tended to be larger in the latter case, as indicated by a statistically significant steeper slope in the relationship shown in Fig. 9 [Student’s comparison of slopes: $t (93) = 2.07$, $P < 0.05$].

Discussion

The results show for the first time that the rostral FN contributes to the control of combined eye-head gaze shifts. We found that unilateral injections of muscimol in the rFN consistently led to the following specific oculomotor and cephalomotor deficits. First, the eyes were rotated in the orbit away from the injected side. Second, the coordinated movements of eye and head toward a visual target became asymmetric such that the resulting gaze saccade missed the target. Ipsiversive movements of eye, head, and gaze were hypermetric, whereas contraversive movements were hypometric. Third, modifications in the contribution of the head to the gaze displacement were also observed: the contribution of the head decreased for ipsiversive gaze shifts and increased for contraversive gaze shifts. In both cases these slight modifications in eye-head coordination were related to a more pronounced asymmetry of the eye in the orbit than of the head on the trunk. Fourth, rFN inactivation also modified the latency of gaze (or eye) and head movements: the time to initiate gaze and head movements toward a target presented in the ipsilesional visual field decreased in five of seven cases, whereas it always increased for a target presented in the contralesional field. Finally, inactivation of the rFN seemed to reduce the speed of large amplitude movements (>35°), but the amount of data available for these large movements was too small to establish statistically the consistency of this trend.

In the following discussion we will first argue that these deficits cannot be accounted for by the diffusion of muscimol to nearby areas and discuss the possible contribution of the rFN to gaze-shift control. Then we will discuss the differences and similarities between the effects of rFN inactivation versus cFN inactivation on gaze shifts in relation to electrophysiological and anatomic data from the literature. This discussion will illustrate a rostrocaudal organization of the FN in controlling the initiation and the accuracy of saccadic gaze shifts.

Implication of the rFN in the control of combined eye-head gaze shifts

Interpreting our findings first requires considering the limits of the inactivation method. Indeed, it could be argued that the deficits observed after each injection are the results of muscimol diffusion toward neurons located outside the rFN and involved in gaze control. However, we believe this possibility is unlikely for the following reasons. First, the deficits reported in this paper were observed as soon as
the postinjection recordings started (i.e., ~15–20 min after the onset of muscimol injection) and remained stable for the whole duration of the recording session. There was only one exception, noticed in experiment L-L, that concerned the head translation that appeared ~6 min after the beginning of the recording session, whereas all other deficits were already present at the beginning of the recording session. Second, according to our previous experience with the same amount of muscimol injected in the FN (Goffart and Pélisson 1994, 1997, 1998; Goffart et al. 1998) and to the autoradiographic measurements of muscimol diffusion in the rat brain (Martin 1991), we are confident that muscimol did not significantly spread out more than ~1 mm from our injection sites. Third, this estimated maximal diffusion distance is compatible with the clear differences, reviewed in the next section, between deficits induced by injecting muscimol in the rFN and those induced in the same animals by injecting 2 mm more caudally. Finally, control experiments indicated that muscimol injections performed outside the FN (i.e., ≥1 mm away from the rFN and cFN reconstructed sites) did not induce any of the deficits reported here, which suggests that the latter deficits could not be related to a diffusion of muscimol into these nearby structures.

Given the reasons listed above, the deficits reported in this paper clearly point toward a contribution of the rFN to the control of combined eye-head gaze shifts. Such a role was previously uncertain and neglected relative to that of the cFN (see INTRODUCTION), but our findings strongly emphasize that the rFN must also be considered as part of the cerebellar circuits engaged in the control of saccadic gaze shifts. Lesion studies in the past examined the effects of large ablations of the cerebellar vermal cortex (Optican and Robinson 1980; Ritchie 1976) or of the FN (Goldberg et al. 1993; Villis and Hore 1981). More recent inactivation or lesion experiments demonstrated conspicuous impairments of saccade accuracy when the cFN (Goffart and Pélisson 1994, 1997, 1998; Goffart et al. 1998; Ohtsuka et al. 1994; Robinson et al. 1993) or the vermal lobules VI–VII projecting to the cFN (Tagaki et al. 1996) were impaired. We are aware of one previous attempt to investigate saccadic eye movements in the head-fixed monkey during rFN inactivation, and no saccadic dysmetria was observed (Robinson et al. 1993). However, because this negative result was only briefly mentioned without demonstration of the injection site nor of the actual data, we are not able to further discuss this finding.

