Background: Patients with intermittent exotropia may have an increase in their angle of strabismus in the distance when the angle is measured either after 1 hour of monocular occlusion or while the patients fixate on a distant target outdoors. The hypothesis that surgery should be performed for this larger deviation has been suggested but not tested.

Objectives: To test the hypothesis that surgery should be performed for the increased angle of strabismus in the distance in patients with intermittent exotropia and to investigate the factors that influence the angle of misalignment.

Methods: A prospective, clinical trial was conducted of patients with intermittent exotropia in whom the angle of misalignment in the distance increased after 1 hour of monocular occlusion or while the patients fixated on an outdoor target. The study group underwent surgery for the largest deviation measured; the control group underwent surgery for the initial angle measured at 6 m. All patients in whom the angle of misalignment increased while the patients were looking at an outdoor target were additionally measured in indoor illumination at 24 m and also at 6 m under floodlights that simulated outdoor illumination. Ninety patients undergoing surgery were randomized.

Results: Forty-three (86.0%) of the 50 patients undergoing surgery for the largest angle measured had a satisfactory outcome vs 25 (62.5%) of the 40 patients in the control group (P < .001). The mechanism for the increase in exotropia while fixating on an outdoor target was studied in 76 patients, and the results were variable.

Conclusions: The angle of strabismus in patients with intermittent exotropia undergoing surgery should be measured while the patients fixate on an outdoor target and after 1 hour of monocular occlusion. Surgery should be performed for the largest angle measured.
SUBJECTS AND METHODS

Subsequent to my previous report on this subject,7 it has been my practice to measure the angle of misalignment of all sufficiently cooperative patients with intermittent exotropia while they look through a window and fixate on a distant outdoor target (typically a flag on top of a building a quarter mile away), in addition to performing the routine strabismus measurements. Also, I obtain a measurement at 6 m after 1 hour of monocular occlusion. For this study, I will refer to the former measurement as the “outdoor measurement” and to the latter measurement as the “postocclusion measurement.” All consecutive patients I operated on for intermittent exotropia between 1985 and 1996 who had either outdoor sensitivity or VA-D were included in this study, subject to the following exclusion criteria: the presence of an A or V pattern requiring treatment, untreated amblyopia, simultaneous oblique muscle surgery, the use of adjustable sutures, a history of strabismus surgery, lateral incomitance of more than 10 prism diopters (Δ),13 follow-up of less than 1 year, insufficient cooperation for obtaining the previously mentioned measurements, or unwillingness to be randomized. Because I wanted to limit this study to patients in whom accurate measurements could be obtained with the prism and alternate cover test while fixation was well maintained on the outdoor target, the lower age for inclusion was 3 years. Also, because I frequently use adjustable sutures on postadolescent patients, and because I wanted to eliminate the confounding variable that would be introduced by adjustable sutures, I set the upper age limit for inclusion at 18 years. Finally, I excluded patients if it was known at the time of surgery that follow-up would be performed by the referring physician. Patients were considered to have intermittent exotropia if the deviation was intermittently manifested at either distance or near. Consequently, patients who had a constant exotropia at distance but an intermittent exotropia at near were included. Because outdoor sensitivity and VA-D have been reported in all forms in patients with intermittent exotropia, regardless of the distance or near discrepancy,6,7 this study includes patients in whom the distance measurement initially exceeded the near measurement, as well as those in whom the distance measurement initially equaled the near measurement. Patients with the convergence insufficiency type of exotropia (near exotropia exceeded distance exotropia by >10Δ) were also excluded because they seem to have a different and poorer prognosis.6,7,12,16 All patients were treated surgically with symmetrical lateral rectus muscle recessions according to a popular surgical formula.2 Because this formula is graduated in Δ increments, deviations were rounded to the closest Δ step for the purpose of quantifying surgery. Consequently, I considered an increase of Δ or more with the outdoor measurement or postocclusion measurement to be clinically important because it would result in an alteration in the amount of surgery performed. The patients were randomized to 1 of 2 groups when they were scheduled for surgery and after they gave informed consent. The study group underwent surgery for either the outdoor measurement or the postocclusion measurement, whichever was larger. The control group underwent surgery for the measurement obtained at 6 m prior to monocular occlusion. If patients had been treated with minus lens therapy or base-in prism prior to surgery, they were put in their appropriate cycloplegic spectacle correction without prism, and it was with those spectacles that the measurements for this study were obtained. For patients with myopia, the full cycloplegic correction was dispensed. For patients with hyperopia, spectacles were prescribed if there was any substantial astigmatic refractive error, anisometropia greater than 0.5 diopters (D), or hyperopia greater than 2 D. In most cases, hyperopic patients with intermittent exotropia were given spectacles that incorporated approximately 1 to 1.5 D less than the full cycloplegic hyperopic correction. Outcome determination was made at the earliest examination date performed at least 1 year after surgery (range, 12-13 months). An outcome was considered satisfactory if there was between 10Δ of exophoria and 3Δ of esophoria. Any intermittent or manifest tropia of any amount, either exotropia or esotropia, was considered an unsatisfactory outcome. Patients who underwent a reoperation, who needed prisms after surgery, or who needed manipulation of their accommodation with plus or minus lenses to meet the previously mentioned criteria were considered to have an unsatisfactory outcome. Patients for whom the angle of strabismus increased with either the outdoor measurement or the postocclusion measurement were subsequently retested again at 6 m after occlusion had been removed for several minutes. This subsequent measurement was obtained to determine if the increase in the angle of exotropia was merely a result of repeated dissociation and testing.

