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How accurate is orthoptic examination at age one? ◇

The Early vs. Late Strabismus Surgery Study Group *°

ABSTRACT. The Early vs. Late Strabismus Surgery Study Group is a group of strabismologists and orthoptists who wish to investigate whether early or late surgery is better in cases of infantile strabismus, in a controlled, multicentre, matched-pair trial: All infants will receive a standardized entry examination at age one and then be operated either before their second birthday in clinics A, or between the 32nd and 60th month of age in clinics B. The children will be evaluated at age six. After completion of the study, one child will be selected from each group, to form a pair of children with the same entry examination, who were operated early or late. Successive pairs will be generated so that finally two smaller groups with the same entry examinations are formed. These two groups can then be compared regarding degree of binocular vision, angle of squint and visual acuity of the worse eye. It was decided to perform first a pilot-study of the examination of infants age nine to 15 months, because we wanted to know to what degree of accuracy infants age one can be examined and what parts of the examination can be carried out most reliably and can therefore be used as parameters to match the pairs in the main study. 190 Children were each examined by three examiners on one day, according to a standardized examination sheet, and differences were quantified. We found that the angle of squint could be measured with reasonable precision: The largest difference between any two of the three measured angles averaged at 6.5°. The angle did not increase when the infant was examined a second or third time. Variability of the angle, vertical divergence and up-/downshoot-in-adduction could not be assessed reliably. On the other hand, restriction of abduction (in a 4-class scale) could be measured with adequate precision: in 58% there were no differences at all between the three examinations. The degree of amblyopia could be well assessed by observing the fixation pattern by means of direct fundoscopy with a fixation mark or by comparing corneal reflexes during monocular fixation. Using a 3-class scale, there were no differences at all between the three examinations of the three orthoptists in 94% of the cases. In addition, amblyopia could be accurately assessed by observing the fixation behaviour of the child with either eye, in a 5-class scale.

Key words: strabismus; esotropia; binocular vision; amblyopia; strabismus surgery

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° The members of the Early vs. Late Strabismus Surgery Study Group are listed in the Appendix.

INTRODUCTION

Infantile strabismus starts before the age of six months. It is a convergent strabismus in most cases. The child concerned will fail to develop binocular vision or lose it rapidly. The child will suppress the image of one eye. Some children will alternate vision with either eye, others will

use one eye preferentially, resulting in partial loss of central vision in that eye, amblyopia. Amblyopia is reversible by patching the healthy eye in most, but not in all cases. Infantile strabismus is common: the incidence is over 1% in the general population. Strabismus operations are, hence, carried out in large numbers. In the United States, surgery for infantile strabismus is now generally performed at an early age (age 1–2), whereas in Europe most eye clinics still operate late (age 4–5). The tendency to operate early developed in the nineteen-seventies. The main argument employed was that binocular vision can be established if the child is operated early enough. However, most reports concerning this controversy sofar are uncontrolled studies or clinical observations.[1–9] One of the few controlled studies, a prospective assessment of acuity and stereopsis in amblyopic infantile esotropes following early surgery[10] showed moderate degrees of stereopsis in 35% of the children who were operated early. In that study, three out of the series of 84 children had full stereopsis. These three did not need surgery, most likely because they had intermittent strabismus.

The most important arguments of the proponents of early surgery are that

a. chances for the development of binocular vision are better,

b. the parent-child relation is not disturbed by the cosmetic appearance of the child.

c. the psychomotor development of the child is better when the eyes are straight and

d. an operation and a hospitalization at age 4–5 constitute a greater psychic trauma.

The most important arguments of the proponents of late surgery are that

a. the correction of the angle of squint can be more precise with surgery at age 4–5.

b. secondary motility disorders (up- and downshoot in adduction, V- and A-pattern), can be corrected together with correction of the horizontal angle of squint.

c. the number of operations necessary with early surgery is larger because of the first two factors and

d. treatment of amblyopia is more difficult after early surgery, because of (1) more difficult assessment by the treating orthoptist of alternating use of both eyes, (2) difficulty in assessing visual acuity at age 0–2, (3) and lack of motivation among the parents of the child to patch one eye when their child has only a small, cosmetically inconspicuous, angle of strabismus postoperatively.

