

**Aus der Universitäts-Augenklinik Tübingen
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**Über den Einfluß der Stimulusgröße und der
Stimulushelligkeit auf die Fläche des Blinden Flecks**

**Eine Untersuchung unter jungen, augengesunden
Probanden am Tübingen Computer Campimeter (TCC)
unter Berücksichtigung der individuellen Reaktionszeiten**

**Inaugural-Dissertation
zur Erlangung des Doktorgrads
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Für meine Eltern und für Nicole

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Originalartikel

Die Ergebnisse meiner Dissertation über den Einfluß der Stimulusgröße und der Stimulushelligkeit auf die Fläche des Blinden Flecks wurden als Artikel bei der Zeitschrift „Acta Ophthalmologica Scandinavica“ unter folgendem Titel eingereicht:

Influence of stimulus characteristics on the area of the blind spot – a study in young normal subjects using semi-automated kinetic perimetry with considerations for individual reaction times.

Auf den folgenden Seiten ist die englische Originalfassung, so wie sie eingereicht wurde, abgedruckt.

Anschließend folgt eine kurze deutschsprachige Zusammenfassung und noch weitere Abbildungen und Tabellen, welche aus Platzgründen keinen Eingang in den Originalartikel finden konnten.

Influence of stimulus characteristics on the area of the blind spot –
a study in young normal subjects using semi-automated kinetic perimetry
with considerations for individual reaction times

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Abstract

Purpose: (i) To determine the effects of various characteristics of moving stimuli on the area of the blind spot using semi-automated kinetic perimetry (SKP) and (ii) to evaluate the repeatability of this method.

Methods: The area of the blind spot of 18 young normal subjects was determined by means of a video-campimetric device, the Tuebingen Computer Campimeter (TCC). Kinetic stimuli were presented for two different sizes, and at four different levels of luminance. Examinations were repeated within two weeks. Measurements were corrected by the individual reaction times, and the area of the blind spot was computed. Individual areas, effects of contrast and size and repeatability standard deviation were evaluated using an analysis of variance.

Results: The area of the blind spot showed considerable inter- and intra-individual variation (least square means ranging from 17 to 49 square degrees), with a standard deviation of 6.8 square degrees. The blind spot size increased with decreasing contrast of the stimuli and appeared larger for the smaller stimulus even after correction for reaction time, which reduced random variation decisively. The sequence or the day of the examination did not affect the area of the blind spot. Repeatability standard deviation was 0.1 square degrees.

Conclusions: Semi-automated kinetic perimetry is a reliable tool to determine the size of small scotomata such as the blind spot with a good repeatability under consideration of individual reaction time. This study revealed high inter-individual differences in the size of the blind spot.

Key words: Blind Spot, semi-automated kinetic perimetry (SKP), Tuebingen Computer Campimeter (TCC), repeatability, stimuli

Introduction

The “gold standard” for examinations of the visual field with moving targets is the manual kinetic technique, using the Goldmann perimeter, which originated in the late 1940s. The results of manual kinetic Goldmann perimetry depend not only on the patient, but also on the investigator (Zehnder-Albrecht 1950; Niesel 1970).

To minimize the influence of the examiner on perimetric results, semi-automated perimetry (SKP), formerly known as computer-assisted kinetic perimetry (CAKP), was introduced (Schiefer et al. 1996; Schiefer et al. 2001a; Rauscher et al. 2002; Rauscher et al. 2003; Schiefer et al. 2003a; Schiefer et al. 2003b; Schiefer et al. 2003c; Schiefer et al. 2004; Nowomiejska et al. 2005). SKP provides a constant angular velocity and an exact localisation of the stimulus together with the possibility to exactly repeat each examination.

We used the Tuebingen Computer Campimeter (TCC), which is equipped with an infrared pupillographic device in order to control fixation and to obtain pupillary data. It offers the ability to minimize not only investigator-related sources of disturbance, but also to provide a constant background illumination, which is a frequent problem in non-calibrated VDUs.

