

Sensitivity of vergence responses of 5- to 10-week-old human infants

Eric S. Seemiller

Indiana University School of Optometry,
Bloomington, IN, USA



Jingyun Wang

Salus University, Pennsylvania College of Optometry,
Elkins Park, PA, USA



T. Rowan Candy

Indiana University School of Optometry,
Bloomington, IN, USA



Infants have been shown to make vergence eye movements by 1 month of age to stimulation with prisms or targets moving in depth. However, little is currently understood about the threshold sensitivity of the maturing visual system to such stimulation. In this study, 5- to 10-week-old human infants and adults viewed a target moving in depth as a triangle wave of three amplitudes (1.0, 0.5, and 0.25 meter angles). Their horizontal eye position and the refractive state of both eyes were measured simultaneously. The vergence responses of the infants and adults varied at the same frequency as the stimulus at the three tested modulation amplitudes. For a typical infant of this age, the smallest amplitude is equivalent to an interocular change of approximately 2° of retinal disparity, from nearest to farthest points. The infants' accommodation responses only modulated reliably to the largest stimulus, while adults responded to all three amplitudes. Although the accommodative system appears relatively insensitive, the sensitivity of the vergence responses suggests that subtle cues are available to drive vergence in the second month after birth.

Introduction

Humans use vergence eye movements to align their eyes on a target in a different depth plane. Maddox (1893) outlined a series of principal cues thought to drive dynamic vergence responses in humans. He included (a) monocular cues such as proximity (Enright, 1987) and looming (Predebon, 1994), which have both been shown to drive these responses; (b) blur cues through an accommodation-convergence coupling (Judge & Cumming, 1986); and (c) retinal disparity,

which acts as the final error-correcting cue (Rashbass & Westheimer, 1961). The vergence system in adults has been shown to respond to initial disparities as small as 0.2° with a linear operating range between -2° and 2° (Busettoni, Fitzgibbon, & Miles, 2001; Erkelens & Regan, 1986), meaning that the vergence response is a linear function of the stimulus demand within that range. Disparities larger than ±2° can also elicit a vergence eye movement, but the nature of the relationship changes and becomes nonlinear (Busettoni et al., 2001).

There is little evidence that human infants are sensitive to disparity before 3 to 5 months of age. Their responses to disparity discrimination tasks have been measured using preferential looking (Atkinson & Braddick, 1976; Birch, Gwiazda, & Held, 1982; Fox, Aslin, Shea, & Dumais, 1980) or the visually evoked potential (Birch & Petrig, 1996; Petrig, Julesz, Kropff, Baumgartner, & Anliker, 1981). Only a small percentage of infants responded to disparity prior to 3 months of age. Newborn infants can make vergence eye movements (Slater & Findlay, 1975), however, and the frequency and accuracy of these movements increases over the first four postnatal months (Aslin, 1977; Hainline & Riddell, 1995; Riddell, Horwood, Houston, & Turner, 1999). This raises an interesting developmental question. As mentioned previously, adults use disparity cues to achieve fully accurate motor alignment. If infants, as a group, do not respond to changes in disparity until 3 to 5 months of age, what drives the motor alignment that allows them to demonstrate these disparity discriminations on the order of minutes of arc at 3 to 5 months (Birch & Petrig, 1996)? Could this be an iterative relationship in which motor and sensory function mature together?

Citation: Seemiller, E. S., Wang, J., & Candy, T. R. (2016). Sensitivity of vergence responses of 5- to 10-week-old human infants. *Journal of Vision*, 16(3):20, 1–12, doi:10.1167/16.3.20.



Other cues are capable of driving rudimentary changes in vergence response during early infancy. Accommodation has been shown to drive vergence in infants as young as 8 weeks (Aslin & Jackson, 1979), although the immature spatial sensitivity of the accommodative system suggests that response accuracy could be limited (Banks, 1980; Green, Powers, & Banks, 1980; Haynes, White, & Held, 1965; Wang & Candy, 2010). Horwood and Riddell (2013) also showed that a small number of 1-month-olds made a vergence response to a Gabor target that suddenly appeared larger on the screen, a potential proximal cue. However, this proximal stimulus failed to drive vergence in adults in that study, although similar proximal stimuli have been shown to do so (Enright, 1987). Additionally, it has been demonstrated that infants as young as 3 to 4 weeks make evasive responses to looming stimuli, such as blinking or leaning backward (Yonas, Pettersen, & Lockman, 1979), although vergence responses were not measured in this study. Of note, proximal and accommodative vergence are considered to be open loop responses (Erkelens & Regan, 1986) with no feedback to provide an estimate of the accuracy of the vergence response. Therefore, they cannot provide error correction to achieve eye alignment.

Another possibility is that disparity actually drives vergence in young infants. Neurons responding preferentially to different amounts of disparity have been found in the cortex of newborn macaques (Chino, Smith, Hatta, & Cheng, 1997; Maruko et al., 2008; Zhang et al., 2013). Additionally, it has been proposed that the cortical architecture necessary to support disparity processing is present prenatally in monkeys (Horton & Hocking, 1996; Hubel & Wiesel, 1977; Rakic, 1977). In considering the impact of immature spatial vision, Brown, Lindsey, Satgunam, and Miracle (2007) demonstrated that adults performed no better than very young infants on a disparity-processing task when the targets were filtered with an infant contrast sensitivity function. They suggested that the relatively fine disparities presented previously to infants in the disparity discrimination tasks were simply filtered out by front-end immaturities before disparity processing could operate (see also Schor, 1985). This does not, however, preclude the possibility that larger disparities could drive a vergence response prior to the previously believed onset of sensitivity to relative disparity, as hypothesized by Riddell et al. (1999).

Some studies of human infant vergence have involved placing a prism in front of one eye, to approximate a full field of absolute disparity (e.g., Aslin, 1977; Riddell et al., 1999) with mixed results. Interestingly, these studies introduced a stimulus on the order of 2.5° or larger, outside the linear response range of disparity-driven vergence in adults found by

Busetтини et al. (2001), and then measured the presence or absence of a refixation disjunctive eye movement. Though Aslin (1977) did not test younger infants, he found that for 4 $\frac{1}{2}$ -month-olds fixating a target at around 30 cm, 2% responded to a 5 prism diopter (PD) prism (equivalent to approximately 2.9°) and 13% responded to a 10 PD prism (equivalent to approximately 5.7°). Riddell et al. (1999) found that 63% of infants between 5 and 8 weeks made refixation responses to 20 PD prisms (equivalent to approximately 11.4°). It was argued that this was indicative of a large disparity threshold for a vergence response that decreased over time.

Previous studies of infant vergence have been largely qualitative (i.e., noting the presence or absence of a response) and have not addressed the sensitivity of the vergence motor response. The current study sought to characterize the sensitivity of 5- to 10-week-old infants' vergence responses to a full cue target (containing retinal disparity, blur, and monocular depth cues). The ultimate goal was to understand the stimulus amplitudes in depth that young infants can make a vergence response to. Stimuli moving in depth at different amplitudes (Wang & Candy, 2010) were presented in the first weeks after birth, before the classical onset of responses to disparity. This performance can then be interpreted in the context of the cues potentially driving the response.

