Visual Field Loss in Young Children and Mentally Handicapped Adolescents Receiving Vigabatrin

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PURPOSE. In adult patients and in children of school age who have been treated with vigabatrin (VGB), persistent visual field defects have been reported as a side effect. To date, it is unknown to what extent VGB causes visual field loss in young children and mentally handicapped adolescents who cannot be tested with conventional perimetric methods. The purpose of the present study was to investigate VGB-induced visual field loss in these patients by using a noncommercial arc perimeter and a forced-choice, preferential-looking method.

METHODS. The visual field size was measured in 30 patients aged 1 to 15 years who had epilepsy and who were treated with VGB. The visual field of these patients was compared to the visual field of 70 control subjects.

RESULTS. In eight (27%) patients who had been treated with VGB, the visual field was constricted compared with the visual field of the children belonging to the control group.

CONCLUSIONS. Arc perimeter shows that mentally handicapped patients and children younger than 6 years treated with VGB have visual field loss compared with the loss reported in adult patients receiving VGB. (Invest Ophthalmol Vis Sci. 2006;47: 3028–3035) DOI:10.1167/iovs.05-0778

Vigabatrin (VGB) is an antiepileptic drug used in the treatment of partial and secondarily generalized seizures and infantile spasms. With conventional perimetric methods, visual field constriction has been found in adult patients and in children of school age who had been treated with VGB.1–38 The prevalence of visual field defects in adult patients who receive VGB ranges between 19%23 and more than 70%.24 In children who receive VGB, a prevalence of visual field defects between 42%37 and 71%28 has been found. However children younger than 6 years and children who were mentally handicapped (IQ <60) had to be excluded from these studies because their visual fields could not be assessed with conventional perimetric methods. In conventional perimeter, which was used to assess the visual field of adult patients and children of school age, patients have to maintain fixation of the central point in the perimetric sphere until the target is presented. When the target is seen, they have to press a button while fixation of the central point is maintained.39 Children younger than 6 years and mentally handicapped adolescents, however, are unable to understand and follow the instructions. Those who understand the instructions are unable to maintain fixation when the target appears, and/or they forget to press the button.40–44 Therefore, the influence of VGB on the extension of the visual field of infants and preschool children has not yet been tested. We therefore assessed the visual field with an improved arc perimeter41–44 using a sufficiently small stimulus, which was only 0.5 degrees of arc larger than the largest stimulus in the Goldmann perimeter. Our arc perimeter is based on the forced-choice, preferential-looking methods41–44 used in earlier studies to assess the visual field in infants. In contrast to conventional perimetry, the method we applied does not require the subjects to understand instructions. When the visual field is assessed with the arc perimeter, the patients are neither required to maintain fixation if they detect the target nor to press a button. The gaze is automatically attracted by a flickering central point. The target appears instead of the fixation point, and the patients are allowed to make an eye movement when the target is presented. The decision about whether the target was detected depends on the kind of eye movement performed when the target is present.41–44 This method made it possible to examine the location and extension of the visual field in very young children and in mentally handicapped patients who had been treated with VGB.

To investigate whether VGB leads to visual field loss in children, the visual field size of children who have been treated with VGB should be compared to the visual field size of normal control subjects who have not been treated with VGB. In healthy children, the visual field reaches normal dimensions at the age of 1 year.41–44 Therefore, the visual field of the control subjects aged between 1 and 15 years is expected to have a normal size.

The targets that are used to assess the size of the normal and the blind visual fields are spots of light on the arc of the perimeter. Hence, the targets are located on the perimetric sphere, as are the blind areas. A comparison of the size of the visual fields of patients who had been treated with VGB with the visual fields of control subjects is, therefore, a comparison of the size of areas on the perimetric sphere.