There is limited data concerning the visual fields of healthy persons in automated kinetic perimetry. Several publications are available concerning the repeatability of automated kinetic perimetry in healthy individuals (Armaly 1969). Moreover, the possibility of the TCC to correct the obtained results with individually determined reaction times is another step towards minimizing deleterious effects and obtaining the most accurate results possible (Rouland et al. 1991; Schiller et al. 1999; Schiefer et al. 2001b). In this regard, we decided to use the blind spot as a model for a small scotomata (Aulhorn et al. 1987) in young, healthy volunteers and to determine its size for different stimulus qualities, including one decrement stimulus and three increment stimuli, one of them at the same contrast as the decrement target. We also evaluated the repeatability of the measurement method in order to estimate the reliability under clinical conditions. To our knowledge, the blind spot has not been investigated for SKP, but rather by means of automated static perimetry (Gramer et al. 1979), (Safran et al. 1993) and manual kinetic perimetry (Armaly 1969), so that a comparison with previously obtained data is possible.

Additionally, the size of the blind spot has gained special interest in the last few years concerning glaucoma (Meyer et al. 1998), influences of the optic disc topography (Meyer et al. 1997) and the acute idiopathic blind spot enlargement syndrome (Fletcher et al. 1988).

The purpose of this study was to (i) evaluate the influence of different stimulus sizes and different stimulus luminance levels (using not only increment targets but also one decrement stimulus) on the reaction time (RT) of the subjects, on the blind spot area, corrected for individual RTs, and to (ii) estimate the repeatability of SKP in regard to blind spot area.

Subjects and Methods

We examined 20 eyes of 20 young (20 to 34 years, criteria for inclusion was age between 20 and 40 years) healthy volunteers, 5 female and 15 male. All eyes were normal on ophthalmologic examination including direct and indirect ophthalmoscopy, intraocular pressure below 20 mm Hg (air pulse tonometry), slit-lamp biomicroscopy, normal stereopsis (according to the Lang I stereotest), normal ocular motility, absence of an afferent papillary defect, and no history of eye injury or lesion of the visual pathway.

Further criteria for inclusion were refraction corrections not higher than ± 4 diopters spherically and ± 2 diopters cylindrically. Corrected visual acuity had to be better than or equal to 20/20. The dominant eye, according to the "Rosenbach's Visierversuch" (alignment test, Rosenbach 1903), was examined. If the dominant eye could not be determined, one eye was randomly chosen. There were 12 right and 8 left eyes investigated. Demographic data is summarised in Table 1.

<Table 1>

Two subjects were excluded from the study, one because of death due to a malignant melanoma and the other because of the refusal of additional ophthalmologic examinations. Our study followed the tenets of the declaration of Helsinki and informed consent was obtained from each participant before examinations.

For SKP, the Tuebingen Computer Campimeter (TCC), which is described in earlier reports (Lutz et al. 2001; Schiefer et al. 2001b), was used. It consists of a calibrated high resolution VDU monitor (BARCO, 8500 Kortrijk, Belgium, model Calibrator, 75 dpi, 1024 x 768 pixel, 21 inch diagonal, max. luminance $L = 64 \text{ c}/(\text{m}^2)$), controlled by a Macintosh computer (Power Macintosh 6100/66, Apple Computer Inc., Apple Computer, Inc. Cupertino, CA 95014) and an infrared pupillographic device for fixation control purposes (Fig.1). All tests were performed at a constant background luminance of $10 \text{ cd}/\text{m}^2$ (31.5 asb).

<Fig. 1>

In order to find co-ordinates of the individual centre of the blind spot, the vertical and horizontal extent were measured by an initial manual kinetic perimetry evaluation using software PeriMac I V2.0, test distance 30 cm, stimulus luminance $41.62 \text{ cd}/\text{m}^2$,

stimulus diameter 13', which is equivalent to a Goldmann II2e stimulus. Detailed calculations for determining the X and Y coordinates of the blindspot are presented in the appendix. The left limit is used, instead of the more common specifications nasal or temporal, to have only one formula, both for right and left eyes.

According to the obtained centre, the individual set of vectors was created using JMP software (SAS Institute Inc., V 3.1.5, SAS Inst. Inc. Cary, NC) and BBEdit software (V 4.0.4, Bare Bones Software Inc., Bedford, Mass).

A vector is defined as the line, along which a stimulus is presented, defined by a starting point and an end point. Two different kinds of vectors were used: *test vectors* served to determine the borders of the blind spot, whereas *reaction time vectors* were presented within seeing areas of the visual field, closely adjacent to the blind spot region in order to determine the individual perceptual latencies in regard to the presentation of moving visual stimuli.

