Deficits in local and global motion perception arising from abnormal eye movements

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Albino mammals exhibit a range of visual deficits including disrupted hemispheric pathways, an underdeveloped central retina, and nystagmus. Recently, it has been reported that albino animals also show deficits in the processing of visual motion, exhibiting higher motion coherence thresholds (MCTs; the proportion of coherently moving elements within a field of randomly moving distracters required to reliably report direction). Here we compare MCTs—collected from human observers with albinism—with an equivalent noise analysis of their fine-direction discrimination and report that their loss in motion sensitivity operates at both the level of local motion processing (of small objects) and at the later stage of global motion pooling. We also compare results from observers with aniridia (characterized by underdeveloped central retina and nystagmus but normal hemispheric visual pathways) and a rare group of observers with albinism who show no nystagmus. For the observers tested, nystagmus proved to be a common feature of individuals showing elevated MCTs. Since it is likely that motion perception is influenced by environmental factors early in development we postulate that the effect of congenital nystagmus on the temporal structure of the natural visual diet disrupts the ability of motion pathways to form normally.

Introduction

Albino mammals have a range of congenital visual abnormalities including underdevelopment of the central retina, abnormal hemispheric pathways into the brain, and nystagmus. While these features have been described structurally, less is known about their impact on visual function. Recently, it has been shown that some albino animals have deficits in motion coherence tasks although the reason for this is unclear (Hupfeld, Distler, & Hoffmann, 2006; Hupfeld & Hoffmann, 2006).

The ability to see motion underpins key visually guided behaviors such as navigation and the breaking of camouflage. Effective motion perception requires an ability to correctly assign direction, velocity, and depth to multiple objects within a scene, which is a challenging computational problem. Our present understanding is that there are two levels of motion processing. The first involves the encoding of *local motion* over small regions by orientation- and direction-selective neurons in V1 (Hubel & Wiesel, 1968) whose operations are well modeled by motion energy or Reichardt detector models. Such motion detectors suffer from an inability to signal motion in any direction other than perpendicular to their preferred orientation (the so-called *aperture problem* for motion). To correctly encode the direction and speed of more spatially extensive objects must therefore require that one pools the output of a series of such local detectors. This takes place in a second level of processing (of global motion), which integrates the individual components of local motion over a larger visual field. This is generally thought to occur in MT(V5) and MST (Mikami, Newsome, & Wurtz, 1986a, 1986b). The receptive fields of neurons in MT and MST are well suited to global motion integration: they are larger than their counterparts in V1 (Born & Tootell, 1992) and tend to receive input from several motion-selective neurons in V1 (Ungerleider & Desimone, 1986). This confers on them the ability to respond to more complex attributes of motion (Movshon, Adelson, Gizzi, & Newsome, 1985) although successful

disambiguation of local motion within contours may also require the involvement of form-responsive mechanisms.

The standard psychophysical paradigm for assessing global motion processing is *motion coherence*: observers report the direction (usually "left" versus "right," or "up" versus "down") of a field of coherently moving signal dots as a function of the number of dots that have been replaced by randomly moving noise elements. The maximum percentage of coherently moving elements that an observer can tolerate being replaced by noise, while still making a reliable judgment of direction, is known as the *motion coherence threshold* (MCT). The MCT paradigm was introduced by Newsome and colleagues (Britten, Shadlen, Newsome, & Movshon, 1992; Newsome, Britten, & Movshon, 1989) and has proved enormously influential for both basic and clinical psychophysical studies of motion perception. It is generally assumed that high motion coherence thresholds (MCTs) result from a global motion processing deficit. This is not necessarily the case, since MCT paradigms cannot quantify the contribution of any early deficits in local motion that have been inherited by global motion integration (Dakin, Mareschal, & Bex, 2005a). Indeed Barlow and Tripathy (1997) have shown that it is largely *local noise,* specifically the false correspondences arising between dots in successive frames of the stimulus, that limits MCTs under varying stimulus conditions such as density, size of region, method of stimulus generation, etc. Nevertheless, MCTs are often (and particularly in a clinical context) taken to be an indicator of competence at *global integration*. Recently some of us (Dakin et al., 2005a; Mareschal, Bex, & Dakin, 2008) have presented evidence that local and global limits on motion perception can be separated using a novel application of an *equivalent noise* (EN) paradigm (Barlow, 1956). The principle underlying the EN paradigm is that performance in tasks requiring visual integration is limited by two factors: precision at estimating the direction of each dot (internal noise) and the number of such direction estimates one can effectively combine (sampling efficiency).

Why albino animals have deficits in motion detection is perplexing, but the abnormal hemispheric projections at the optic chiasm in these animals may be a contributing factor. All albino mammals share the common phenotype of misrouted retinal ganglion cell axons at the optic chiasm, where the uncrossed projection is reduced in favor of the crossed projection resulting in disruptions to binocular vision (Creel, Witkop, & King, 1974; Guillery, Okoro, & Witkop, 1975; Kinnear, Jay, & Witkop, 1985; Kriss, Russell-Eggitt, Harris, Lloyd, & Taylor, 1992; Lund, 1965; Oetting, Summers, & King, 1994). In humans with albinism, pigmentation of the eyes, skin, and hair correlate with the degree of misrouting of the hemispheric projections (von dem Hagen, Houston, Hoffmann, & Morland, 2007). The size of the abnormally large crossed projection found in albinos varies considerably between individuals, extending up to 15 degrees into temporal retina (Hoffmann, Lorenz, Morland, & Schmidtborn, 2005; Hoffmann, Tolhurst, Moore, & Morland, 2003; Schmitz et al., 2004). However, other

deficits may also play a role. The central retina in albino animals is underdeveloped, and in man, the fovea is absent resulting in marked reductions in visual acuity (Oetting et al., 1994). Further, the majority of humans with albinism suffer from nystagmus, although this is not exclusive to them as this condition arises spontaneously in man whenever the fovea is absent. Indeed nystagmus also occurs in observers with a normal fovea, such as individuals with congenital nystagmus. Motion perception is impaired in individuals with congenital nystagmus, which is predominantly horizontal in orientation (Dieterich & Brandt, 1987; Shallo-Hoffmann, Bronstein, Morland, & Gresty, 1998). Dieterich, Grünbauer, and Brandt (1998) also described motion perception deficits in downbeat and upbeat nystagmus. Shallo-Hoffmann, Bronstein et al. (1998) showed that individuals with congenital nystagmus, including two subjects with ocular albinism, had elevated motion discrimination thresholds, particularly in the direction of their nystagmus. This could be due to abnormal eye movements or the adaptive mechanisms that reduce oscillopsia in these individuals. It was concluded that the impaired motion discrimination was probably due to adaptive mechanisms as the thresholds remained elevated even when the subjects observed the stimulus in the null position, where nystagmus was minimal or absent. Congenital nystagmus is also known to disrupt the optokinetic response (OKN; Abadi & Bjerre, 2002; Collewijn, Apkarian, & Spekreijse, 1985).