Methods

Subjects

Nineteen full-term infants between the ages of 5 and 10 weeks and nine optically-corrected typical adults, with no abnormalities of binocular vision, participated in the study. Informed consent was obtained from all adult subjects or the infants' guardians. The study was approved by the Indiana University Institutional Review Board and adhered to the tenets of the Declaration of Helsinki.

Stimulus

Subjects viewed a high-contrast commercial cartoon movie presented on a 6.8×6.8 cm LCD screen (Caltron Industries, Fremont, CA) (Figure 1). The images were naturalistic, in that they had approximately $1/f$ spatial amplitude spectra (Field, 1987). The screen was mounted on a motorized track that was moved forward and backwards in depth linearly in dioptic (D) and meter angle (MA) units. The stimulus moved as an approximate triangle wave in depth at a frequency of 0.1

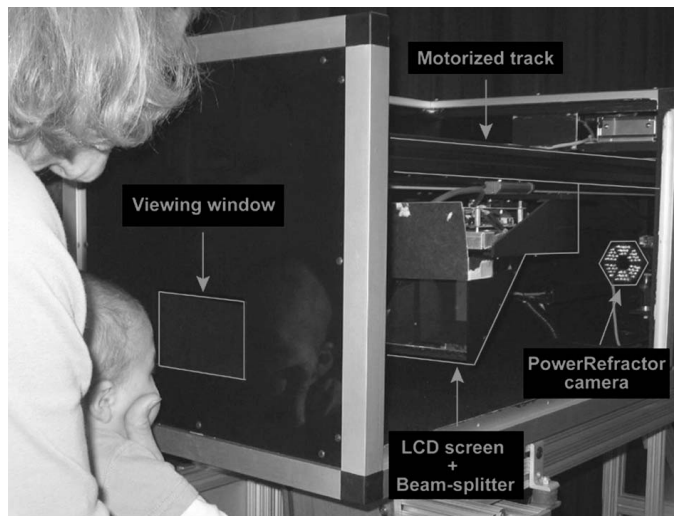


Figure 1. An LCD screen and beam splitter were mounted on a motorized track to permit movement of the stimulus in depth. A PowerRefractor mounted at a viewing distance of 1 m recorded the eye position and refractive state of the subject, who viewed the stimulus through a viewing aperture (from Bharadwaj & Candy, 2008). The side of the box was removed temporarily for the purposes of this Figure.

Hz, around a mean distance of 2.0 MA (50 cm). Each trial consisted of three full cycles of movement at each of three stimulus amplitudes: 1.0 MA (33 to 100 cm), 0.5 MA (40 to 67 cm), and 0.25 MA (44 to 57 cm). Because the temporal frequency remained constant, the velocities differed between amplitudes. Each amplitude took 30 s to complete (Figure 2). An unpredictable movement was included between amplitudes to prevent the subject from continuing on to make predictive eye movements at the frequency of the stimulus during the next, smaller amplitude stimulus (van der Wildt, Bouman, & van de Kraats, 1974). A complete trial took approximately 1 min 45 s, and proceeded continuously after it started, regardless of the attention of the subject. No effort was made to randomize the order of the amplitudes as a previous study showed that the order of amplitudes presented had no effect on the infant accommodation response (Wang & Candy, 2010). Therefore, in an effort to attract the attention of the infant, the largest amplitude stimulus was presented first.

Data collection

A PowerRefractor (MultiChannel Systems, Reutlingen, Germany) was positioned at a viewing distance of 1 m from the subject, behind the moving target and beam splitter (Figure 1). It is an eccentric photorefractor and Purkinje image tracker that measures refractive state and eye position simultaneously at 25 Hz (Choi et al., 2000; Schaeffel, Wilhelm, & Zrenner,

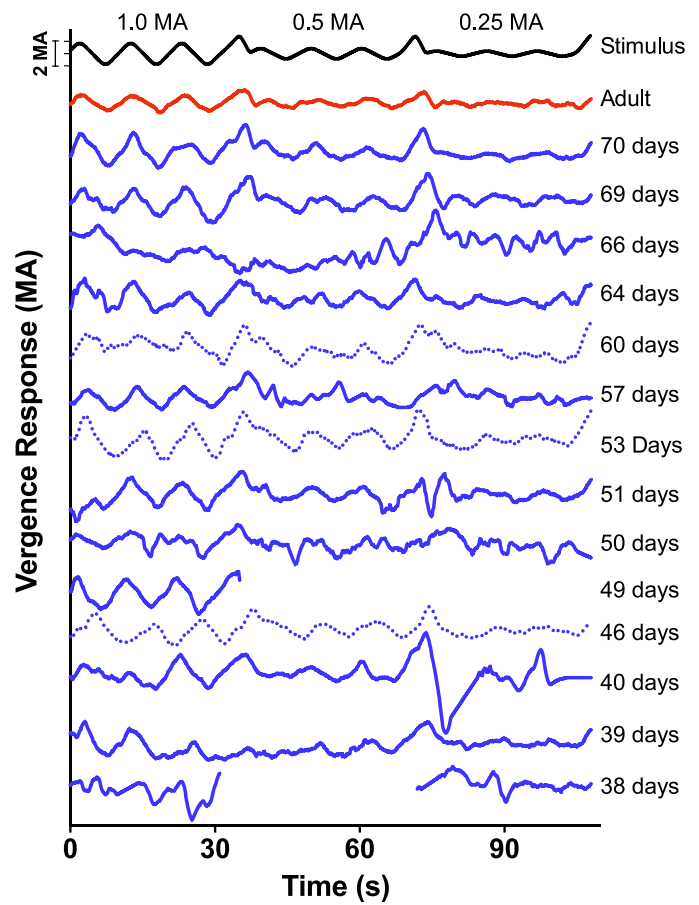


Figure 2. The profile of the stimulus (in MA; black) with a typical adult response (red) and responses from each infant (blue). All responses are smoothed over 1 s, but were not smoothed for analysis. The same smoothing window was also applied to the stimulus trace in this Figure for consistency. The dotted functions represent data collected from a single infant who provided data at three ages.

1993). Briefly, vergence position is estimated by comparing the relative positions of the first Purkinje images and the centers of the images of the pupils in the two eyes. No estimate of angle lambda was made in this study (the angular difference between the line of sight and the pupillary axis [Lancaster, 1943; Slater & Findlay, 1972]), and therefore absolute gaze position was not known. It was not necessary, however, as the analysis only addressed relative change in eye position. A standard adult Hirschberg ratio of 20.86 PD/mm was used to approximate the gain of the eye tracker, which is also a reasonable estimate of the Hirschberg ratio for infants (Riddell, Hainline, & Abramov, 1994). Change in refractive state was estimated with the slope of the intensity of reflected light across the pupil, using the principle of eccentric photorefractive (Howland & Howland, 1974; Schaeffel et al., 1993).

The stimulus and PowerRefractor were positioned inside a dark box. The subject viewed the stimulus

through a small rectangular opening in the box while the room lights were dimmed or turned off to reduce distractions. Infant subjects had their heads gently held in place either by their guardian or a trained member of staff. If an infant became restless in the middle of a trial, they were briefly moved away from the stimulus until they became calm again.