Twelve test vectors, which were numbered as indicated in Fig. 2, originated from the centre of the individual blind spot at radial angles 30° apart, namely at 15°, 45°, 75°, 105°, 135°, 165°, 195°, 225°, 255°, 285°, 315° and 345° to the first meridian. The reaction time vectors originated automatically at the same eccentricity as the blind spot, each aiming towards the fixation point. Their origins were shifted by an angle of 8° upwards or downwards from the centre of the blind spot. All vectors had a length of 9 degrees.

<Fig. 2>

The semi-automated kinetic perimetry was performed using software PeriMac II V0.38 with stimuli moving at a constant angular velocity of 2 degrees/s, at a test distance of 50 cm in order to gain a high spatial resolution .

In order to reduce the examination time, origins of all vectors, except for the reaction time vectors, were shifted adaptively depending on the location where the previous repetition of the same stimulus was perceived: after the initial presentation, vectors did not obligatorily originate from the centre of the blind spot, but were moved to two degrees (which is equivalent to a time interval of one second at an angular velocity level of two degrees/s) inside from the location, in which this stimulus was perceived at the previous presentation. Thus, most vectors originated approximately two degrees inside the border of the blind spot (Fig. 3). The time between two stimulus presentations was set to one second.

<Fig. 3>

During each examination, 4 different stimuli were presented, either at increment luminance levels (the corresponding Goldmann classification is given in squared brackets) of 110 cd/m² (346 asb) [3e] and 41.62 cd/m² (131 asb) [2e], or at luminance levels of 20 cd/m² (63 asb) [1e] and 0 cd/m² (0 asb) (i.e. decrement “black”). At each luminance level, both stimulus sizes 13’ (Goldmann II) and 26’ (Goldmann III), were presented.

Each examination comprised four of the eight combinations of stimulus size and luminance. Stimulus presentations were repeated four times. Eight reaction time stimuli were presented along each RT vector. All stimuli were presented in random order. There were 12 (directions) × 4 (stimuli) × 4 (repetitions) + 2 (RT vectors) × 4 (stimuli) × 8 (repetitions) = 256 stimulus presentations in one examination, of which 25% served as reaction time vectors.

Three such examinations were performed on each of two days. In any one examination either bright stimuli with luminance 110 cd/m² and 41.62 cd/m² were presented or dark stimuli with luminance 20 cd/m² and 0 cd/m². Subjects were randomised to all six possible combinations of three examination types in advance. This cross-over design (see Table 2) repeated the examination with bright stimuli in one half of the subjects and the examination with dark stimuli in the other half.

<Table 2>

Examinations were repeated in strictly the same order as in the initial session on another day. The retest session followed within 3 days in 67 % of all subjects, and within two weeks for all participants.

All results were recorded as a BBEdit file and converted to JMP files. The PeriMac II software saved all data on the stimulus presentation (e.g. start co-ordinates, “seen” co-ordinates, luminance level, size, the total time of stimulus presentation), and also the time passed since the beginning of the examination together with the pupillographic data.

For evaluation, as a first step, all vectors marked as “not seen” were excluded (0.07 % of all presentations). As a second step, all responses to stimulus presentations along reaction time vectors, which were perceived within 125 ms, were rated as false-positive catch trials and excluded (0.6 % of all reaction time vectors)(Greve 1973; Olsson et al. 1997).

A linear model was fitted to reaction times, in order to estimate specific reaction times, for which blind spot measurements were to be corrected. After estimation of

the Box-Cox transformation, the logarithm of the reaction times (RT) were computed so that the residuals' distribution resembled a normal distribution with a variance that did not vary according to any factor. The analysis of covariance (ANCOVA) used to estimate specific geometric mean RTs by the restricted maximum likelihood method considered luminance level, size, their interaction, day, examination, covariable time since the examinations commenced as dependent factors, and subject as a random factor.

Subsequently, each measured eccentricity from the individual blind spot centre (blind spot eccentricity) ec (in degrees) was corrected by the predicted reaction time RT_{pred} (in seconds) as follows:

$$ecc = ec - 2 \cdot RT_{pred}$$

where ecc is the corrected blind spot eccentricity (in degrees).

The individual blind spot area was approximated as a sum of 12 triangles, which were defined by the corrected blind spot eccentricities (Fig. 4).