Cosmetic considerations are also very important. It seems possible that there is a critical threshold in the swing towards early surgery: in a society where a very high percentage of the squinting children is operated upon at an early age, the remaining squinting children will become less cosmetically acceptable, and this may decide the balance in favour of early surgery.

The Early vs. Late Strabismus Surgery Study Group is a group of strabismologists and orthoptists who wish to investigate the controversy on early or late surgery in infantile strabismus in a controlled, multicentre trial. During its founding meeting in Nürnberg on June 4th, 1991, it was decided that the study would be a matched-pair study: All infants entering the study would receive a standardized examination at age one and then be operated before their second birthday in clinics A or between their 32nd and 60th month of age in clinics B. After evaluation of the children at age six, a child from each group with the same entry examination would be selected, to form a pair of children with the same entry examination. Successive pairs

would be generated, so that finally two smaller groups with the same entry examinations are formed that can be compared regarding, for instance, degree of binocular vision, angle of squint and visual acuity of the worse eye.

During the meeting it was suggested to perform first a pilot-study of the examination of infants, before starting the main study, to establish which examination parameters can be determined most accurately in infants age one.

METHODS

For the pilot-study we have devised an examination sheet with questions concerning the following five groups of parameters.

1. *History*: age in months, sex, onset of strabismus, periodic or constant strabismus, onset of amblyopia treatment, occlusion pattern, onset of wearing glasses.
2. *Cycloplegic refraction* and strength of glasses.
3. *Horizontal angle of squint*, measured with prisms and corneal reflexes during fixation of an object with a light at 50 cm or by estimation of the location of the corneal reflexes during fixation of an object with a light at 50 cm, variability over time of the horizontal angle of squint, variation of the horizontal angle of squint with up- or downgaze.
4. *Eye motility*: degree of abduction possible, dissociated vertical deviation, up- or downshoot in adduction, concomitant vertical deviation.
5. *Visual acuity*: eye dominance, type of fixation behaviour when covering the other eye, fixation in fundus or by judging corneal reflexes, latent nystagmus, torticollis.

In each participating clinic, five infants age 9 to 15 months were examined on one day by three orthoptists or ophthalmologists. Whenever possible, only one of the three examiners worked at the participating clinic and the two other examiners were invited from other clinics or practices, as we anticipated that the differences would be smaller if all examiners were working at the same clinic. The parents were informed of the purpose of the study, for instance 'to determine what can be examined accurately in infants this age'.

In each case, a short history was taken by the three examiners together, so that each had the same starting information. The forms were filled out immediately after examining the child, and before contact with the other examiners. The examination sheets were distributed and collected by the country coordinators of the study (see appendix). The results were entered in a spreadsheet computer programme by Miss Grosglauser, the research-orthoptist of the pilot study and Dr. Kolling, and the data have been transferred to Heidelberg where statistical analysis was carried out by Dr. U. Haag and PD Dr. H. Schäfer from the Zentrum zur Betreuung von Therapiestudien of the University of Heidelberg.

RESULTS

In total, the filled-out examination sheets of over 200 children were received, 190 of which met the preset criteria of age limits, etc. (= 570 examinations).

A comparison between age groups (younger/older than 12 months) did not show differences between the angles of strabismus, standard deviations and intraclass correlation coefficients of the various examinations. It seems that, although in general older children can be examined more easily, this tendency is not present in an age group of under 15 months of age.

Onset of strabismus followed a very skewed distribution, with 78.5% of the onsets being in the first four months of life.

Refraction (spherical equivalent) followed a symmetrical distribution with a single maximum at about 2.5 dioptres, very few being under 0 and very few being over 5 dioptres.