We sought to assess local and global motion processing in humans with albinism to determine whether they have deficits in processing coherent motion and identify the mechanisms that underlie them. Using both motion coherence and equivalent noise paradigms we compare individuals with albinism displaying the common phenotype with a rare sub-group that do not have nystagmus. Further, we also compare these with data from observers with aniridia. These are of interest because similar to observers with albinism they lack a fovea, exhibit nystagmus, and have a structurally abnormal calcarine fissure; however, the hemispheric pathways at the optic chiasm are normal (Azuma et al., 1999; Neveu, Holder, Sloper, & Jeffery, 2005; Neveu, von dem Hagen, Morland, & Jeffery, 2008; Young, 2003). Aniridia is also associated with other non-visual cortical abnormalities, such as the absence of the anterior commissure (Sisodiya et al., 2001). Hence, they represent a comparison in which it should be possible to ascribe the etiology of deficits to either a retinal or a cortical location.

Methods

Observers

We tested five groups of observers:

1. Six observers with albinism and nystagmus (Table 1, Observers 1–6, 3 males, 3 females), aged 23–56 years.

Obs. no.	Gender	Age (years)	RVA	LVA	Steroeacuity (sec of arc)	Foveal hypo.	Fundal hypo.	Iris trans.	Nystagmus	Squint	OCA
1	M	18	20/80	20/80	Nil	+	+	−	+	Yes	No
2	M	23	20/400	20/63	Nil	+	+	+	+	No	Yes
3	F	24	20/125	20/125	Nil	+	+	+	+	Yes	Yes
4	F	36	20/32	20/32	?	+	+	−	+	Yes	Yes
5	M	38	20/125	20/125	Nil	+	+	+	+	Yes	HP
6	F	56	20/125	20/40	Nil	+	+	+	+	Yes	Yes
7	F	22	20/40	20/40	Nil	+	+	+	−	No	Yes
8	M	15	20/32	20/32	Nil	+	+	−	−	No	Yes
9	F	36	20/80	20/80	Nil	+	−	−	+	No	
10	F	42	20/125	20/200	Nil	+	−	−	+	No	
11	M	72	20/63	20/80	Nil	+	−	−	+	Yes	
12	M	22	20/63	20/63	Nil	−	−	−	+	No	

Table 1. Clinical details of each observer from observer groups 1–4. *Note*: HP—Hermansky–Pudlak Syndrome; "+" present; "−" absent.

Five with oculocutaneous albinism (OCA, 4 with Type I, 1 with Type II) and one with Hermansky–Pudlak Syndrome. Visual acuities ranged from 20/32 to 20/400. All observers had bilateral foveal hypoplasia, fundus hypopigmentation, and nystagmus. Visual evoked potential (VEP) testing revealed misrouting of the visual pathways at the optic chiasm in all observers. One observer with OCA had an esotropic right eye and another observer with OCA had an exotropic right eye.

2. Two observers with albinism and without nystagmus (Table 1, Observers 7 and 8), aged 22 years (female) and 15 years (male). Both observers had OCA Type 1B. Visual acuities were 20/40 bilaterally in the female observer and 20/32 bilaterally in the male observer. Both observers had bilateral foveal hypoplasia and fundus hypopigmentation. The female observer had mild iris transillumination. VEP testing revealed misrouting of the visual pathways at the optic chiasm in both observers.

3. Three observers with aniridia and nystagmus (Table 1, Observers 9–11, 2 females, 1 male), aged 36, 42, and 72 years. Visual acuities ranged from 20/63 to 20/400. All observers had bilateral foveal hypoplasia and nystagmus. One observer (Observer 11) had ptosis and another had exotropia in the left eye (Observer 10). The projections of the visual pathways at the optic chiasm are normal in aniridia (Neveu et al., 2005).

4. One 22-year-old male observer with idiopathic horizontal nystagmus but no other visual or neurological abnormalities (Table 1, Observer 12). Visual acuities were 20/63 bilaterally.

5. Six age-matched controls (2 males, 4 females) to the group with albinism and nystagmus (#1). Visual acuities were 20/20 or better in both eyes and all observers were healthy, with no ophthalmological or neurological pathology.

Informed consent was obtained prior to testing. The research followed the tenets of the Declaration of Helsinki and was approved by the Institute of Ophthalmology ethics committee.

By visual inspection, all observers with nystagmus had horizontal nystagmus. Observers with albinism had either horizontal jerk nystagmus or periodic alternating nystagmus. All aniridic subjects and the observer with idiopathic nystagmus had horizontal jerk nystagmus. We did attempt to quantify the amplitude and phase of the oscillation using an infrared eye tracker (Cambridge Research Systems) but iris transillumination renders the albino pupil invisible under such conditions.

Apparatus

Experiments were carried out on a PC computer under the MATLAB programming environment (MathWorks) and incorporated elements of the Psychtoolbox (Brainard, 1997). Stimuli were presented in grayscale on a CRT monitor (LaCie Electron Blue 22″), which was calibrated with a Minolta LS110 photometer. We used a video processor (Bits++; Cambridge Research Systems, UK) to give true 14-bit contrast resolution. The display had a mean background luminance of 50 cd/m^2. A centrally presented fixation marker (a 0.5 cd/m^2 "+" with arms subtending 32 arc min) was continuously visible onscreen to (a) help observers maintain fixation and (b) provide a static orientation reference for the direction discrimination judgements.

Equivalent noise paradigm

Motion perception involves the processing of both local motion over small regions of the visual field by