<Fig. 4>

The area of one triangle (in square degrees), $A_{triangle}$, was calculated from the height of the triangle h and the corrected blind spot eccentricity measured with vector n , ecc_n , $n = 1, 2, 3, \dots, 12$, (see Fig. 2) as:

$$\begin{aligned} A_{triangle} &= \frac{1}{2} \cdot h \cdot ecc_n \\ &= \frac{1}{2} \cdot (\sin 30^\circ \cdot ecc_{n+1}) \cdot ecc_n \\ &= \frac{1}{4} \cdot ecc_n \cdot ecc_{n+1}, \end{aligned}$$

as indicated in Fig. 4.

Blind spot area (in square degrees) $A_{blindspot}$ was the sum:

$$A_{blindspot} = \frac{1}{4} \cdot ecc_{12} \cdot ecc_1 + \frac{1}{4} \cdot \sum_{n=1}^{n=11} ecc_n \cdot ecc_{n+1}.$$

The factors considered in the ANOVA of blind spot areas were the same as above. Estimation of the Box-Cox transformations showed a nearly normal distribution of residuals. Where two means are compared, 95 %-confidence intervals (CI) are given.

JMP software (SAS Institute Inc., Cary, NC, 2003, V 5.0.1.2) was used for analyses.

Results

Reaction times (RTs)

RTs showed a high inter-individual variation with individual geometric means ranging from 332 to 469 ms in the middle of the examinations (coefficient of variation 9.4 %). The small stimulus size (13') resulted in significantly longer RTs than the 26' stimulus (geometric means 435 vs. 369 ms, CI 16.5 % to 19.0 %), and the RTs were shorter for high contrast stimuli (geometric means 440, 420, 383 and 364 ms for luminance levels of 20, 0, 41.62 and 110 cd/m², respectively, $P < 0.001$) Stimulus size had a greater effect on RT for the lower luminance levels; see Fig. 5.

<Fig. 5>

From the first examination day to the second, a learning effect could be shown: the reaction times decreased significantly (geometric means 411 vs. 391 ms, CI 3.7% to 5.8 %). During the second examination of a day, subjects had slightly longer RTs (geometric means 395, 409 and 398 ms for the first, second and third examination, $P < 0.001$).

The elapsed time was also regarded in the correction formula for the blind spot eccentricities: the current examination duration significantly reduced the RTs by approximately 5 % from start to end of a 12 minute examination (CI 3 % to 7 %). Predicted RTs were used to correct blind spot eccentricities by a mean 0.81 deg (SD 0.13 deg).

Examination time

Adaptive shift of the vector origins resulted in an average examination time of 12.0 minutes, ranging from 11.2 min to 13.5 min (SD 23 sec).

Blind spot area

The blind spot area showed remarkable variation between the subjects, least squares means (LSM) ranging from 17 to 49 square degrees, with a mean of 28.6 square degrees, and an inter-individual SD of 6.8 square degrees (Fig. 6).

<Fig. 6>

That *inter*-individual variance component contributed 78 % to random variance, whereas the *intra*-individual variance contributed only 22 % to the total variance, with the residual SD being 3.6 square degrees.

The area of the blind spot decreased with increasing stimulus contrast (LSM 32, 31, 27 and 24 square degrees for luminance levels of 20, 0, 41.62 and 110 cd/m², $P < 0.001$) and the blind spot size was also significantly smaller for the greater (26′) stimuli than for the smaller (13′) ones (LSM 26 square degrees vs. 31, CI from 5.0 to 6.4). This size effect was more pronounced for the low contrast stimuli, see Fig. 7. RT-corrected areas were 16.8 square degrees smaller on average than uncorrected ones (SD 4.78 square degrees). Without RT-correction (corresponding SD *with* RT-correction given in brackets), the residual and the inter-individual SD were 4.8 (3.6) square degrees and 9.1 (6.8) square degrees, respectively. Their contributions to random variance did not differ, and random variance was 63% of total variance. All fixed factors explained greater parts of variation, when they effected both, blind spot size and RT.

<Fig. 7>

Sequence and day of the examination

The sequence of the examination showed only small changes of blind spot area with increasing perimetric experience of the subjects, but not at a significant level (LSM 28.6, 28.8 and 28.3 square degrees for first, second and third examination, $P = 0.50$). The repetition of the examination also resulted in a negligible mean difference of the blind spot area between the first and second day (LSM 28.6 and 28.5 square degrees). Repeatability accuracy was 0.13 square degrees (CI from -0.5 to +0.8) and repeatability SD was 0.1 square degrees. In our investigation, the repeatability variance contributes only 0.07% to the total variance, see Table 3.

