Signals from the bilateral vestibular labyrinths work in tandem to generate robust estimates of our motion and orientation in the world. The relative contributions of each labyrinth to behavior, as well as how the brain recovers after unilateral peripheral damage, have been characterized for motor reflexes, but never for perceptual functions. Here we measure perceptual deficits in a heading discrimination task following surgical ablation of the neurosensory epithelium in one labyrinth. We found large increases in heading discrimination thresholds and large perceptual biases at 1 wk postlesion. Repeated testing thereafter improved heading perception, but vestibular discrimination thresholds remained elevated 3 mo postlesion. Electrophysiological recordings from the contralateral vestibular and cerebellar nuclei revealed elevated neuronal discrimination thresholds, elevated neurometric-to-psychometric threshold ratios, and reduced trial-by-trial correlations with perceptual decisions [“choice probabilities” (CPs)]. The relationship between CP and neuronal threshold was shallower, but not significantly altered, suggesting that smaller CPs in lesioned animals could be largely attributable to greater neuronal thresholds. Simultaneous recordings from pairs of neurons revealed that correlated noise among neurons was also reduced following the lesion. Simulations of a simple pooling model, which takes into account the observed changes in tuning slope and correlated noise, qualitatively accounts for the elevated psychophysical thresholds and neurometric-to-psychometric ratios, as well as the decreased CPs. Thus, cross-labyrinthine interactions appear to play important roles in enhancing neuronal and perceptual sensitivity, strengthening interneuronal correlations, and facilitating correlations between neural activity and perceptual decisions.

Reduced choice-related activity and correlated noise accompany perceptual deficits following unilateral vestibular lesion

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The search for the neural basis of perception has fascinated neuroscientists for a long time. Traditional tools for assessing functional links between single neurons and perceptual decisions include quantification of trial-by-trial correlations between neuronal activity and perceptual reports for ambiguous stimuli (1). Such “choice probabilities” (CPs) have been reported in visual (2–9), parietal (10), and somatosensory (11) cortical areas. Computational studies have also shown that the extent of correlated noise in a pool of neurons profoundly affects CPs (12–14). Until recently, these properties were largely considered the province of cerebral cortex.

To better understand how peripheral sensory signals are processed centrally to generate perceptual decisions, Liu et al. (15) used a vestibular heading discrimination task to explore the relationships between neuronal sensitivity, CPs, and correlated noise in vestibular nucleus (VN) and cerebellar nucleus (CN) neurons. These areas receive afferent signals from the vestibular periphery and are interconnected with the thalamo-cortical system (16, 17), the midline vestibulocerebellum (18), the spinal cord (19), and each other (20). Perhaps surprisingly, subcortical neurons exhibited robust correlations with perceptual decisions during a vestibular heading discrimination task and showed a steeper relationship between CP and neuronal sensitivity than typically found in visual cortex (15). Remarkably, strong CPs were observed almost exclusively for VN/CN cells that selectively represent head translation (21). In contrast, neurons that respond to net gravito-inertial acceleration, which are presumably not useful for heading perception, do not show significant CPs. These findings support the hypothesis that CPs emerge when sensory signals are represented in an appropriate format for mediating the trained behavior (22).

Simultaneous recordings from pairs of neurons also revealed highly structured correlated noise among subcortical vestibular neurons (15). Although average noise correlations were close to zero, pairs of VN/CN neurons frequently exhibited large positive or negative noise correlations, and these showed a dependence on tuning similarity that was stronger than that typically seen for cortical neurons. A population-decoding model that takes into account the measured noise correlations could predict the greater CPs observed in VN/CN relative to visual cortex. Thus, the emergence of strong choice-related response modulations in the brainstem/cerebellum may be attributable to a robust structure of interneuronal correlations.

Noise correlations are thought to arise from shared connectivity and common input. One source of common input in the vestibular brainstem is convergence between the ipsilateral and contralateral labyrinths (23). This bilateral convergence might contribute to the large noise correlations observed in VN and CN (15). If so, one would expect that a unilateral vestibular lesion would reduce correlated noise and decrease the magnitude of CPs. Although reflex-related effects of unilateral lesions have

Significance

Correlations between single-neuron activity and perceptual decisions are used to probe functional links between sensory neurons and perception, but the roles of correlated noise and decoding strategy in shaping these correlations remain unclear. The peripheral vestibular system provides an ideal model system to explore these questions, due to interactions between afferent signals from the two sides of the brain. We made a unilateral lesion to the vestibular labyrinth and recorded from neurons in the contralateral vestibular and cerebellar nuclei. The lesion led to reduced neural sensitivity, reduced correlations with perceptual decisions, and less correlated noise among neurons. Simulations show that these changes could account for the effects of the lesion on behavior.

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been studied, noise correlations, CPs, and neuronal thresholds have not been measured in this context. Furthermore, perceptual deficits following unilateral labyrinthectomy have never been tested, and most previous studies have focused on the rotational vestibulo-ocular reflex (VOR), driven by the semicircular canals. Examination of otolith function following unilateral lesions has been limited to measuring mean firing rate changes in anesthetized animals (24). Here we quantitatively compare behavioral and neuronal heading discrimination thresholds, CPs, and interneuronal correlations in unilaterally lesioned macaques with those recorded in normal animals. We found weaker correlated noise among neurons, weaker CPs, and elevated neuronal thresholds, in support of the hypothesized relationships among these properties.