We will now detail which movement parameters were modified by rFN inactivation to provide some clues regarding the two following questions: 1) what are the functional processes in the generation of saccadic gaze shifts that are influenced by rFN and 2) what is the neurophysiological substrate of the contribution of rFN in gaze control?

Two observations provide some clues regarding the nature of gaze dysmetria induced by rFN inactivation. First, for both movement directions, gaze dysmetria was proportional to the initial target eccentricity (retinal error) and could therefore be described as an increase in the gain of ipsiversive gaze shifts and a decrease in the gain of contraversive ones. Second, in permanent target trials, visual feedback was used by the animals to generate correction saccades and to compensate for the error of fixation that resulted from the gaze dysmetria. Although a small error remained uncorrected, these correction saccades suggest that biased information about target position cannot account alone for the dysmetria. Together these findings strongly indicate that rFN inactivation modified a gain either in the processes that specify the metrics of the impending gaze shift, leading to up-or down-scale desired displacement signals, or in the feedback mechanisms controlling the ongoing movement.

These possibilities can be discussed in light of the dynamic characteristics of the gaze shifts. We found that the velocity of eye, head, and gaze movements tended to be reduced during rFN inactivation, although the large variability of the data precluded a statistical confirmation. In contrast, according to the above hypothesis postulating a modulation by rFN of a feedback gain, opposite modifications of gaze dynamics could be expected for ipsiversive (decrease) or contraversive (increase) movements. For example, by simulating a model incorporating the local feedback loop concept first introduced by Robinson (1975), Keller (1989) showed that increasing the gain along the negative feedback path led to hypometric saccades with an increased maximum velocity. In our study a significant increased velocity of contraversive gaze shifts was observed in only one of seven experimental cases (see Fig. 12C). Therefore the main sequence data as a whole do not support the hypothesis postulating a modulation by rFN of the gain of the local feedback loop. Note that, as already discussed in our investigation regarding the cFN (Goffart et al. 1998), changes in movement dynamics after muscimol injection in the rFN may not be related to the modifications in movement metrics. In addition, the markedly slowed movements and the increased latency observed for all responses in cat H might possibly result from some nonspecific factors such as a decreased arousal or prenauseous state. This possibility is consistent with the appearance of nausea soon after the end of the recording sessions in this animal and with a fastigial involvement in various aspects of autonomic control (Blanks 1988; Chida et al. 1989).

Inactivation of the rFN also modified the latency of eye-head orienting movements: the time to initiate eye and head movements toward targets presented in the ipsilesional visual field shortened (except for cat H), whereas it lengthened for targets presented in the contralesional field. These results indicate that the rFN acts on neuronal circuits involved in triggering these movements.

Although both eye and head participated in the dysmetria of gaze shifts, changes in their relative contribution to the amplitude of gaze shifts were observed. These changes can be interpreted in two ways. They could be related to the initial deviation of the eyes in the orbit. Indeed, because this deviation was contralateral to the inactivated side, ocular saccades associated with ipsiversive gaze shifts benefited from a larger field before reaching their orbital limits, whereas those associated with contraversive gaze shifts had a more restricted oculomotor range. Consequently, the amplitude of ipsiversive eye saccades could have increased, whereas that of contraversive eye saccades reduced. This fluctuation was shown to occur in the normal subject (Freedman and Sparks 1997; Fuller 1996) and in this case was associated with modifications in the timing of movement initiation (the body segment starting earlier contributing more). Note that the overall accuracy of gaze was preserved in normal subjects because the amplitude of the head coun-
terbalanced these changes in eye excursion in the orbit. However, because rFN inactivation strongly altered the accuracy of gaze with only subtle changes in eye-head delay (∼10 ms), we propose a second, nonexclusive explanation for the modifications in the relative contributions of the eye and head to the gaze displacement. This explanation assumes different effects of rFN inactivation on eye and head motor systems. Considering first ipsiversive responses, gaze hypermetria could mainly result from an hypermetric response of the eye. Such an explanation would account for the observation that eye hypermetria was present even for small retinal errors that did not elicit any head response. For contraversive responses gaze hypometria resulted from decreases in both eye and head responses, but again eye dysmetria exceeded head dysmetria, especially for retinal errors less than ∼30°.

