Introduction to strabismus

**Strabismus is a symptom**

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Neuchâtel

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**Why do eyes not cross?**

1. Orbital ANATOMY favors divergence
2. ESOTONUS regulation early in life
3. MOTOR FUSION loop for fast tuning
4. PROPRIOCEPTION of extraocular muscles
5. HEREDITY

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**Esotonus regulation in early life**

- Cortical area for pursuit eye movements have an innate bias for nasal drift.
- Afferences from binocular layer of V1 correct this nasal bias.
- If binocular connexions fail to develop in V1 during early life (months 3 to 6):
  - Nasal drift becomes clinical
  - Esotonus increases
- Resulting in convergent strabismus, latent nystagmus, asymmetric monocular OKN.
Exaggerated esotonus results in convergent strabismus.

Esotonus is the baseline innervation of the rectus medialis muscles.

‘When binocular visual input is abnormal in early life [months 2 - 8], ESOTONUS becomes dissociated, [“non-synchronized”], resulting in Infantile Esotropia’

Michael Brodky

‘Motor fusion’

Disparity-driven vergence - vergence fusionnelle / fusion motrice / Vergenza / Motorische Fusion

Disparity perception in V1 (V2, MT, MST,...)
Midbrain
near response
cells

III / VI
Vergence cells

Vergence eye movements to align the eyes

Various cortical areas can generate a signal to initiate vergence movements (parietal, frontal, superior colliculus, midbrain, pons)

Vergence movement is initiated (= motor response to disparity)

Disparity-driven vergence - vergence fusionnelle / fusion motrice - Vergenz / Motorische Fusion

Disparity is corrected and allows images to fuse

Disparity is corrected

Disparity-driven vergence - vergence fusionnelle / fusion motrice - Vergenz / Motorische Fusion

Disparity is corrected and allows images to fuse

Remaining minimal horizontal disparity is corrected by 'sensory fusion' allowing stereoscopic impression

Sensory fusion

Disparity is corrected and allows images to fuse
Disparity-driven vergence (‘Motor Fusion’) is a strong correcting mechanism dedicated to maintain eye alignment. It requires normal binocular connections. Its efficiency can be measured with prisms: ‘fusional amplitude’.

PROPRIOCEPTION of extraocular muscles

Proprioceptive pathways of extra-ocular muscles are partly known: (Superior colliculus, vestibular nuclei, cerebellum, frontal premotor areas)

HEREDITY

Comitant strabismus is thought to be multifactorial with variable genetic predisposition. Familial weakness of binocularity suspected in some cases. Susceptibility gene for exotropia: 1: 14q21.3, dominant. Susceptibility genes for convergent strabismus (chr. 6, 8, 10, 15, 17).

The major mechanisms of ocular alignment rely on an adequate maturation of the binocular connections during early life (months 3 to 8).
**Maturation of binocularity**

At 6-8 mo: 100% of children have acquired a stereoscopic vision. Those who have not will not develop this binocular competence

**Conditions for the development of binocularity:**
- Adequate visual acuity development
- Intact visual cortex
- Ocular alignment during critical period
- Normal chiasmatic and callosal decussations

**Clinical signs of abnormal binocularity:**
- Exotropus (convergent strabismus)
- Absent motor fusion, absent stereoscopy
- Latent nystagmus
- Dissociated deviations
- Abnormal retinal correspondence

**Consequences of very early strabismus**

- Definitive abnormal binocularity
- If strabismus is unilateral: deep amblyopia

**Clinical signs of binocular immaturity: latent nystagmus**

- Latent nystagmus is defined clinically as nystagmus which appears on covering one eye and beats in the direction of the uncovered, fixating eye. When covering the other eye, the nystagmus will change direction.
  - The slow phase typically shows decreasing speed.
  - This very particular form of nystagmus is pathognomonic of binocular immaturity.
In patients with an early-onset defect of binocular function, the occlusion of one eye may induce an elevation of the occluded eye, secondary to an imbalance in vestibular system. The eye elevates slowly and extorts. The phenomenon is generally bilateral although asymmetric.
Abnormal retinal correspondance is a 'sensorial abnormality'. It is a cortical adaptive process to prolonged eye deviation in early infancy.

