



# *Typical and atypical development of ocular alignment and binocular vision in infants – the background*

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Accepted Version

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Horwood, A. M. (2019) Typical and atypical development of ocular alignment and binocular vision in infants – the background. American Academy of Ophthalmology. (Online article) Available at <http://centaur.reading.ac.uk/84149/>

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Publisher: American Academy of Ophthalmology

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## Typical and atypical development of ocular alignment and binocular vision in infants – the background

### Overview and context.

These pages cover the outcomes of research into the typical **motor** aspects of development of binocular vision in very early childhood. Separate pages on the clinical Examination of Ocular Alignment and Binocular Vision in Infants under six months of age (link to it) deals with the their clinical assessment and the recognition of atypical signs.

The development and assessment of visual acuity, stereopsis, refraction and the process of emmetropization has a large literature, and will only be covered here where it affects motor systems. Specific ocular motor anomalies such as esotropia, exotropia, incomitant strabismus, congenital dysinnervation syndromes and paralytic strabismus will also not be covered as their management extends well beyond infancy

### The First Months

Infants are born with practically no visual experience, but by around four months of age, have learned, or will have developed, a complex range of interrelated visual skills.

Many visual processes – fixation, ocular alignment, visual acuity (VA), mature motion detection, convergence (C), accommodation (A), convergence/accommodation linkages, stereopsis, emmetropization, develop concurrently post-natally, and if all goes well, re-inforce each other as they develop (Fig 1a). It is impossible for clinicians to consider any of these systems in isolation. If there is an abnormality or even a mis-match of the developmental trajectories or critical periods in any of these systems, it can quickly lead to concurrent or subsequent maldevelopment of many others (Fig 1b). In very early infancy, it is important to be able to differentiate typical from atypical development in these inter-related systems so that only appropriate interventions are applied.

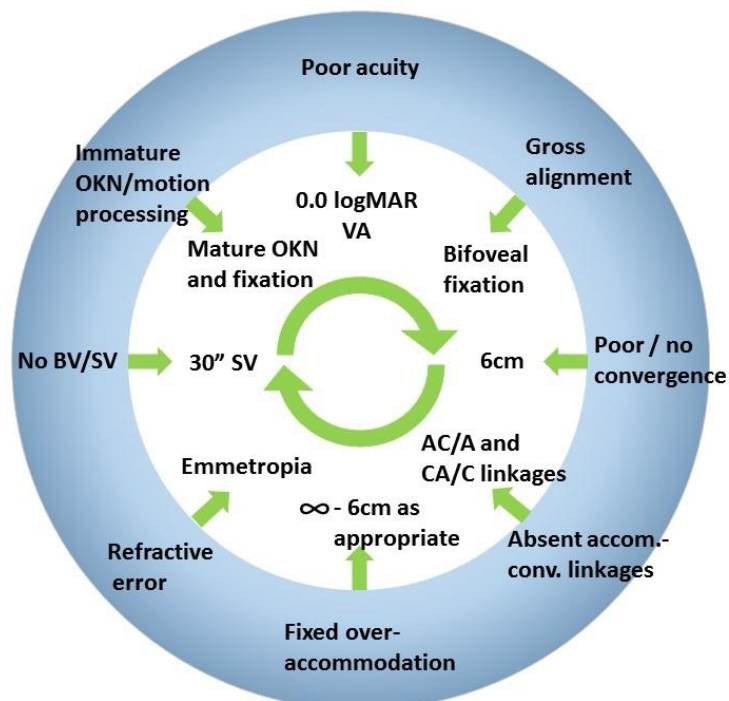


Fig 1a. Typical development. Outer ring – state of visual skills at birth. Inner section- mature visual skills which reinforce each other

