Neonatal ocular misalignments reflect vergence development but rarely become esotropia

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Background: 214 orthoptists’ infants have been followed for up to 15 years, relating neonatal misalignment (NMs) behaviour to onset of convergence and 20 Δ base out prism response, and also to later childhood ocular abnormalities.

Methods: In a prospective postal survey, orthoptist mothers observed their own infants during the first months of life and regularly reported ocular behaviour and alignment, visual development, and any subsequent ocular abnormalities.

Results: Results confirm previously reported characteristics of NMs. Infants who were misaligned more frequently were misaligned for longer periods (p < 0.01) and were later to achieve constant alignment (p < 0.001) but were earlier to attempt first convergence (p = 0.03). Maximum NM frequency was usually found at or before the onset of first convergence (p = 0.0002).

Conclusions: NMs occur in the first 2 months of life and usually reflect a normally developing vergence system. They appear to represent early attempts at convergence to near targets. Emerging infantile esotropia is indistinguishable from frequent NMs before 2 months.

Ocular behaviour in early infancy is immature. Acuity and contrast sensitivity are low (for reviews see Atkinson and Held) and refractive error common until later childhood. There is a consensus that binocular vision, in terms of the ability to resolve random dot stereograms, does not develop until 12–16 weeks of life. Vergences and accommodation are immature and largely unresponsive to varying target demand. There is no clear evidence that any reliable accommodation/convergence linkages are present at this time, and if present, convergence accommodation may be just as, or more, influential than accommodative convergence. Nevertheless, when active convergence is not required, most infants’ eyes appear broadly aligned (once corrections for the large angle lambda of infancy have been made) and studies suggest that a primitive vergence system may exist before 12 weeks that is not dependent on cortical binocularity.

Parents of visually normal children often comment that their eyes had been “all over the place” in their first weeks. In a booklet issued to all new parents in the United Kingdom, the advice is given “at birth a baby’s eyes may roll away from each other occasionally”. General practitioners and health visitors only refer intermittent squinting if it persists after about 3 months of age. However, if the intermittent “strabismus” reaches an orthoptist before the infant is 4 months of age, these misalignments may be considered pathological. Two recent papers suggest that early intermittent esotropia resolves in 27% of referred cases, especially if they present under 12 weeks of age. The relatively small numbers reported (175 subjects provided by 137 investigators at 104 clinical paediatric orthoptism sites) suggest that these early deviations form a very small part of the clinical ophthalmology caseload. But perhaps, instead of being rare, early squinting is so common and normal that it rarely reaches eye professionals.

A longitudinal study by the author of a group of 75 normal infants of orthoptists found that most neonates’ eyes were broadly aligned for most of the day, but the majority (88%) of infants showed brief periods of intermittent squinting. The deviations were overwhelmingly short lived, convergent, large angle, unilateral, and alternating. I term these “neonatal misalignments” (NMs) because “esotropia” implies an abnormality that may not be present. Although the time scale sometimes falls outside the 1 month limit of “neonatal,” the majority of NMs do occur within the first month and are generally reducing by 2 months of age.

In later infancy, intermittent strabismus is always pathological, but the 1993 data, along with anecdotal reports, suggested that NMs are of little significance. It is possible that instead of being part of a pathological spectrum of esotropia, intermittent misalignment is normal behaviour that may “tip over” into, or overlap with, pathology, especially if excessive in early infancy, or abnormally persistent.

A second, longitudinal cohort study of 1150 children showed that there were subtle consequences of NMs. There was a small but significant association of frequent NMs in the first 8 weeks with later hyperopia and myopia, as well as with clinically significant esotropia or esophoria at 4 years of age, while never showing NM was significantly associated with later astigmatism.