Clinical Entities

- Deviation more than seconds - minutes per day
- Always the same eye deviates
- No improvement during M2
- Persistence after M3

Neonatal ocular misalignment is a physiological, transient instability of eye alignment during the first few weeks of life. Eye position stabilized at ± 5 w (46 WGA).
Infantile esotropia

Prevalence: 0.1-0.5%
Onset: 2 to 6 (8) months
No neurological defect
RF: heredity, prematurity

- Large angle of deviation, constant, comitant
- Crossed fixation (pseudo abduction palsy)
- Latent nystagmus (25-95%)
- Monocular pursuit asymmetry (TN-NT)
- DVD (50-90%)
- Alphabetical syndrome, V >> A (68%)
- Torticollis (6-70%)
- Amblyopia: 35%
- Always abnormal retinal correspondance (ARC)
- ‘Absent’ binocularity

Infantile esotropia

Management:

1. Exclude organic disease, urgently
2. Optical correction and follow-up after cycloplegic refraction
3. Amblyopia surveillance / treatment if needed
4. Repeat examination to test for reproducible angle of deviation

Surgery can be proposed as early as 18 months, as soon as:
- Angle is stable and measure reproducible
- Spontaneously alternating fixation
- Parents ready to proceed to surgery

Many surgeons will prefer to wait until angle measurement is reliable (4-5y)

A minority resolve spontaneously to ‘ocular alignment with no binocularity’

Differential diagnosis to comitant strabismus: VIth nerve palsy

- Most frequent CN palsy in the child
- Incomitance (VOR: true abduction palsy)
- Head turn

- Congenital:
  - 3% of traumatic birth
  - 0% of cesarean birth
  - Frequent resolution if traumatic
  - Stilling - Duane syndrome

- Acquired (child):
  - Intracranial tumor 30%
Symmetrical corneal reflex
Central, stable fixation RE/LE
Occlusion accepted RE/LE
No foveation movement after unilateral cover test
Fixates (recognizes) Lang’s stereogram

Differential diagnosis to comitant strabismus: pseudostrabismus

Symmetrical corneal reflex
Central, stable fixation RE/LE
Occlusion accepted RE/LE
No foveation movement after unilateral cover test
Fixates (recognizes) Lang’s stereogram

Microstrabismus / monofixation syndrome

Stable abnormality of binocular connexions, with:
1. Monocular deviation of 2.5° - 5° (4-8 DP)
2. Slight amblyopia (3/4 cases)
3. Subnormal stereopsis
4. Small central suppression scotoma present during binocular viewing

Accommodative esotropia

- Accommodation is strongly connected to convergence in the midbrain
- Newborns and children are physiologically hyperopic
- Most accommodative esotropias do not have high hyperopia
I. Pure accommodative esotropia (not so common)
   Correct with glasses (full cyclopegic correction)

II. Partial accommodative esotropia (most cases). ARC frequent.
   Correct hyperopia with full correction + surgery for residual angle of deviation

III. Accommodative convergence excess, high AC/A ratio (the squint is stronger at near vision, due to accommodation effort)
   correct with bifocals or progressive glasses
   (If non-accommodative convergence excess : proceed to surgery)
Acquired convergent strabismus may have no accommodative component:

- Decompensated microstrabismus (ARC) → treat amblyopia + operate
- Decompensated esophoria (NRC) → prism + operate; no delay
- Acute normosensorial esotropia (NRC) → prism + operate, no delay
- Acute VIth CN palsy (incomitant!) emergency
- Neurological Et (rare) emergency

Look for: signs of (transient) diplopia; strong ocular dominance / amblyopia; neurological signs or nystagmus; intact abduction; angle far > near; papilledema.

Acquired non-accommodative strabismus:

Strabismus that was clearly not present during first year of life is called ‘acquired’, as opposed to ‘infantile’ or ‘congenital’.

As binocular connexions may be normal and could regress if misalignment persists, surgical correction should be proposed early in the management of acquired strabismus.