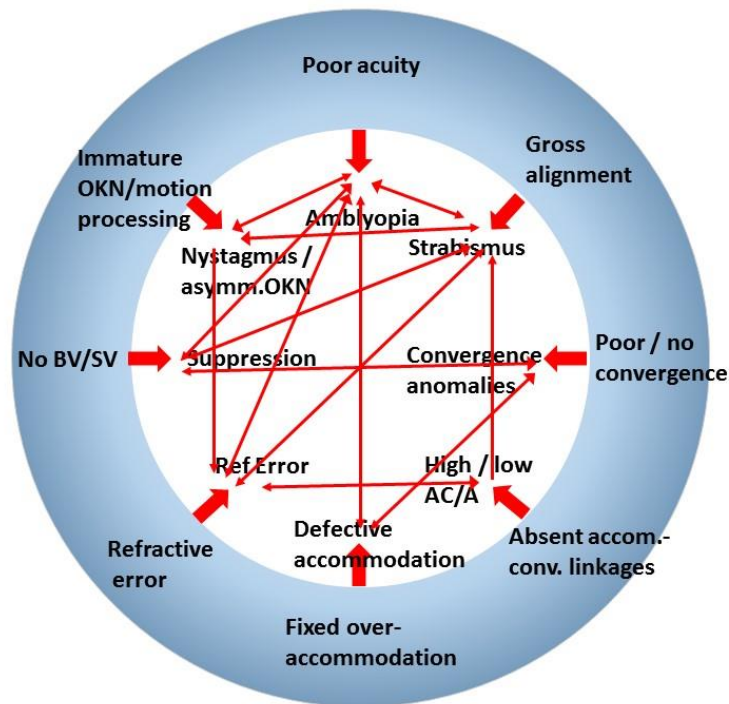


Fig 1b. Atypical development. Outer ring – state at birth. Inner section – abnormal consequences of maldevelopment and examples where abnormal feedback affects other systems

### Co-ordinated systems

We have two horizontally separated eyes, so they need to be co-ordinated to line up when fixating objects anywhere in a visual scene. In addition, they must also cope with binocular fixation of objects as they move in depth between near and distance fixation (convergence) and must also concurrently alter focus of the lenses to keep the images clear in each eye. These interlinked processes of alignment, ocular vergence and accommodation are fundamental to mature binocular single vision in order to take advantage of fine stereopsis, which requires two clear retinal images to fall within Panum's area. Most of the literature on these topics supports the notion that ocular versions, convergence and accommodation are yoked systems which act in fixed relationships, with limited flexibility to act independently, although no clear anatomical pathways have been identified. What is less clear is whether these relationships are learned or hard wired. More recent research suggests that these linkages may be less fixed than previously thought.

Deficiencies and abnormalities of alignment, vergence and accommodation result in the common childhood visual problems of concomitant strabismus (which in turn is associated with suppression, loss of stereopsis, amblyopia, nystagmus and dissociated vertical divergence (DVD)), heterophoria and convergence and accommodation anomalies. Some of these conditions emerge and present well beyond infancy, but understanding the visual skills and associations learned in infancy are fundamental in managing these patients

## **Concurrent Development**

### **Visual acuity**

Infants have poor visual acuity at first (Dobson and Teller, 1978). A useful rule of thumb is that acuity improves by approximately 1 cycle per degree per month (Atkinson, 2000). Newborn acuity is no more than 20/600 or 6/180 and reaches 20/200 or 6/60 at one year of age. Contrast sensitivity is also poor at first (Banks and Salapatek, 1978), but infants have sufficient vision to be able to recognise their own mother's face within the first days of life (Bushnell et al., 1989). Visual acuity develops very rapidly in the first six months of life, then more slowly as infancy progresses. Teller gave a good overview of visual acuity development (Teller, 1997), but for the purposes of these pages, it is reasonable to assume that typical infants have sufficient acuity to fixate and follow slowly objects of interest such as faces and large bright unambiguous targets from birth (Fig 2).

*Fig 2 Simulation of adult compared with newborn visual acuity of a face at 30cm. Image cropped from larger illustration in (von Hofsten et al., 2014)*

### **Emmetropisation**

The majority of infants will demonstrate hyperopia when refracted under cycloplegia, but otherwise they generally show a myopic refraction (Mohindra and Held, 1981) as accommodation frequently fails to relax into the distance. The range of cycloplegic errors is wide, but with a high prevalence of hyperopia and astigmatism, and has a much flatter distribution curve than that of older children and adults.