The decision to perform surgery on a given patient was not made according to a rigid predetermined protocol; however, certain factors consistently influenced the decision. In general, surgery was recommended if there was a deterioration of the exotropia with respect to either frequency or magnitude, despite nonsurgical therapy (eg, alternate occlusion, prisms, or minus lens therapy). These nonsurgical modalities were attempted in most patients who were younger than 7 years; typically, I have found such treatment approaches to be most effective in this age range. In addition, surgery was advised if there was a manifest tropia present more than 50% of the time as determined by either ocular examination or ocular history.

In addition, to investigate the nature of outdoor sensitivity, the angle of strabismus in patients who exhibited that phenomenon was measured in 2 additional manners. First, it was measured while the patients fixated on an indoor accommodative target 24 m away in standard indoor illumination (44 lux). Second, it was measured while the patients fixated on an accommodative target at 6 m while the Snellen chart and the patient’s face were illuminated with floodlights simulating outdoor illumination (1400 lux).

The range of light intensity for the outdoor measurements in this study varied with the season and climate from a low of 350 to a high of 44 000 lux.

RESULTS

Ninety of the 118 patients who had outdoor sensitivity, VA-D, or both underwent surgery and met the criteria for inclusion in this randomized, clinical trial. Six patients were unavailable for follow-up by the outcome date: 2 were from the study group, and 4 were from the control group. This left 50 patients randomized to the study group and 40 patients randomized to the control group who completed this study. Table 1 depicts a comparison of the 2 groups for sex, mean angle of exotropia at 6 m, mean increase in the angle of exotropia with the outdoor measurement or post-
occlusion measurement, and distribution for distance and near differences according to the Burian classification. The 2 groups were similar for all these parameters. The mean (±SD) age of the patients at the time of surgery was 5.1±4.4 years for the study group and 5.6±3.1 years for the control group. Of the 50 patients in the study group and 40 patients in the control group, 43 (86.0%) had a satisfactory outcome 1 year after surgery compared with 25 (62.5%) of the 40 patients in the control group. Of the 50 patients in the study group and 40 patients in the control group, 43 (86.0%) had a satisfactory outcome 1 year after surgery compared with 25 (62.5%) of the 40 patients in the control group. Of the 50 patients in the study group (those undergoing surgery for the maximum deviation measured), 43 (86.0%) had a satisfactory outcome 1 year after surgery compared with 25 (62.5%) of the 40 patients in the control group. This difference was significant (P<.001, χ² test). Although patients in the study group underwent surgery for an average of 11.7±5.2 years for the study group and 10.3±5.7 years for the control group, this did not result in an increase in overcorrections. There was 1 overcorrection in each group. Table 2 provides the surgical outcome for patients in this clinical trial based on the subsets of patients who had outdoor sensitivity, VA-D, or both. Although the sample size in each of these subsets was too small to permit meaningful statistical analysis, it seems that the results were similar for each subset.