Data analysis

If the infant was restless or not looking into the box during most of the trial, their data were excluded. Occasionally, because of blinking, head movements or eccentric gaze, small periods were missing in usable data. When considering the response to each stimulus amplitude separately, if there were greater than 2 s of consecutive missing data (50 samples) the whole response was excluded, although the responses to the other stimulus amplitudes could be included. Missing data within an otherwise usable amplitude were interpolated using the slope between the two adjacent available data that were collected.

Fast Fourier transforms (FFT) were performed on the stimulus and response vectors to obtain the amplitude spectra for each stimulus amplitude. The highest amplitude in the stimulus, as intended, occurred at 0.1 Hz. Because the stimulus approximated a triangle wave and not a pure sinusoid, there was additional energy at higher harmonics and the energy at 0.1 Hz represented only a portion of the stimulus. The amplitudes of the accommodation and vergence responses at 0.1 Hz were used as estimates of the responses to the stimulus. Although these responses may consist of a stimulus-driven component plus noise, they are defined as the “signal” for the purposes of the analyses performed here. An initial estimate of response noise was made by averaging the amplitudes at the adjacent frequencies in the FFT (0.067 Hz and 0.132 Hz).

Conditions

The primary stimulus condition incorporated all cues to drive vergence or accommodation, including retinal disparity, blur, and monocular cues. If data from one amplitude within a trial were poor, the full trial could be run again in an attempt to collect data for all three amplitudes over multiple trials.

A comparison condition was performed to generate a second estimate of the response noise. The subjects viewed a static target for 30 s (the length of time equivalent to three cycles of one amplitude in the full-cue condition). The FFTs of the vergence and accommodation vectors were computed for this condition and the amplitude of the response at 0.1 Hz was

used as an alternative estimate of response noise for comparison with the primary condition.

If possible, a second full-cue primary trial was also attempted to assess test-retest repeatability.

Statistical analyses

The normality of the response amplitude distribution across observers was assessed for each stimulus amplitude using a Shapiro–Wilk test. After confirming that all response amplitudes were normally distributed, paired *t* tests comparing the 0.1 Hz response amplitude and noise estimates were performed. Significance was set at $p < 0.05$ and adjusted for multiple comparisons within each age group using a Bonferroni correction ($p < 0.0167$). Reported *p*-values are uncorrected.

Results

Vergence sensitivity

Usable data were collected from 12 of 19 infants and all nine adult subjects. The vergence response vector from each individual infant is plotted in Figure 2 together with the stimulus profile and a typical example of adult data. One subject was followed longitudinally at 46, 53, and 60 postnatal days, and all three visits are included in figures (although for statistical analyses, only results from the first visit were included). The data were smoothed for the purposes of generating Figure 2 using a running average over 500 ms before and 500 ms after each data sample. This was done to highlight the lower frequency content in the response (nearer to the frequency of the stimulus) for visual inspection of individual trials. All further analyses, however, were performed using the raw, unsmoothed data. The amplitude spectra of the stimulus and vergence responses of two infants are shown in Figure 3. Both the signal value (the response at 0.1 Hz) and the noise estimate (the mean of the adjacent frequencies) are presented in Figure 4. For adults and infants, both the signal and noise responses were normally distributed. For all amplitudes tested, the signal response was significantly different from the adjacent frequencies noise estimate for both adults (1.0 MA: $t = 11.28$, $p < 0.001$; 0.5 MA: $t = 9.05$, $p < 0.001$; 0.25 MA: $t = 3.54$, $p = 0.004$) and infants (1.0 MA: $t = 5.40$, $p < 0.001$; 0.5 MA: $t = 3.12$, $p = 0.005$; 0.25 MA: $t = 3.03$, $p = 0.006$).

The mean signal response amplitudes for infants were 0.76 ($SD \pm 0.27$), 0.37 (± 0.17), and 0.24 (± 0.09) MA for the 1.0, 0.5, and 0.25 MA stimuli, respectively. For adults they were 0.66 (± 0.13), 0.34 (± 0.07), and 0.17 (± 0.05) MA, respectively. Because the stimulus