*Fig 3. Four distributions of refraction from two different studies (Mutti et al., 2005, Ingram and Barr, 1979) from 3 months of age to 3.5 years. (a) 3–9 months. (b) 1–3 years. Illustration taken from (Flitcroft, 2014)*

The process of emmetropisation means that, for a population of typical infants, the distribution of refractive errors becomes more closely bunched around emmetropia as they grow (Gwiazda et al., 1993, Flitcroft, 2014). Within moderate limits, the closer to zero the refraction starts, the lower the rate of change towards emmetropia (Woodhouse et al., 1994). Emmetropisation appears to be an active growth process in response to visual input, with blur, light levels and genetic factors being implicated (Flitcroft, 2014) (Troilo, 1992). Some specific groups are known not to emmetropise as well as others, and these groups comprise much of the paediatric ophthalmology population e.g. children with strabismus, high refractive error, amblyopia, Down syndrome, other developmental delays, albinism and nystagmus.

### **Ocular alignment**

Neonatologists, midwives and “early days” professionals generally tell parents not to worry if their infant has short periods of ocular misalignment in their first weeks, because they will resolve. In contrast, the older clinical ophthalmology literature suggested that any neonatal strabismus was a sign of “congenital” esotropia.

Sondhi et al (Sondhi et al., 1988) assessed the ocular alignment in infants on a neonatal unit and reported that 70% showed a manifest exotropia at some time, but also commented that some infants showed “convergence spasm” at times. Other studies suggest infants’ eyes are broadly aligned. Thorn (Thorn et al., 1994) reported most infants’ eyes were broadly aligned in their first month. Another study asked orthoptist mothers, trained in the assessment of strabismus (Horwood, 1993) to observe their own newborn infants from birth throughout their first year. Few of these mothers reported exotropia in their infants, even in their first days, but many reported that fleeting esotropias or over-convergence were common, and these appeared to be most common as infants attempted fixation on a near object (Fig 4). Most deviations were momentary and soon corrected, but 8% of infants’ eyes were misaligned for more than 15% of their waking hours. These neonatal misalignments generally were becoming less frequent by two months of age and, in typical children, had disappeared by four months.



*Figure 4. Intermittent neonatal misalignments in the same infant in the first month of life, which resolved by three months of age*

The difference between the Sondhi and Horwood studies may be that many newborns may look divergent to eye professionals but not parents, that exodeviations are only present in the first few days, or that infants interact differently with professionals and their main caregiver, but *parents* generally only notice intermittent esodeviations. Initial speculation that these eso-misalignments were a sign of an emerging accommodation / convergence linkage, was disproved by a subsequent laboratory study (Horwood and Riddell, 2004) which showed that they were rarely associated with concurrent accommodation. Many typically developing infants appeared to “get stuck” in

convergence and lacked the ability to relax their vergence appropriately after fixating a target that had loomed towards them.

**Epicanthus.** Prominent epicanthic folds can be a major cause of pseudo strabismus, particularly noticeable if the infant is fixating slightly to the side, or is fixating a fixation light but with a small head turn. The reduced nasal scleral show caused by the epicanthus as the eye adducts can give a very strong illusion of esotropia (Fig 5)



Figure 5 Pseudo strabismus due to epicanthus <https://www.aapos.org/terms/conditions/88>

### **Angle kappa**

Angle kappa is a measure of the displacement of the corneal reflex (first Purkinje image) from the centre of the pupil. It is sometimes also referred to as angle alpha or lambda – angles which are mathematically very similar, but refer to slightly different measurement points within the eye. It occurs because the fovea is temporal to the optic disc so there is an angle between the optic and visual axes. A typical angle kappa is positive (corneal reflex nasal to the centre of the pupil). Angle kappa relates to axial length, and so a shorter eye (neonatal or hyperopic) will have a larger positive angle. The posterior chamber of the neonatal eye develops very rapidly in the first six months of life, so the neonatal angle kappa of around  $17^\circ$  per eye at birth, declines rapidly in the first nine months of life. In older children it is around  $5^\circ$  per eye (Riddell et al., 1994). A large positive angle kappa is a cause of pseudo exotropia and can be especially misleading for clinicians accustomed to using corneal reflection position to assess a strabismus angle in older children (Fig 6).