direction-selective neurons in V1 and global motion that integrates the individual components of local motion over a larger visual field in MT(V5) and MST. Local and global limits on motion perception can be separated using a novel application of an equivalent noise (EN) paradigm (Dakin et al., 2005a; Mareschal et al., 2008). Figure 1 illustrates the principle underlying the EN paradigm; that performance in tasks requiring visual integration is limited by two factors: internal noise and sampling efficiency. For directional integration these factors translate to: precision at estimating the direction of each dot and the number of such direction estimates one can effectively combine. An EN experiment for direction discrimination involves presenting the observer with a field of moving elements whose directions are drawn from a random distribution with some associated mean and variance and then estimating the smallest discriminable change in mean direction. One then measures these direction discrimination thresholds as a function of the level of directional variability in the stimulus (i.e., the width of the direction distribution). Because the threshold measure employed is effectively a measure of the variance of some internal representation of direction one can exploit the additivity of variance to predict the effects of noise on performance. Specifically one can fit a simple two-parameter model to the data that allow one to read off directly (a) the number of samples that the observer is integrating and (b) the precision of each of those samples. Note that such estimates are not bound to any particular model of motion processing; no matter how an observer performs a task EN will reveal that the observer is using n samples with a particular precision. This is a useful behavioral tool that has now been applied to various issues related to motion processing; for example, poorer direction discrimination performance in the periphery and around oblique angles have both been shown to be attributable to less precise estimates of local motion (Dakin, Mareschal, & Bex, 2005b; Mareschal et al., 2008).
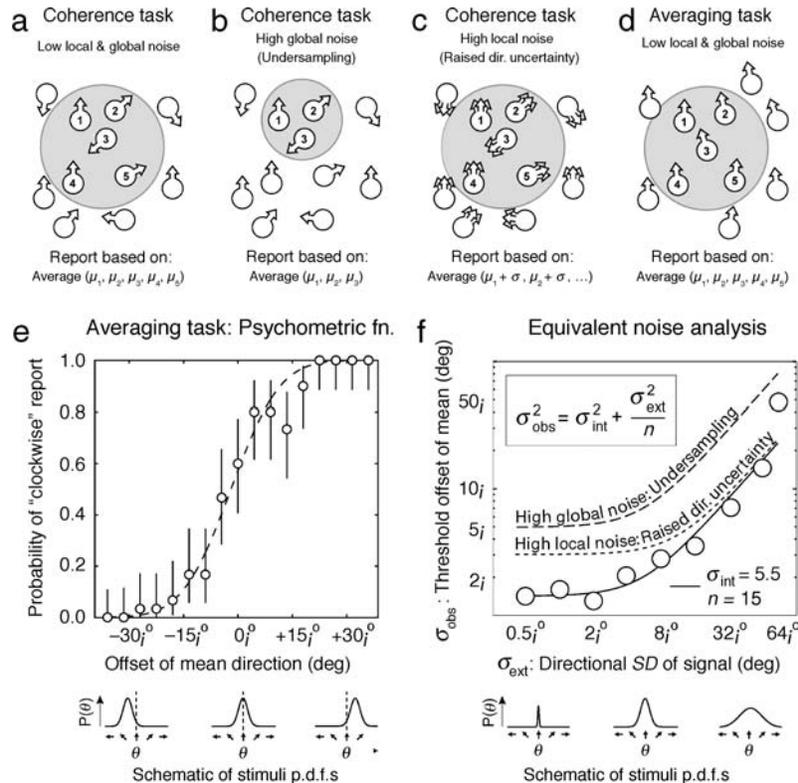

Figure 1. Assessing local and global limits on motion processing using motion coherence and equivalent noise paradigms. (a) Motion coherence tasks involve presenting observers with a set of coherently moving dots and then estimating how many of those dots can be replaced with random motion while supporting the observers' ability to discriminate the (gross; e.g., up versus down) overall direction. (b) Although generally assumed to be limited by the observers' ability to (globally) pool motion samples, poor performance could arise from (c) a noisy representation of individual (local) direction. To disambiguate the contribution of these two factors, we also used (d) an averaging task where the observers make a fine-direction discrimination of elements whose directions are drawn from a Gaussian random distribution. (e) Our performance measure (the direction discrimination threshold) is the slope of the psychometric function for the observers' ability to say if the overall direction of the element set lay clockwise or anti-clockwise of some reference direction. (f) Plotting threshold as a function of the range of directions gives data (open symbols) that can then be fit by an equivalent noise (EN; boxed equation) whose parameters yield direct estimates of both the number of samples being averaged and the precision with which each estimate is being made.

Stimuli

Stimuli were 18-frame movies (presented for 240 ms at the monitor frame rate of 75 Hz) showing 64 patches of drifting spatial frequency (SF) band-pass filtered noise randomly located within a circular aperture (radius 12.6 deg). A single frame from a representative stimulus is shown in Figure 2. Each patch consisted of a static 2D raised-cosine contrast envelope (radius 54 arc min with a tapered edge extending 8 arc min) multiplied by a drifting isotropic noise carrier (Log-Gabor filtered: peak SF = 2.2 c/deg, SF bandwidth = 0.5 octaves). The carrier drifted at 2.2 deg/sec with its motion being generated using OpenGL on the computer's graphics card accessed via the Psychtoolbox (QUEST, Watson & Pelli, 1983). This procedure allowed us to set the noise direction independently at each patch location. We chose to use this procedure over other, e.g., random dot stimuli because (a) we can concentrate energy at lower SFs to enhance visibility, (b) the directions drifting noise can move in are not—unlike dot stimuli—limited by the raster of the stimulus display making it more suitable for fine-direction discrimination, and (c) the use of static apertures minimizes the induction of pursuit eye movements.

The directions that the drifting noise carriers moved in depended on the condition. In the motion coherence condition, some proportion of the elements moved in the same direction while the remainder moved in random directions. In two separate runs observers had to determine whether the overall direction was (a) "up" versus "down;" or (b) "left" versus "right." In equivalent noise conditions, the directions of all elements were generated using a Gaussian probability density function with a mean that varied around some reference direction (either vertical/upward or horizontal/leftward, in two separate conditions) and a standard deviation that was either 1°, 8°, or 32°. These values were selected based on previous studies (Dakin et al., 2005a) since they are known to elicit a range of direction discrimination performance suitable for equivalent noise modeling.

Design

We assessed motion perception using three behavioral measures: contrast detection thresholds, motion coherence detection thresholds, and fine-direction discrimination thresholds. Thresholds were tested around both vertical and horizontal directions for all observers. Fine-direction discrimination thresholds were measured at various levels of direction variability allowing us to conduct an equivalent noise analysis (see above and Introduction section) and specifically to determine how much performance was governed by local noise (observers ability to see the motion of one patch) or global noise (observers ability to pool motion estimates across patches).

Procedure

Observers were seated in front of the display monitor, at a viewing distance of 75 cm. They were presented with a field of drifting noise patches (described above) and asked to perform one of two responses depending on condition. The observers viewed the stimulus binocularly. The first (used in the contrast detection and motion coherence conditions) was a coarse judgment of direction (either "left" versus "right," or "up" versus "down" assessed in separate runs). The second (used in the equivalent noise condition) was a fine-direction judgment: to determine if the overall direction of the drifting elements was clockwise or counterclockwise of some reference direction. The observers responded by either pressing the appropriate key on a keypad or (if they were uncomfortable with this) by making a verbal response (in which case the experimenter made the keyboard response for them). Auditory feedback was given for incorrect responses.