Results
Perceptual Deficits in Heading Discrimination. Using a motion platform (SI Methods), we trained animals to perform a heading discrimination task (5), in which they reported their perceived self-motion direction (leftward vs. rightward relative to straight ahead) by making a saccade to one of two choice targets that appeared at the end of each trial. Monkeys were initially trained to perform this task based on either platform motion in the absence of optic flow (vestibular condition) or optic flow cues alone (visual condition) (for details, see ref. 4). Both animals reached asymptotic performance before being subjected to unilateral labyrinthectomy, a procedure that incapacitates the vestibular labyrinth in one ear (25).

Behavioral performance was quantified by plotting the proportion of rightward choices as a function of heading, as illustrated in Fig. 1. When first tested 1 wk after surgery, the animals’ performance on the vestibular heading task was poor, showing both impaired sensitivity and large biases (Fig. 1, red), and these deficits partially recovered by 14 d postlesion (Fig. 1, green). The direction of the bias depended on the side of the lesion. Specifically, psychometric functions shifted rightward for animal W (left labyrinthectomy) and mostly leftward for animal C (right labyrinthectomy). Thus, when first tested 1 wk postlesion, animals tended to report their perceived heading with a bias toward the lesioned side.

Although significant recovery was seen with repeated testing during the first few weeks following the surgery, deficits in vestibular heading discrimination thresholds persisted even after 3 mo (Fig. 1, compare blue and black symbols/curves). For animal W, vestibular thresholds increased from a prelesion average baseline of 3.9° [95% confidence interval (CI): 3.2–4.5°] to 16.1° [2.5–28.4°] 7 d after labyrinthectomy, and subsequently gradually recovered to 11.6° [9–14.3°] and 9.2° [5.5–13°] when measured 14 d and 3 mo after the lesion, respectively (Fig. 2A and Table S1). For animal C, vestibular thresholds increased from a baseline value of 2.3° [2–2.7°] to 17.7° [6.7–27.4°], 6.6° [3.6–10.1°], and 4.8° [3.2–7°] when measured 7 d, 14 d, and 3 mo after the operation, respectively (Fig. 2B and Table S1).

How perceptual thresholds and biases evolved over time after the lesion is summarized in Fig. 2 A–D. Note that thresholds for the visual heading task were also substantially elevated during the first days of testing postlesion (Table S1). However, visual heading thresholds returned to preoperation values within 10–14 d after surgery. The reason for this transient increase in visual heading thresholds is not clear, but it might simply be the case that animals were still a bit disoriented following surgery and thus did not perform their best. In contrast to the rapid recovery of visual thresholds, vestibular thresholds remained elevated for at least 3 mo postlesion.

Effects of Labyrinthectomy on Neuronal Thresholds and CPs. Neural recordings from the VN/CN contralateral to the lesioned labyrinth commenced 1 mo after the lesion, as illustrated in Fig. 2 E and F, which plots distributions of the number of cells recorded as a function of time after labyrinthectomy. As summarized above, vestibular psychophysical thresholds measured during this period of neural recordings (W, 9.8° ± 1.2°; C, 4.6° ± 1.2°) remained significantly elevated compared with control values (W, 3.7° ± 1.1°; C, 2.3° ± 1.1°) (P < 0.001; Wilcoxon rank sum test; see also Table S2). We now consider how neuronal thresholds after unilateral labyrinthectomy compare with those in control animals (from ref. 15). To obtain sufficient data in a limited time and because few (if any) VN/CN neurons are tuned to optic flow, recordings were only obtained in the vestibular condition.

Sixteen VN and 17 CN neurons with significant vestibular heading tuning in the horizontal plane were recorded following labyrinthectomy. Data from these neurons were compared with those from a sample of 41 VN and 56 CN cells recorded from intact monkeys in a previous study, which included animal W (15). Data from an illustrative neuron are shown in Fig. 3. This cell was monotonically tuned over the narrow range of headings tested in the discrimination task, with stronger responses to rightward headings (Fig. 3A). To quantify neural sensitivity for discriminating heading, we analyzed distributions of firing rates. Response histograms for leftward and rightward headings overlapped for small angles and were well separated for large angles (Fig. 3B). Receiver operating characteristic (ROC) analysis was used to convert distributions of firing rates into neurometric functions, as illustrated for this cell in Fig. 3C. The neuronal threshold was then computed as the SD of the cumulative Gaussian that best fit the neurometric function. These data were collected simultaneously with behavior, allowing a direct comparison of neurometric and psychometric functions (Fig. 3C). This neuron was typical in that it was substantially less sensitive than the animal. Finally, responses of the example neuron were also sorted into two groups according to the animal’s heading percept (which may differ from the true stimulus direction), and ROC analysis was again applied to compute the CP, as illustrated for the ambiguous (0°) heading stimulus in Fig. 3D. The CP value of 0.54 was not significantly greater than chance (0.5) for this example cell (P = 0.08; permutation test), as was the case in lesioned animals.