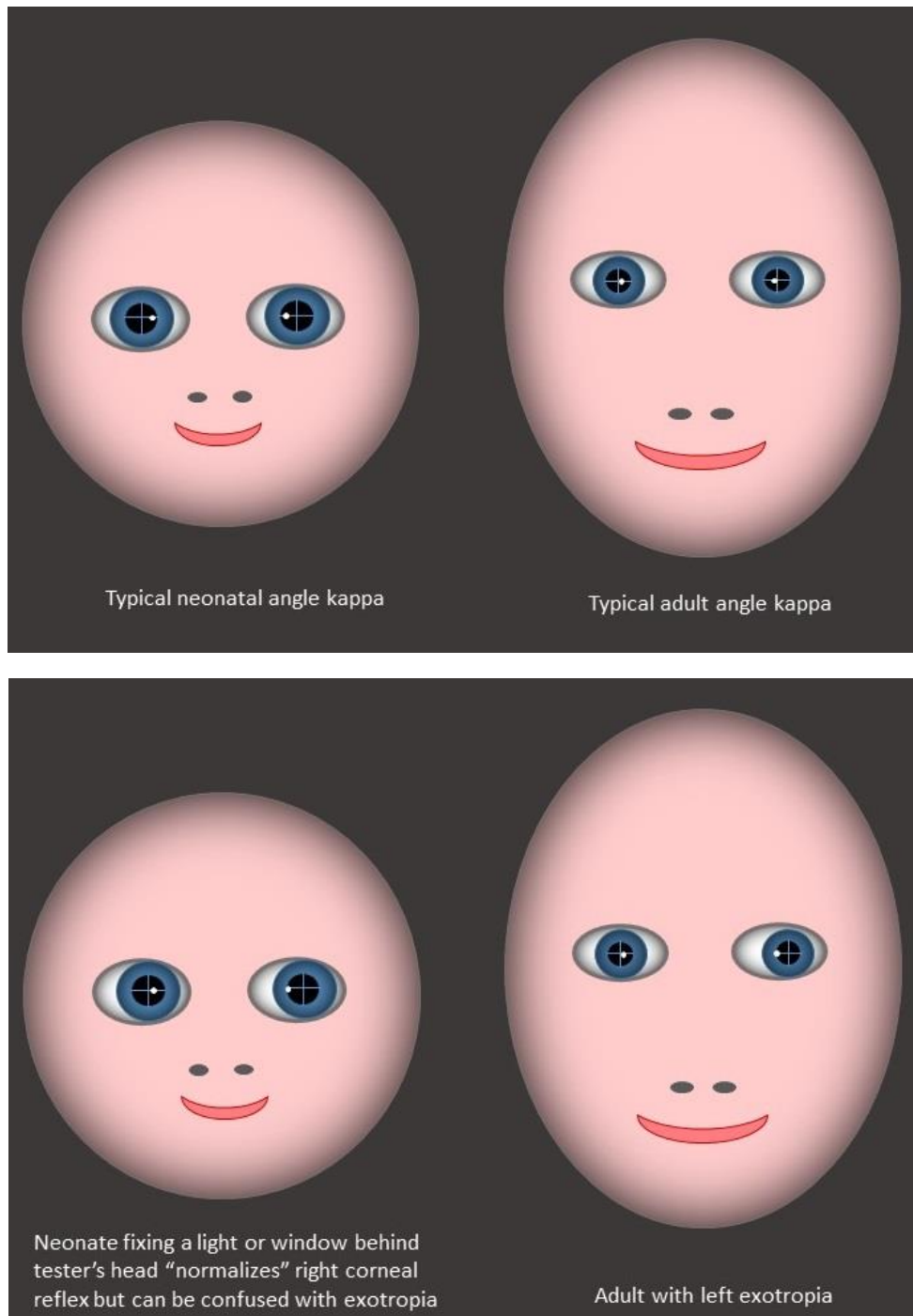


Figure 6. The large angle kappa of infancy makes corneal reflections appear more nasal than in adults. The effect is especially misleading if the infant fixes a bright light behind the examiner's head, when corneal reflections are identical to those of an adult with exotropia (+ Link to Powerpoint with narration to illustrate effect)

### **Fixation and following**

Infants will fixate and follow a very slowly moving face or unambiguous bright target from soon after birth. They are rarely engaged by distant targets except bright windows or lights. Once engaged with a target, very young infants may exhibit "sticky fixation", where they appear to have difficulty disengaging fixation from one target to the next (Hood and Atkinson, 1993)



### ***Binocularity and Stereoacuity***

There is a large literature on the development of cortical binocularity and stereopsis (and the subtle neurological and technical differences between the two terms) (e.g. (Birch et al., 1982, Braddick et al., 1983)). The consensus is that adult-like binocular vision emerges relatively rapidly from between 12-16 weeks of age (Birch, 1993). Before this, infants prefer rivalrous (so simultaneous but different) targets in each eye, before switching to a preference for fusible (similar) ones (Shimojo et al., 1986).

Normal binocularity depends on the postnatal development of binocular cells in the visual cortex, and their connections are acutely sensitive to disruption by unequal visual input from the eyes in the critical period. The critical period for binocularity is thought to start a few weeks after birth and its onset appears concurrent with the development of cortical binocular cells and stereopsis. Before this, frequent neonatal misalignments or even genuine VIth cranial nerve palsy (Elston and Timms, 1992) do not appear to have the damaging effects that they would have later in infancy. The acquisition of binocular connections at a cellular level is also the first time that pathological suppression of one eye is likely to be possible.