The experimental variable (either contrast, motion coherence, or directional offset) was always under the control of an adaptive staircase procedure. This procedure converges on the threshold level of the independent variable, i.e., the level that elicits 75% correct identification performance from the observer. At least two runs of 45 trials were undertaken for all thresholds reported. Runs were never interleaved. Error bars are the 95% confidence intervals on threshold estimates obtained using a bootstrap.
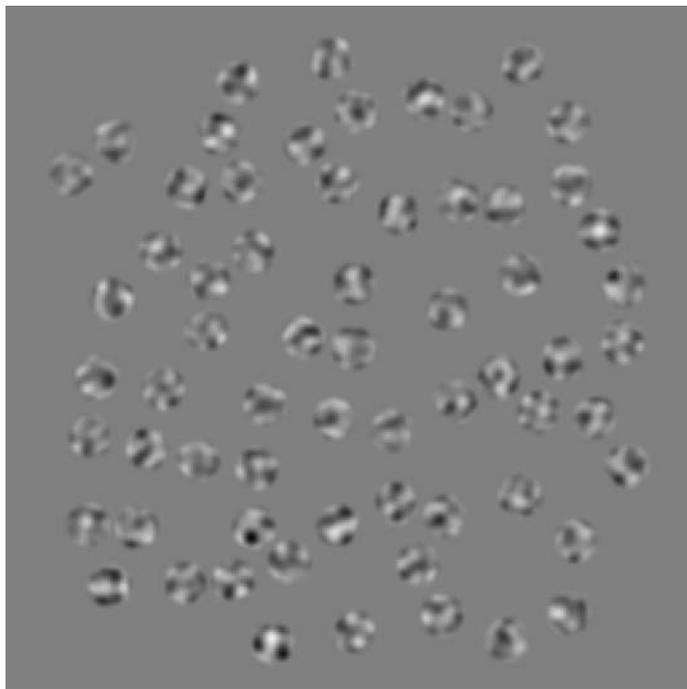

Figure 2. Single frame from typical stimuli employed in the study. Stimulus contained 64 patches of drifting spatial frequency (SF) band-pass filtered noise randomly located within a circular aperture (radius 12.6 deg).

In all cases when estimates of significance are given we report the *p* value from a two-tailed *t*-test.

Three sets of measurements were made for each observer. We first estimated contrast thresholds for a coarse direction judgment with vertical (90° versus 270°) and horizontal directions (0° versus 180°). These thresholds were used to determine the Michelson contrast of elements in the two subsequent test conditions: either 5 times the contrast threshold or 100%, whichever was the lower value. We next estimated motion coherence thresholds using the same stimuli at 5 times the contrast threshold or 100% contrast. Observers made a coarse direction judgment deciding if a pattern was moving either "up" versus "down" or "left" versus "right," within two separate runs. Our QUEST procedure yielded the signal-to-noise ratio supporting 75% correct performance on this task.

The third and final sets of measurements we made was a set of fine-direction discrimination thresholds, at multiple levels of directional variability, which allow us to perform an equivalent noise analysis (Dakin et al., 2005a; Hess, Mansouri, Dakin, & Allen, 2006; Mareschal et al., 2008), in the vertical and horizontal directions. QUEST estimated the minimum directional offset that reliably (75% correct) supports observers reporting the overall stimulus direction as clockwise or anti-clockwise of some reference direction (either horizontal or vertical in separate runs). Having estimated such thresholds at multiple levels of directional variability we used the equivalent noise model to derive estimates of local noise and global sampling efficiency on this task. To reiterate this technique allows one to directly "read off" (a) the precision with which an observer can estimate the direction of each noise patch and (b) the number of noise patches observers are pooling over.

Data analysis

Having determined motion coherence thresholds and equivalent noise parameters from our various observer groups, we sought to compare differences between groups using a bootstrapping technique. Specifically, for the two largest groups (control, $n = 6$; and albino patients with nystagmus; $n = 5$) we used the mean threshold as best estimate of average performance and QUEST's estimates of threshold as the best estimate of performance standard deviation. Bootstrapping works by assuming that every real/measured data point represents one observation drawn randomly from a distribution of possible data points with the given mean and standard deviation. Under this assumption one can generate new data sets by resampling those distributions (using the mean and *SD* estimates described). If one generates a whole series of such data sets the end overall mean and standard deviation of each point will match the original estimate of those parameters (by definition). We generated 1024 new data sets for each condition. We then estimated the average (across observers, within a group) (a) motion coherence threshold and

(b) equivalent noise parameters for each one of these 1024 resampled data sets. These data allow us to construct a distribution of likely group-mean motion coherence thresholds and group-mean equivalent noise parameters, which can (a) be compared to one another and (b) be compared to individual estimates from members of the smaller experimental groups.

Results

Results from all conditions are summarized in Table 2. The following is a descriptive summary of the results presented in Table 2.

Motion detection thresholds

Motion detection thresholds are the lowest Michelson contrast level, which supported the observer being able to discriminate either "left" versus "right" (horizontal, 0°) or "up" versus "down" (vertical, 90°) directions of motion. There was no significant difference between the two conditions for the control observers ($p > 0.5$, Table 2). Similarly, motion detection thresholds in two observers with albinism and without nystagmus were normal in both the horizontal and vertical directions (Table 2).

Motion detection thresholds in 5/6 observers with albinism and nystagmus were elevated compared to control observers ($p < 0.001$, Table 2) but did not differ significantly between horizontal and vertical motion conditions ($p > 0.05$). One observer with albinism and nystagmus was unable to see the stimulus, even at maximum contrast. This observer was excused from participation in the next two experiments. The motion detection thresholds in one observer with idiopathic nystagmus were highly variable and several estimates were made to obtain thresholds in both directions of motion. This observer described extreme difficulty seeing the stimulus.

Motion detection thresholds were highly variable in observers with aniridia and the mean of the three observers is given in Table 2. Only the first observer could perform the test reliably. The second observer had an elevated threshold in the horizontal direction but was unable to register a reliable threshold in the vertical direction. After several attempts, the third observer had variable thresholds in both directions of motion. Two out of three observers were only able to see high contrast stimuli compared to observers with albinism and controls.

Motion coherence thresholds

Motion coherence stimuli were presented at either 5 times the motion contrast detection threshold determined

	Direction	Controls (n = 6)	Albino with nystagmus (n = 6)	Albino without nystagmus (n = 2)	Aniridic (n = 3)	Idiopathic nystagmus (n = 1)
Motion detection threshold (%)	Horiz	1.5 ± 0.3	10.5 ± 3.6*	2.1	35.8 ± 18.8*	?4.8
	Vert	1.9 ± 0.4	12.8 ± 4.2*	1.9	20.8 ± 5.9*	?4.1
Motion coherence threshold (%)	Horiz	45 ± 18	80 ± 18*	46	74 ± 28*	100
	Vert	46 ± 17	75 ± 27*	53	65 ± 35*	100
Direction discrimination thresholds	Horiz 1	6.4 ± 2.2	12.9 ± 4.7*	6.5	52.5 ± 30.6*	21.8
	Horiz 8	7.0 ± 1.6	14.8 ± 6.3*	6.9	37.1 ± 16.5*	25.2
	Horiz 32	27.8 ± 5.2	37.6 ± 10.2*	23.8	70.8 ± 12.1*	100
	Vert 1	6.9 ± 1.3	30.7 ± 13.8*	8.6	42.1 ± 21.0*	83.7
	Vert 8	9.5 ± 3.8	34.1 ± 13.7*	12.6	49.9 ± 25.8*	34.4
	Vertl 32	25.2 ± 16.6	60.7 ± 28.9*	43	50.3 ± 13.2*	100
Internal noise	Horiz	4.3 < 6.6 < 8.9	16.4 < 22.3 < 30.4*	8.6	39.7 ± 45.9*	7.5
	Vert	8.6 < 12.8 < 18.8	15.2 < 16.8 < 18.5	5.2	35.5 ± 47.9*	30.2
Sampling efficiency	Horiz	1.3 < 1.56 < 1.9	1.8 < 3.15 < 6.6*	2.8	0.2 ± 0.2*	0.1
	Vert	3.3 < 5.2 < 8.8	6.2 < 6.3 < 6.3*	0.9	0.3 ± 0.2*	0.2