At the population level, neural heading discrimination thresholds were greater in animals with only one functional labyrinth, compared with controls (Fig. 4A). Neuronal thresholds averaged 75.5° ± 2.3° for CN (geometric mean ± SD) and 57.9° ± 2.5° for VN (Table S2). These values, which were not significantly different from each other (P = 0.46; Wilcoxon rank sum test), were
Neuronal thresholds can theoretically depend on two factors: the slope of the tuning curve around straight ahead and response variance. We found significant differences between control and lesioned animals only for tuning slope ($P < 0.001$; Wilcoxon rank sum test; $0.58 \pm 0.06$ spikes per second per degree for intact animals vs. $0.19 \pm 0.03$ spikes per second per degree for lesioned animals) and not for response variance ($P = 0.6$). Thus, the greater neuronal thresholds in labyrinthectomized animals can be attributed to changes in heading tuning that reduce the slope of the tuning curve around the straightforward reference. This finding is illustrated further in Fig. S1 C and D, which plots population-tuning curves in the horizontal plane, as measured during a passive fixation task (SI Methods). Tuning curve amplitudes, computed by fitting a wrapped Gaussian function to each heading-tuning curve, were significantly smaller in lesioned animals (25.5 spikes per second prelesion vs. 13.7 spikes per second postlesion; $P < 0.001$; bootstrap), with no significant difference between VN and CN neurons ($P = 0.8$). Tuning bandwidth, as assessed by the SD of the fitted Gaussian, was also narrower in lesioned animals (68.7° prelesion vs. 38.4° postlesion; $P < 0.001$; bootstrap). Although the narrower tuning curves following labyrinthectomy might partially counteract the reduced response amplitudes, the net effect is a reduction of the average slope of tuning curves postlesion.

Interestingly, the increase in neuronal thresholds following the lesion was greater than the increase in psychophysical thresholds, as illustrated by the fact that the average neuronal-to-psycho-physical (N/P) threshold ratio after labyrinthectomy (11.4 ± 2.5; geometric mean ± SD) was significantly greater than the N/P ratio in intact animals (6.6 ± 3.7; $P = 0.003$; Wilcoxon rank sum test; see also Table S2). We also computed the N/P ratio based on sensitivity, defined as 1/threshold$^2$, which is directly proportional to Fisher information (26), and the difference remained significant ($P = 0.003$).

Unilateral labyrinthectomy also affected CPs, which quantify correlations between neuronal activity and perceptual decisions (SI Methods and Fig. 4B). As shown previously (15), robust and significant CPs are found in VN and CN neurons, especially those that have high sensitivity (low neuronal thresholds) (Fig. 4C). CPs generally decreased after labyrinthectomy (Fig. 4 B and C), although the difference was only significant for VN [0.61 ± 0.1 (SD) vs. 0.54 ± 0.07; $P = 0.01$; Wilcoxon rank sum test], but not CN (0.59 ± 0.1 vs. 0.55 ± 0.09; $P = 0.2$). In addition, the percentage of cells with CPs significantly greater than chance (0.5) also decreased from 38.1% (37/97) in control animals to 18.2% (6/33) in lesioned animals.

Because CPs are inversely correlated with neuronal thresholds [analysis of covariance (ANCOVA); $P < 0.01$; Fig. 4C], the reduced CPs in lesioned animals might simply be a consequence of the greater neuronal thresholds observed postlabyrinthectomy. Indeed, the best-fitting linear relationship between CP and threshold, although less steep postlesion, was not significantly
Correlated Noise. As in cortical areas, the spike counts of subcortical neurons in response to an identical stimulus vary from trial to trial, and these fluctuations can be strongly correlated among heading-selective neurons in the brainstem and cerebellum (15). It is generally thought that these noise correlations arise from common input and/or shared connectivity (27). In the vestibular brainstem, noise correlations could arise from the bilateral convergence between the two labyrinths (23). To test this hypothesis, we recorded from 38 pairs of VN cells and 32 pairs of CN neurons while fixing monkeys with unilateral labyrinthectomy. We found that vestibular heading discrimination thresholds show a fast (~2–3 wk) phase of recovery, but remain elevated as long as 3 mo postlesion. We also found elevated neuronal thresholds in the two main thalamo-cortical projection nuclei, the VN and CN. However, neuronal thresholds increased more than expected from the observed changes in behavioral thresholds, thus resulting in higher N/P ratios compared with labyrinth-intact animals. VN/CN neurons in lesioned animals were also characterized by reduced correlations between neural responses and perceptual choices (CPs). However, the relationship between CP and neuronal threshold, although a bit shallower, was not significantly altered, suggesting that the smaller CPs may be mainly attributable to higher neuronal thresholds.

It has been suggested that the high CPs in VN/CN neurons may be linked to strong interneuronal noise correlations (15). We found that noise correlations in labyrinthectomized animals were reduced compared with intact animals. In addition, the dependence of noise correlations on tuning similarity, which is a strong predictor of the magnitude of CPs (15), was found to be less steep postlesion. We conclude that cross-labyrinthine interactions play important roles in enhancing neuronal and perceptual sensitivity, strengthening interneuronal correlations, and facilitating higher correlations between neural activity and perceptual decisions.