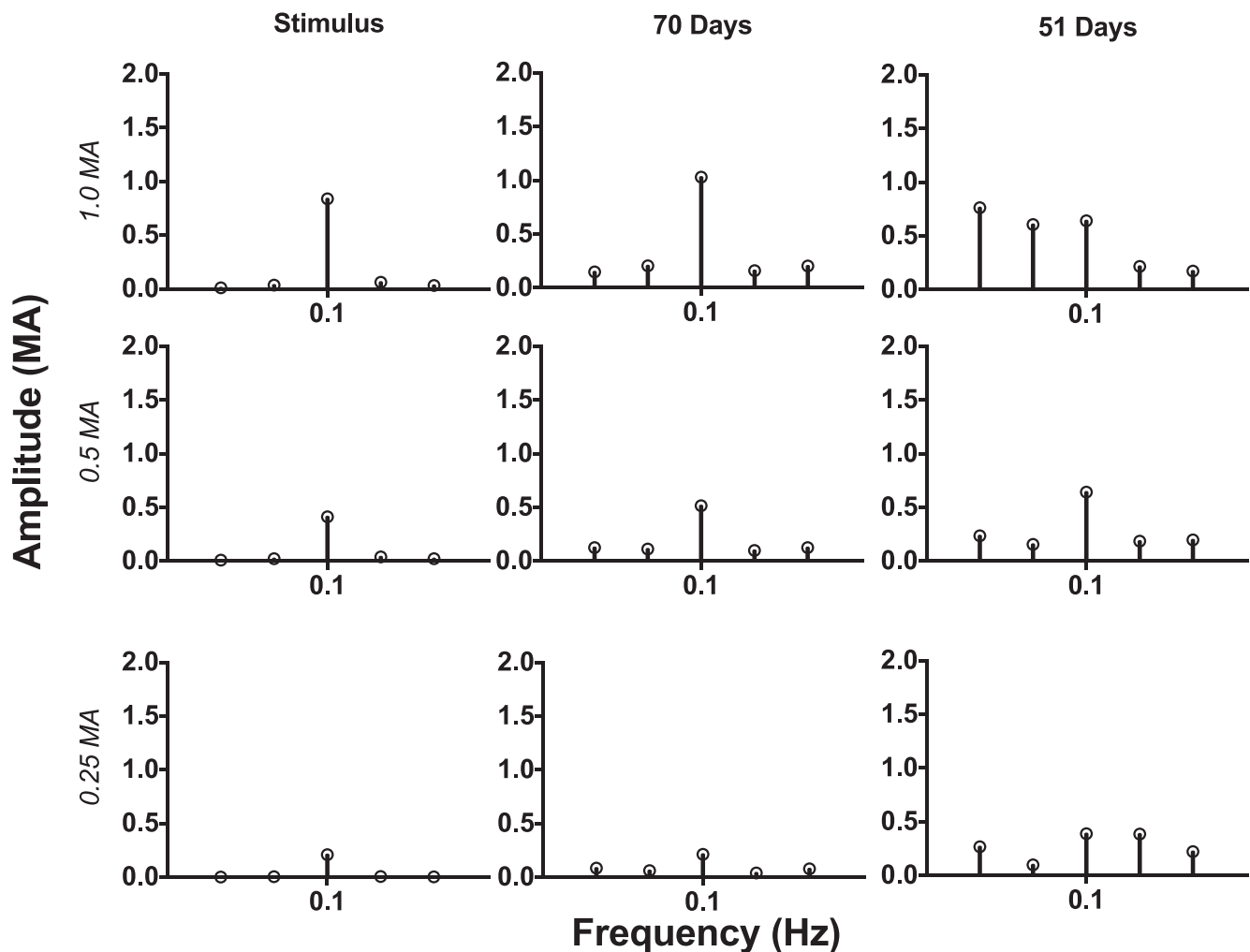


Figure 3. Amplitude spectra of the stimulus and the responses of two infant subjects. The rows from top to bottom represent the 1.0 MA, 0.5 MA, and 0.25 MA amplitude stimuli, respectively. The response at 0.1 Hz, the fundamental frequency of the stimulus, will be referred to as “signal” while the mean of the adjacent frequencies, 0.067 Hz and 0.132 Hz, will be referred to as “noise.”

approximated a triangle wave, the actual stimulus amplitudes at 0.1 Hz were less than the entire stimulus modulation (0.83, 0.41, and 0.21 MA). The mean response gains for adults were 0.79, 0.83, and 0.81. For infants they were 0.91, 0.90, and 1.14. It should be noted that the gain of the PowerRefractor was not calibrated for individual Hirschberg ratios and so individual differences in corneal curvature and anterior chamber depth that affect the Hirschberg ratio may contribute to the variation in response estimates seen here.

Tukey mean-difference plots for adult and infant vergence responses are shown in Figure 5. These plots demonstrate the consistency in responses across two trials from each individual, as a function of the magnitude of the result. Multiple trials were collected from seven out of 12 infants and all adults. Limits of agreement were ± 0.30 MA for adults and ± 0.46 MA for infants, with little bias.

Additional, previously unreported, vergence data from a study conducted by Wang and Candy (2010) are also shown in Figure 4. This experiment was performed in a largely similar way on 2- to 4-month-old infants. The stimulus amplitudes for that experiment were 0.75, 0.50, and 0.25 MA or D, all modulating at a temporal frequency of 0.1 Hz. For infants in that experiment, vergence signals were also significantly larger than the noise at all three amplitudes (0.75 MA: $t = 16.04$, $p < 0.001$; 0.50 MA: $t = 6.71$, $p < 0.001$; 0.25 MA: $t = 6.23$, $p < 0.001$).

Accommodation responses

All adult and infant subjects who provided usable vergence data also provided accommodation data, as the two were measured simultaneously. Example amplitude spectra for infant accommodation responses

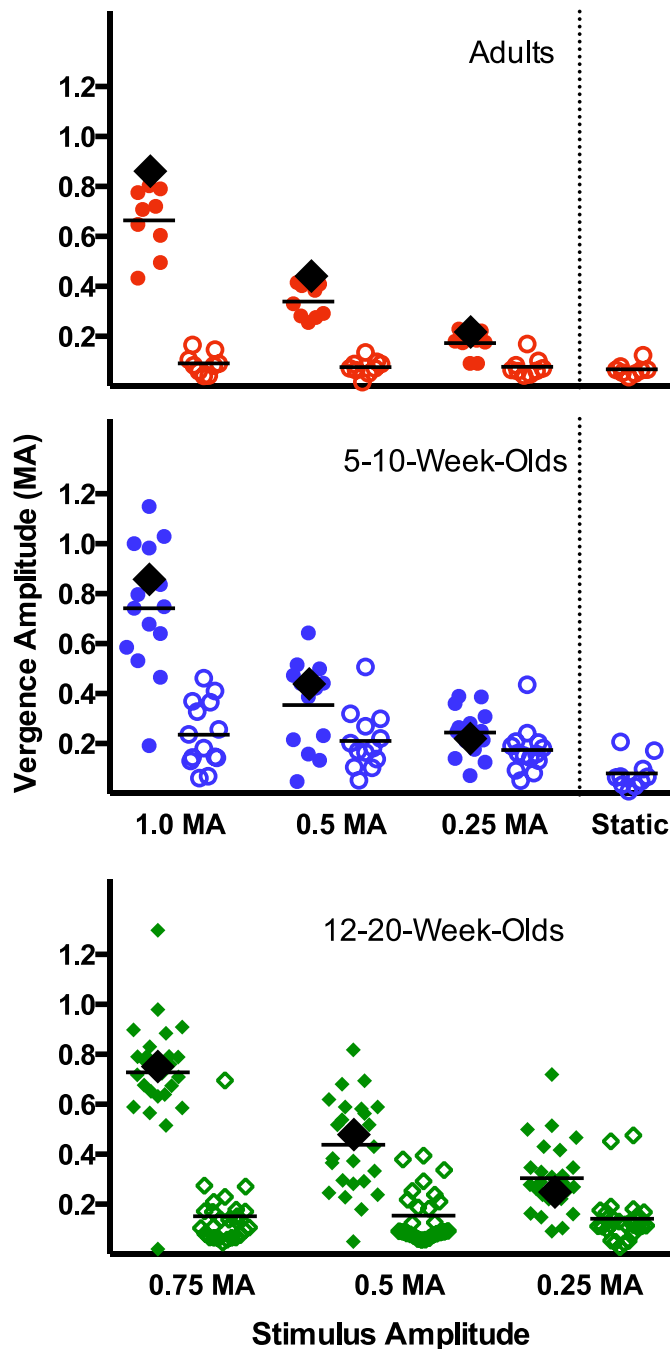


Figure 4. Signal and noise vergence amplitudes for adults (top, red), 5- to 10-week-olds (middle, blue), and 12- to 20-week-olds from Wang and Candy (2010; bottom, green). Filled symbols represent the signal response at 0.1 Hz while the stimulus was moving. Open symbols represent the noise estimates from the adjacent frequencies (0.067 Hz and 0.132 Hz). Black diamonds represent the amplitude of the stimulus at 0.1 Hz and horizontal black lines are the mean response values. The noise estimate from the static stimulus condition is included for subjects run in this study.

are shown in Figure 6. Adult signal and adjacent frequencies noise estimates were normally distributed, as shown in Figure 7, and paired t tests confirmed that the mean accommodation signal was larger than the mean noise at all amplitudes (1.0 MA: $t = 6.43$, $p < 0.001$; 0.50 MA: $t = 5.70$, $p < 0.001$; 0.25 MA: $t = 4.30$, $p = 0.0013$; Figure 7). For infants, only the largest of the three stimulus amplitude responses was significantly different from the noise after a Bonferroni correction for multiple comparisons (1.0 MA: $t = 2.88$, $p = 0.007$; 0.50 MA: $t = 1.88$, $p = 0.043$; 0.25 MA: $t = -1.72$, $p = 0.94$; the p -values reported here are uncorrected, but should be compared to a corrected significance level of 0.0167). Inspection of the infant data plotted in Figure 7 suggests that both the signal and noise estimates are more variable than found in adults. This is consistent with data previously reported by Wang and Candy (2010), who found noisy accommodative responses in the 2- to 4-month-old infants.