Table 1. Characteristics of the Control and Study Groups

<table>
<thead>
<tr>
<th>Group</th>
<th>M/F Ratio (Percentage Ratio)</th>
<th>Initial Angle of Exotropia at 6 m, Δ*</th>
<th>Increase in the Angle of Exotropia With Occlusion or Outdoors, Δ†</th>
<th>Classification‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (n=40)</td>
<td>14:26 (35:65)</td>
<td>25.3±5.1</td>
<td>10.1±6.2</td>
<td>0</td>
</tr>
<tr>
<td>Study (n=50)</td>
<td>16:34 (32:68)</td>
<td>27.3±6.3</td>
<td>11.7±5.8</td>
<td>21</td>
</tr>
</tbody>
</table>

* Data are given as the mean (±SD). Δ indicates prism diopters.
† Refers to the mean increase in the angle of exotropia with outdoor or postocclusion measurement, whichever is greater. Outdoor and postocclusion measurements are defined in the “Subjects and Methods” section.
‡ Data are given as the number of patients. Burian classification.

Table 2. Results of Surgery by Subsets of Patients With Outdoor Sensitivity, VA-D, or Both*

<table>
<thead>
<tr>
<th>Patient Description (N=118)</th>
<th>Patients Not Operated On or Excluded From the Study</th>
<th>Study Group</th>
<th>Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Satisfactory Outcome</td>
<td>Unsatisfactory Outcome</td>
<td>Satisfactory Outcome</td>
</tr>
<tr>
<td>Patients with outdoor sensitivity only (n=69)</td>
<td>11</td>
<td>25</td>
<td>4</td>
</tr>
<tr>
<td>Patients with VA-D only (n=24)</td>
<td>8</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Patients with outdoor sensitivity and VA-D (n=25)</td>
<td>9</td>
<td>12</td>
<td>0</td>
</tr>
</tbody>
</table>

* All data are given as the number of patients. VA-D indicates vergence aftereffect at distance.

Table 3. Outdoor Sensitivity and VA-D by Distance or Near Difference (N=118)*

<table>
<thead>
<tr>
<th>Distance or Near Relationship†</th>
<th>Increased Angle of Exotropia After Occlusion Measurement (VA-D)</th>
<th>Increased Angle of Exotropia After Outdoor Measurement</th>
<th>Increased Angle of Exotropia After Occlusion and Outdoor Measurement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distance angle of exotropia&gt;near angle of exotropia (divergence excess)</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Distance angle of exotropia=near angle of exotropia (basic)</td>
<td>6</td>
<td>29</td>
<td>23</td>
</tr>
<tr>
<td>Distance angle of exotropia&gt;near angle of exotropia and distance angle of exotropia=near angle of exotropia after occlusion (simulated divergence excess)</td>
<td>14</td>
<td>39</td>
<td>2</td>
</tr>
<tr>
<td>Distance angle of exotropia&lt;near angle of exotropia (convergence insufficiency)</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

* All data are given as the number of patients. Outdoor and postocclusion measurements are defined in the “Subjects and Methods” section. VA-D indicates vergence aftereffect at distance.
† The classification of exotropia according to Burian is given in parentheses.

A total of 202 patients with intermittent exotropia were measured for outdoor sensitivity and VA-D; many of these patients did not undergo surgery. There were 125 girls and 77 boys in the study. Of the 202 patients, 118 exhibited an increase of 3Δ or more with the outdoor measurement or the postocclusion measurement. As previously reported, the presence of outdoor sensitivity or VA-D was not limited to any 1 type of patient with respect to distance or near discrepancies (Table 3 shows the distribution). The mean (±SD) increase in the angle of exotropia with the postocclusion or outdoor measurement was 10.3±5.2Δ (range, 5Δ-30Δ). The mean (±SD) increase in the angle of exotropia with the outdoor measurement alone was 10.3±5.7Δ (range, 5Δ-30Δ); after monocular occlusion, the mean (±SD) increase was 7.7±4.3Δ (range, 5Δ-19Δ). No relationship was noted between the increase in the angle of exotropia with the outdoor measurement and the outdoor light level (350 or 44 000 lux). Of the 202 patients who were measured for outdoor sensitivity, 22 had constant exotropia at distance but had intermittent exotropia at near. Of these 22...
patients, 10 (45%) had an increased angle of exotropia with the outdoor measurement; the mean (±SD) increase was $7.8\pm3.4\Delta$ (range, $5\Delta$-$15\Delta$). Six (27%) of the 22 patients had an increased angle of exotropia with the postocclusion measurement; the mean (±SD) increase was $7.2\pm2.5\Delta$ (range, $5\Delta$-$10\Delta$). Although the increase in the angle of exotropia with the outdoor and postocclusion measurements seems to be smaller in patients with constant exotropia at distance than in patients with intermittent exotropia, the sample size in these subgroups is too small to permit meaningful statistical comparison.