Bilateral Organization of the Vestibular System. The semicircular canals are characterized by a cross-labyrinth push–pull organization, which is based on the fact that pairs of canals have opposite preferences for direction of head rotation. In contrast, each of the otolith organs contains a broad representation of preferred directions of linear acceleration within the macula, including opposite-directed responses across an imaginary line known as the striola (29). Thus, appropriate push–pull signals in the otolith system could arise either from computations that operate across the two labyrinths (as in the canal system) or from computations that occur within the same otolith macula via crossed-striolar inhibition. Indeed, extensive convergence of otolith-driven signals has been documented experimentally: VN neurons receive convergent inputs from both the ipsilateral and contralateral otolith organs, both the utricle and the saccule, as well as both sides of the neuroepithelium across the striola of a single
sensory organ (23, 30). Whether this type of organization also characterizes otolith-driven responses in the CN is unknown.

It is commonly assumed that correlated noise arises either from common input or from interconnections among neurons (27). Thus, we hypothesized that the strong noise correlations observed previously in the VN/CN (15) are at least partly due to strong signal convergence from the bilateral labyrinths. The large decrease in correlated noise that we report here following unilateral labyrinthectomy (Fig. 5) provides strong support for this hypothesis. In turn, this result implies that correlated noise at the level of VN or CN is not driven primarily by top-down signals from other parts of the brain including the cortex, although our results do not exclude some contribution of top-down signals.

One can think of correlated noise as a direct consequence of interneuronal communication within large interconnected networks. Its functional consequences for population encoding and decoding, however, are more difficult to generalize. It is thought that the information capacity of a population code depends on the correlated noise among neurons, and the impact of correlations could be particularly strong for large populations (26, 31, 32). In addition, the effect of correlated noise on decoding efficacy is also of considerable interest. At least theoretically, the impact of correlated noise on population decoding could be negligible if an optimal decoder has complete knowledge of these correlations and if the correlations are not concentrated in the same portion of response space as the stimulus variations. However, incomplete or inaccurate knowledge of the correlation structure could cause a decoder to fail to extract all of the information that is available in a population code.

These considerations suggest that correlated noise induced by computations (such as push–pull interactions) that occur within or across the two labyrinths may play critical roles in constraining the amount of information that can be extracted from vestibular neurons. Our findings are consistent with the idea that cross-labyrinth interactions contribute substantially to the correlated noise measured at the level of pairs of neurons.

**Effects of Labyrinthectomy on the VOR.** Two phases of compensation for unilateral vestibular damage have been reported in well-characterized postural and motor deficits, including the VOR (33, 34). First, there is an acute phase (~1 wk) in which VOR gain recovery is fast, likely involving restoration of spontaneous activity in central VOR pathways. Subsequently, compensation proceeds more slowly. For low acceleration sinusoidal rotations, a nearly complete recovery of the yaw VOR within the first month postlesion has been documented. However, substantial asymmetries in the high-frequency VOR, specifically in the form of lower gain during rotations toward the lesion side, persist over the long term (33, 35, 36).

Large asymmetries and reduced gains have also been reported for the translational VOR following unilateral vestibular damage, even after 3 mo of recovery (37). These persistent translational VOR deficits, along with the elevated heading thresholds reported here, demonstrate that both labyrinths are vital for normal perceptual and motor functions of the otolith system. This finding may be surprising given that push–pull convergence of otolith afferent signals could arise either from computations that span the two labyrinths (as in the canal system) or from within the same otolith macula through cross-striolar inhibition (23, 30). Although cross-striolar convergence may contribute, our findings demonstrate that convergence of otolith signals from the two labyrinths is critical for enhancing perceptual sensitivity during heading discrimination.

**Compensatory Changes in VN/CN Neurons Following Unilateral Labyrinthectomy.** Neural correlates of the relatively rapid recovery of the rotational VOR have been found in VN neurons contralateral to the lesion side, which return to prelesion modulation gains within 3 wk after labyrinthectomy (38). This recovery may be mediated by changes in the intrinsic membrane properties of central vestibular neurons and synaptic reorganization of central vestibular pathways (39). Recovery of VN responses ipsilateral to the lesion side is much weaker and never becomes complete.

Here we have focused on the responses of neurons without eye-movement sensitivity because this cell type was shown to project to the thalamo-cortical system (16). Because we recorded from the VN/CN contralateral to the lesion side and all recordings were done at least 1 mo after the lesion, we expected to find small, if any, neuronal deficits, given the smooth, low-acceleration stimuli used here. Instead, we found tuning curves with substantially reduced response amplitudes and shallower slopes, which resulted in greater heading discrimination thresholds in lesioned animals. Thus, it is possible that recovery of otolith-driven responses is either less complete or slower than recovery of horizontal canal-driven signals.

We have described a constellation of changes in neural response properties that accompany the reductions of behavioral sensitivity resulting from labyrinthectomy. To gain intuition into how these neural changes contribute to the behavioral outcomes, we simulated responses of populations of VN/CN neurons in the contraleisonal hemisphere, and we used population decoding to make predictions of psychophysical thresholds and CPs (see SI Methods and Fig. S2 for details). These simulations qualitatively reproduce the main findings of this study. Specifically, modeling the empirically observed changes in tuning curves and correlated noise predicts increased psychophysical thresholds, reduced CPs, and a small reduction in slope of the relationship between neuronal thresholds and CPs (Fig. S2). The simulations also

provide insight into the finding that N/P threshold ratios were significantly greater after labyrinthectomy. By simulating separately the effects of labyrinthectomy on tuning curves and correlated noise (Fig. S2, green and blue curves, respectively), the model demonstrates that the effects of the lesion on tuning curve slopes and noise correlations pull the predicted psychophysical threshold in opposite directions. In contrast, only tuning slope changes affect neuronal thresholds. As a result, the simulated lesion produces a greater elevation in neuronal thresholds than psychophysical thresholds, thus explaining why the neurometric/psychometric ratio increases after labyrinthectomy.