<Table 3>

Discussion

To our knowledge, the blind spot has not yet been systemically examined with automated kinetic perimetry, but only with automated static perimetry (Safran et al. 1993), manual kinetic perimetry (Armaly 1969) and also with SLO microperimetry, using both automated static and manual kinetic testing (Meyer et al. 1997; Glück et al. 1999). The majority of prior studies were conducted using the blind spot as a well-defined model of a small scotoma (Aulhorn et al. 1987), in order to evaluate applicability and detection rates of automated static perimetry with different strategies (Gramer et al. 1979; Funkhouser et al. 1988; Safran et al. 1993), the influence of stray light and optic disc topography on the detection and size of the blind spot (Fankhauser et al. 1980; Meyer et al. 1997) and to compare the influence of different stimulus qualities on the differential luminance thresholds at the border of the blind spot (Bek et al. 1989; Glück et al. 1999).

Using static perimetry for detection of small scotomas, a considerable problem consists of either limited resolution (Jonas et al. 1991) or long examination times (Meyer et al. 1997) or both, even when applying adaptive strategies. Therefore, conventional automated static perimetry, as used in clinical routine, hardly ever provides any detailed quantitative information concerning the blind spot, although there is possible evidence for a diagnostic meaning not only in neuro-ophthalmology but also in glaucoma (Meyer et al. 1998).

The recently developed tool of SKP could be a solution for most of the above mentioned problems occurring with static perimetry. Additionally, it eliminates various disturbing factors arising from manual kinetic perimetry (Nowomiejska et al. 2005). Not only the investigator-related disturbances can be eliminated with this method, but also the influence of individual reaction time can be estimated even within a pre-defined region of the visual field and taken into consideration. RT depends to a great extent on the stimulus quality (Schiefer et al. 2001b). RT-correction reduces inter-individual, residual and repeatability variance considerably, which was demonstrated in our study. As a consequence, it might be useful in (semi-) automated kinetic perimetry, not only to cope with inter-individual differences in RT, but also with differences emerging from the stimulus quality and the special conditions in the vicinity of scotomas.

Even after RT correction, our study showed additional dependencies of the blind spot area on the stimulus quality: higher stimulus contrast resulted in significantly smaller blind spot areas (Armaly 1969) and large stimuli produced significantly smaller blind spots than small targets (Bek et al. 1989).

The decrement stimulus produced significantly smaller blind spots (as well as shorter RTs) than the increment stimulus at the same contrast (10 cd/m²). As there is almost no data on comparability of increment and decrement stimuli in perimetry, this is a strong hint that there is no general equality of decrement and increment stimuli in perimetry, in contrast to a former study (Wabbels et al. 1995). Nevertheless, there has been evidence for differences (Mutlukan 1994). Attenuation is $-\infty$ for the 0 cd/m²-stimulus but just +3 dB for the 20 cd/m²-stimulus. As a consequence a -3 dB stimulus of 5 cd/m² should be considered for further studies.

The other influencing factors like stray light (Fankhauser et al. 1980) or light scatter at the optic disc (Meyer et al. 1997) could not be investigated in this study, due to the use of comparatively small stimuli (i.e., 13' and 26', which equals Goldmann sizes II and III), which in addition were also comparatively dim due to technical reasons (maximal luminance difference 100 cd/m², equivalent to Goldmann level 3e).

Former studies found a great variation regarding the area of the blind spot, ranging from approximately 100 square degrees (Armaly 1969) to 19.44 square degrees (Armaly 1969; Niesel 1970). Results may also vary because of inadequate spatial resolution due to comparatively coarse test point arrangements in the blind spot area, when applying automated static perimetry (Stepanik 1986). Another reason for differing means may be the comparatively small sample size in some studies. In such cases, the inter-individual variability, which turned out to be the most important influence on blind spot size (Table 3), causes random variation of the mean. Inter-individual SD of 20 blind spot areas in this study was 6.8 square degrees, a little greater than among 20 slightly older subjects (5.7 square degrees) assessed by automated static perimetry (Safran et al. 1990). However, our repeatability SD of 0.1 square degrees translates into a mean absolute difference between examinations of 2.8 square degrees, which is far lower than that of Safran et al. (3.82 square degrees).