Table 2. Motion detection thresholds, MCTs, direction discrimination thresholds, internal noise, and sampling efficiency for 5 observer groups. *Note*: *Significantly different to normal; *n* = number of subjects; ? = minimum value of several attempts.

individually for each observer or at 100% if "5 times the motion contrast threshold" exceeded the value of 100. The stimulus consisted of elements moving either predominantly in the horizontal or vertical direction (depending on condition) mixed with elements moving in random directions. Observers were required to determine the overall direction of motion (2AFC, "up" versus "down" or "left" versus "right"). The threshold is the percentage of elements required for observers to determine the direction of motion correctly 75% of the time. The motion coherence thresholds (MCTs) for control observers and observers with albinism are plotted as group means in Figure 3 alongside data from the smaller groups—observers with aniridia (squares), observers with albinism and without nystagmus (circles), and observer with idiopathic nystagmus (stars). In all cases error bars indicate standard deviations of the threshold estimates for each individual.

Controls required approximately 46% of the stimulus elements to be moving in the same direction before the direction of motion could be detected correctly (Table 2). As in the previous condition, there is no significant difference in the control group between vertical and horizontal motions (*p* > 0.5), and once again, observers with albinism and without nystagmus had normal MCTs (Table 2, Figure 3, circles) in both directions of motion. By contrast, coherence thresholds in observers with albinism and nystagmus were grossly elevated (5/6 observers, Figure 3, yellow and burgundy bars for horizontal and vertical motions, respectively), but we observed no significant difference between MCTs in the horizontal and vertical directions (*p* > 0.2).

Motion coherence thresholds were highly variable in both observers with aniridia and idiopathic nystagmus (Figure 3, squares and stars, respectively). The first
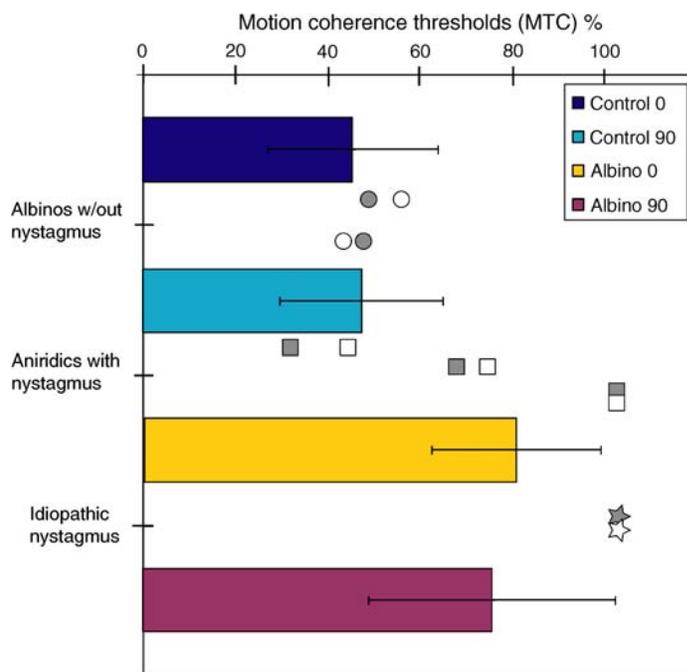

Figure 3. Motion coherence thresholds (MCTs) for control (blue bars) and albino (yellow and burgundy bars) groups in the horizontal (0) and vertical directions (90) of motion. Stimuli were presented at either 5 times the contrast threshold or 100%, whichever was the lower value. MCTs from observers with albinism and nystagmus (5/6 observers) are elevated compared to control observers. One observer with albinism and nystagmus and the observer with idiopathic nystagmus were unable to detect any motion in the stimulus. MCTs from the smaller groups, i.e., aniridics (squares), albinos without nystagmus (circles) and idiopathic nystagmus (stars), are shown for each individual observer in the horizontal (unshaded) and vertical (shaded) directions of motion.

observer with aniridia had markedly elevated MCTs compared to controls. The second observer with aniridia was unable to detect any motion in the stimulus at maximum contrast in both directions and the third observer with aniridia had MCTs comparable to controls. Due to the small sample size, the highly variable MCTs from these observers were unsurprisingly not significantly different from controls or observers with albinism ($p > 0.2$). The single observer with idiopathic nystagmus described extreme difficulty seeing the stimulus under all conditions.

Even on occasions when all elements were moving in the same direction, the observer was unable to detect any motion in the stimulus.

Direction discrimination thresholds

Figure 4 plots direction discrimination thresholds for each observer in the control and albinism groups (Figure 4), as a function of the directional variability of the stimulus.
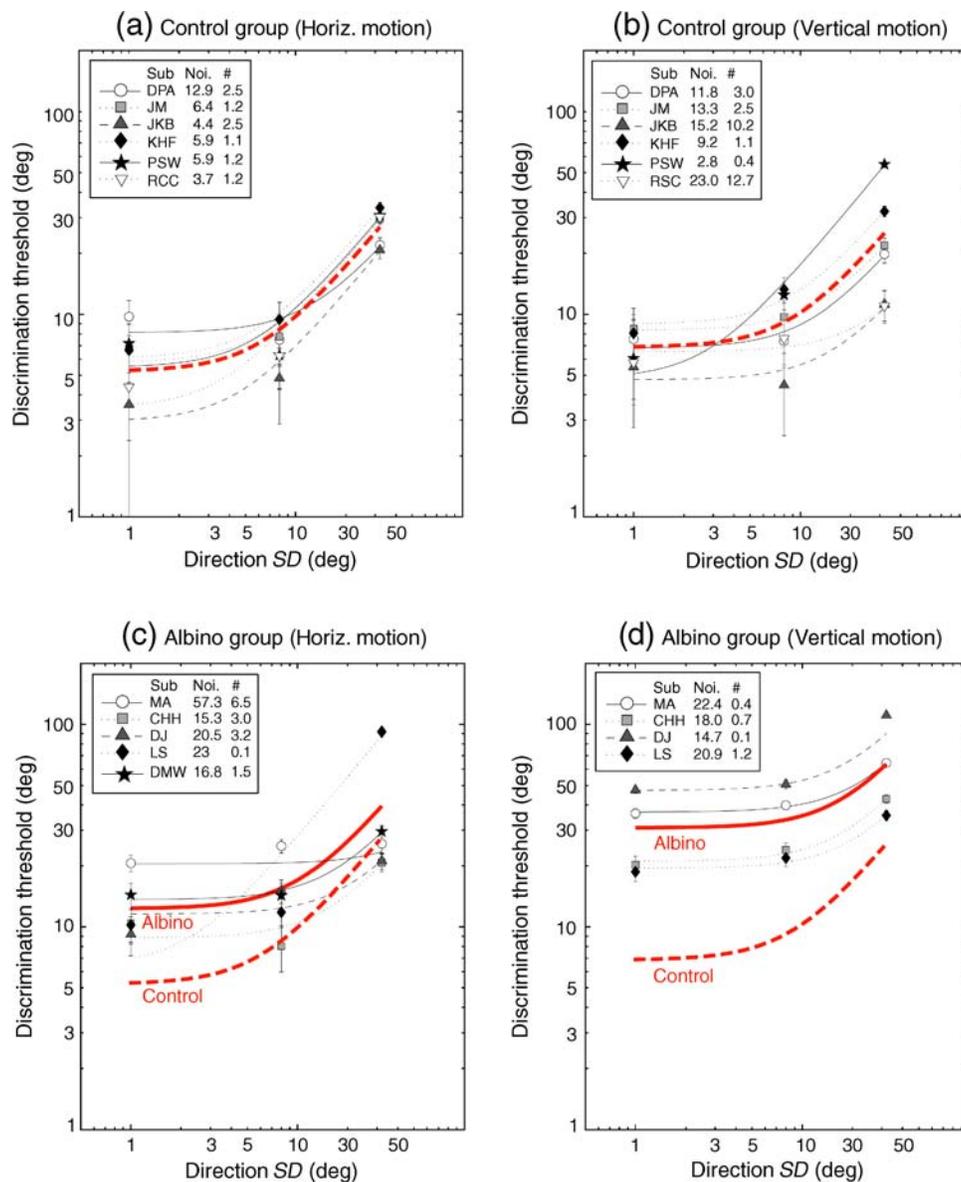