It should be noted that our estimate of the noise covariance structure in the neural populations is derived from pairwise recordings and might not adequately capture all types of correlated noise that limit information in a population of neurons. Despite these caveats, the simulations suggest that the basic pattern of results that we observe could be a straightforward consequence of the measured effects of labyrinthectomy on basic neural response properties in the contralateral hemisphere. Understanding how early sensory signals are transformed and decoded to maximize perceptual performance is critical for understanding the neural correlates of behavior, and the circuitry of the vestibular system may provide unique opportunities for exploring these issues.

Methods

Two rhesus monkeys (Macaca mulatta) were trained to perform a heading discrimination task based on visual (optic flow) or vestibular (platform motion) cues (4, 5). Behavioral data were collected beginning 1 wk postlesion, whereas neuronal data were collected during the second and third months postlesion (Fig. 2 E and F). Postlesion cells were recorded from the right VNC/ CN after the left labyrinth in animal W was surgically ablated (n = 57) and from the left VNC/CN after the right labyrinth in animal C was lesioned (n = 88). These responses are compared with data from 312 cells previously recorded in labyrinth-intact macaques (15). Details about experimental protocols and analyses can be found in SI Methods.

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Supporting Information

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SI Methods

Subjects and Apparatus. Two rhesus monkeys (Macaca mulatta) were subjects in the present experiments. A circular delrin ring was chronically implanted to restrain and stabilize the head during experiments, and a recording grid was implanted to allow precise positioning of microelectrodes [see Liu et al. (1, 2) for details]. Stainless steel inverted T bolts and dental acrylic were used to attach the implant to the skull. In addition, a scleral coil was implanted to measure eye movements. Following training and control data collection, the left labyrinth was surgically ablated in animal W, whereas in animal C this operation was performed on the right labyrinth. The surgical and experimental procedures conformed to National Institutes of Health guidelines and were approved by the Institutional Animal Care and Use Committee at Washington University. Motion stimuli, in the form of passive whole-body translations, were delivered by using a six-degree-of-freedom motion platform [Moog 6DOF2000E; for details see Gu et al. (3)].

Heading Discrimination Task. Animals were trained to perform a heading discrimination task based on visual (optic flow) or vestibular (platform motion) cues (4, 5). In each trial, the monkey experienced forward motion with a small leftward or rightward component while maintaining fixation (2 × 2° electronic window) on a head-fixed target located at the center of the screen. The motion trajectory (30-cm displacement) was 2 s in duration and followed a Gaussian velocity profile (peak velocity: 45 cm/s), with a correspondingly biphase linear acceleration profile (±0.1 G = ±0.98 m/s²). At the end of the trial, the fixation point disappeared, two choice targets appeared, and the monkey had to make a saccade to one of the targets to report his perceived motion as leftward or rightward relative to straight ahead. Correct choices were rewarded with a drop of juice. For the ambiguous heading direction (0°), rewards were delivered randomly on half of the trials. If fixation was broken at any time before appearance of the choice targets, the trial was aborted and the data were discarded.

Psychophysical performance in the heading discrimination task was quantified for the vestibular condition (platform motion only, no optic flow) and the visual condition (stationary motion platform, optic flow simulates self-motion). A broad range of headings was used to be able to measure the impaired performance following lesions: ±32°, ±16°, ±8°, ±4°, ±2°, ±1°, and 0° (straightforward). Behavioral data were collected beginning 1 wk postlesion because there is a strong static imbalance due to deficits in spontaneous activity of central neurons following unilateral labyrinthectomy. As a result, animals generally have difficulty fixating visual targets during the first few days after unilateral vestibular damage because of strong spontaneous nystagmus. Recovery of these static symptoms is rapid and generally complete after the first week postlesion (6–9). The goal of this study was to quantify the prevailing deficits in perception after the static vestibular imbalance had been mostly resolved. The visual task condition provides an important control for any residual nonspecific effects of the lesion on behavioral performance. Both of these animals showed optimal cue integration in previous studies (4).

Neural Recordings. Neuronal data collection started 1 mo postlesion, after behavioral thresholds had approached steady-state values (Figs. 1 and 2). We recorded extracellularly the activities of single neurons in the vestibular nucleus (VN) and cerebellar nucleus (CN) using epoxy-coated tungsten microelectrodes (FHC; 5–7 MΩ) that were inserted into the brainstem and cerebellum through transdural guide tubes. CN recordings concentrated on the rostral fastigial nucleus but might also have extended into the anterior interposed nucleus (1, 10, 11). Electrode penetrations were guided by the location of the abducens nuclei, which were identified in initial experiments for each animal. Experiments used either a single electrode (n = 19) or two microelectrodes (n = 70) to record from a pair of neurons simultaneously. For the latter case, the microelectrodes were placed inside two different guide tubes separated by 0.8–2.8 mm. Raw neural activity was amplified, filtered (0.1 Hz to 10 kHz), and discriminated by using a dual time–amplitude window discriminator (BAK Electronics). Once a VN/CN cell was satisfactorily isolated, it was first tested with eye movement protocols in which trained animals pursued a target that moved along the horizontal and vertical axes (Gaussian velocity profile, ±9°, 2s, five repetitions). The mean firing rate for each trial was computed from the middle 1 s of the response to the pursuit stimulus, and this activity was used online to determine whether the cell was tuned for the direction of smooth pursuit eye movements (P < 0.05; one-way ANOVA).