PATIENTS AND METHODS

The patients were 30 children and adolescents aged 1 to 15 years (mean age, 98.7 ± 45.7 months [SD]) who had been treated with VGB for epileptic seizures. The ages of the children, duration of treatment with VGB, and dose of VGB are summarized in Table 1. Nine patients had infantile spasms: seven from focal epileptic seizures, five from grand mal seizures, and nine from other kinds of epileptic seizures. The mean dose of VGB that the patients received was 62.4 ± 35.7 (SD) mg/kg body weight (range: 12–160 mg/kg body weight). The mean age at the beginning of the treatment was 52 ± 37 (SD) months (range: 1–13 years). The mean duration of treatment was 46 ± 32 months (SD, range: 6–88 months). Five patients were treated for less than a year, 9 were treated between 1 and 3 years, 6 were treated between 3 and 5 years, and 10 were treated longer than 5 years. Twenty-three children belonging to this group received additional antiepileptic medication. The visual fields of patients could not be examined with conventional perimetric methods, because the patients were either too young (8 children were younger than 6 years) or mentally handicapped (22 children). Cognitive functioning was assessed with the HAWIK-R (Hamburg-Wechsler Intelligenztest für Kinder),15 an adapted German version of the WISC-III (Wechsler Intelligence Scale for Children-Revision III). Scores of cognitive functioning could not be tested in nine patients older than 6 years because they did not understand...
instructions. Thirteen patients had an IQ below 60 (HAWIK-R). In all children, the optokinetic nystagmus, threat response, eye movements, optical alignment, and pupillary reflex were normal. Spontaneous eye movements occurred to the left and to the right. All children reacted to acoustic and tactile stimuli in the left and right halves of space. Patients were excluded from arc perimeter if they had damage to the primary or secondary visual pathway, if they were unable to hold their head upright and if they did not open their eyes and did not direct their eyes spontaneously to the flickering fixation point in the perimetric arc. Six patients who had been treated with VGB had to be excluded from the study due to the listed exclusion criteria.

Control Subjects

Group 1. The monocular visual fields of 30 children and adolescents matching the patients of the VGB group in age and mental category, but without a sign of visual disturbance (mean age, 96.73 ± 43.67 months) were assessed on eight meridians with the arc perimeter. There was no significant difference between the mean age of the children and adolescents of control group 1 and the mean age of the patients who had been treated with VGB (t-test: P = 0.62). The visual fields of these children and adolescents were assessed with the arc perimeter because the children could not be tested with conventional perimetric methods. The children were unable to understand and follow the instructions, because they were too young or because they were mentally handicapped. Eight children were less than 6 years of age. Scores of cognitive functioning could not be tested in 10 patients older than 6 years because they did not understand instructions. Twelve patients had an IQ below 60 (HAWIK-R).

Group 2. The monocular visual fields of 20 children with cerebral palsy but without involvement of the visual system (mean age, 26.8 ± 10.3 months) were assessed on eight meridians with the arc perimeter. Spontaneous eye movements occurred to the left and to the right. All children reacted to acoustic and tactile stimuli in the left and right halves of space. In all children the optokinetic nystagmus, threat response, eye movements, optical alignment, and pupillary reflex were normal. Children were excluded from arc perimeter if they had damage to the primary or secondary visual pathway, if they were unable to hold their heads upright and if they did not open their eyes and did not direct their eyes spontaneously to the flickering fixation point in the perimetric arc.

Group 3. To compare the cerebral palsy group with a healthy control group, we investigated an age-matched group of 20 normal children (mean age, 27.0 ± 9.9 months). The visual fields of these children were assessed during a comprehensive medical checkup. There was no significant difference between the ages of the children in control group 3 and in the cerebral palsy group (t-test: P = 0.71). The monocular visual fields of these children were also assessed on eight meridians within the arc perimeter. Spontaneous eye movements occurred to the left and to the right. All children reacted to acoustic and tactile stimuli in the left and right halves of space. In all children the optokinetic nystagmus, threat response, eye movements, optical alignment, and pupillary reflex were normal.

Group 4. To determine the maximum error of measurement, we assessed the monocular visual fields of 16 patients aged 6 to 18 years (mean age, 12.6 ± 3.5 years) who had a homonymous hemianopia on eight meridians with the Goldmann perimeter (target luminance, 320 cd/m²; background luminance, 5 cd/m²; target diameter 2 and 4 mm) and with the arc perimeter. All patients had an IQ above 81 (HAWIE and HAWIK-R). Spontaneous eye movements occurred to the left and to the right. All patients reacted to acoustic and tactile stimuli in the left and right halves of space. Optokinetic nystagmus was disturbed in 11 patients, and pursuit eye movements were disturbed in six. Threat response, optical alignment, and pupillary reflex were normal in all patients. Optokinetic nystagmus was tested by showing the children a rotating drum with black and white stripes of a frequency of 0.07 c/deg. Visual threat response was tested by moving a 14 × 14-cm object rapidly toward the child’s eyes.