To our knowledge, the repeatability of SKP in young, healthy subjects has not been evaluated before. The results of this study indicate that this method has the potential

to become a useful tool to detect even small scotomas in a well reproducible way. Quantitative measures of the blind spot are of considerable clinical value e.g. in neuro-ophthalmological diseases, such as papilledema, unilateral optic disc swelling or (translational and torsional) displacement of the blind spot due to ocular motility disorders. This method could be also applied to small steeply bordered glaucomatous visual field defects (Meyer et al. 1998), which seem to occur frequently, especially in case of low tension glaucoma. Furthermore, it may be useful in case of advanced field loss resulting in only small residual islands of vision or clear-cut extensive visual defects, such as in tapeto-retinal degeneration, in advanced glaucoma or in (post-)chiasmal lesions of the visual pathway.

In conclusion, RT-corrected semi-automated kinetic perimetry is a reliable tool to determine the size of even small scotomas with a good repeatability. This study revealed high inter-individual differences in the size of the blind spot and stimulus dependencies independent from RT. RT-correction could be showed to be useful in order to reduce inter-individual, residual and repeatability variance considerably. Additionally, this study proves a need for further investigation concerning the comparability of increment and decrement stimuli in perimetry.

Figures, Tables & Legends

Subject Nr.	Age [years]	Sex	Eye	Visual acuity	Refraction	Remarks
1	28	F	R	10/10	-2.50 sph	
2	27	M	L	16/10	none	
3	27	F	L	12/10	-1.50 sph	excluded because of death
4	23	M	L	10/10	none	excluded, refused further examinations
5	23	M	R	16/10	none	
6	28	M	R	12/10	none	
7	26	M	R	16/10	none	
8	20	M	R	12/10	none	
9	20	M	L	16/10	none	
10	23	F	R	10/10	-1.25 sph	
11	21	M	R	12/10	none	
12	23	M	R	12/10	none	
13	33	M	R	10/10	none	
14	23	M	L	12/10	0.50 sph -1.25 cyl/ 70°	
15	21	M	L	12/10	none	
16	30	F	R	12/10	none	
17	25	M	L	12/10	-2.00 sph	
18	21	M	R	10/10	-1.75 sph	
19	21	M	L	10/10	-0.50 sph -1.00 cyl/ 95°	
20	29	F	R	12/10	none	

Table 1 Demographic and refractive data

Subjects	First examination	Second examination	Third examination
9, 15, 16	BRIGHT	BRIGHT	DARK
7, 10, 13	BRIGHT	DARK	BRIGHT
2, 6, 18	DARK	BRIGHT	BRIGHT
5, 12, 20	DARK	DARK	BRIGHT
8, 14, 17	DARK	BRIGHT	DARK
1, 11, 19	BRIGHT	DARK	DARK

Table 2

Order of examinations: stimuli at luminance levels of 41.62 cd/m² and 110 cd/m² were denoted as “BRIGHT”, at 20 cd/m² and 0 cd/m² as “DARK”. Subjects were randomised. Please note that subjects 3 and 4 were excluded.

Source	DF	Sum of Squares	Mean Square	<i>F</i>	<i>P</i>	SS [%]
Subject (random)	17	18966	1116	.	.	59.3
Luminance	3	3740	1257	94.1	$3 \cdot 10^{-46}$	11.7
Size	1	3476	3476	262.4	$8 \cdot 10^{-46}$	10.9
Size * Luminance	3	406	135	10.2	$2 \cdot 10^{-6}$	1.3
Day	1	2	2	0.2	0.67	0.007
Examination	2	18	9	0.7	0.50	0.058
Model	27	26609	986	74.4	0	83.3
Residual	404	5351	135	.	.	16.7
Total	431	31959	.	.	.	100

Table 3

Effect test table of used model for Blind spot size, DF: degrees of freedom, SS: sum of Squares.