The angle of strabismus had been measured with reasonable accuracy. The intraclass correlation coefficient (differences between three examiners examining one infant; 1.0 signifying complete agreement between examiners and 0.0 signifying no agreement between examiners) was 0.8, which is sufficient for matching. The largest difference between any two of the three measured angles averaged at 6.5°. In 10% of the infants the largest difference between any two of the three measured angles exceeded 10°. The distribution peaked at 5°-intervals, *i.e.*, at 0°, 5°, 10° and 15°, which is understandable, as angles measured with the corneal reflex method are usually rounded to the nearest 5°-value. This at least partly explains the conspicuously high proportion (16.8%) where there was no difference at all between all three examinations. Interestingly, standard deviations and intraclass correlation coefficients were the same for both methods of measurement (prisms and corneal reflexes). The angle of strabismus averaged 21° for the first, second and third examinations, with approximately equal standard deviations for all three examinations.

For variability of the angle of strabismus, the data were very incomplete and the distribution of the data was very skewed. Apparently, it was not possible to determine the variability of an angle of strabismus with sufficient precision. The restriction of abduction was quantified in a 4-class scale: (1) free using pursuit eye movements, (2) free using doll's-head eye movements, (3) passing midline but not free using any method and (4) not passing midline using any method. It was measured with adequate precision: in 58% there were no differences at all between the three examinations. Cohen's kappa-statics coefficient (approximately the same as the intraclass correlation coefficient, but for a series of qualitative instead of quantitative measurements) was 0.57.

The doll's-head eye-movement option had been subdivided in two, in one of which the infant was supposed to sit with the parent on a swivel-chair. However, the swivel-chair option was taken only in 2% of the examinations, so we had to leave out this subdivision in the analysis.

The degree of amblyopia could be assessed well by observing the fixation pattern by means of direct fundoscopy with a fixation mark or by comparing corneal reflexes during monocular fixation. Using a 3-class scale (central/eccentric/far eccentric), in 96% (right eye) and 92% (left eye), there were no differences at all between the three examinations of the three orthoptists. Amblyopia could be equally well assessed by observing the fixation behaviour of the child with either eye, quantified in a 5-class scale (poor fixation/failure to maintain fixation/alternating but preference of fixation/cross-fixating/alternating freely). Cohen's kappa-statics coefficients were 0.75 (right eye) and 0.80 (left eye).

The data on up- or downshoot-in-adduction and for concomitant vertical divergence were incomplete and diverse. This partly resulted from a mistake in the form: it was not clearly indicated that these values were to be estimated quantitatively. Nevertheless, sufficient accuracy in the determination of associated vertical divergence and up- or downshoot-in-adduction is not to be expected.

DISCUSSION

The pilot-study on the accuracy and reproducibility of orthoptic examination at age one has shown results that were partly to be expected, partly disappointing and partly surprising.

The angle of squint can be measured with reasonable accuracy in infants age 9–15 months, sufficient to use it as a matching criterium in the main study. Interestingly, and to the disappointment of some purists, the accuracy was the same whether the angle was measured with prisms and corneal reflexes or only by assessing the location of the corneal reflex. In addition, the angle did not, on average, become larger when the child was examined for a second or third time.

The results for refraction were as expected. Refraction can be measured by the participating ophthalmologists with great precision and is an important prognostic factor. The measurement procedure and the policy for glasses must be agreed upon to some extent before starting the main study. In the study protocol, it is suggested to perform retinoscopy as part of the standardized examination between four and 18 months of age, and at least yearly until evaluation at age six, after atropine or cyclopentolate. Glasses (subtracting no more than 0.5 D from retinoscopy-in-cycloplegia values) are prescribed in case of: spheric equivalent $>$ 1.5 D (before early surgery this should at least have been tried), anisometropia $>$ 1 D, astigmatism (after age 2) $>$ 1.5 D or $>$ 1 D when oblique or against the rule, and astigmatism (before age two) $>$ 2 D or $>$ 1.5 D, because young infants can have large and rapidly changing astigmatism. Bifocals are prescribed when, in cases of accommodative convergence excess, the angle of squint at near is reduced, and binocular vision at near is demonstrably improved.