### ***Motion detection***

Infant motion sensitivity and response is another area with a large literature, but for clinicians it is useful to know that slow (probably subcortical) binocular optokinetic nystagmus can usually be elicited from birth. Monocular opto-kinetic nystagmus (OKN) and response to motion (Atkinson, 1979, Wattam-Bell, 2003) are asymmetrical in the first year of life, with much better temporal to nasal responses than nasal to temporal. Before (or in the absence of) the onset of binocularity, this monocular bias towards following a target approaching the nose, rather than receding, may be one reason that neonatal misalignments and infantile strabismus are typically convergent (Horwood and Riddell, 2004). Some asymmetry is still detectable in the second year (Lewis et al., 2000), and larger asymmetries persist into later life in infantile esotropia.

### ***Vergence eye movements and motor fusion***

Infants have not been shown to be able to converge to near targets at birth, but conversely, parents do not comment on significant lack of convergence for near fixation (when feeding for example). Thorn et al (Thorn et al., 1994) studied the development of vergence and random dot stereopsis and found that "first" convergence to an illuminated toy developed at around 12 weeks of age (just before preference for fusional targets), but "full", more precise, vergence developed approximately a week later. Riddell et al (Riddell et al., 1999) found that younger infants from 5 weeks of age could overcome a 20Δ base out prism, if enough time was given, and the target was isolated and unambiguous (an illuminated toy in a darkened room), demonstrating that vergence movements were possible much earlier. These very young infants would occasionally overcome the prism, then "get stuck" in a convergent deviation and even appear to try to correct their misalignment in the wrong direction (so becoming more convergent) before eventually correcting to binocular alignment. This behaviour often occurred in the same infants, and at the same time, that as their parents were noting occasional esotropias (neonatal misalignments) at home.