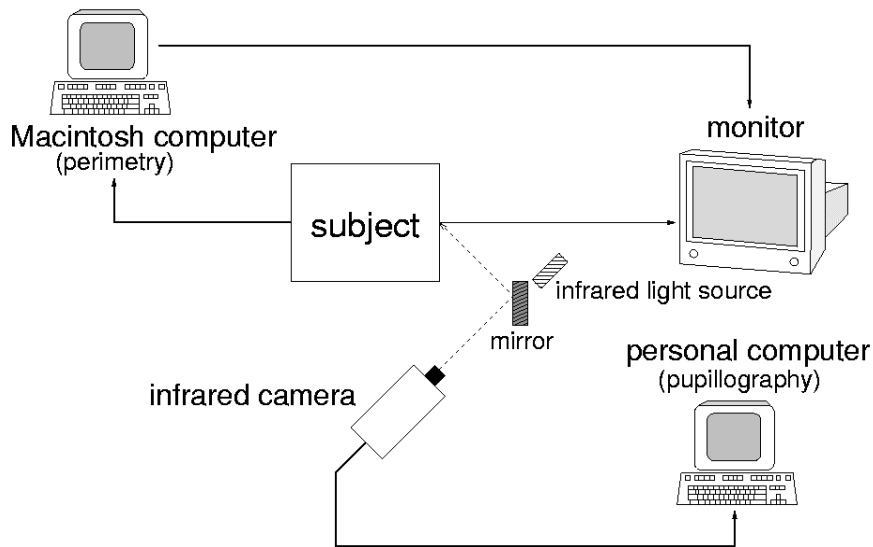


Fig.1

Scheme of the TCC. The Macintosh computer is controlling perimetry (display of the moving stimuli and background on the monitor), and recording the data; the personal computer is controlling infrared pupillography. The pupil is displayed on a monitor during the examination, so the investigator is able to detect fixation errors immediately.

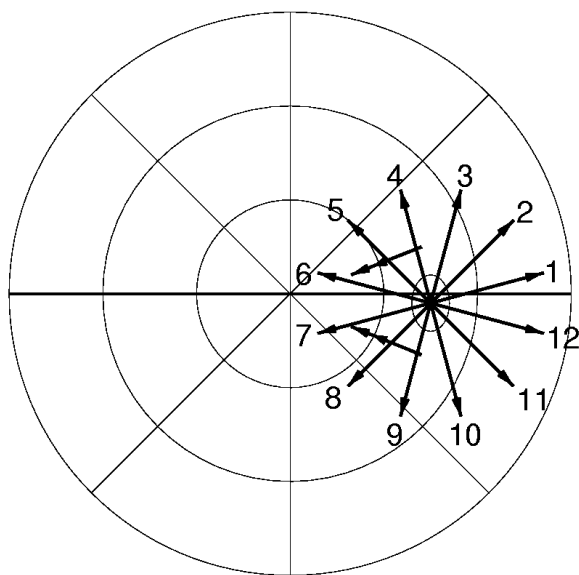


Fig. 2

Set of vectors; the test vectors are starting in the centre of the blind spot, reaction time vectors are the oblique ones beyond and below the blind spot, marked with double arrow heads.

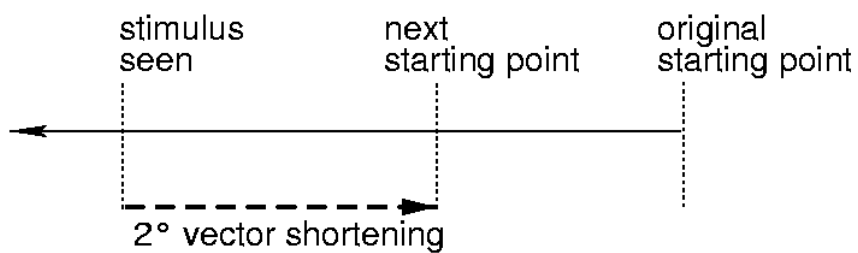


Fig. 3 Vector shortening: Depending on the point a stimulus was seen, the next presentation of this certain stimulus did not start at the original starting point, but at a new starting point 2 degrees away (back on the vector) from the location the stimulus was seen the presentation before.

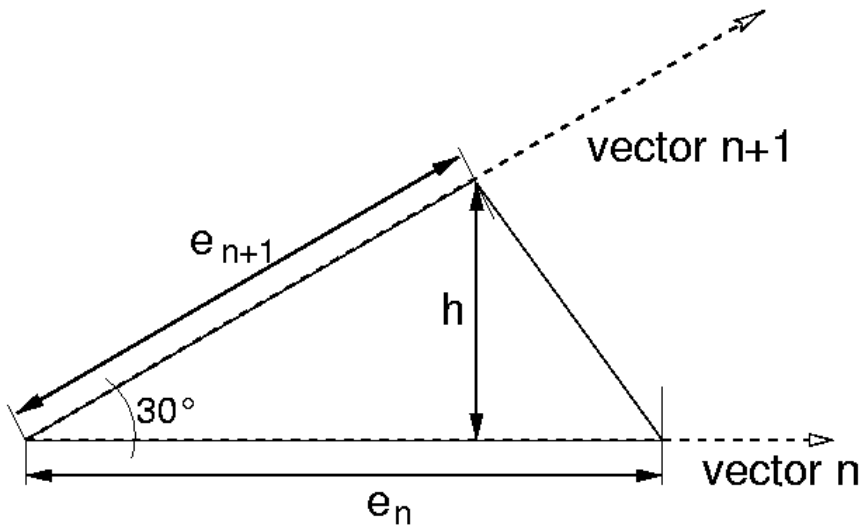


Fig. 4 One triangle used for calculation of the blind spot area, where e_{cc_n} and $e_{cc_{n+1}}$ are the RT corrected eccentricities measured on vector n and vector $n+1$, and h is the height of the triangle