Of the 118 patients who had either VA-D or outdoor sensitivity, 69 had an increase in the angle of exotropia while looking at a distant target but did not have an increase after monocular occlusion. Twenty-four patients only had an increase in the angle of exotropia after monocular occlusion but did not have an increase while looking at an outdoor target. The angle of exotropia increased in the remaining 25 patients after monocular occlusion and while they looked at an outdoor target. It seems that measuring the angle of strabismus of a patient while the patient fixates on an outdoor target vs after 1 hour of monocular occlusion may increase the initial angle by different mechanisms in many patients.

**Figure 1** shows diagrammatically how the initial measurement at 6 m, the postocclusion measurement, and the outdoor measurement compare for each of the 118 patients. In most cases (92%), the repeated measurement at 6 m performed after the testing for outdoor sensitivity and VA-D was essentially identical to the initial 6-m measurement. This suggests that outdoor sensitivity and VA-D are real phenomena and not merely functions of repeated testing.

Of the 94 patients who had outdoor sensitivity (the 69 with outdoor sensitivity alone plus the 23 with outdoor sensitivity and VA-D), 76 underwent further testing to elicit the mechanism of this phenomenon. The initial 6-m measurement for these patients was $21.0\Delta\pm4.8\Delta$ (range, $5\Delta$-$25\Delta$); the amount by which the angle of exotropia increased with the outdoor measurement was $10.7\Delta\pm5.5\Delta$ (range, $5\Delta$-$30\Delta$). The amount by which the angle of exotropia increased when measured indoors at 24 m compared with the initial measurement was $4.2\Delta\pm4.8\Delta$ (range, $-5\Delta$ to $15\Delta$); the amount by which the angle of exotropia increased when measured at 6 m indoors but with outdoor illumination compared with the initial measurement was $4.8\Delta\pm5.0\Delta$ (range, $-5\Delta$ to $15\Delta$). (All the data are provided as the mean [±SD]; a negative number denotes a decrease in the angle of exotropia.) **Figure 2** graphically depicts the measurement obtained for each of these 76 patients in the previously mentioned testing modalities. It seems from these data that, in some patients, outdoor sensitivity is a function of the increased illumination outdoors; in others, it is a function of the increased distance; and in some, it is both.

**COMMENT**

The data suggest that the angle of strabismus in patients with intermittent exotropia should be measured while the patients fixate on a distant target and after 1 hour of monocular occlusion. Surgery should be performed for the largest deviation obtained. Although an outdoor measurement and a measurement after monocular occlusion may reveal a larger underlying exotropic deviation, neither test is a replacement for the other. Both tests must be performed on each patient to determine the appropriate deviation for which surgery should be planned. As reported by others, the presence of outdoor sensitivity and VA-D is not limited to patients with greater exotropia at distance than near (divergence excess or simulated divergence excess types of exotropia). Consequently, testing for these phenomena should not be limited to patients in whom the distance deviation exceeds the near. Several authors have suggested a role for prism adaptation to determine the angle of strabismus for which surgery should be planned in patients with intermittent exotropia. This study did not investigate the use of prism adaptation. Shippman and coworkers have suggested that prism adaptation in patients with intermittent exotropia gives essentially the same information as a 1-hour patch test for distance or near differences. However, its role relative to the distance measurement obtained after monocular occlusion or with an outdoor fixation target still needs to be investigated. Whether prism adaptation will reveal the same deviation that can be elicited by monocular occlusion or an outdoor measurement is an important question. The data in this study also show that although the angle of strabismus may increase in a patient with intermittent exotropia at distance, this increase is not always related to an increase at near. This suggests that some patients may have a greater angle of exotropia at distance than near in a patient with intermittent exotropia at distance but not at near.
tropia when measured at a distance of 24 m indoors or with outdoor illumination at 6 m neither of these measurements is a replacement for either the outdoor or the postocclusion measurement. This finding is similar to that reported by Fleming and Cassin.21

One might argue that these data merely indicate that the standard surgical formula for patients with intermittent exotropia is not sufficient. Possibly, larger amounts of surgery should just be performed. However, this argument is contradicted by data that show good results with the same formula in patients with intermittent exotropia who do not have an increase in their deviation at 6 m after prolonged occlusion or while looking out a window.7

Some authors have suggested that increased luminance may play a role in the cause of exotropia because studies show an increase in exotropia in sunnier climates.11,22 Eustace and coworkers23 found that increased luminance caused an increase in the near deviation in patients with divergence excess exotropia. Wirtschafter and von Noorden24 found that greater luminance increased the deviation of intermittent exotropia but did not affect constant exotropia. Although the data in this study do not directly address the role of light on the cause of exotropia, the fact that many patients had an increase in their deviation under floodlights at 6 m does support the hypothesis that light plays a role. Other factors (eg, increased fixation distance) are also important.