All patients directed their gazes spontaneously to a flickering fixation point in the perimetric arc and maintained fixation for at least 4 seconds. Patients were excluded if they were unable to understand and follow the instructions or if they were unable to maintain fixation of the central point in the Goldmann perimeter for at least 1 minute.

Measurement of the Visual Field Size

The size of the visual field was assessed with a noncommercial arc perimeter consisting of a semicircular semitranslucent white screen of 41-cm radius.

During the perimetric testing of the visual field, the child was held on an assistant’s or a parent’s lap. The child’s head was positioned at the center of the perimeter facing the semicircular screen at a distance of 41 cm and was supported and stabilized by hand. On the screen, the fixation point (diameter, 1.5°) and the target (2.5°) appeared. Target luminance could be varied between 0 and 26,000 cd/m². Background luminance was 0.05 cd/m². The head position, fixation, and eye movements were controlled by an infrared-sensitive video camera displayed on a high-resolution monitor. During perimetric testing, an assistant controlled fixation of the central fixation point and eye and head movements on the video monitors. Two investigators independently judged whether an eye movement was directed toward a target. The investigators did not know where the targets would appear and received no information about whether the child had cerebral lesions or epileptic seizures or about the medication the child received. To exclude the presence of a hemispatial neglect, spontaneous eye movements were recorded when no visual stimulus was present in the perimetric arc.

The visual field was examined in steps of 5° or 10° along eight meridians. The borders of blind areas were assessed in steps of 2° with stationary targets along the meridians. The luminance of the target was 5 cd/m². If the target was not detected, the measurement was repeated with a target luminance of 40 cd/m², since targets with a luminance below 50 cd/m² had no light scatter.5,44

At the beginning of each trial, the fixation point flickered with a frequency of 4 Hz. When the child directed his or her gaze to the fixation point, the flicker frequency of the fixation point was reduced.
When the fixation point had disappeared and the child still directed his or her gaze to the center of the perimetric screen where the fixation point had been shown, the target was presented for four seconds (experimental trials). If eye movement had not occurred within 4 seconds after the onset of the target, the target was removed, and the trial was terminated. Half of the trials were blank trials that were identical with the experimental trials, except that no target appeared after the offset of the fixation point. Experimental trials and blank trials were of equal length and followed in random order. The intertrial intervals varied randomly between 5 and 8 seconds. A target was regarded as detected only if (1) it elicited a saccadic eye movement (one saccade followed by a small correction saccade) directed toward the target followed by fixation of the target in at least three successive trials; (2) the eye movement occurred within a time interval of 4 seconds after the onset of the target; and (3) in at least three successive blank trials, there was either no eye movement directed to the side on which the target was shown in the experimental trials or if in at least two of three successive blank trials eye movements were directed opposite the side where the target was shown in the experimental trials. Searching eye movements consisting of a succession of saccades were not allowed. Further details of the method and precision of arc perimeter and the control of scattering light have been reported earlier.43,44

An area of the visual field was regarded as blind if the targets presented in this area were not detected by the method just described and if all targets that were presented in the same area were detected in the control groups.

This study was approved by the ethics committee of the University of Munich and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. The parents of all children gave their informed consent before their children’s inclusion in the study.

Determination of the Blind Areas of the Visual Field and Statistical Evaluation

Because the size of the blind areas were assessed with the arc perimeter, the borders of the perimetrically blind areas are represented by lines through the measurement points on the perimetric sphere. Perimetrically blind areas delineated by the lines through the measurement points are therefore not areas on a plane, but areas on the perimetric sphere. The intact visual field and the visual field defects assessed with perimetric methods can be conceived as being composed of spherical triangles, the sides of which are lines of the great circles of the perimetric sphere. As the location of points on the perimetric sphere was known as a result of the perimetric measurement, the angles of the spherical triangles were calculated on the grounds of the cosine rules for spherical triangles (Neper’s rule). The area of the blind visual field between 5° and 15° eccentricity, between 15° and 30° eccentricity, between 30° and 60° eccentricity, and between 60° and 85° eccentricity was calculated from the spherical excess of the angles of the spherical triangles and the radius of the perimetric sphere (i.e., the radius of the arc perimeter) for each quadrant of the temporal visual field of each eye. The area of the blind visual field was calculated between 5° and 15°, between 15° and 30°, and between 30° and 50° for each quadrant of the nasal visual field of each eye. The influence of VGB on the size of the visual field was determined as the area of visual field in the patients who had been treated with VGB compared with the area of visual field in the control subjects. The significance of the difference between the areas of visual fields in the VGB group and the control groups was calculated using the t-test. The significance of the difference of the percentage of visual field defects in the VGB group and the control groups was calculated using the chi-squared test: overestimations, $\chi^2 = 1.15; df = 5; P > 0.05$. All children responded promptly to the target, which was presented on eight meridians of each monocular visual hemifield.