The mean accommodative signal responses for adults were 0.62 ($SD \pm 0.29$), 0.36 (± 0.17), and 0.19 (± 0.09) D for the 1.0 D, 0.5 D, and 0.25 D stimuli, respectively, while the mean infant accommodation response to the largest stimulus was 1.09 (± 0.81) D. These responses correspond to gains relative to the energy at 0.1 Hz of 0.74, 0.87, and 0.90 for adults and 1.33 for infants responding to the largest stimulus. The inaccuracy of the gain may be at least partially related to the absence of individual calibrations of refractive state.

Static stimulus

Responses to the static stimulus were collected from seven of 12 infants and all adults. In this condition the screen was held stable at 2.0 MA (50 cm) for a period of 30 s, equivalent to the duration of one amplitude of the triangle wave stimulus. An FFT was used to determine the response at 0.1 Hz. For vergence, plotted in Figure 4, the mean amplitudes were 0.068 MA for adults and 0.071 MA for infants, which were not significantly different from each other ($t = -0.11$, $p = 0.54$). For accommodation, plotted in Figure 7, the mean amplitudes were 0.05 D for adults and 0.45 D for infants, which were significantly different from each other ($t = 2.76$, $p = 0.008$; Candy & Bharadwaj, 2007).

Comparing the two estimates of noise, the static condition estimates were lower than the adjacent frequencies estimates for the vergence condition in both infants and adults. As only seven infants provided usable data for the static condition, no statistical analysis was performed. The difference between the two types of noise estimate presumably reflects the spread of the response energy in the full cue condition into adjacent frequencies. The difference appears smaller for

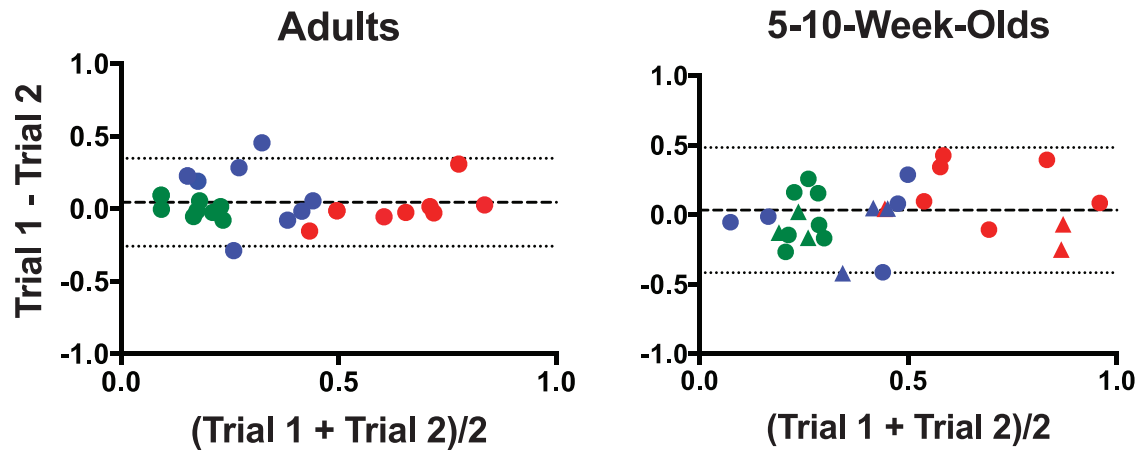


Figure 5. Tukey mean-difference plots of the vergence response amplitude at 0.1 Hz for all adults (left) and seven infants (right). Responses to 1.0 MA stimuli are plotted in red, 0.5 MA are plotted in blue and 0.25 MA are plotted in green. One infant subject was followed longitudinally and denoted by a triangle. The mean bias and 95% limits of agreement are also plotted.

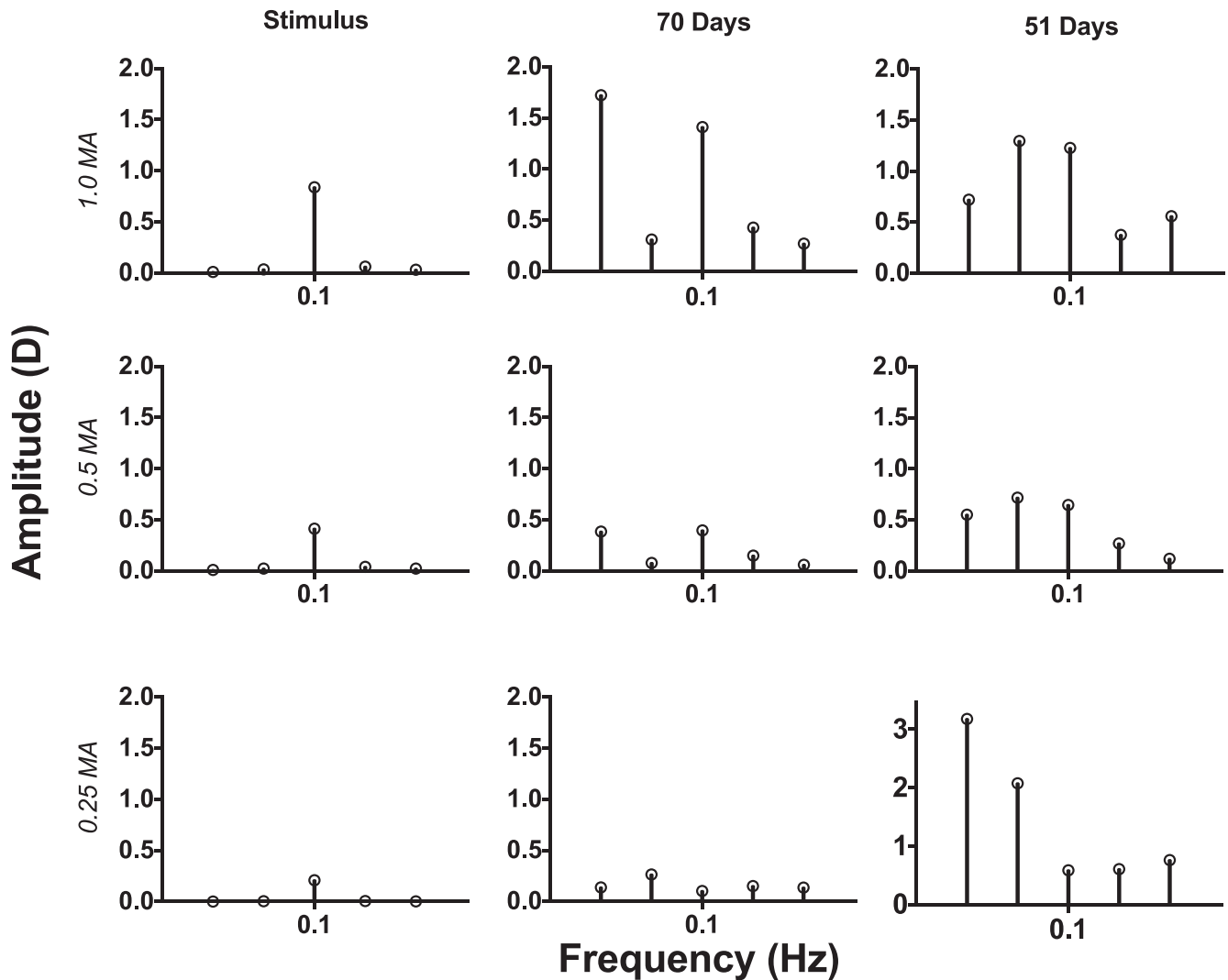


Figure 6. The amplitude spectra of the stimulus and the accommodation responses of the same two infants shown in Figure 3. Note that the vertical scale of the lower right graph has increased relative to the rest of the Figure to show increased response amplitudes.