(i) The “3D heading protocol” involved translation of the motion platform along 26 directions sampled evenly around a sphere (3). The animals were simply required to maintain visual fixation on a head-fixed target during this protocol. The duration of the heading stimulus was 2 s, the displacement was 13 cm, and the velocity profile was Gaussian with a peak velocity of ~30 cm/s, corresponding to a biphase acceleration profile with peak acceleration of ~0.1 G = 0.98 m/s². Note that the width of the Gaussian velocity profile was narrower than in the discrimination task, which resulted in a smaller displacement and peak velocity but similar peak acceleration. This change was necessary because of mechanical limits of the motion platform during vertical heading directions. Responses from this protocol were used to compute heading tuning curves, as well as noise and signal correlations (Data Analysis).

(ii) Neurons with significant heading tuning in the horizontal plane (P < 0.05; one-way ANOVA) for at least five consecutive 400-ms time bins (computed every 25 ms; Chen et al., 12) were further tested during the heading discrimination task, as summarized above [for additional details, see Gu et al. (5) and Liu et al. (1)]. During neural recordings, a narrower range of nine logarithmically spaced headings (±16°, ±6.4°, ±2.6°, ±1°, and 0°, expressed relative to straight-ahead, with positive angles corresponding to rightward directions) were randomly interleaved. The range and spacing of headings were chosen carefully to obtain near-maximal psychophysical sensitivity while allowing neural sensitivity to be reliably estimated for most neurons (Data Analysis).

The neurons included in this study were all of the NEM type, and all were recorded from the side of the brain contralateral to the lesion (i.e., from the right VN/CN after the left labyrinth in animal W was ablated and from the left VN/CN after the right labyrinth in animal C was lesioned). All neural recordings were completed during the second and third months postlesion (Fig. 2 E and F), with n = 57 for animal W and n = 88 for animal C. These responses are compared with data from 312 cells previously re-
corded in labyrinth-intact macaques (1). Of these, 134 cells were recorded from animal W before the lesion (control neural data were not obtained from animal C). Note that there are no visually-only neurons in the VN/CN, and few, if any, VN/CN cells are tuned for heading defined by optic flow (13). Thus, no attempt was made to record neural responses during the visual stimulus condition.

Data Analysis. Behavioral performance was quantified by plotting the proportion of rightward choices as a function of heading direction. Psychometric functions were fit with a cumulative Gaussian function (5), and behavioral threshold was defined as the SD of the Gaussian fit. All behavioral data shown here (e.g., Figs. 1 and 2) had fits with $R^2 > 0.8$ (median: 0.97).

Neural responses were quantified as mean firing rates computed over the middle 400-ms interval of each stimulus presentation. To characterize neuronal sensitivity, we used receiver operating characteristic (ROC) analysis to compute the ability of an ideal observer to discriminate between two opposite-directed headings based solely on the firing rate of the recorded neuron, as well as that of a presumed “antineuron” with opposite tuning (1, 5, 14). ROC values were plotted as a function of heading direction, resulting in neurometric functions that were also fit with a cumulative Gaussian function. Neuronal thresholds were defined as the SD of these functions. Only neurons with a minimum of 10 repetitions per distinct stimulus condition were included in this analysis.

To quantify the relationship between neural responses and the monkey’s perceptual decisions, we also computed choice probabilities (CPs) using ROC analysis (15). For each heading, neuronal responses were sorted into two groups based on the choice that the animal made at the end of each trial. Specifically, each choice was classified as “preferred” or “null” according to the tuning of the neuron under study, where a preferred choice is one that favors the preferred sign of heading of the neuron being recorded. ROC values were calculated from these distributions, and a CP was computed for each heading at which the monkey made at least three choices in favor of each direction. We further computed a single “grand” CP for each neuron by combining responses across all heading directions that met this criterion. This calculation was done by first normalizing (Z-scoring) the data for each heading and then combining them into a single pair of distributions for preferred and null choices. ROC analysis on this pair of distributions yielded the grand CP. The statistical significance of CPs (i.e., whether they were significantly different from the chance level of 0.5) was determined by using permutation tests (1,000 permutations).

For the analysis of simultaneously recorded pairs of neurons, noise correlation ($r_{\text{noise}}$) was computed as the Pearson correlation coefficient of responses of two simultaneously recorded neurons driven by the same stimulus (1, 16, 17). The response of each neuron in each trial was taken as the number of spikes during the middle 400 ms of the stimulus duration. For each heading direction, responses were first z-scored by subtracting the mean response and dividing by the SD across stimulus repetitions, to remove the stimulus effect on the mean response such that the measured noise correlation reflected only trial-to-trial variability [see Gu et al. (16) and Liu et al. (1) for more details]. Then we pooled data across different heading directions to compute $r_{\text{noise}}$. In addition to noise correlation, signal correlation ($r_{\text{signal}}$) was computed as the Pearson correlation coefficient between the 3D tuning curves (average firing rate during the middle 400 ms of the stimulus duration) of two simultaneously recorded neurons.