In 16 patients aged 6 to 18 years who had a homonymous hemianopia, the visual field was assessed with the Goldmann perimeter and the arc perimeter (control group 4). In all cases, the difference between the measurements (i.e., the possible error of measurement) was smaller than 5° (mean difference at the horizontal meridian $x = 3.3° \pm 0.7°$ [SD]). The size of the visual field measured with the Goldmann perimeter did not differ significantly from the measurement with the arc perimeter (Wilcoxon test: overestimations, $z = 0.54$; $P > 0.05$; underestimations, $z = -0.33; P > 0.05$; Pearson $r = 0.897; P = 0.000003$).

In the group of children who had been treated with VGB, 8 (27%) of 30 had visual field loss (Fig. 1). This means that these patients did not respond to stimuli in areas of the visual field in which the control subjects responded to the same visual stimuli. The difference between the percentages of patients with visual field defects in the VGB group (26.6%) and the control groups (0%) was highly significant ($z = -7.34; P < 0.001$). The difference between the area of visual field in the VGB group (right eye: $x = 5790 \pm 441.1$ cm² [SD]; left eye: $x = 5889 \pm 452.3$ cm²) and the control groups (right eye: $x = 6018 \pm 19.0$ cm²; left eye: $x = 5912 \pm 18.1$ cm²) was also highly significant (for both eyes, $t$-test: $P < 0.01$). The area of visual field defect and the percentages of visual field loss are summarized in Table 3.

Right Eye, Nasal Visual Field

One patient (PA) treated with VGB had a visual field defect measuring 36 cm² in the superonasal quadrant between 5° and 15° eccentricity, which corresponds to 46% of the superonasal quadrant field between 5° and 15° eccentricity in control subjects—an area of 78 cm². This patient also had a 36-cm² defect in the inferonasal quadrant between 5° and 15° eccentricity, which is 46.2% of control subjects. In normal control subjects, this area of the visual field was 78 cm².

Five patients treated with VGB had visual field defects measuring 44 to 194 cm² in the superonasal quadrant between 30° and 50° eccentricity, which corresponds to 10.6% to 46.8% of the superonasal quadrant field between 30° and 50° eccentricity in control subjects—an area of 415 cm². These patients also had a 44- to 132-cm² defect in the inferonasal quadrant between 30° and 65° eccentricity, which is 8% to 23.9% of that in control subjects. In normal control subjects, this area of the visual field was 553 cm².

Right Eye, Temporal Visual Field

Three patients treated with VGB had visual field defects measuring 8 to 561 cm² in the superotemporal quadrant between...
30° and 60° eccentricity, which corresponds to 0.9% to 63.5% of the superotemporal field between 30° and 60° eccentricity in control subjects—an area of 883 cm². One patient also had a 52-cm² defect in the inferotemporal quadrant between 30° and 60° eccentricity, which is 5.5% of that in control subjects. In normal control subjects, this area of the visual field was 946 cm². Seven patients treated with VGB had visual field defects measuring 132 to 517 cm² in the superotemporal quadrant between 60° and 85° eccentricity, which corresponds to 25.5% to 100% of the superotemporal quadrant field between 60° and 85° eccentricity in control subjects—an area of 517 cm². Six of these patients also had a 97- to 561-cm² defect in the infero-

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<td>$x = 46.4^\circ$</td>
<td>$x = 46.5^\circ$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SD = 1.1°</td>
<td>SD = 1.6</td>
<td>SD = 1.6°</td>
</tr>
<tr>
<td>Right</td>
<td>Nasal VF 120° meridian</td>
<td>$x = 45.9^\circ$</td>
<td>$x = 46.0^\circ$</td>
<td>$x = 46.1^\circ$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SD = 1.0</td>
<td>SD = 1.3</td>
<td>SD = 1.2°</td>
</tr>
<tr>
<td>Right</td>
<td>Nasal VF 210° meridian</td>
<td>$x = 46.7^\circ$</td>
<td>$x = 46.6^\circ$</td>
<td>$x = 46.7^\circ$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SD = 1.2°</td>
<td>SD = 1.4</td>
<td>SD = 1.4°</td>
</tr>
<tr>
<td>Right</td>
<td>Nasal VF 240° meridian</td>
<td>$x = 52.2^\circ$</td>
<td>$x = 51.9^\circ$</td>
<td>$x = 52.4^\circ$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>SD = 2.9°</td>
<td>SD = 2.2°</td>
<td>SD = 2.3°</td>
</tr>
</tbody>
</table>
### Table 3. Areas and Visual Fields in Control Subjects and Areas of Visual Field Defect in VGB-Treated Patients

