Infantile strabismus inaugurates a constellation of dissociated eye movements that correspond to visuovestibular reflexes in lateral-eyed animals. These visual reflexes are generated by subcortical visual pathways that use binocular visual input to modulate central vestibular tone. In this article, I present evidence that the accessory optic system is uniquely suited to provide an innervational substrate for visuovestibular eye movements in humans with infantile strabismus.

Infantile strabismus is characterized by dissociated binocular vision, which is the normal condition in lateral-eyed animals.1,2 Early binocular misalignment gives rise to dissociated eye movements (changes in eye position evoked by unequal visual input to the 2 eyes).3 These include latent nystagmus, dissociated vertical divergence, and dissociated horizontal deviation,1,3 all of which have a prominent torsional component. Primary oblique muscle overaction, which accompanies infantile strabismus but is not dissociated in nature, is also characterized by a torsional misalignment of the eyes.4

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These binocular deviations all correspond to normal visuovestibular reflexes that are operative in lateral-eyed animals.1,4 Evolutionarily, these visual reflexes antedate development of the visual cortex, which does not generate torsional eye movements in humans.9 Therefore, any attempt to anatomize infantile strabismus must explain the reemergence of these atavistic reflexes, as well as their prominent torsional components. I propose that the accessory optic system (AOS), an atavistic subcortical visual motion detection system, could generate the dissociated and non-dissociated torsional eye movements that accompany human infantile strabismus.

WHAT IS THE AOS?
The AOS consists of 3 nuclei at the mesodiencephalic border that receive direct retinal input from the accessory optic tract (AOT)6-9 (Figure 1). The AOT comprises an inferior and a superior fasciculus, with its superior fasciculus divided into a posterior branch, a middle branch, and an anterior branch that is identical to the original transpeduncular tract (tractus peduncularis transversus) discovered in 1870 by Gudden.10,11 The number of accessory optic fibers is small. In almost all mammalian species, most optic fibers reach the accessory optic nuclei via the transpeduncular tract, which is visible as it courses over the brachium of the superior colliculus.12

In most mammalian species, the AOS is composed of 3 paired terminal nuclei, namely, the dorsoterminal nucleus (DTN), the lateroterminal nucleus (LTN), and the medioterminal nucleus (MTN), which receive innervation from primary optic fibers.7,9 Input to these 3 accessory optic terminal nuclei is predominantly from the contralateral eye.7,9,11,12 Along with the nucleus of the optic tract (NOT), these 3 terminal nuclei project differentially to the dorsal cap of the inferior olive,13-15 which
Figure 1. Neuroanatomical connections of the accessory optic system. The brainstem is depicted from the front (with the left-hand side of the animal on the right-hand side of the drawing). Accessory terminal nuclei include the dorsoterminal nucleus (DTN), which lies adjacent to the nucleus of the optic tract (NOT); medial terminal nucleus (MTN); lateral terminal nucleus (LTN); and principal part of the inferior olive (IOp). Optokinetic input from the right retina crosses to the left accessory optic nuclei (depicted), which send ipsilateral projections to the left dorsal cap (DC) of the inferior olive and then back to the right flocculus (not shown), resulting in a double decussation of motion pathways from each eye. Adapted with permission from Simpson et al.7-9 CP indicates posterior commissure; D, nucleus of Darkschewitsch; DMNm, deep mesencephalic nucleus, pars medialis; EW, nucleus of Edinger-Westphal; INC, interstitial nucleus of Cajal; inSFp, intersitial nucleus of the superior fasciculus, posterior fibers; MAO, medial accessory nucleus, inferior olivary complex; ML, medial lemniscus; MLF, medial longitudinal fasciculus; PAGm, periaqueductal gray, medial part; pdl, dorsolateral division, basal pontine complex; pm, medial division, basal pontine complex; pv, ventral division, basal pontine complex; PVG, periventricular gray; RN, red nucleus; rpc, pontine reticular nucleus, pars caudalis; rpo, pontine reticular nucleus, pars oralis; vl, lateral vestibular nucleus; vLO, ventrolateral outgrowth, inferior olivary complex; vm, medial vestibular nucleus; vs, superior vestibular nucleus; vsp, spinal vestibular nucleus; VTRZ, visual tegmental relay zone; β, nucleus β of the inferior olive; 3n, oculomotor nerve; 4n, trochlear nerve; and 6n, abducens nerve.

provides the only source of climbing fibers to the flocculonodular lobe of the cerebellum.7-9,13-17 In this way, cells of the AOS converge with those of the vestibular system in the vestibulocerebellum.7,9

Despite its name, the AOS is a primary visual system receiving direct visual information from the retina via 1 or more AOTs13 that are responsible for visuovestibular interaction in afoveate animals.7,16,17 Its retinal input is derived from ON-type direction-sensitive ganglion cells. The AOS neurons have large receptive fields (averaging about 40° vertically and 60° horizontally), are direction selective, and have a preference for slow-moving stimuli.7,9,12,11 The AOS processes information about the speed and direction of movement of large textured parts of the visual world.7,9 The AOS signals self-motion as a function of slip of the visual world over the retinal surface and generates corrective eye movements to stabilize the retinal image.7,9 As an analyzer of self-motion, the AOS subserves visual proprioception in the afoveate animal.7-9

The AOS is a visual system that is organized in vestibular coordinates.7-9 According to results of experimental studies by Simpson and colleagues, visual and vestibular signals that produce compensatory eye movements are organized about a common set of axes derived from the orientation of the semicircular canals (Figure 2).7,9,12,16,17 Because the AOS is directionally sensitive to low-velocity movements while the vestibular system typically responds to movements of higher velocity, the AOS and vestibular labyrinths form 2 complementary systems to detect self-motion and promote image stabilization so that objects in the visual world can be quickly and accurately analyzed.7,9,12,13