- Occurs in 15-25% of strabismus of early onset (often with abnormal binocularity).
- Dysfunction in oblique muscle tonic innervation (V syndrome sometimes called ‘strabismus sursoadductorius’ because eye elevates when adducted).

- May also be associated with abnormal orbital shape or craniofacial dysmorphism
- 1st choice treatment: inferior oblique muscle recession

Alphabetic syndromes

Elevation in adduction due to hyperactivity of left IO

V syndrome with orbital dysmorphia

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Dysfunction in oblique muscle tonic innervation (V syndrome sometimes called ‘strabismus sursoadductorius’ because eye elevates when adducted)

- May also be associated with abnormal orbital shape or craniofacial dysmorphism
- 1st choice treatment: inferior oblique muscle recession

Positive Bielschowsky test on right side

Differential diagnosis of elevation in adduction: “superior oblique palsy”

No association with obstetric trauma

- No diplopia
- Secondary inferior oblique overaction with V-Syndrome and upshoot in adduction
- Torticollis

1st choice treatment: inferior oblique recession (+/- superior oblique plication if strong vertical deviation)
### Divergent Strabismus

- Intermittent exotropia (80% of cases)
- Sensory exotropia (due to lost afference)
- Primary exotropia (rare)

- Incomitant exotropia (III rd nerve palsy; Thyroid Orbitopathy ; myasthenia ; Duane Type II ; CFEOM)

- Neurological exotropia:
  - Diffuse cerebral lesions (leukomalacia ; encephalopathies ; perinatal ventricular hemorrhage)
  - Pontine X (WEBINO)
  - Bilateral INO (REINO)

In a child with constant exotropia, probability of finding an associated systemic or ocular disease is higher than with a constant esotropia.

(Hunter. Ophthalmology 1999)

### Intermittent Exotropia

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operate only if:</td>
<td></td>
</tr>
<tr>
<td>1. Eye tends to remain divergent</td>
<td></td>
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<tr>
<td>2. X(t) decompensates also at near</td>
<td></td>
</tr>
<tr>
<td>3. Angle of deviation</td>
<td></td>
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<tr>
<td>4. Social / professional handicap</td>
<td></td>
</tr>
</tbody>
</table>

- Alternance between
  - Normal binocular vision (straight)
  - Monocular vision and suppression (divergent)
- Loss of alignment far > near
- No diplopia
- No amblyopia
- Generally no measurable binocular abnormality

Recurrence rate: 20-60%

### Secondary Strabismus

Strabisme sensoriel (secondaire) / sekundärer Strabismus

Any organic disease that causes visual impairment can cause strabismus
Step-by-step approach

Findings that may suggest benign strabismus

- Heredity
- Congenital cerebral lesions
- Prematurity
- Absence of neurologic signs

Think of neurological strabismus and investigate if:

- Incomitance
- Acute acquired strabismus with Alphabetic syndrome
- Loss of fusion amplitude
- Exotropia angle far > near
- Nystagmus (non-latent)
- Headache, awkwardness, vomiting, neuro signs
- Papilledema

Management principles

Normal retinal correspondance (NRC) / acquired strabismus:

1. Rule out organic disease
2. Correct hyperopia
3. Prisms to allow bifoveal fixation
4. In the child, proceed to surgery no delay

Abnormal retinal correspondance (ARC) / early strabismus:

1. Rule out organic disease
2. Correct hyperopia
3. Amblyopia prevention / treatment
4. Proceed to surgery only when:
   - amblyopia is treated or stabilized
   - fixation alternates spontaneously
   - angle measurement is reproducible
Management principles

Weakening procedures:
- Recession (1.5° / mm)
- Retroequatorial myopexy (on rectus muscles)

Strengthening procedures:
- Resection or plication (1.5° / mm)

Transposition surgery:
- Muscle transpositions are used for extra-ocular muscle paralysis

Further reading - contact

Further reading:
B. Lorenz, M. Brodsky. Strabismus - new concepts in pathophysicsology, Diagnosis and treatment. 2010