#### A. Right Eye

<table>
<thead>
<tr>
<th>Areas of Visual Field</th>
<th>Eccentricity of Investigated Areas (deg)</th>
<th>Eccentricity of Investigated Areas (deg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper quad.</td>
<td>30–50</td>
<td>15–30</td>
</tr>
<tr>
<td>Lower quad.</td>
<td>30–65</td>
<td>15–30</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Areas of Visual Field</th>
<th>Eccentricity of Investigated Areas (deg)</th>
<th>Eccentricity of Investigated Areas (deg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper quad.</td>
<td>5–15</td>
<td>5–15</td>
</tr>
<tr>
<td>Lower quad.</td>
<td>5–15</td>
<td>5–15</td>
</tr>
</tbody>
</table>

Control subjects

- Upper quad.
  - 415 cm² 100%
  - 262 cm² 100%
  - 78 cm² 100%
  - 78 cm² 100%
  - 262 cm² 100%
  - 883 cm² 100%
  - 517 cm² 100%
- Lower quad.
  - 553 cm² 100%
  - 262 cm² 100%
  - 78 cm² 100%
  - 78 cm² 100%
  - 262 cm² 100%
  - 946 cm² 100%
  - 746 cm² 100%

Patients

- AS
  - Upper quad.
    - 194 cm² 46.82%
  - Lower quad.
    - 116 cm² 20.98%
- RO
  - Upper quad.
    - 407 cm²
  - Lower quad.
    - 46.09%
- PA
  - Upper quad.
    - 36 cm² 46.15%
  - Lower quad.
    - 36 cm² 46.15%
- FA
  - Upper quad.
    - 88 cm² 21.20%
  - Lower quad.
    - 132 cm² 23.87%
- ME
  - Upper quad.
    - 75 cm² 18.10%
  - Lower quad.
    - 90 cm² 16.27%
- BT
  - Upper quad.
    - 44 cm² 10.60%
  - Lower quad.
    - 44 cm² 7.96%
- BG
  - Upper quad.
    - 48 cm² 11.56%
  - Lower quad.
    - 48 cm² 8.68%
- OK
  - Upper quad.
    - 8 cm² 0.91%
  - Lower quad.
    - 8 cm² 0.91%

B. Left Eye

<table>
<thead>
<tr>
<th>Areas of Visual Field</th>
<th>Eccentricity of Investigated Areas (deg)</th>
<th>Eccentricity of Investigated Areas (deg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper quad.</td>
<td>60–85</td>
<td>15–30</td>
</tr>
<tr>
<td>Lower quad.</td>
<td>60–85</td>
<td>15–30</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Areas of Visual Field</th>
<th>Eccentricity of Investigated Areas (deg)</th>
<th>Eccentricity of Investigated Areas (deg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper quad.</td>
<td>5–15</td>
<td>5–15</td>
</tr>
<tr>
<td>Lower quad.</td>
<td>5–15</td>
<td>5–15</td>
</tr>
</tbody>
</table>

Control subjects

- Upper quad.
  - 517 cm² 100%
  - 883 cm² 100%
  - 262 cm² 100%
  - 78 cm² 100%
  - 262 cm² 100%
  - 262 cm² 100%
  - 415 cm² 100%
- Lower quad.
  - 746 cm² 100%
  - 946 cm² 100%
  - 262 cm² 100%
  - 78 cm² 100%
  - 262 cm² 100%
  - 262 cm² 100%
  - 553 cm² 100%

Patients

- AS
  - Upper quad.
    - 294 cm² 56.87%
  - Lower quad.
    - 313 cm² 41.96%
- RO
  - Upper quad.
    - 12 cm² 15.54%
  - Lower quad.
    - 6.6 cm² 7.8%
- PA
  - Upper quad.
    - 219 cm² 42.36%
  - Lower quad.
    - 225 cm² 30.16%
- FA
  - Upper quad.
    - 193 cm² 37.33%
  - Lower quad.
    - 240 cm² 32.17%
- ME
  - Upper quad.
    - 102 cm² 24.58%
  - Lower quad.
    - 108 cm² 18.22%
- BT
  - Upper quad.
    - 132 cm² 25.53%
  - Lower quad.
    - 253 cm² 33.91%
temporal quadrant between 60° and 85° eccentricity, which is 13% to 75.2% of that in control subjects. In normal control subjects, this area of the visual field was 746 cm².