When patients are looking at an outdoor distant target while looking through a window, they are indoors but the object of regard receives outdoor illumination. The area of the retina of each eye that is being stimulated with outdoor illumination is, therefore, a function of the size of the window and the distance of the subject from the window (Figure 3). Therefore, when obtaining an outdoor measurement, it is important that the patient be positioned as close to the window as possible, yet sufficiently far away as to permit the examiner to stand between the subject and the window to obtain measurements.

This study did include patients who had constant exotropia at distance if they had an intermittent exotropia at near. Some of these patients did have outdoor sensitivity or VA-D. This suggests that possibly either of these 2 phenomena might also be present in patients who have constant exotropia at distance and near. However, because this study did not include any patients with constant exotropia at all fixation distances, the data cannot be extrapolated to such patients. Also, this study only included patients with intermittent exotropia without A or V patterns, oblique dysfunction, lateral incomitance, or a history of surgery. The results cannot be extrapolated with confidence from this study to patients who have those criteria that were excluded. Although there is no reason to suspect that patients with those characteristics would behave differently, there are no data to substantiate that.

Although I believe this study confirms the hypothesis that I suggested in 1987, the study needs to be viewed in the light of the following limitations. Although it was prospective and randomized, the outcome was not masked. This has the potential of introducing some examiner bias. Ideally, a separate randomization should have been performed for patients in whom only outdoor sensitivity was manifest and for patients in whom only VA-D was manifested. By combining patients who had either of these phenomena in 1 randomization protocol, I may have obscured the relative importance of 1 of these factors compared with the other. Although not statistically significant because of the small sample size, the evaluation of subsets in Table 2 suggests that this limitation does not have an important effect on the conclusions of this study. It would, in fact, be quite difficult to perform a separate randomization for these 2 subsets because a few patients had an increase in the deviation with only 1 of the 2 tests. Ideally, there would have been better control of light levels for the investigation of outdoor sensitivity. Although the level of luminance under the indoor floodlights was substantially more than the level of standard indoor illumination, it was less than the level of outdoor luminance on brighter days. Finally, the criteria that I chose to define the successful outcome were arbitrary and may be subject to question. I chose these criteria because they were the same ones used in my earlier report on this subject and I wanted to be able to make meaningful comparisons with my previous data.7 Some authors have used more liberal outcome criteria in studying intermittent exotropia, and some have used more stringent criteria.25-28 Some authors suggest that 1 year after surgery is too soon to determine the outcome of patients undergoing surgery for intermittent exotropia.27,28 It is for this reason that I specifically avoided describing patients as being “cured”; instead, I chose to describe them as having a satisfactory outcome. I was mainly interested in comparing the outcome of 2 different treatment modalities rather than defining a true cure.

This article is the first of a 3-part series. The second part will appear next month.

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Figure 3. As the distance between an eye and a window increases (right), the angle that the window subtends on the retina is smaller than if the distance decreases (left).
References


In Other AMA Journals

Diabetes Insipidus and Blindness Caused by a Suprasellar Tumor: Pieter Pauw’s Observations From the 16th Century

Tero Kivelä, MD; Risto Pelkonen, MD; Matti Oja, PhD; Olli Heiskanen, MD

Tumors in the suprasellar region may cause both visual and endocrinologic symptoms. This association, well known to modern physicians, was established during the 19th century. However, we have identified a 16th-century autopsy report, written by the Dutch professor of anatomy Pieter Pauw (1564-1617), which describes an 18-year-old girl who developed marked polyuria and subsequently became totally blind from a cystic tumor compressing the optic chiasm. Based on prevailing theories on the nature of diabetes, Pauw attributed the disease to the kidneys. Undoubtedly, however, his lucid report is the earliest known account of diabetes insipidus caused by an arachnoid cyst, the Rathke cleft cyst, or craniopharyngioma in the region of the pouch of Rathke. The description also gives insights into the role of anatomic dissections in late 16th-century northern Europe. JAMA. 1998;279:48-50

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