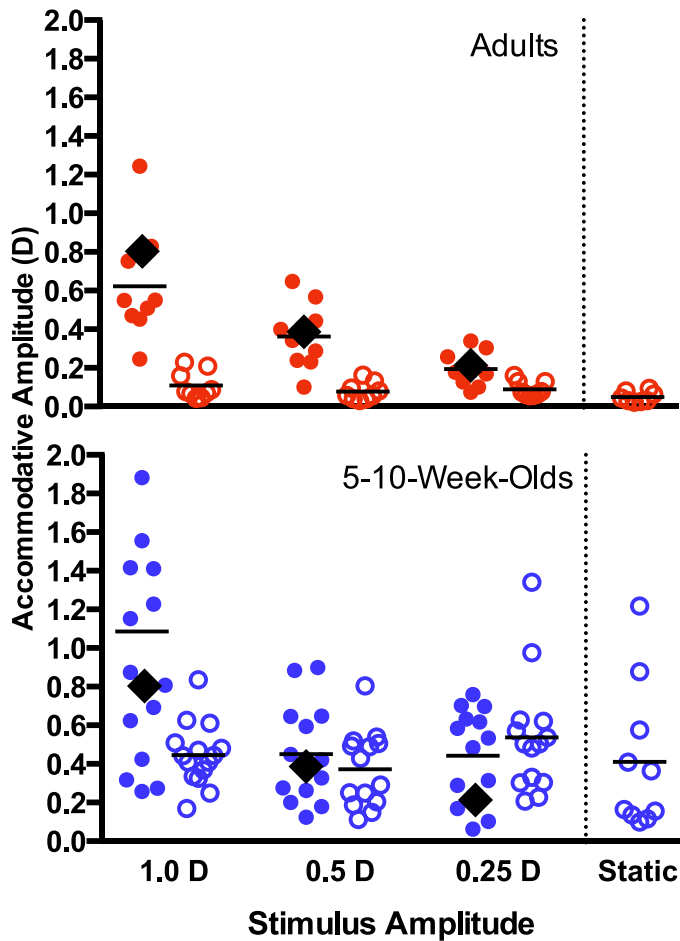


Figure 7. Accommodation signal and noise amplitudes for adults (top, red) and 5- to 10-week-old infants (bottom, blue). Filled circles are the signal responses at 0.1 Hz and open circles are the noise responses derived from the adjacent frequencies (0.067 Hz and 0.132 Hz). Black diamonds represent the amplitude of the stimulus at 0.1 Hz and horizontal black lines represent the mean. Signals are significantly larger than noise for all the amplitudes in adults, but only for the largest amplitude in infants. Noise estimates from the static condition are also shown.

accommodation for infants, while adult differences for vergence and accommodation are comparable.

Discussion

The findings reported here suggest that, as a group, 5- to 10-week old infants can exhibit reliable vergence responses to targets modulating in depth at an amplitude of 0.25 MA. For the infants in this study with an average interpupillary distance of 4.0 cm (range = 3.9–4.1) this is equivalent to an angular stimulus of approximately 1° in each eye, from nearest to farthest point, which is about 2° of interocular disparity. Some

individual responses in Figure 2 demonstrate structure in the response that mimics the stimulus, suggesting that even smaller changes in stimulus distance might be able to elicit a tracking vergence response. Though no amplitude smaller than 0.25 MA was tested in this experiment, the true sensitivity might be finer than that based on this structure.

These responses are generated to stimuli that are close to the range of disparities tested in the classic disparity discrimination studies. For example, Petrig et al. (1981) failed to find evidence of cortical responses to 40 min of disparity until 3 months of age, while Atkinson and Braddick (1976) found some evidence of disparity detection for stimuli of this size in one infant at 2 months. Held, Birch, and Gwiazda (1980) found few responses to 1° of disparity until about 16 weeks. A later study found little evidence, either behaviorally or cortically, of responses to disparities of 30 min until 3 months of age (Birch & Petrig, 1996). How might young infants be able to generate these vergence responses given the classical findings regarding the development of disparity discrimination? Perhaps the individuals in the current study were ones that had developed disparity detection already. Braddick, Watam-Bell, Day, and Atkinson (1983) testing subjects from birth found substantial variation in the earliest cortical responses to binocular stimuli (correlograms), the youngest being at 54 days. However, this only occurred in a small percentage of subjects, and younger subjects in the current study exhibited vergence responses. It is also an unlikely possibility that only subjects with active disparity detection were cooperative and those with immature disparity detection were prohibitively fussy. If this were true and seven of 19 (37%) were uncooperative because of disparity insensitivity, 11 of 19 (57%) were still responding to the largest amplitude based on their signals being larger than the entire noise distribution (see Figure 4, 1.0 MA). This is still inconsistent with previous literature on binocular function at these ages.

Another possibility is that young infants are using cues other than disparity to drive their vergence response, such as the coupling between accommodation and vergence. Infants between 5 and 10 weeks of age have been shown to generate vergence responses to accommodative stimuli (Aslin & Jackson, 1979), but it is thought that the blur detection that drives accommodation may have limited sensitivity due to limited spatial vision (Green et al., 1980). The accommodative responses in this study and others (Wang & Candy, 2010) suggest that the vergence response is more robust than that of accommodation and therefore the likelihood that accommodation is responsible for this vergence response appears limited. It is possible that the difference between the measured accommodation and vergence responses is the result of measurement

noise, given that Purkinje image eye tracking and photorefractive are two different forms of image analysis. However, the adult control group in the current study showed no significant difference in their vergence and accommodative responses to a static target, suggesting that the measurement noise in the two methods is comparable.

In Maddox's terminology the final possibility would suggest that monocular cues such as looming or proximity are driving these vergence responses. These looming or proximal cues were available in the current stimulus. The angular subtense of the target changed from 11.76° to 3.90° during the largest amplitude stimulus, 9.71° to 5.81° during the middle stimulus, and from 8.83° to 6.83° during the smallest amplitude stimulus. This is much smaller than the change in stimulus size that Yonas et al. (1979) used (25.9° to almost full-field) and that Horwood and Riddell (2013) used (2° to 25°) when they demonstrated behavioral responses to looming stimuli, and therefore it is difficult to compare these studies. Without further investigation, looming can be neither confirmed nor ruled out as a component in the infant vergence responses recorded here.