Left Eye, Nasal Visual Field
Two patients treated with VGB had visual field defects measuring 102 to 141 cm² in the superonasal quadrant between 30° and 50° eccentricity, which corresponds to 24.6% to 34% of the superonasal quadrant field between 30° and 50° eccentricity in control subjects—an area of 415 cm². These patients also had a 108- to 198-cm² defect in the inferonasal quadrant between 30° and 50° eccentricity, which is 18.2% to 35.8% of that in control subjects. In normal control subjects, this area of the visual field was 553 cm².

Left Eye, Temporal Visual Field
One patient (PA) treated with VGB had a visual field defect measuring 12 cm² in the superotemporal quadrant between 5° and 15° eccentricity, which corresponds to 15.5% of the superotemporal quadrant field between 5° and 15° eccentricity in control subjects—an area of 78 cm². This patient also had a 6.6-cm² defect in the inferotemporal quadrant between 5° and 15° eccentricity, which is 7.8% of that of control subjects. In normal control subjects, this area of the visual field was 78 cm².

Four patients treated with VGB had visual field defects measuring 193 to 517 cm² in the superotemporal quadrant between 60° and 85° eccentricity, which corresponds to 37.3% to 100% of the superotemporal quadrant field between 60° and 85° eccentricity in control subjects—an area of 517 cm². These patients also had a 225- to 716-cm² defect in the inferotemporal quadrant between 60° and 85° eccentricity, which is 30.2% to 100% of that in control subjects. In normal control subjects, this area of the visual field was 746 cm².

Seven children who showed visual field defects had taken VGB for 4 to 7 years at doses between 12.5 and 66 mg/kg body

The third and the fourth rows indicate the eccentricities of the borders of the visual fields in the upper and lower quadrants in a given visual hemifield being investigated. The area of visual field (cm²) between these eccentricities is dealt with in the fifth and sixth rows. Percentages indicate the portion of the visual field area that corresponds to the area given in square centimeters. An area between 30° and 50° eccentricity in the upper quadrant of left visual field has, for example, an extension of 415 cm², which corresponds to 100% of the area between 30° and 50°.

The patients’ initials are listed in the first column. The third and the fourth rows indicate the eccentricities of the borders of the visual fields in the upper (upper) and in the lower (lower) quadrants in a given visual hemifield being investigated. The rows below indicate areas of visual field defects (cm²). Percentages indicate the portion of the visual field loss that corresponds to the area of visual field defect given in cm². Patient AS, for example, had a visual field defect measuring 194 cm² in the superonasal quadrant between 30° and 50° eccentricity. This corresponds to 46.8% of the superonasal quadrant field between 30° and 50° eccentricity in control subjects.

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**TABLE 3 (continued). Areas and Visual Fields in Control Subjects and Areas of Visual Field Defect in VGB-Treated Patients**

<table>
<thead>
<tr>
<th>Areas of Visual Field</th>
<th>Areas of Visual Field</th>
</tr>
</thead>
<tbody>
<tr>
<td>BG</td>
<td></td>
</tr>
<tr>
<td>Upper quad.</td>
<td>517 cm²</td>
</tr>
<tr>
<td>Lower quad.</td>
<td>746 cm²</td>
</tr>
<tr>
<td>OK</td>
<td></td>
</tr>
<tr>
<td>Upper quad.</td>
<td></td>
</tr>
<tr>
<td>Lower quad.</td>
<td></td>
</tr>
</tbody>
</table>