A more detailed longitudinal study by Horwood & Riddell, found that infants could converge to a single unambiguous target with a gain not significantly different from adult levels by 8-9 weeks of age (Horwood and Riddell, 2013b). Before the onset of binocularity, it is not clear whether

simultaneous alignment of both eyes on a near target is “motor fusion” or just two simultaneous monocular adduction movements to achieve fixation on the macular regions of each eye.

### **Accommodation**

A myopic non-cycloplegic refraction (Mohindra and Held, 1981), but hyperopia when under cycloplegia, demonstrates that accommodation is being exerted from the first days of life, but is not necessarily related to target distance or necessarily under any visual control. Horwood & Riddell’s group (Turner et al., 2002) (Horwood and Riddell, 2013b) found that in the first weeks of life accommodation varies little with fixation distance, in agreement with earlier literature (Aslin, 1993) but by 8-9 weeks mean response gains across a group of infants to a dynamic, engaging, binocular target were not significantly different from those of adults. These mean data mask the much wider variability within the accommodation data in comparison to the simultaneously collected vergence data in the same infants. Many young infants demonstrated a characteristic “all or nothing” accommodation response, with flat accommodation slopes for three more distant targets, then accommodating for the closest target only, while vergence responses were largely linear for target demand (Figure 7).

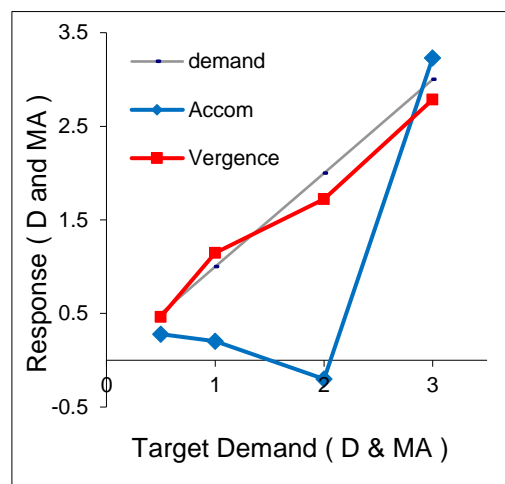


Figure 7 Typical “all or nothing” accommodation response (with concurrent appropriately linear vergence) to targets moving in depth from 2m to 33cm in a two month infant. Accommodation shown in diopters (D) and vergence in metre angles (MA) so equivalent responses for the stimulus demand are plotted on the same chart.

### **Accommodation-convergence linkages**

Older literature suggests that the accommodation and convergence systems are related in a fixed and innate relationship – usually expressed as the accommodative convergence to accommodation (AC/A) ratio. There is very limited data on vergence and accommodation in the very first weeks, but if accommodation is unresponsive to fixation distance, but convergence is more active, there is unlikely to be a link at first. Although Tunrenr et al (Turner et al., 2002) found that beyond 8 weeks of age mean AC/A ratios did not change significantly over development, this does not mean that linkages are similar in infants and adults. Accommodation is much less precise than convergence at all ages, but particularly so in infants, where linear stimulus/response curves are common for convergence, but “all or nothing” accommodation responses occur simultaneously (Fig7). The poor acuity of infants may make them insensitive to small changes in blur cues, while the precision of the

main vergence cue (disparity) is much greater. This suggests that the accommodation and vergence systems are relatively independent at first, although driven by common cues.

There is large literature on the stability of the AC/A ratio in (often highly experienced) adults, but evidence from more naturalistic experiments, or using clinical methods, on infants, children and adults suggest that fixed “ratios” are rarely repeatable using different methods e.g. (Gage, 1996, Horwood and Riddell, 2013a, Murray and Newsham, 2010) and on an individual basis are not nearly as “fixed” as data which report means suggest. It seems quite possible that AC/A relationships are learned associations because accommodation and convergence need to work in parallel for any near task and become broadly associated but could still remain two more separate systems driven by the same cues.

### ***Visual Cues***

Professionals often think in terms of “accommodation driving vergence” or “vergence driving accommodation”, but this implies that internal drives and cross-linkages are stronger than cues from the environment. It may be more useful to think of how common cues drive both systems.