Might infants of this age control their vergence response using disparity signals? In the simplest sense this contradicts the aforementioned behavioral and electroencephalography studies that suggest infants do not respond to disparity until 3 to 5 months of age. However, these studies dealt primarily with relative disparity and did not assess oculomotor control. Reflex vergence is frequently considered to be driven by absolute disparity (Busetini et al., 2001; Mitchell, 1970). Absolute disparity detectors are thought to operate in V1 (Cumming & Parker, 1999) while relative disparity detectors have been studied in V2 (Thomas, Cumming, & Parker, 2002), suggesting differences in neural substrate. It has also been shown that stimuli can be designed to drive vergence without a stereoscopic percept and vice versa in adults. Masson, Busetini, and Miles (1997) demonstrated that anticorrelated disparity stimuli could drive a vergence response opposite in sign (i.e., crossed anticorrelated disparity drives divergence and uncrossed drives convergence) without subjects reporting a depth percept. Conversely, Lughtigheid, Wilcox, Allison, and Howard (2014) were able to drive a depth percept independently of vergence responses using the after-images of disparate lines. These results suggest that disparity for vergence and stereopsis may be processed somewhat separately. Thus, it may be possible that young infants are able to use absolute disparity to drive vergence prior to the time when they can demonstrate responses to relative disparity.

It is also possible that infants are simply sensitive to larger disparities prior to the ages at which responses to

smaller disparity were noted in the previous literature. This could indicate maturation of neurons tuned to disparity, but is also consistent with the proposal explored by Brown et al. (2007) and Schor (1985) that front-end immaturities limit infants' disparity sensitivity. The largest disparities tested prior to 3 to 5 months of age in the previous literature were in most cases less than 1° , while the smallest interocular disparity tested in this experiment was approximately 2° . It may be that infants in this experiment were responding to larger disparities than in previous experiments, although the structure in their responses in Figure 2 implies that they can be sensitive to stimuli of less than 2° .

One possibility beyond Maddox's cues that cannot be ruled out entirely in the present study is that of "monocular foveation" or "bifoveal fixation" (Hainline & Riddell, 1995; Held, 1985, 1993). This hypothesis suggests that apparently disjunctive eye movements measured in young infants may not truly be a vergence response. Rather, the two eyes arrive independently at the target, giving the outward appearance of a vergence eye movement. Riddell et al. (1999) suggested this was how young infants were able to refixate when a prism was placed in front of one eye; one eye maintained fixation while the other eye refixated the target. It has also been proposed that cortical immaturities limit binocular interaction, forcing the two eyes to operate independently (Held, 1985, 1993). However, it has been shown that the neural architecture necessary for binocular comparisons is present prenatally (Rakic, 1977) and neonatally (Horton & Hocking, 1996) in monkeys. Additional evidence suggests that some neurons in both V1 (Chino et al., 1997) and V2 (Maruko et al., 2008) in neonatal macaques respond to relative disparity, with sensitivity limited only by the spatial frequency tuning of the cell (Zhang et al., 2013). Thus, the present anatomical and physiological evidence supports disparity processing within the first weeks of life in macaque (thought to be roughly equivalent to the first two months of life in humans [Boothe, Dobson, & Teller, 1985]). Further research is necessary to reveal the role of disparity and other cues in these fine scale responses.

Keywords: vergence, accommodation, development, disparity, infant

Acknowledgments

The authors wish to thank Stephanie Biehn for her support with subject recruitment and data collection, Bill Monette for developing the experimental equipment and two anonymous reviewers for their valuable recommendations. This work was supported by R01

EY014460 (TRC) and P30 EY019008 “Core Grant for Vision Science.”

Commercial relationships: none.

Corresponding author: Eric S Seemiller.

Email: eric.seemiller@gmail.com; eseemill@indiana.edu.

Address: Indiana University School of Optometry, Bloomington, IN, USA.

References

- Aslin, R. N. (1977). Development of binocular fixation in human infants. *Journal of Experimental Child Psychology*, 23(1), 133–150. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/839156>
- Aslin, R. N., & Jackson, R. W. (1979). Accommodative-convergence in young infants: development of a synergistic sensory-motor system. *Canadian Journal of Psychology*, 33(4), 222–231. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/546490>
- Atkinson, J., & Braddick, O. (1976). Stereoscopic discrimination in infants. *Perception*, 5(1), 29–38.
- Banks, M. S. (1980). The development of visual accommodation during early infancy. *Child Development*, 51(3), 646–666. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/7418504>
- Bharadwaj, S. R., & Candy, T. R. (2008). Cues for the control of ocular accommodation and vergence during postnatal human development. *Journal of Vision*, 8(16):14, 1–16, doi:10.1167/8.16.14. [PubMed] [Article]
- Birch, E. E., Gwiazda, J., & Held, R. (1982). Stereoacuity development for crossed and uncrossed disparities in human infants. *Vision Research*, 22(5), 507–513. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/6981241>
- Birch, E. E., & Petrig, B. (1996). FPL and VEP measures of fusion, stereopsis and stereoacuity in normal infants. *Vision Research*, 36(9), 1321–1327. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/8711910>
- Boothe, R. G., Dobson, V., & Teller, D. Y. (1985). Postnatal development of vision in human and nonhuman primates. *Annual Review of Neuroscience*, 8, 495–545. doi:10.1146/annurev.ne.08.030185.002431.
- Braddick, O., Wattam-Bell, J., Day, J., & Atkinson, J. (1983). The onset of binocular function in human infants. *Human Neurobiology*, 2(2), 65–69. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/6629875>
- Brown, A. M., Lindsey, D. T., Satgunam, P., & Miracle, J. A. (2007). Critical immaturities limiting infant binocular stereopsis. *Investigative Ophthalmology & Visual Science*, 48(3), 1424–1434. [PubMed] [Article]
- Busettini, C., Fitzgibbon, E. J., & Miles, F. A. (2001). Short-latency disparity vergence in humans. *Journal of Neurophysiology*, 85(3), 1129–1152. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/11247983>
- Candy, T. R., & Bharadwaj, S. R. (2007). The stability of steady state accommodation in human infants. *Journal of Vision*, 7(11):4, 1–16, doi:10.1167/7.11.4. [PubMed] [Article]
- Chino, Y. M., Smith, E. L., III, Hatta, S., & Cheng, H. (1997). Postnatal development of binocular disparity sensitivity in neurons of the primate visual cortex. *Journal of Neuroscience*, 17(1), 296–307. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/8987756>
- Choi, M., Weiss, S., Schaeffel, F., Seidemann, A., Howland, H. C., Wilhelm, B., & Wilhelm, H. (2000). Laboratory, clinical, and kindergarten test of a new eccentric infrared photorefractor (Power-Refractor). *Optometry and Vision Science*, 77(10), 537–548. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/11100892>
- Cumming, B. G., & Parker, A. J. (1999). Binocular neurons in V1 of awake monkeys are selective for absolute, not relative, disparity. *Journal of Neuroscience*, 19(13), 5602–5618. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/10377367>
- Enright, J. T. (1987). Perspective vergence: Oculomotor responses to line drawings. *Vision Research*, 27(9), 1513–1526. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/3445485>
- Erkelens, C. J., & Regan, D. (1986). Human ocular vergence movements induced by changing size and disparity. *Journal of Physiology*, 379, 145–169. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/3559991>
- Field, D. J. (1987). Relations between the statistics of natural images and the response properties of cortical cells. *Journal of the Optical Society of America A*, 4(12), 2379–2394. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/3430225>
- Fox, R., Aslin, R. N., Shea, S. L., & Dumais, S. T. (1980). Stereopsis in human infants. *Science*, 207(4428), 323–324. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/7350666>
- Green, D. G., Powers, M. K., & Banks, M. S. (1980). Depth of focus, eye size and visual acuity. *Vision*