---

**FIGURE 1.** Visual field defects of eight patients who had been treated with VGB. (A) Left eye: patient ME: white squares; patient BG: white squares and horizontal stripes; patient PA: small scotoma between 7° and 12° eccentricity and between the 195° and the 165° meridian (not indicated); patients RO and FA: white squares. Blind areas of patients ME and RO are superimposed on the black area. The numbers outside the visual fields indicate the meridians tested. The radius of the inner circle is 10°; the radius of the outer circle is 90°; the radii of the two other circles are 50° and 70°. (B) Right eye. Right visual field. Patient BT: black squares; patient FA: oblique stripes + black squares; patients ME and AS: oblique stripes + dots + black squares; patient OK: all areas except gray; patient BG: all areas except black, gray, and broken lines; patient RO: all areas except black and horizontal stripes. Left visual field: patients AS, ME, and FA: all areas except horizontal stripes; patient BG: oblique stripes; patient PA: horizontal stripes.
weight. In four children, VGB was administered together with other anticonvulsant drugs such as phenytoin, orphiril, pirimidon, valproic acid, sultiam, or ergenyl (Table 1). There was no correlation between the area of visual field and age at the beginning of VGB medication (Pearson $r = -0.0068; P = 0.97$), the duration of VGB medication (Pearson $r = 0.26; P = 0.16$), and the dose of VGB (Pearson $r = 0.18; P = 0.33$).

**Discussion**

The purpose of the present study was to investigate whether VGB medication causes visual field loss in children and adolescents who cannot be tested with conventional perimetric methods. Using arc perimetry, we showed that mentally handicapped patients and children younger than 6 years receiving VGB have visual field defects compared with visual field defects reported in adult patients who had been treated with VGB.

The visual field defects that we found cannot be regarded to be an error in measurement. Although there was a statistically significant difference between the size of the visual fields of the VGB group and that of the control groups, the presence of a visual field defect in the VGB group could not be assumed. An area of the visual field was only regarded as a defect if all the control subjects detected all targets in this area.

The finding that the visual fields of the children belonging to the cerebral palsy group (control group 2) have the same size as the visual fields of the children belonging to control group 3 shows that the measurement of the size of the visual field is not influenced by cerebral damage, which does not involve the geniculostriate visual system. Although the children in control groups 2 and 3 were much younger than the children and adolescents in control group 1, the size of the visual fields was not significantly different. This result shows that age does not play a part in the size of the visual field if the children are older than 1 year, when the visual field reached its full size.

The results of the present study support earlier findings that showed that VGB causes visual field constriction in children of school age who are not mentally handicapped. Comparing the results of these earlier studies with those of the present study, one can conclude that VGB-induced visual field constriction is not more frequent in children younger than 6 years or in mentally handicapped persons. The incidence of visual field constriction in our patients (27%) is in agreement with the report of Daneshvar et al.,8 who found visual field defects in 29% of 41 adults after treatment with VGB. Other researchers4,10,17,20,21,24,26,31,37,47,48 have found visual field defects in up to 73% of the patients who were treated with VGB. Our results are in agreement with the findings of Best and Acheson17 who have shown that visual field defects due to VGB therapy do not progress when VGB medication is continued. They assume that there is no dose-dependent toxicity. Other investigators17,21 reported a slight increase in visual field when VGB medication was stopped. An improvement of the visual field after withdrawal of VGB has even been reported.17,33,34,47

As most children who had visual field constriction had taken VGB for at least 4 years, it may be assumed that visual field constriction develops within 4 years. A more detailed analysis of the data has shown, however, that there was no correlation between the size of the visual field and the duration of VGB medication. It may also be assumed that the retina or optic nerve of young children is more vulnerable to the side effects of VGB than is the retina or optic nerve of older children. There was no correlation, however, between the age when VGB treatment began and the extension of the visual field.

The example of patient BG shows that visual field constriction may develop within 1 year. Ten months after the beginning of treatment with VGB, the visual field had a normal size but 1 year later 41.5% of the area of visual field of the right eye and 25.3% of the area of visual field of the left eye were blind.

We found also no correlation between the VGB dose and the size of the visual field. Visual field defects developed in children who had received a VGB dose (patient A5, 12.5 mg/kg; patient RO, 33.5 mg/kg; patient ME, 35.7 mg/kg) that was well below the mean dose of VGB ($\bar{x} = 62.4$ mg/kg), which was given to the children in the treated group. Visual field defects also developed during monotherapy with VGB. It is important to detect early constriction of the visual fields to prevent progression. Arc perimetry is a means of measuring visual fields in patients who cannot be tested with other perimetric techniques because they are too young to understand or follow instructions or are mentally handicapped.

**References**