Simulations. To relate the observed changes in neural tuning and correlated noise to effects of the lesion on behavior and CPs, we simulated population activity and used a decoder to make predictions. To decode heading from a population of neurons, we implemented a standard maximum-likelihood decoder that assumes Poisson spiking statistics (for details, see refs. 1 and 18) and computes the likelihood function over possible stimulus headings. The spike count of each neuron was multiplied by the logarithm of its tuning curve, and the result represented each neuron’s contribution to the likelihood function. The full log likelihood function was obtained by summing the contributions across neurons. Correlated noise was introduced into simulated population responses by constructing a covariance matrix based on the observed relationship between noise correlation and signal correlation (for details, see ref. 1).

In each simulated trial, the decoder determined whether the comparison heading was leftward or rightward relative to the reference (straightforward) heading according to the relative peak locations of the likelihood functions. If the peak of the likelihood function for a given heading, computed from one trial of activity from the population, was to the right of the peak for the reference heading, the ideal observer would report “rightward,” and vice versa.

To simulate results for populations of neurons of different sizes, we generated simulated populations of neurons that were based as closely as possible on measured data. For each population size, correlated noise was generated based on the empirical relationship between signal and noise correlations (see ref. 1 for details). Firing rates were generated based on the mean response that was determined from the tuning curve of each simulated neuron.

Tuning curve slopes were drawn from a Gaussian distribution having the same mean and SD as the relevant population of neurons from either intact or lesioned animals. In all simulations, we only simulated responses of neurons from the contralesional VN or CN. Because we have not measured responses from the ipsilesional side, we effectively assume that they have properties similar to those of neurons on the contralesional side. For intact animals, this assumption is likely valid. For animals with a unilateral labyrinthectomy, good data are not available to constrain assumptions further. If neurons on the ipsilesional side have sensitivity that is substantially lower than the contralesional side, these neurons would likely contribute little to behavior and would not likely affect our results much. If neurons on the ipsilesional side are substantially more sensitive, then our simulations may have larger errors, but this possibility seems unlikely (19, 20).

We simulated psychophysical thresholds and CPs for intact animals based on tuning curve and noise correlation data from those animals (black symbols in Fig. S2). Similarly, simulation results for lesioned animals were based on data recorded from those animals (red symbols in Fig. S2). In addition, to explore the relative contributions of changes in tuning slope and changes in correlated noise, we also simulated additional neuronal pools. To assess the effect of the changes in noise correlation, we performed a simulation with tuning slope parameters obtained from intact animals and correlation structure from lesioned animals, (blue symbols in Fig. S2). Similarly, to isolate the effects on tuning, we simulated pools with the same correlation structure as the intact animals but with tuning slopes that were, on average, 1/3 of those seen in intact animals (green symbols in Fig. S2). For each distinct stimulus condition, we decoded responses to 30 simulated trials. The “choice” of the decoder on each simulated trial was stored and used to compute CPs for each neuron in the simulated population. This method allowed quantitative predictions of CPs for neural populations of different sizes.

Fig. S1. Summary of population heading tuning curves. (A) Scatter plot of neuronal threshold against each cell’s preferred direction, relative to straight-forward (°). In this plot, 90° corresponds to both rightward and leftward heading preferences. Marginal distributions (top) summarize the direction preferences separately for intact (black) and lesioned (red/magenta) animals. (B) Polar plot of the data in A, where the radius corresponds to neuronal threshold and the polar angle illustrates the preferred direction relative to the cell’s location (ipsilateral vs. contralateral relative to the lesion). Because all postlesion recordings were made in the contralateral brainstem/cerebellum, this distinction also separates ipsilesional and contralesional preferred directions. For each dataset, the distribution of preferred directions was not significantly different from uniform (P > 0.15; uniformity test). There was also no significant difference between the distributions of heading preferences in control and lesioned animals (A, P = 0.5; B, P = 0.6; Kolmogorov–Smirnov test), suggesting that the balance of ipsilesional and contralesional heading preferences was not substantially altered by labyrinthectomy. Different symbols show data from different animals postlesion (circles, animal W; diamonds, animal C). (C and D) Control (70 VN and 107 CN; black) and postlesion (27 VN and 31 CN; red/magenta) population tuning curves before (B) and after (C) subtraction of spontaneous activity. Heading was varied in the horizontal plane (8 directions, 45° apart) while monkeys passively fixated a head-fixed visual target. Responses from each neuron were shifted along the horizontal axis to align the peaks of all tuning curves (at 0°) before averaging across the population.
Fig. S2. Predicted psychophysical and neuronal sensitivity, based on a standard maximum-likelihood decoder that assumes Poisson spiking statistics. (A) The predicted psychophysical threshold (±SD) plotted as a function of the number of neurons in the simulated neural population. The population responses were generated based on the properties of the intact VN/CN neurons, with simulated tuning slopes randomly drawn from the observed Gaussian distribution. Data points represent averages across 30 iterations. (B) Average CP (±SD) as a function of population size. (C) Average slope of type II linear regression fit to CP (±SD) vs. neuronal threshold relationship as a function of population size. (D) Average neuronal-to-psychophysical threshold ratios (±geometric SD) as a function of population size. Black symbols/lines, simulated population response based on intact data (1); red symbols/lines, postlesion; blue symbols/lines, simulated population responses based on tuning slopes from intact animals and noise structure from postlesion animals; green symbols/lines, simulation population responses based on tuning slopes from intact animals but reduced by 1/3 (as is observed postlesion) and noise structure from intact animals. The observed changes in tuning slope and correlations pull the predicted psychophysical threshold in opposite directions (A, green vs. blue), whereas only tuning slope affects the neuronal thresholds. This effect is why the neurometric/psychometric ratio becomes larger after labyrinthectomy (D). In contrast, changes in both tuning slope and correlations decrease the average CP (B, green/blue), and the two effects add, thus resulting in small postlabyrinthectomy CPs (B, red). Finally, note that reduced correlations predict a decrease in the slope of the relationship between CP and neuronal threshold, whereas reduction in tuning slopes, if anything, leads to the opposite effect (C, blue vs. green). As a result, the CP vs. neuronal threshold relationship changes modestly (C, red), consistent with the experimental data (Fig. 4C).