- Research*, 20(10), 827–835. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/7467137>
- Hainline, L., & Riddell, P. M. (1995). Binocular alignment and vergence in early infancy. *Vision Research*, 35(23–24), 3229–3236. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/8560794>
- Haynes, H., White, B. L., & Held, R. (1965). Visual accommodation in human infants. *Science*, 148(3669), 528–530. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/14263778>
- Held, R. (1985). Binocular vision - Behavioral and neuronal development. In J. Mehler & R. Fox (Eds.), *Neonate cognition: Beyond the blooming buzzing confusion*. Hillsdale, NJ: Lawrence Erlbaum Associates.
- Held, R. (1993). Two stages in the development of binocular vision and eye alignment. In K. Simons (Ed.), *Early visual development, normal and abnormal*. New York, NY: Oxford University Press.
- Held, R., Birch, E., & Gwiazda, J. (1980). Stereoacuity of human infants. *Proceedings of the National Academy of Sciences USA*, 77(9), 5572–5574. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/6933571>
- Horton, J. C., & Hocking, D. R. (1996). An adult-like pattern of ocular dominance columns in striate cortex of newborn monkeys prior to visual experience. *Journal of Neuroscience*, 16(5), 1791–1807. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/8774447>
- Horwood, A. M., & Riddell, P. M. (2013). Developmental changes in the balance of disparity, blur, and looming/proximity cues to drive ocular alignment and focus. *Perception*, 42(7), 693–715. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/24344547>
- Howland, H. C., & Howland, B. (1974). Photorefraction: a technique for study of refractive state at a distance. *Journal of the Optical Society of America*, 64(2), 240–249. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/4815102>
- Hubel, D. H., & Wiesel, T. N. (1977). Ferrier lecture. Functional architecture of macaque monkey visual cortex. *Proceedings of the Royal Society B: Biological Sciences*, 198(1130), 1–59. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/20635>
- Judge, S. J., & Cumming, B. G. (1986). Neurons in the monkey midbrain with activity related to vergence eye movement and accommodation. *Journal of Neurophysiology*, 55(5), 915–930. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/3711972>
- Lancaster, W. B. (1943). Terminology in ocular motility and allied subjects. *American Journal of Ophthalmology*, 26, 122–132.
- Lutigheid, A. J., Wilcox, L. M., Allison, R. S., & Howard, I. P. (2014). Vergence eye movements are not essential for stereoscopic depth. *Proceedings of the Royal Society B*, 281(1776), 20132118, doi:10.1098/rspb.2013.2118.
- Maddox, E. E. (1893). *The clinical use of prisms and the decentering of lenses* (2nd ed.). Bristol, UK: J. Wright & Sons.
- Maruko, I., Zhang, B., Tao, X., Tong, J., Smith, E. L., III, & Chino, Y. M. (2008). Postnatal development of disparity sensitivity in visual area 2 (v2) of macaque monkeys. *Journal of Neurophysiology*, 100(5), 2486–2495, doi:10.1152/jn.90397.2008.
- Masson, G. S., Busetini, C., & Miles, F. A. (1997). Vergence eye movements in response to binocular disparity without depth perception. *Nature*, 389(6648), 283–286, doi:10.1038/38496.
- Mitchell, D. E. (1970). Properties of stimuli eliciting vergence eye movements and stereopsis. *Vision Research*, 10(2), 145–162. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/5440779>
- Petrig, B., Julesz, B., Kropfl, W., Baumgartner, G., & Anliker, M. (1981). Development of stereopsis and cortical binocularity in human infants: Electrophysiological evidence. *Science*, 213(4514), 1402–1405. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/7268443>
- Predebon, J. (1994). Convergence responses to monocularly viewed objects: implications for distance perception. *Perception*, 23(3), 303–319. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/7971108>
- Rakic, P. (1977). Prenatal development of the visual system in rhesus monkey. *Philosophical Transactions of the Royal Society B: Biological Sciences*, 278(961), 245–260. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/19781>
- Rashbass, C., & Westheimer, G. (1961). Disjunctive eye movements. *Journal of Physiology*, 159, 339–360. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/14490420>
- Riddell, P. M., Hainline, L., & Abramov, I. (1994). Calibration of the Hirschberg test in human infants. *Investigative Ophthalmology & Visual Science*, 35(2), 538–543. [PubMed] [Article]
- Riddell, P. M., Horwood, A. M., Houston, S. M., & Turner, J. E. (1999). The response to prism deviations in human infants. *Current Biology*, 9(18), 1050–1052. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/10508620>

- Schaeffel, F., Wilhelm, H., & Zrenner, E. (1993). Inter-individual variability in the dynamics of natural accommodation in humans: relation to age and refractive errors. *Journal of Physiology*, *461*, 301–320. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/8350267>
- Schor, C. M. (1985). Development of stereopsis depends upon contrast sensitivity and spatial tuning. *Journal of the American Optometric Association*, *56*(8), 628–635. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/4031353>
- Slater, A. M., & Findlay, J. M. (1972). The measurement of fixation position in the newborn baby. *Journal of Experimental Child Psychology*, *14*(3), 349–364. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/4658480>
- Slater, A. M., & Findlay, J. M. (1975). Binocular fixation in the newborn baby. *Journal of Experimental Child Psychology*, *20*(2), 248–273. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/1194845>
- Thomas, O. M., Cumming, B. G., & Parker, A. J. (2002). A specialization for relative disparity in V2. *Nature Neuroscience*, *5*(5), 472–478. doi:10.1038/nn837.
- van der Wildt, G. J., Bouman, M. A., & van de Kraats, J. (1974). Effect of anticipation on transfer-function of human lens system. *Optica Acta*, *21*(11), 843–860. Retrieved from <Go to ISI>://WOS:A1974U681400001
- Wang, J., & Candy, T. R. (2010). The sensitivity of the 2- to 4-month-old human infant accommodation system. *Investigative Ophthalmology & Visual Science*, *51*(6), 3309–3317. [PubMed] [Article]
- Yonas, A., Pettersen, L., & Lockman, J. J. (1979). Young infant's sensitivity to optical information for collision. *Canadian Journal of Psychology*, *33*(4), 268–276. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/546493>
- Zhang, B., Tao, X., Shen, G., Smith, E. L., III, Ohzawa, I., & Chino, Y. M. (2013). Receptive-field subfields of V2 neurons in macaque monkeys are adult-like near birth. *Journal of Neuroscience*, *33*(6), 2639–2649. doi:10.1523/JNEUROSCI.4377-12.2013.