Restriction of abduction, quantified in a 4-class scale, could be assessed accurately and can therefore be used as a matching parameter in the main study. Interestingly, the restriction of abduction could be assessed a first time in 181 infants, a second time in 159 infants and a third time only in 48 infants.

It is surprising that orthoptists can estimate amblyopia in infants age 9–15 months with such accuracy and reproducibility as is evident from the results of this pilot study. Amblyopia could be assessed accurately by observing the fixation with direct fundoscopy or by comparing corneal reflexes during monocular fixation (3-class scale), as well as by observing the pattern of fixation behaviour during monocular viewing (5-class scale). As both methods turn out to be reliable and because occasionally unlikely discrepancies were observed in the forms between the results of the two measurements, it seems wise to combine the two, for the main study, into one continuous scale encompassing the two others:

1. Poor fixation behaviour and far eccentric fixation in fundus (or by comparing corneal reflexes during monocular fixation).
2. Poor fixation behaviour and eccentric fixation in fundus (or by comparing corneal reflexes during monocular fixation),
3. Failure to maintain fixation, but central fixation in fundus (or by comparing corneal reflexes during monocular fixation),
4. Alternating, but preference of fixation.
5. Cross-fixating or alternating freely.

The question which eye is dominant should be kept as an accessory, because occasionally unlikely discrepancies were observed in the forms between amblyopia and dominance.

It was initially suggested that the time of onset of strabismus should be used as a matching criterion in the main study, because a later onset may indicate a better prognosis. Now that we

have found that in 78.5% of the infants the onset of strabismus occurred during the first four months of life, it seems wise to restrict entry into the study instead to patients who had their strabismus begin in the first four months of life. The reason for taking the first four instead of taking the first six months of life is that (a) the time of onset of strabismus is an important prognostic parameter and we want the study groups to be as homogeneous as possible and that (b) it is generally assumed that binocular vision and stereopsis develop approximately in the fourth month of life.

Based on the results of the pilot-study, we suggest that the main study proceeds (entry of infants starting May 1st, 1993), using the matched-pair procedure described above.

We suggest that the following four parameters of the standardized entry examination are used to match pairs at the end of the main study: refraction (spherical equivalent), angle of squint, degree of amblyopia and restriction of abduction; listed in sequence of priority, spherical equivalent having the highest priority. The pilot study has shown that these parameters can be determined reliably and they are critical for the prognosis.

We suggest that the main study should evaluate the following major parameters of success of treatment at age six: (1) degree of binocular vision: no simultaneous vision, simultaneous vision, fusion or stereopsis (reach-test, Bagolini glasses, Housefly, circles, Lang or TNO), (2) manifest angle of squint during fixation at distance, measured with full corrected glasses in primary position with prisms and unilateral cover, and (3) visual acuity of the worse eye. (Note that, to limit the number of major parameters of the study, manifest angle of squint during fixation at near had to be made a minor parameter.)

Amblyopia has been subject to intense debate: Does the success of the amblyopia treatment have anything to do with a study that compares early with late strabismus surgery? Is not the success of amblyopia treatment influenced by many other factors that cannot be controlled? These are good questions and one would tend to leave the issue of amblyopia entirely out of the study. This would, however, disregard the fact that the main argument employed by ophthalmologists operating late is that amblyopia treatment can be far more difficult against a background of early surgery (see *Introduction*). To reconcile these contrasting lines of reasoning, it seems best to split the aim and methods of the study into two: Instead of the question whether early or late surgery is better regarding the three parameters mentioned above, two questions have to be answered, each with their own parameters: (1) Is early or late surgery better, as regards binocular vision and angle of squint at age six? (2) Is amblyopia treatment against the background of early surgery more difficult than amblyopia treatment against the background of late surgery, as determined by visual acuity of the worse eye at age six?