Figure 4. Direction discrimination thresholds (response variability of the observer) against the stimulus variability (standard deviation of the directions present in the stimulus) for control (a, b) and albino (c, d) groups determined using the equivalent noise paradigm (Dakin et al., 2005a). Stimuli were presented at either 5 times the contrast threshold or 100%, whichever was the lower value. Discrimination thresholds for each observer are plotted and errors bars demonstrate variability of the response at a given orientation deviation. (a, b) Direction discrimination thresholds from controls (red dashed lines) show no significant difference between (a) horizontal and (b) vertical motions. (c, d) Observers with albinism (5/6 observers) have elevated thresholds compared to controls and the difference in the horizontal direction of motion is less than that in the vertical direction (compare red solid and dashed lines in (c) and (d)).

Performance shows the pattern of results observed in equivalent noise experiments, with an initial plateau (where variability has little effect) followed by a steep increase in threshold at higher levels of directional noise. There was no significant difference between performance with horizontal and vertical directions at any directional standard deviation tested ($p > 0.2$) in the control group. This is similar to previous studies on normal observers (Dakin et al., 2005a).

As in previous conditions the performance of observers with albinism and without nystagmus was essentially identical to the control group, while discrimination thresholds were elevated in the horizontal (5/6 observers, Figure 4c) and vertical (4/6 observers, Figure 4d) directions of motion in observers with albinism and nystagmus. Again the latter group showed a significant difference in performance between the horizontal and vertical conditions ($p < 0.05$, Table 2).

Discrimination thresholds in both horizontal and vertical directions in observers with aniridia were grossly elevated compared to normal observers ($p < 0.001$, Table 2). As the variance in the direction of motion increased, observers demonstrated a greater than normal variability in detecting the direction of motion. Thresholds recorded in both directions of motion were similar ($p > 0.5$, Table 2). The observer with idiopathic nystagmus had difficulty seeing the stimulus during testing and the thresholds were highly variable but were generally elevated compared to controls.

Internal noise and sampling efficiency

Given our estimates of direction discrimination performance as a function of stimulus variability we were able to use an equivalent noise model to derive estimates of internal noise and sampling efficiency for direction integration (using the logic described above). These factors translate to: precision at estimating the direction of each dot (internal noise) and the number of such direction estimates one can effectively combine (sampling efficiency). Estimates of these parameters for the control observers (blue bars) and observers with albinism (green/red bars) are plotted in Figure 5. Observers from the smaller groups, i.e., observers with aniridia (squares), observers with albinism and without nystagmus (circles), and the observer with idiopathic nystagmus (stars) are plotted as individual estimates with confidence intervals (error bars).

Control observers demonstrated the lowest internal noise levels and therefore were best able to discriminate the direction of local motion within the stimulus (Table 2, Figure 5, left graph, blue bars). Similar to previous findings (Dakin et al., 2005a) internal noise estimates were lower for horizontal ($4.3 < 6.6 < 8.9$) compared to vertical directions ($8.6 < 12.8 < 18.8$), respectively (Table 2; $p < 0.014$). The average effective number of samples pooled was 1.6 and 5.2 in the horizontal and vertical directions of motion, respectively, which is low compared to previous estimates of efficiency with comparable numbers of moving two-dimensional elements (typically nearer 8, Mansouri, Allen, Hess, Dakin, & Ehrt, 2004). This is likely attributable to a combination of our using shorter exposure durations (240 ms compared to 450–500 ms previously) and to our use of windowed noise as our local elements (we have previously used filtered dot stimuli). This may have been less effective in promoting grouping. No significant difference was observed in the estimated efficiency between the two directions of motion ($p > 0.5$). Consistent with both previous experiments, the two observers with albinism and without nystagmus demonstrated normal internal noise levels and sampling efficiency (Table 2, Figure 5, circles).
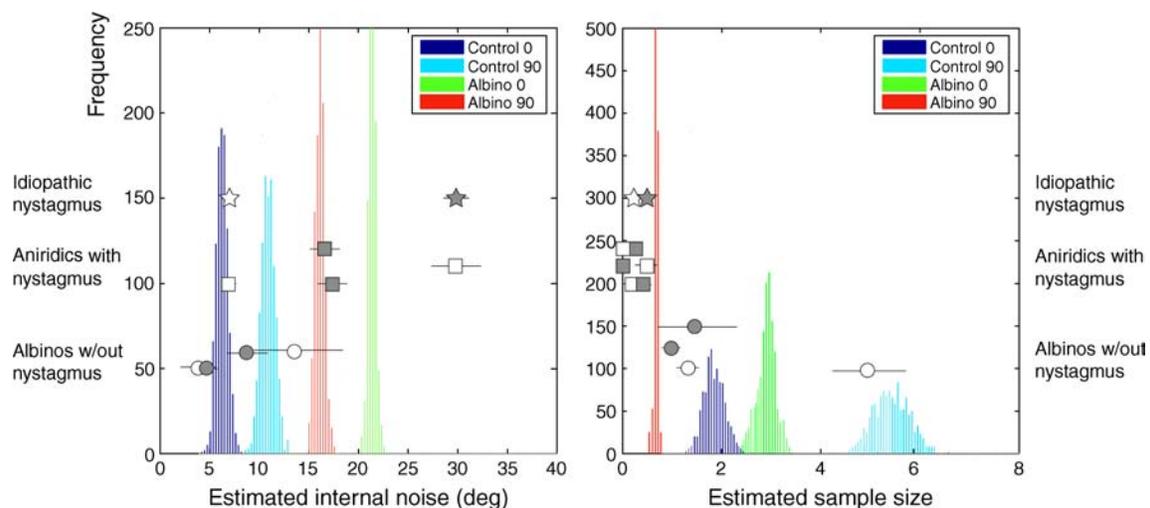

Figure 5. Frequency distributions of estimated internal noise and sample size for control (blue bars) and albino (green and red bars) groups using a bootstrapping technique. The estimated internal noise and sample size from individual observers within the smaller groups, i.e., aniridics (squares), albinos without nystagmus (circles) and idiopathic nystagmus (stars), are shown in the horizontal (unshaded) and vertical (shaded) directions of motion. The bars show the individual variance in the estimate (error bars). One aniridic subject had internal noise estimates of 90 deg in both directions (not shown).