Table S1. Summary of behavioral performance during the heading discrimination task

<table>
<thead>
<tr>
<th>Animal/condition</th>
<th>Control</th>
<th>7 d</th>
<th>9 d</th>
<th>14 d</th>
<th>1 mo</th>
<th>2 mo</th>
<th>3 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bias</td>
<td>0.2 [−0.3 to 0.8]</td>
<td>47.6 [33.8 to 67.5]</td>
<td>12.8 [10.1 to 15.8]</td>
<td>4.4 [−1.1 to 9.1]</td>
<td>−0.1 [−2 to 1.3]</td>
<td>−1.6 [−3.3 to 0.9]</td>
<td></td>
</tr>
<tr>
<td>Visual Threshold, °</td>
<td>3.6 [2.4 to 4.6]</td>
<td>15.5 [11.2 to 20.2]</td>
<td>2.1 [1.4 to 3.8]</td>
<td>3.6 [2.2 to 6.1]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bias</td>
<td>0.9 [0.3 to 1.6]</td>
<td>20 [15.1 to 26.2]</td>
<td>−3 [−3.5 to 0.2]</td>
<td>−3.4 [−6 to 2.3]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monkey C Vestibular Threshold, °</td>
<td>2.3 [2 to 2.7]</td>
<td>17.7 [6.7 to 27.4]</td>
<td>12.7 [8.8 to 16.2]</td>
<td>6.6 [3.6 to 10.1]</td>
<td>7 [3.5 to 12]</td>
<td>5.2 [3.7 to 7.3]</td>
<td>4.8 [3.2 to 7]</td>
</tr>
<tr>
<td>Bias</td>
<td>1 [0.7 to 1.3]</td>
<td>−6.8 [−12.7 to 1.2]</td>
<td>−4.4 [−6.9 to 2]</td>
<td>1.1 [−0.6 to 2.7]</td>
<td>0.1 [−1.8 to 1.5]</td>
<td>0.7 [−0.6 to 1.8]</td>
<td>−0.35 [−1.6 to 0.7]</td>
</tr>
<tr>
<td>Visual Threshold, °</td>
<td>1.6 [1.3 to 1.9]</td>
<td>2.1 [1.6 to 2.5]</td>
<td>2 [1.2 to 2.3]</td>
<td>1.5 [0.9 to 2]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bias</td>
<td>−1.2 [−1.5 to 1]</td>
<td>−0.4 [−0.3 to 1.1]</td>
<td>0.4 [−0.3 to 0.8]</td>
<td>−0.2 [−0.7 to 0.2]</td>
<td></td>
<td></td>
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</tbody>
</table>

Each parameter is shown along with its 95% confidence interval, computed by using bootstrapping. Empty cells illustrate data not collected or data with poor fits ($R^2 < 0.8$).

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<table>
<thead>
<tr>
<th>Condition</th>
<th>Neuronal threshold, ° (n)</th>
<th>Behavioral threshold, °</th>
<th>Neuron to behavior threshold ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>VN</td>
<td>CN</td>
<td>VN</td>
</tr>
<tr>
<td>Control</td>
<td>22 ± 3.7 (41)</td>
<td>25.1 ± 3.4 (56)</td>
<td>3.6 ± 1.5</td>
</tr>
<tr>
<td>Lab–lesion</td>
<td>57.9 ± 2.5 (16)</td>
<td>75.5 ± 2.3 (17)</td>
<td>5.8 ± 1.8</td>
</tr>
<tr>
<td>Monkey W–control</td>
<td>29.4 ± 4.1 (15)</td>
<td>22.4 ± 3.1 (16)</td>
<td>3.8 ± 1.2</td>
</tr>
<tr>
<td>Monkey W–laboratory–lesion</td>
<td>136 ± 2.5 (5)</td>
<td>70.1 ± 2.4 (4)</td>
<td>9.8 ± 1.2</td>
</tr>
</tbody>
</table>

All values represent geometric mean ± SD.