Some minimal requirements have to be met during the treatment of amblyopia in both groups. For instance, all infants should be seen at least twice a year by the clinic that does the surgery, even when the child is treated for amblyopia by the referring ophthalmologist, in order to be able to correct early when the compliance of the child or its parents is waning. How to treat amblyopia cannot be proscribed, but this problem is less serious than it may seem, because there is a general consensus that the final goal of treatment of amblyopia is equal and good visual acuity of both eyes: The differences that may result from a slightly different treatment goal (for instance, patching less to disrupt

fusion less) are small in comparison to the differences caused by lack of compliance of child or parents.

Three committees have been installed that will (1) set guidelines for amblyopia treatment for the participants in the study, (2) set guidelines for surgical procedure and policy (when to operate a second time, etc.) and age limits for all surgeons operating early and (3) set guidelines for surgical procedures, policy and age limits for all surgeons operating late. The first infants will probably be enrolled in the trial in May 1993.

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APPENDIX: LIST OF PARTICIPANTS

Austria: *Graz*: Langmann, Alge, Stückler, Unger, *St. Pölten*: Mayer (country coordinator), Scharf, Hofer, Kumpera, Fuchsberger, *Wien*: Thaler, Hafner, Grainer.
Belgium: *Liège*: Paris (country coordinator).
France: *Nantes*: Quéré (country coordinator), Lavenant, Prud'Homme, *Toulouse*: Thouvenin, Nogue, Gajan.
Germany: *Braunschweig*: Gutzeit, *Dresden*: Hering, Sommer, Muchamedjarow, *Erlangen*: Gusek, Förster, Schürhoff, *Frankfurt*: Stärk, Zubcov, Schneider, *Freiburg*: Lorenz, Lieb, Mattheus, *Halle-Wittenberg*: Weidlich (country coordinator), Wittenbacher, Teubner, Hoffmann, *Hamburg*: Pohlmann, Wibbelt, Dannheim-de Decker, Verlohr, Czerwonka, Nisch, *Heidelberg*: Stoll, Baader, Wüst, Renken, Pink, Kolling (country coordinator), Haag & Schäfer (statistical analysis, Zentrum zur Betreuung von Therapiestudien), *Köln*: Brandl, Seipel, Kirsch, Böhm, *Marburg*: Balke-Jbler, *Kaas*, Müller, *München*: Boergen, *Münster*: Rittmann-Burchert, Markodimitrakis, *Saarburg*: Kleinschmidt.
Great-Britain: *London*: Fells (country coordinator), McIntyre, Kousoulides, McLeod, *Manchester*: Hunter, Gray, Ansons, *Oxford*: Reynolds, Elston, Dodridge.
Hungary: *Szeged*: Déak (country coordinator).
Italy: *Firenze*: Frosini (country coordinator), Campa, Fabrucci, *L'Aquila*, Sabetti, Biordi, Segator, *Milano*: Blini, Persico, Vegetti, *Milano*: Nucci, Alfarano, Piantanida, *Roma*: Bagolini, Dickmann, Mengione, *Catania*: Di Pietro, Mangano, Lombardo, Bari, Bellizzi.
The Netherlands: *Amsterdam*: Prick (country coordinator), Polman, Lantau, van Mourik-Noordenbos, *Groningen*: de Vries, *Rotterdam (Oogziekenhuis)*: Grootendorst, Kingma-Wilschut, Verhoeff, van Wijnen-Segeren, *Rotterdam (University Eye Clinic)* Simonsz (corresponding author).
Norway: *Bergen*: Haugen (country coordinator).
Poland: *Cracov*: Prociej-Zero, Krcystkowa (country coordinator), Kubatko-Zielinska, Rasszewska, *Gdansk*:

