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Enhancement of the Bias Component of Downbeat Nystagmus after Lesions of the Nodulus and Uvula

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Abstract

In two monkeys, we recorded spontaneous eye movements before and after ablation of the cerebellar nodulus and uvula (Nod/Uv). In both monkeys, there was an increase in upward ocular drift (downbeat nystagmus, DBN) in darkness (M1: 1.5 °/s pre, 3.4 °/s post; M2: 1.3 °/s pre, 7.0 °/s post), but not in light. There was little effect of orbital position on drift velocity. These findings suggest that the Nod/Uv may play a role in the bias component of DBN.

Keywords

Cerebellum; Rhesus; Monkey; Ataxia; Oscillopsia

INTRODUCTION

Spontaneous downbeat nystagmus (DBN) is seen commonly in patients with cerebellar degeneration and is clinically important because it causes blurred vision and oscillopsia. Prior studies have shown that DBN has at least two components: 1) an orbital-position-dependent component that is likely due to a disturbance of the vertical neural integrator, and 2) an orbital-position-independent “bias” component that may include impaired processing of otolith signals. The bias component can be further divided into gravity-dependent and gravity-independent portions¹. A recent model² showed that loss of floccular Purkinje cells could account for many aspects of DBN, as well the vertical pursuit asymmetry that is commonly seen in these patients³. Here we asked whether the nodulus and uvula (Nod/Uv) might also play a role in DBN.

METHODS

Two juvenile rhesus monkeys were studied before and after neurosurgical aspiration of the nodulus and uvula. Eye movements were recorded using the magnetic field scleral search coil technique. Spontaneous gaze was recorded in complete darkness and with the room lights on. Analysis was performed using custom programs written in MATLAB and Python. Coil signals

were converted to rotation vectors, from which the angular eye velocity vector was calculated. Slow-phase segments were selected manually, using an interactive program. All experimental procedures were performed under a protocol that was approved by the Animal Care and Use Committee of the Johns Hopkins University.

RESULTS

As is commonly seen in rhesus monkeys, both animals had a weak downbeat nystagmus in the dark before the lesions. Post-operatively, the intensity of downbeat nystagmus increased. The biggest change was seen in M2; example recordings are shown in Figure 1. The overall median slow-phase velocity (SPV) increased from 1.5 to 3.4 °/s in M1 and from 1.3 to 7.0 °/s in M2. In both monkeys, the change in SPV was statistically highly significant (M1: $p=0$, M2: $p=0$, Wilcoxon rank-sum). The increase in upward drift was seen only in the dark; with the lights on, the drift was still suppressed (M1: SPV 0.26 °/s; M2: SPV 0.71 °/s).

We determined the relationship of SPV to the horizontal and vertical positions of the eyes in the orbits, over the animals' range of natural gaze (in the dark, they seldom look down, especially in the presence of a substantial upward drift). The results are shown in Figure 2, before and after the Nod/Uv lesions. Overall, there was little effect of orbital position on the vertical SPV. In particular, we did not find the pattern commonly observed in patients with cerebellar disease, namely a decreased SPV in upward gaze and increased SPV in lateral gaze.

Finally, we determined the effect of head orientation relative to gravity on vertical nystagmus, over a limited range of head pitch (~ 20 – 30°). In M1, there was a large effect; with the head pitched back, there was a brisk upbeat nystagmus (downward SPV: $16.9^\circ/\text{s}$, nose up 31°). In M2, there was little effect over the tested range.

DISCUSSION

These results suggest that the Nod/Uv play a role in the bias component of DBN. Other aspects of DBN, including its orbital-position-dependence and the failure of fixation suppression, are likely mediated through other cerebellar structures, such as the floccular complex^{4, 5}. Thus, our findings lend further support to the idea that DBN in humans involves a combination of mechanisms, likely with different anatomical substrates.

Patients with DBN have asymmetric vertical pursuit: downward slow phases are impaired³. It has been suggested that the upward eye velocity biases of pursuit and DBN may be related². Our findings are consistent with this idea, in that Nod/Uv lesions in our monkeys both enhanced DBN and produced a vertical pursuit asymmetry similar to that seen in humans⁶.

The effect of head orientation was different in our two monkeys. In M1, there was a large effect, and nystagmus became upbeat in the nose-up position. This suggests that otolith inputs play an important role in vertical nystagmus after Nod/Uv lesions, consistent with the known function of the Nod/Uv in the processing of otolith signals in other contexts^{7–9}. Nystagmus in M2, however, was modulated little. The significance of this is uncertain, but it is possible that we would also have observed a gravity dependence of SPV in M2, had we been able to record responses over a wider range of head orientations. Alternatively, this may have been due to a difference in the exact extent of the lesions in the two monkeys.

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Figure 1.
Representative eye position recordings in darkness (left panel) and light (right panel) before and after Nod/Uv lesion in M2.

Figure 2.

Vertical SPV as a function of the vertical (upper panels) and horizontal (lower panels) orbital position. Each bar represents the median SPV for all data in the corresponding eye position bin (bin width 5°). Upward velocities are positive.