The three main cues to accommodation and convergence are blur, binocular disparity (in its broadest sense that if the eyes are not directed at the target, they get displaced images on the retinae) and proximal cues such as looming, motion parallax, perspective, size, etc. Each of these cues is capable of driving a significant amount of convergence and accommodation when presented in isolation. If these individual response gains were added, the total response would be excessive; so they must be weighted. Older literature suggests that blur drives accommodation, and also two-thirds of convergence (leading to traditionally “typical AC/A ratio” of around 4Δ:1D), with proximal and disparity cues making up the difference. The role of disparate images to drive vergence and accommodation (the CA/C – convergence accommodation to convergence relationship) is rarely considered in the clinical literature because it is technically very difficult to measure.

More recent research has shown that the disparity drive to both convergence and accommodation may be the most important, at least in typical older children and adults, with minor roles for blur and proximal cues. Horwood & Riddell (Horwood and Riddell, 2013b) studied the development of these cue weightings over infant development. In the first weeks of life, infants respond best to proximal /looming cues. This may explain why neonatal misalignments are more common just after infants watch a target which has loomed towards them. In “middle infancy” between three months and one year, blur disparity and proximal cues can all drive responses equally. By 5 years of age disparity drive the best responses, and proximal cues wane significantly in influence. Although blur might be expected to become a more important cue as visual acuity improves and emmetropization occurs, its weighting does not appear to change throughout development.

Many other biological systems follow a parsimonious developmental model, pruning back the least efficient parts of system and reinforcing the most efficient or precise. Vergence and accommodation behave similarly, using the best cue available at first (proximal/looming), but shifting to disparity, with much smaller dead-zones, as it is made available by emerging binocularity and fine acuity. Bharadwaj and Candy (Bharadwaj and Candy, 2008) also support a strong role for disparity cues in driving vergence and accommodation in infants beyond 1.9 months of age.

If something should occur to interfere with this typical developmental trajectory – suppression to disrupt BV, or refractive error to give excessive blur, different weightings may emerge (Horwood and

Riddell, 2014). This may help explain the wide clinical variation in children with strabismus or heterophoria. If some children can vary in their responses to blur, disparity and proximal visual cues, this might explain why spectacles help one child's strabismus and not another's.

### ***Hard wired or learned?***

Most aspects of infant visual development appear to be pre-programmed (hard-wired), so in premature infants they will develop according to gestational (corrected), not chronological, age. Convergence and accommodation appear similarly pre-programmed (Horwood et al., 2015), but a clue to a possible cause of infantile esotropia may be provided by a paper by Jando et al (Jando et al., 2012) who reported that development of the response to dynamic random dot correlograms (a marker for cortical binocularity) appears experience dependent. Convergence and accommodation are normally fairly stable by 8-9 weeks, well before cortical binocularity emerges at 12-16 weeks. But in premature infants, they may still be more erratic (so the eyes less well aligned and focused) at a time when experience-dependent binocular connections (and so the potential for suppression) are emerging - providing a possible risk factor for strabismus.

### ***When does neonatal misalignment become infantile esotropia?***

At what point can normal, but frequent neonatal misalignments be differentiated from pathological infantile esotropia? The tipping point seems to be in the third month of age. Typical neonatal misalignments are reducing by two months and most have resolved completely by four months, while children destined to develop infantile esotropia are seen to be strabismic more frequently and the esotropic angle gradually increases (Horwood, 2003). It is probably no coincidence that this tipping point is the time that stereopsis is typically emerging. Motion detection and OKN are asymmetrical in early infancy, and infants converge best to looming targets which involve motion cues, resulting in a bias towards convergence rather than divergence. As typical binocularity emerges, the adult-like disparity control increasingly corrects for this eso-bias. If binocularity does not emerge or is extinguished by suppression, neonatal biases to esodeviation and convergence (or maybe two monocular adductions), and better responses to looming cues as an object approaches rather than recedes, may persist without any counteracting influence.

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