This paper reports the orthoptists’ infants study in more detail, including additional data on the nature and frequency of NMs in an extended group that was not analysed in the original publication. The original group now also includes a number of infants who developed pathological strabismus and refractive error, who were excluded from the 1993 report. Unreported data on the development of convergence in relation to NMs and later refractive error are also presented. A companion paper reports in more detail the NM behaviour of those children who went on to develop referable abnormalities...
Can be misleading reflection position because the large angle lambda of infancy to misalignment were made (specifically not using corneal
Table 1.
and then at 1.0, 3.5 and 5.0 years. Numbers are detailed in
infant’s ocular behaviour on postal questionnaires at the end
tist mothers were recruited while pregnant and reported their
malities were detected.
omizations were made before any subsequent ocular abnor-
mental defects were reported at diagnosis. All neonatal
data and base out prism response from 3 months. Refractive, visual, or
Analyses were carried out using SPSS software. 1 Tests,
transient esodeviations are common in months 1–4. In
month 1, 73.2% were misaligned at some time (21.6% less
than once a day, 15% once a day, 23.2% up to 10% of the time,
7.8% for 11–30% of the time, and 4.7% for more than this).
They were reducing by 2 months (when only 49% of
subsequently normal infants showed any deviation at all) and,
in the visually normal infants, gone by 4 months.
The only infants (n = 2) still misaligned at 4 months were in
the process of developing true infantile esotropia, confirming
the findings of The Pediatric Eye Disease Investigator Group.12 14 All other infants were constantly aligned at 4
months. Those destined to develop subsequent manifest
deviations of later onset were all aligned, with normal binocu-
lar and acuity responses, until at least 2 years of age.
The two infants destined to be infantile esotropes were
indistinguishable from the subsequently normal children in
the first 2 months with frequent, but not constant, esodeviation.
However, when the “norms” started to show fewer NMs at
around 2 months, these infants were becoming more
constantly misaligned. Although constantly manifest by 4
months, the angle of deviation continued to increase until
strabismus surgery on both infants was undertaken at around
9 months. Two further infants with similar characteristics
have been observed in the infant vision laboratory in a group
to be reported separately. One infant who needed frequent
general anaesthetics was misaligned for 48 hours after each
anaesthetic during her first year but at no other time and is
now visually normal.
A one way ANOVA showed a highly significant effect of fre-
quency of NMs on age at which NMs ceased (F5, 205 = 6.662, p
< 0.001). Those with most frequent NMs were later to cease
squinting (Fig 2).
Of the infants who squinted in the first month, 29.3%
squinted momentarily, 59.6% for a few seconds, 8.8% for a few
minutes, and 0.6% (two infants) for 10–60 minutes at a time
(neither of whom later proved to be infantile esotropes). There
was a weak, but significant, correlation between frequency
and duration of misalignment when it occurred (Spearman’s
rho: r = 0.18, p < 0.01). Infants who squinted most frequently
generally squinted for longer—for example, only 0.05% of
infants who squinted only once daily did it for more than a
few seconds, whereas 19% of those who squinted 11–30% of
the time squinted for a few minutes. There were no sex differ-
cences in severity of any squint (t = 0.037, p = 0.7), age to start
squinting (t = 0.2, p = 0.8), age at time of worst squinting (t
= −0.93 p = 0.3), or age to stop squinting (t = 0.6, p = 0.5).
In week 1, 48.6% of NMs were unilateral (one eye fixing),
13.7% were bilateral (neither eye fixing the target) and 37.7%

![Figure 1](https://example.com/figure1.png)

Figure 1 Neonatal misalignments in a normal infant aged 5
weeks. These deviations were observed for a few seconds at a time
for up to 10% of waking hours. They were reducing at 2 months and
resolved by 3 months. She is now orthophoric and has normal
binocular vision and acuity.

in later childhood. NMs will be shown to be a common occur-
rence of early infancy with important relevance to the develop-
ment of vergence eye movements and later abnormalities.

**METHODS AND SUBJECTS**
Recruitment has already been described in detail.14 15 Orthop-
tist mothers were recruited while pregnant and reported their
infant’s ocular behaviour on postal questionnaires at the end
of the first and second weeks of life, monthly up to 6 months
and then at 1.0, 3.5 and 5.0 years. Numbers are detailed in
Table 1.
Observations of the frequency, characteristics, and stimuli
to misalignment were made (specifically not using corneal reflection position because the large angle lambda of infancy
can be misleading2 24–27). Basic orthoptic tests were also carried
out by the mothers, looking at quality of fixation, gross pursuit
movements, convergence to near point from birth, and 20Δ base out prism response from 3 months. Refractive, visual, or
motility defects were reported at diagnosis. All neonatal
observations were made before any subsequent ocular abnorm-
alities were detected.

Analysis was carried out using SPSS software. 1 Tests,
ANOVA, and Tukey’s post hoc tests were used for parametric
data and χ² tests for non-parametric data.