Observers with albinism and nystagmus and observers with aniridia demonstrated higher levels of internal noise in both directions of motion compared to control observers, indicating they are less able to distinguish local direction of motion. Observers with albinism and nystagmus showed lower sampling efficiency in the vertical direction of motion only compared to control groups, whereas observers with aniridia showed substantially lower sampling efficiency in both directions of motion. One observer with aniridia demonstrated normal local noise in the horizontal direction. Local noise did not exhibit the same degree of anisotropy as sampling efficiency.

Note that the internal noise estimates in the observer with idiopathic nystagmus differed between directions of motion (Table 2, stars), but this likely results from a generally unconstrained fit of the EN function (performance was so poor that threshold data were essentially flat).

Conclusions

Summary

We report (a) no significant differences in any subject group for motion coherence or contrast detection thresholds for the two directions tested (either horizontal or vertical) and (b) substantial deficits in fine-direction discrimination of the patient groups, with directions perpendicular to the direction of nystagmus. The latter results are indicative of marked deficits in local and global motion processing in human observers with albinism and nystagmus or aniridia and nystagmus. We have demonstrated that these deficits in motion processing depend upon individuals exhibiting abnormal eye movements; when nystagmus is absent in albinos, motion processing is normal. Observers with these disorders tend to suffer from poor acuity, but our presenting stimuli at constant multiple contrast thresholds (in the majority of subjects) rules out any simple explanation in terms of the visibility of the stimulus. Further, the one observer with idiopathic nystagmus who was neither an albino nor an aniridic observer also exhibits significant deficits in this task.

All humans with albinism have a misrouting of the visual pathways that is consequent upon a lack of melanin synthesis during development. Irrespective of eye movement deficits, melanin deposition varies considerably across the population and it has been shown that pigmentation of the eyes, skin, and hair correlate with the degree of misrouting of the hemispheric projections (von dem Hagen et al., 2007) extending up to 15 degrees into temporal retina (Hoffmann et al., 2005, 2003; Schmitz et al., 2004). This study has shown significant differences in direction discrimination thresholds between subjects with albinism and nystagmus and subjects without nystagmus. On clinical observation both subject groups had similar degrees of hypopigmentation. Therefore the deficits in motion processing described here cannot be fully explained by variations in pigmentation or misrouting of the visual pathways.

Relationship to previous motion studies

It has been reported that motion detection thresholds are eight times greater than normal in observers with horizontal idiopathic congenital nystagmus (Abadi, Whittle, & Worfolk, 1999). Similarly motion detection thresholds to the stimulus motion parallel to the direction of nystagmus are elevated in these individuals (Bedell, 1992). At low temporal frequencies of motion (e.g., 0.5 Hz), thresholds are approximately six times greater than normal, and at higher temporal frequencies (e.g., 4 Hz) thresholds are approximately 20 times greater. Here we report little difference in motion coherence thresholds or contrast detection thresholds. The likely explanation for this discrepancy is that we equated the visibility of our stimuli across subjects and across stimulus directions.

As far as we are aware this is the first report of fine-direction discrimination deficits in albinism. Direction discrimination thresholds in the horizontal direction of motion (i.e., parallel to the direction of nystagmus) were better than those in the vertical in observers with albinism and nystagmus and one observer with aniridia. The most likely explanation for this relates to the mechanisms that underpin fine-direction discrimination. When making discriminations of stimuli around, say, near-vertical upward directions, the one set of mechanisms that are completely uninformative are those tuned to the vertical upward motion (since they cannot help one discriminate between say slightly clockwise or slightly anti-clockwise of vertical directions). Instead, perhaps counterintuitively, the most informative directional structure in the pattern will tend to fall off-vertical or, in the limit, perpendicular to the direction of reference motion. That the human visual system relies on such channels has been demonstrated by comparing the effects of motion adaptation on detection and fine-direction discrimination (Hol & Treue, 2001). Thus because structure within the near-horizontal directions will be maximally disrupted by the presence of horizontal nystagmus, we would expect to see poorest direction discrimination around vertical when these directions are maximally informative.

Visual environment

While the impact of physical motion on the stimulus imposed by nystagmus likely contributes to the performance we have observed we cannot rule out a developmental component to the deficits observed. It is known

that the early visual environment can have a profound impact on the visual brain. The development of orientation tuning and binocular connectivity in V1 requires normal visual experience and can be disrupted when it is not present (Blakemore & Cooper, 1970; Hubel & Wiesel, 1970). It is also established that an inability to detect normal movement in adult animals occurs when they are reared in a stroboscopic environment where no motion can be identified. This environmental manipulation has a profound impact on the development of movement-sensitive cells in the superior colliculus (SC), which is a multi-modal brain stem structure associated with orientation to novel objects (Chalupa & Rhoades, 1978; Rhoades & Chalupa, 1978; Stein, Wallace, Stanford, & Jiang, 2002).

In such a context, it is likely that the observed thresholds in motion coherence result from the lack of eye stability present from birth in human observers with aniridia and the vast majority of observers with albinism. The instability of the retinal image is suppressed by adaptive mechanisms that reduce the effects of oscillopsia (Abadi & Dickinson, 1986; Abadi et al., 1999; Bedell, 2000; Dell'Osso, 1991; Leigh, Dell'Osso, Yaniglos, & Thurston, 1988). These adaptive mechanisms may also impair motion perception in individuals with congenital nystagmus (Dieterich & Brandt, 1987; Shallo-Hoffmann, Bronstein et al., 1998). Further, it is possible that a lack of eye stability may directly impact regions of the brain responsive to movement, and that these regions fail to establish appropriate response properties to moving stimuli. MT is the main structure in the primate brain responsive to global motion (Born & Bradley, 2005). Its removal or that of its homologue in carnivores, the lateral suprasylvian cortex (LS), results in impaired motion perception (Lauwers, Saunders, Vogels, Vandenbussche, & Orban, 2000; Rudolph & Pasternak, 1996).