**Rostrocaudal organization of the fastigial nucleus in the control of saccadic gaze shifts**

A comparison of the data reported in the preceding paragraphs with those obtained after muscimol injection into the cFN (Goffart and Pelisson 1994, 1997, 1998; Goffart et al. 1998) showed some similarities and several differences. The observations common to both studies were the ipsilateral hypermetria and contralateral hypometria pattern of gaze inaccuracy and the changes in movement latency. These similarities suggest an overall involvement of the FN in controlling the initiation and the amplitude of combined eye-head gaze shifts. Beyond this remark, note that these similarities could be accounted for by the involvement either of a single structure contacted by both rFN and cFN (see INTRODUCTION) or of two functionally redundant structures separately influenced by rFN and cFN through segregated projections. Besides, the effects of muscimol inactivation of cFN and rFN differed in several aspects, detailed in the following paragraphs.

First, very strong postural deficits were systematically observed after rostral but not caudal injections. Indeed, inactivation of the rFN consistently impaired postural control to the extent that the animals could no longer stand or walk on the ground when examined after completion of the postinactivation session. All three cats had their forelimbs positioned laterally far away from the inactivated side so that they systematically fell toward the ipsilateral side. We suspect that this postural deficit could be responsible for the ipsilesional head translation, noticed in most experiments, when the animal was lying in the hammock during the recording session. Such a role of rFN in the control of stance and gait is consistent with its anatomic links with the spinal cord (Fukushima et al. 1977; Matsushita and Hosoya 1978; Wilson et al. 1978) and the vestibulospinal system (Batton et al. 1977; Homma et al. 1995), with electrophysiological studies showing vestibular and optokinetic sensitivities (Buttner et al. 1991; Gardner and Fuchs 1975; Gruart and Delgado-Garcia 1994; Siebold et al. 1997), and with recent experiment showing a predominance of neuronal responses to the stimulation of vertical semicircular canals or otolith (Siebold et al. 1997). That these properties are classically defined as specific of the rFN is supported by the lack of postural deficits when the cFN of the same animals was inactivated.

Second, after caudal injections the hypometria of ipsiver-
sive gaze shifts mainly resulted from a constant error (bias), whereas the dysmetria induced by rostral injections essentially was related to an increased gain in the visuomotor transformation. In addition, a large fixation offset was consistently observed during inactivation of the cFN, whereas the fixation offset induced by rFN inactivation was significantly smaller. In our previous reports (Goffart and Pelisson 1994, 1997, 1998; Goffart et al. 1998) we argued that the bias of ipsiversive gaze shifts and the fixation offset during cFN inactivation resulted from a disturbance in the processes that specify the metrics of an impending gaze shift (target localization or production of a desired gaze displacement information). We further proposed that the bilateral fastigial projections toward the superior colliculus and thalamic nuclei likely mediate a cFN influence on these processes. Because these fastigiofugal pathways originate predominantly from the cFN, the lack of significant bias for ipsiversive gaze shifts and of a large fixation offset during inactivation of its rostral part is consistent with this hypothesis.

Third, caudal injections modified the relative contribution of the eye and of the head to the gaze displacement (Goffart et al. 1998) in a lesser extent than muscimol injections in the rFN. A related difference concerned the tonic deviation of the eyes in the orbit, which occurred only during inactivation of the rFN. These two differences, which may be related to each other (see previous section), suggest that, as compared with the cFN, the role of the rFN in gaze control takes place at a level where eye and head motor signals are separately represented.

Finally, although inactivation of either rFN or cFN modified both the accuracy and the latency of gaze shifts, an interaction between the hypometria and the increased latency of contraversive gaze shifts was observed only when the inactivation was confined to the cFN.

**Conclusions**

These findings indicate a contribution of the rFN to the control of combined eye-head gaze shifts. Muscimol inactivation of the rFN affects the latency and metrics of gaze- and head-orienting movements in a way that depends on their direction relative to the injected side (reduced latency and hypermetria for ipsiversive movements and increased latency and hypometria for contraversive movements). Although further demonstrations are required, our data suggest that these deficits result from disturbance in both the oculomotor and the cephalomotor systems rather than in neural processes controlling the orientation of the visual axis in space. Finally, our results provide evidence for a functional distinction between the rostral and caudal parts of the medial cerebellar nucleus in the control of visually triggered orienting gaze shifts.

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**Address for reprint requests:** D. Pelisson, Espace et Action, INSERM U 94, 16 Avenue Doyen Lépine, 69500 Bron, France.
Gaze shifts during inactivation of FNF


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