**RESULTS**
**Characteristics of neonatal misalignments**
The additional dataset collected since 1993 showed no
systematic difference from the original study results.24 The
data have been pooled to provide greater power to the analy-
sis. These extended results will be described briefly.

| Table 1 Numbers followed at each age group |
|---|---|
| Age | No |
| Up to 3 months | 215 |
| Up to 6 months | 188 |
| up to 1 year | 159 |
| Up to 3.5 years | 98 |
| Up to 5 years | 66 |
| >6 years | 55 |

Mean age (weeks) to stop NMs (SEW)

![Figure 2](https://example.com/figure2.png)

Figure 2 Mean age in weeks when neonatal misalignment (NMs)
ceased by neonatal frequency category. More frequently misaligned
infants were older when NMs ceased. Constant misalignments
excluded because of unreliable data [see text].
showed a significant effect of neonatal frequency group \( (F_{2.653}, \text{df } 1203, p=0.006) \) for the more frequently squinting infants. A sign of very early, but inaccurate, convergence. Indeed their frequent NMs might have been a spontaneous comment, so the true incidence cannot be established. Further details were unavailable. This appears to be the first time that this has been reported in normal neonates.

**Relation to convergence**

The mothers were asked when their infants first attempted convergence. This was similar to the “first vergence” assessed by Thorn et al., and did not specify a specific near point or quality of movement. The target was whatever the mothers found most successful, generally the mother’s face. Convergence was generally more delayed in most infants than was steady fixation or following, which were usually elicited by the second week of age; 42.9% attempted convergence in week 1, with the percentage rising logarithmically with age \( (r^2 = 0.97) \) (Fig 3). By month 4, only four infants (2%) were still not seen to converge. There were no sex differences \( (t = -0.4, p = 0.6) \).

Figure 4 appears to illustrate that both frequent and rare NMs are associated with later first convergence. However, the data from the seven infants with NMs for >30% of the day (not shaded in Fig 4) have been excluded as unreliable. The wording of the question was “Is normal convergence attempted?” NMs are usually reported to occur at the time of attempted near fixation. An orthoptist could easily interpret very frequent NMs, which occurred on attempted near fixation, as “abnormal” convergence and so would answer “no” to the question. A “yes” response would only be used once NM had stopped when older. Second, if NMs occurred every time convergence was attempted, it is impossible to differentiate NM from attempted convergence. They would therefore answer “no” to the normal convergence question. Usually these few children may not have been genuinely later to start to converge; indeed their frequent NMs might have been a sign of very early, but inaccurate, convergence.

If these seven infants (3%) are excluded, one way ANOVA showed a significant effect of neonatal frequency group \( (F_{2,110}, \text{df } 4,203, p = 0.03) \) with a highly significant linear trend \( (F_{1,110}, \text{df } 1203, p = 0.006) \) for the more frequently squinting infants (in the groups up to 30% of the time) to be earlier to converge.
Neonatal ocular misalignments reflect vergence development but rarely become esotropia

Change in frequency of NMs over the first 3 months of life may be a more important diagnostic clue than age of onset or time spent misaligned per se. Misalignments that are worsening at 2 months are likely to develop into infantile esotropia, while non-pathological NMs generally reduce from 1 month of age, but may still be seen until 3 months.

The orthoptists reported overwhelmingly large, intermittent exodeviations, not exodeviations as reported by Archer et al. It is improbable that these are pseudo-deviations because the angles are generally very large and orthoptists, unlike lay parents, are unlikely to be misled by epicanthus. If pseudo-strabismus were to be the cause of an apparent squint, the large angle lambda of early infancy, if anything, creates a significant bias towards pseudo-esotropia if corneal reflections are used to assess alignment.

Convergence was reported from the very first weeks, earlier than previously reported by some authors, but not others. NMs appear to occur at or just before the time that convergence emerges and rapidly cease once vergence becomes reliable. If vergence develops early, infants are initially likely to spend more of their waking hours misaligned, but unless these misalignments are very frequent and worsening after the first month, they are less likely to go on to have a later abnormality (see companion paper).

NMs also appear to provide a useful research tool for the study of the emerging vergence system because they are large and easy to detect. The relation of NMs to accommodation measured objectively in a laboratory setting will be the subject of a future paper in preparation. In a clinical setting, awareness of what parents are describing when they say their babies’ eyes are “all over the place” or “unfocused” can help to differentiate pathology more accurately in the few, and avoid anxiety for many others.

REFERENCES