The AOS exists in all vertebrate classes6,7,18,19 including humans20 but it has been studied most extensively in the rabbit. The 3 preferred directions for cells in the accessory optic terminal nuclei define 3 directions in visual space, namely, horizontally from posterior to anterior for the DTN, vertically up and down for the MTN, and vertically down for the LTN.7,9,11-14,21 Its 3 pretectal accessory optic nuclei are closely related to the NOT and receive input predominantly from the contralateral eye.7,9,12,13 Direction-sensitive ON-type retinal ganglion cells encode retinal image slip22,23 and transmit this information to the AOS, inferior olive24 floccular climbing fibers,25 and floccular Purkinje cells.26 These 3 pairs of channels remain anatomically distinguishable within the AOS, inferior olive, and floccular zones, which (when stimulated) elicit eye movements organized in a canal-like coordinate system.18,27-29 Each pair conveys signals about flow of the visual surround about 1 of 3 rotation axes, which are approximately collinear with the best-response axes of the semicircular canals and the rotation axes of the extracocular muscles.28

The rabbit flocculus ipsilateral to the seeing eye is optimally sensitive to optokinetic stimulation about a 135° axis, while the flocculus con-
contralateral to the seeing eye is optimally sensitive to optokinetic stimulation around a horizontal 45° axis (Figure 3). For horizontal stimulation, the DTN and its adjacent NOT are selectively sensitive to nasally directed optokinetic stimulation presented to the contralateral eye. Conversely, electrical microstimulation in the alert rabbit’s flocculus produces abduction of the ipsilateral eye or dissociated torsional and vertical rotations of the 2 eyes, corresponding to the plane of 1 semicircular canal. Because floccular motion detection for each eye is not fully represented on its own side of the body, monocular optokinetic responses must be derived from the synthesis of bilateral floccular representations. Therefore, the flocculus provides a subcortical binocular visual system that generates asymmetrical torsional eye movements under dissociated conditions of optokinetic stimulation. Studies using decortication have revealed contributions from the visual cortex to the AOS. Disruption of contributions from the visual cortex to the AOS by strabismus may alter the inherent biases of the accessory optic nuclei. The ipsilateral visual cortex is necessary for several response properties that distinguish DTN and LTN neurons in the cat from those in the rabbit. Following decortication, cat DTN and LTN neurons lose their binocularity and become almost totally dominated by the contralateral eye. For example, LTN neurons excited by upward movement, which in the cat are equal in number to those excited by downward movement, become less numerous so that the cat LTN becomes like that of the rabbit, consisting of neurons excited by slow downward movements to the contralateral eye. Unlike the LTN and DTN, neurons in the cat MTN are largely monocular and similar to those in the rabbit. The monocular nasotemporal optokinetic asymmetry that characterizes infantile strabismus is known to result from monocular cortical input to the NOT and DTN, unmasking a subcortical visuovestibular bias that generates latent nystagmus. The AOS provides a neuroanatomical substrate whereby vertical monocular subcortical motion biases could generate the canal-based torsional eye movements that characterize primary oblique muscle overaction and dissociated vertical divergence. Although we observe and analyze these eye movements in yaw, pitch, and roll, they are encoded in a canal-oriented push-pull bilateral coordinate system that detects optokinetic flow in every direction.

Photic stimulation can activate the AOT in the rabbit. The AOS neurons show the same responses to retinal illumination as ON-type direction-sensitive retinal ganglion cells, being excited only at the onset of retinal stimulation, and generate a firing response that is related to light intensity. In this way, the AOS may implement the visuovestibular reflexes that characterize infantile strabismus. However, because the AOS is primarily a motion detector, central modulation of the primitive luminance reflexes that characterize infantile strabismus may require input from additional subcortical visual pathways. It is possible that other primitive luminance pathways may provide parallel subcortical luminance input to the visuovestibular system. Like the AOS, luminance input that modulates the dorsal light reflex in fish (which corresponds to dissociated vertical divergence and primary oblique muscle overaction in humans with infantile strabismus) is transmitted to the central pretectal nucleus in the contralateral midbrain and then down to the vestibulocerebellum, which integrates visual and vestibular input. These luminance and motion pathways may constitute the subcortical equivalents of the “what” and “where” visual streams within the association visual cortex. How these subcortical visual streams intercommunicate to consolidate spatial and temporal summation of visual information at the subcortical levels remains a mystery. But the likelihood that they provide the innervational substrate for the atavistic eye movements that characterize infantile strabismus should not be ignored.

CONCLUSIONS

The AOS provides a critical piece of the puzzle for infantile strabismus by serving as a neuroanatomic substrate for visuovestibular eye movements. The AOS is atavistic, present in humans, subcortical, crossed, and sensitive to optokinetic motion. It operates in a canal-based coordinate sys-
This analysis implies that mutations involving the AOS or its target zones within the cerebellar flocculus could provide a potential template for infantile strabismus. If so, then the age-old dichotomy posited by Worth (congenital defect in cortical fusion) and Chavesse (early binocular misalignment) could be explained by binocular subcortical dysfunction intrinsic to the visuovestibular system.

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REFERENCES

15. Maekawa K, Takeda T. Afferent pathways from the visual system to the cerebellar flocculus of the rabbit.

Error in Figure 4F. In the Clinical Sciences article titled “Spectral-Domain Optical Coherence Tomographic Assessment of Severity of Cystoid Macular Edema in Retinopathy of Prematurity,” by Maldonado et al, published in the May issue of the Archives (2012;130[5]:569-578), an error occurred in the γ-axis of Figure 4F on page 573. The axis range should not be from 0 to 300 μm but from 0.00 to 2.00, as in Figure 4D and E. This article was corrected online.