Fabiszewska, Budzynska, Porozynska, Porozynska, *Katowice*: Buchta-Demel, Trzcionka, Swiatnicka, *Katowice*: Samochowiec, Koraszewska, Pieczara, *Lublin*: Bazelan, Malec, Nowinski, *Rzeszow*: Dobrodzka, Reichhart, Skorzak, *Szeczecin*: Baranowska, Andrzejewska, *Wroclaw*: Agopsowicz, Domagalska, Kapica.
Portugal: *Lissabon*: Reich-d'Almeida (country coordinator).
Spain: *Madrid*: Gomez de Liaño (country coordinator), Gomez de Liaño, Gomez de Liaño, Rodriguez.
Sweden: *Huddinge*: Lennerstrand (country coordinator), Gustavsson, Derouet-Eriksson, Waern, *Linköping*: Axelsson, Andersson, Jakobsson, *Sundsvall*: Grandell, Eames, Lindberg.
Switzerland: *Basel*: Doll, Ammann, Gerok, *Lausanne*: Klainguti (country coordinator), De Maria, Huguenin, Strickler, *St. Gallen*: Schmal, Noske, Behlau, Grossglauser (research orthoptist of the study).

EXAMINATION SHEET

This examination sheet is filled out by examiner (designate the examiners beforehand as A, B or C) A / B / C
I am the first / second / third to examine this particular infant 1st / 2nd / 3rd
I am an ophthalmologist / orthoptist ophthalm / orthopt
I work at the same clinic or practice as examiner(s) A / B / C
In our clinic, operations for infantile strabismus are carried out before / after 2nd anniversary before / after

1. History (to be taken only once, before the examination, all three examiners being present)

Age in months: .....
Sex: M / F
Onset of squint (age in months): .....
Periodic or constant strabismus: periodic / constant
Onset of amblyopia (occlusion) treatment (age in months): .....
occlusion pattern: .....
Started to wear glasses at (age in months): .....

2. Cycloplegic refraction (measured only once - not to be repeated if done recently. Only subtract 1, 1.5 or 2 dioptres for 1m, 0.67m or 0.50m retinoscopy distance, do not subtract or add anything else.)

Which drops were used for retinoscopy: .....

		retinoscopy:			glasses:
OD:	Sphere	.....	1st meridian:	Sphere	.....
	Cylinder	.....	2nd meridian:	Cylinder	.....
	Axis	.....	**OR:** Axis of 1st m:	Axis	.....
OS:	Sphere	.....	1st meridian:	Sphere	.....
	Cylinder	.....	2nd meridian:	Cylinder	.....
	Axis	.....	Axis of 1st m:	Axis	.....

3. Horizontal angle of squint (with glasses, if present)

Either: Measured with prisms and corneal reflexes
during fixation of an object with a light in 50 cm .....
Or, if that fails: By estimation of the location of the corneal reflexes
during fixation of an object with a light in 50 cm .....
This and the following angles of squint are in (please mark) prisms-diopters / degrees
Variation of the angle of squint during the examination: largest / smallest angles seen: ..... / .....
V / A: Angles in ± 25° up- and ± 25° down-gaze (approximately): upgaze: ..... / downgaze: .....

4. Motility

Abduction: (please mark)
Free, using pursuit movements: R ... L ...
Free using doll's-head eye movements, head turned only: R ... L ...
parent and child turned on swivel-chair: R ... L ...
Passing midline but not free, using any method: R ... L ...
Not passing midline, using any method: R ... L ...
Dissociated vertical deviation: yes / no
Up- / downshoot in adduction / congenital trochlear palsy:
vertical deviation of the right eye, this eye being in ± 25° adduction: ..... R/L or L/R
of the left eye: ..... R/L or L/R
Concomitant (associated) vertical deviation (approximately): ..... R/L or L/R

5. Visual acuity:

Dominant eye: right / left / neither
Type of fixation: (please mark)

Poor fixation	R... L...
Failure to maintain fixation	R... L...
Alternating but preference of fixation	R... L...
Cross-fixating	R... L...
Alternating freely	R... L...

Fixation in fundus (or by comparing corneal reflexes, monocularly):

centrally	R... L...
eccentric	R... L...
far eccentric	R... L...

Latent nystagmus yes / no
Torticollis .....