Annexes

1. Estimation of angle of deviation

Hirschberg's method
(measure in degrees: 1mm displacement of corneal reflex = 1°)

A Normal
B 1° ET
C 30° ET
D 45° ET

Krimsky test
(measure in prismatic diopters [cm/m])

A LE fixing
B
C Corneal reflex centered
2. Classification of Esotropia according to von Noorden

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**Table 16-1. Classification of Esodeviations**

<table>
<thead>
<tr>
<th>I. Concomitant esodeviations</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Accommodative esotropia</td>
</tr>
<tr>
<td>1. Refractive accommodative esotropia (normal AC/A)</td>
</tr>
<tr>
<td>2. Nonrefractive accommodative esotropia (high AC/A)</td>
</tr>
<tr>
<td>3. High accommodative esotropia (reduced NPA)</td>
</tr>
<tr>
<td>B. Nonaccommodative esotropia</td>
</tr>
<tr>
<td>1. Inertile esotropia</td>
</tr>
<tr>
<td>2. Nonaccommodative convergence excess</td>
</tr>
<tr>
<td>Inertial (AC/A)</td>
</tr>
<tr>
<td>3. Acquired basic esotropia</td>
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<tr>
<td>4. Acute-onset esotropia</td>
</tr>
<tr>
<td>5. Divergence insufficiency or paralysis*</td>
</tr>
<tr>
<td>6. Cyclic esotropia*</td>
</tr>
<tr>
<td>7. Recurrent esotropia</td>
</tr>
<tr>
<td>C. Microtropia</td>
</tr>
<tr>
<td>1. Primary microtropia</td>
</tr>
<tr>
<td>2. Secondary microtropia</td>
</tr>
<tr>
<td>D. Nystagmus “blockage” syndrome*</td>
</tr>
<tr>
<td>II. Incomitant esotropia*</td>
</tr>
<tr>
<td>A. Paralytic</td>
</tr>
<tr>
<td>B. Nonparalytic</td>
</tr>
<tr>
<td>1. A- and V-pattern esotropia</td>
</tr>
<tr>
<td>2. Depression syndrome</td>
</tr>
<tr>
<td>3. Mechanical-restrictive esodeviations</td>
</tr>
<tr>
<td>a. Congenital anomalies of extraocular muscles</td>
</tr>
<tr>
<td>b. Acquired restriction (lensborne myopathy, trauma to orbital wall, excessive resection of medial rectus muscles, mydriasis)</td>
</tr>
<tr>
<td>strabismus syndromes</td>
</tr>
<tr>
<td>Don’t forget: ocular myasthenia can mimic any oculomotor paresis.</td>
</tr>
</tbody>
</table>

3. Extraocular muscles of the right eye

| Annexes |

- Lid levator (III)
- Superior rectus (III)
- Lateral rectus (VI)
- Inferior oblique (III)
- Inferior rectus (III)
- Superior oblique (IV)
- Medial rectus (III)

4. Actions of the extraocular muscles

- Superior oblique muscle, from above
- Inferior oblique muscle, from below
5. Actions of the extraocular muscles

### Table 6.1. Action of the Extraocular Muscles from the Primary Position

<table>
<thead>
<tr>
<th>Muscle*</th>
<th>Primary</th>
<th>Secondary</th>
<th>Tertiary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medial rectus</td>
<td>Adduction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lateral rectus</td>
<td>Abduction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inferior rectus</td>
<td>Depression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior rectus</td>
<td>Elevation</td>
<td>Inversion</td>
<td></td>
</tr>
<tr>
<td>Inferior oblique</td>
<td>Depression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior oblique</td>
<td>Inversion</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*The superior muscles are inversions; the inferior muscles, eversions. The lateral rectus muscles are adductors; the oblique muscle, abductors.