Electrophysiological recordings clearly show that MT/LS is highly responsive to direction-selective stimuli, with many responding to optical flow and to large area random dot patterns (Brosseau-Lachaine, Faubert, & Casanova, 2001; Lagae, Maes, Raiguel, Xiao, & Orban, 1994; Maunsell & Van Essen, 1983; Rauschecker, von Grünau, & Poulin, 1987; Saito et al., 1986; Strong, Malach, Lee, & Van Sluyters, 1984; Tusa, Demer, & Herdman, 1989). In pigmented and albino ferret, recordings from LS cortex reveal that cells are strongly directionally selective (Philipp, Distler, & Hoffmann, 2006). However, response strength in the preferred direction and tuning sharpness of these neurons were significantly reduced in albino animals compared to the pigmented phenotype. Further, the interspike intervals during stimulation were significantly shorter in pigmented compared to albino animals. Unfortunately, such detailed comparisons have not been made between pigmented and albino primates. However, data from fMRI studies on normal observers and observers with albinism do confirm motion response abnormalities at both higher and lower regions of the albino brain.

Schmitz et al. (2004) using fMRI report that both MT and the SC in human observers with albinism remained active when the stimulus being employed was stationary. This was thought to be due to the presence of congenital nystagmus. Consequently, it is possible that the nystagmus may act partly as a mask that restricts the ability to detect appropriate stimuli.

Eye movement abnormalities

Humans make approximately 100,000 involuntary eye movements' everyday, yet we do not perceive a continually moving image. These micro-saccades trigger the process of saccadic suppression, which markedly suppresses the perception of motion during a saccade (Burr, Morgan, & Morrone, 1999; Ilg & Hoffmann, 1993; Ross, Burr, & Morrone, 1996; Shioiri & Cavanagh, 1989). Saccadic suppression develops earlier than motion processing and selectively suppresses the magnocellular pathway and leaves the parvocelullar pathway unaffected (Burr, Morrone, & Ross, 1994; Kleiser, Seitz, & Krekelberg, 2004). The onset of a saccade modulates activation of LGN and V1 to briefly presented stimuli and triggers suppression of the retinal image at the cortical level (Sylvester, Haynes, & Rees, 2005; Vallines & Greenlee, 2006). The amplitude of the responses decreases as stationary stimuli are presented closer to the onset of a rapid eye movement. This subsequently suppresses the magnocellular pathway. When visual stimulation is absent, activation of LGN and V1 can still be observed (Sylvester et al., 2005; Vallines & Greenlee, 2006).

The direct effects of congenital nystagmus on the process of saccadic suppression have not been investigated. However, motion processing is abnormal in congenital nystagmus (Bedell, 1992; Shallo-Hoffmann, Wolsley, Acheson, & Bronstein, 1998), which may suggest that abnormal eye movements superimposed onto normal micro-saccades may further enhance saccadic suppression, thereby reducing motion sensitivity. Thus, although the findings of Bedell (1992) indicate that the retinal motion due to nystagmus alone can disrupt motion processing there is evidence that saccadic suppression may also contribute to the motion deficit observed. Elevated thresholds are observed even when subjects were maintaining a null position of gaze, where eye movements are absent or minimal, therefore the suppression of motion perception in congenital nystagmus may be due to saccadic suppression (Leigh et al., 1988; Shallo-Hoffmann, Wolsley et al., 1998). This explains the data presented here, where all albino and aniridic subjects with congenital nystagmus have abnormal motion perception and an albino subject without nystagmus has normal motion perception.

Oscillopsia can also develop in the absence of vestibular function (Brandt, 1996; Bronstein, 2004; Rinne, Bronstein, Rudge, Gresty, & Luxon, 1998). When both unilateral and bilateral vestibular failure occurs, rapid head movements

increase retinal image slip hence resulting in oscillopsia. However oscillopsia can decrease with time as adaptive mechanisms suppress the effects of retinal image motion (Grunfeld, Morland, Bronstein, & Gresty, 2000). Similar to the observations presented here, this suppression increases motion detection thresholds (Deutschländer et al., 2008; Grünbauer, Dieterich, & Brandt, 1998; Shallo-Hoffmann & Bronstein, 2003). Deutschländer et al. (2008) also used fMRI to show that the activation of MT/V5 is reduced during visual motion stimulation in these individuals. The fMRI response to visual motion stimuli has not been investigated in individuals with albinism.

Stability

An interesting observation regarding nystagmus and the ability to see motion is that none of the observers with this condition ever reported an unstable visual world or oscillopsia. Rather, to them the visual environment remained stable (Abadi & Dickinson, 1986; Bedell, 2000; Dell'Osso, 1991; Leigh et al., 1988) in spite of the fact that some of them had minimal ability to perceive motion. All could read clearly and only had problems "concentrating" toward the end of the day when tired or following alcohol consumption. Hence, while MT and SC may have abnormal response properties and on a grosser level may remain active even when motion does not form part of the visual scene, such activities are not translated into perceptual events in their observers. A possible explanation for this is that individuals with congenital nystagmus perceive a stable visual world because they sample the visual scene at specific velocities of the nystagmus waveform. However, Jin, Goldstein, and Reinecke (1989) showed that these individuals were able to detect a flashing spot across a range of velocities including the null position and the maximum velocity of their nystagmus. This suggests that the lack of oscillopsia is not due to sampling. This is remarkable considering the degree of retinal image motion demonstrated by individuals with congenital nystagmus due to involuntary eye movements (Abadi et al., 1999; Bedell & Bollenbacher, 1996; Leigh et al., 1988). When this degree of retinal image motion was simulated in normal observers, they described obvious movement of the visual world and profound motion smear. Abadi et al. (1999) therefore suggested that the perceptual stability in congenital nystagmus observers was probably due to extraretinal signals such as the control of eye movements by the extra-ocular muscles (Abadi et al., 1999; Bedell & Currie, 1993; Dell'Osso, 1997; Leigh et al., 1988).

We speculate that the absence of perceived motion may also arise from chronic adaptation of neural mechanisms sensitive to motion in the direction of nystagmus. A direct measure of motion perception following motion adaptation has not been documented in observers with congenital nystagmus, however Shallo-Hoffmann, Wolsley et al.

(1998) report that observers with congenital nystagmus exhibit weaker motion adaptation compared to controls.

While the absence of a stable retinal image is likely to be the key factor in the motion deficits found in human observers with aniridia and most observers with albinism, such a link is not always present in animal models of albinism. Hence, albino ferrets have marked deficits in their motion coherence thresholds, similar to those revealed in this study, but do not display nystagmus. In spite of this these animals do not have an optokinetic response, and as such do not have normal eye movements (Hupfeld et al., 2006). It is probable that the absence of an optokinetic response is due to abnormal visual projections to the dorsal terminal nucleus of the accessory optic system (Hoffmann, Garipis, & Distler, 2004). Whether such projections are abnormal in human observers with albinism remains to be determined. However, there is no evidence for disruptions to visual pathways in humans with aniridia (Neveu et al., 2005).

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