6. Incomitant, non paretic strabismus

**Causes of mechanical restrictive Strabismus**:
- Thyroid orbitopathy
- Orbital fracture with muscle adhesions or entrapment
- Other muscle fibrosis, as in Duane retraction syndrome or CFEDM
- Brown syndrome (inflammation of the tendon sheath of superior oblique muscle at the level of the trochlea, leading to a restriction of passive gliding of the tendon in upgaze in adduction)

**Causes of mechanical non-restrictive Strabismus**:
- Orbital dysmorphia (A-/V-pattern deviations)
- "Heavy eye" syndrome in high myopia (esotropia and hypotropia due to an abnormal length eye: the lateral rectus muscle slips down along the lateral wall of the bulbus, the eye rotates inside and down)

7. Sherrington's law - loi de l'agoniste - antagoniste

**Figure 6-10.** Electromyographic evidence for reciprocal innervation of extracocular muscles. Upper tracing from left lateral rectus muscle (LLR); lower tracing from left medial rectus muscle (LMR). In extreme right lateral gaze (LLG), the LLR is electrically silent and the LMR is electrically active. In extreme left lateral gaze (LLG), the LMR is electrically silent and the LLR is electrically active. (Courtesy of Dr. Goodwin M. Brenn.)
Herings’ law – loi d’égale innervation

III VI

Lateral rectus Medial Rectus

This physiological principle explains why, in paretic Strabismus, the yoke muscle becomes hyperfunctional, and why the secondary angle of deviation is larger than the primary angle of deviation. Primary angle is measured when the non paretic eye is fixating; the secondary angle is measured when the paretic eye is fixating.

Yoke muscles move the eyes in the same direction (ex. Lateral rectus of RE and medial rectus of LE)

Pathogenetic definition (W. Haase):
Low vision that results from a disturbed visual development, in spite of a normal neuronal potential

Commonly used clinical definition:
Reduced BCVA that is not explained by an organic cause

Mostly unilateral, may be bilateral

Sensitive period for development of amblyopia (= critical period of vulnerability of visual acuity development): 0 to 7-8 y.

The earlier the amblyogenic factor is present, the deeper the amblyopia. The longer the amblyogenic factor is present, the deeper the amblyopia.

Deep amblyopia secondary to early and prolonged deprivation or neutralisation is not reversible. Vision can be as low as ‘hand movements’.

Age up to 3 is particularly sensitive to deprivation and strabismic amblyopia

Amblyopia : sensitive periods of development, damage and recovery of visual acuity
Causes of amblyopia

A. Strabismic amblyopia (suppression)
   1. Congenital exotropia
   2. Congenital exotropia
   3. Acquired constant tropia in adulthood
   4. Accommodative exotropia
   5. Small-angle tropia (monofixation syndrome)
   6. Intermittent exotropia (rarely associated with amblyopia)

B. Monocular pattern distortion (suppression and pattern distortion)
   1. Anisometropia
      a. Hyperopia > +1.50
      b. Myopia > -3.00
      c. Meridional > +1.50
   2. Media opacities
      a. Unilateral cataract
      b. Unilateral corneal opacity (Peter's anomaly)
      c. Unilateral vitreous hemorrhage or vitreous opacity

C. Bilateral pattern distortion (pattern distortion)
   1. Anisometropia
      a. Bilateral high hypermetropia > +3.00
      b. Bilateral meridional (astigmatic) > +2.50
   2. Media opacity
      a. Bilateral congenital cataracts
      b. Bilateral corneal opacities (Peter's anomaly)
      c. Bilateral vitreous hemorrhages

Amblyopia treatment

Pre-requisite: best adapted optical correction

Occlusion therapy by patching of the better eye (Lancet 2006; Cochrane 2009)

- Some recommend initiating treatment by full-time occlusion and control after a few days or weeks to monitor visual improvement. We initiate treatment with half wake-time occlusion, then adapt according to age and importance of amblyopia.

- As a general rule: occlusion 1h/day pro year of age (ex.: 2y old will have 2h occlusion/ day, 7/7 until next control).

- Atropine 2x/week in the better eye as penalisation is efficient for moderate amblyopia as an alternative if patching is not tolerated. CAVE risk of inverse amblyopia if uncontrolled.

* The major part of improvement occurs within 3 months of treatment begin.

- A treatment attempt is sometimes recommended up to age 17 if never treated before, although treatment after 6 years seldom results in significant improvement of VA. Early begin of treatment is the key to success.