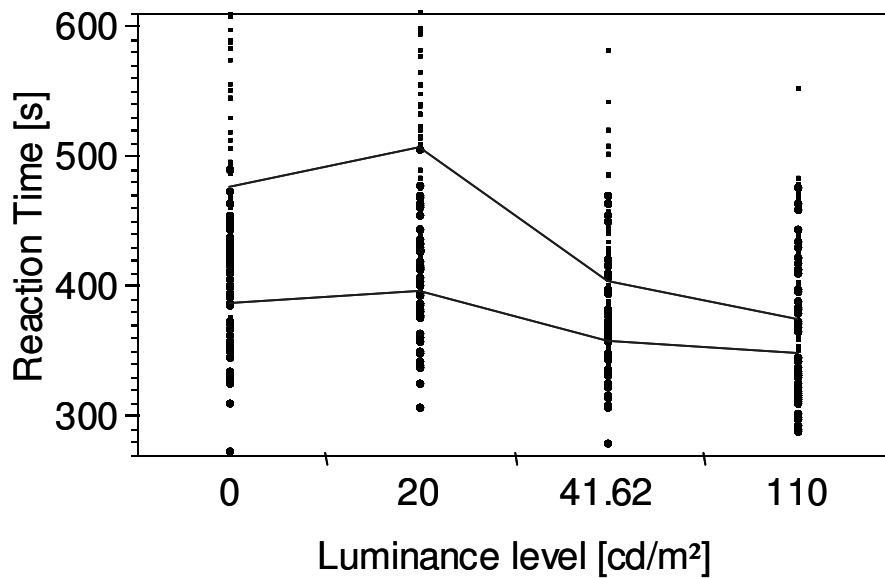


Fig. 5 Influence of stimulus size (13' small symbols, upper line, 26' large dots lower line) and luminance level on the reaction time. Geometric means are connected.

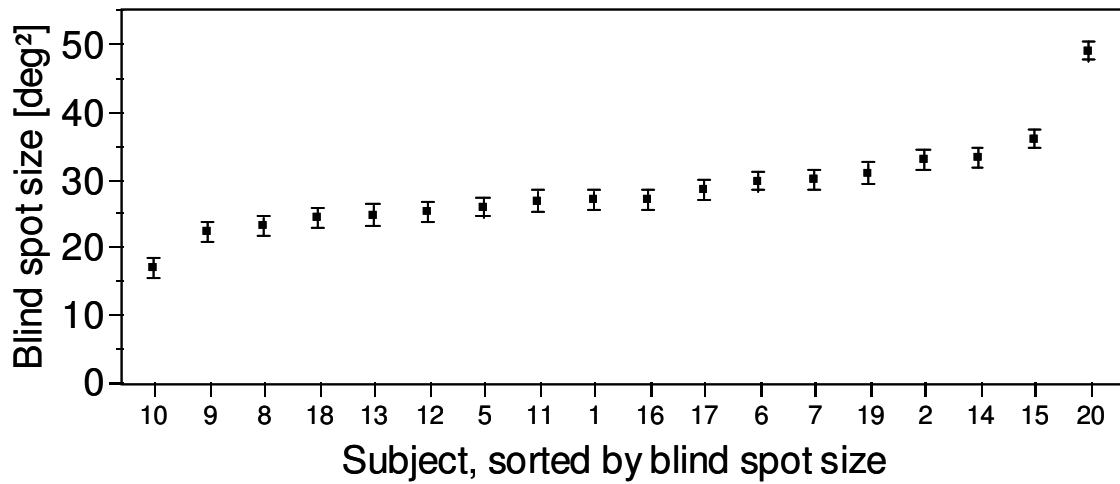


Fig. 6 Blind spot size by subject (least square means CI). Please note, that subjects 3 and 4 were excluded

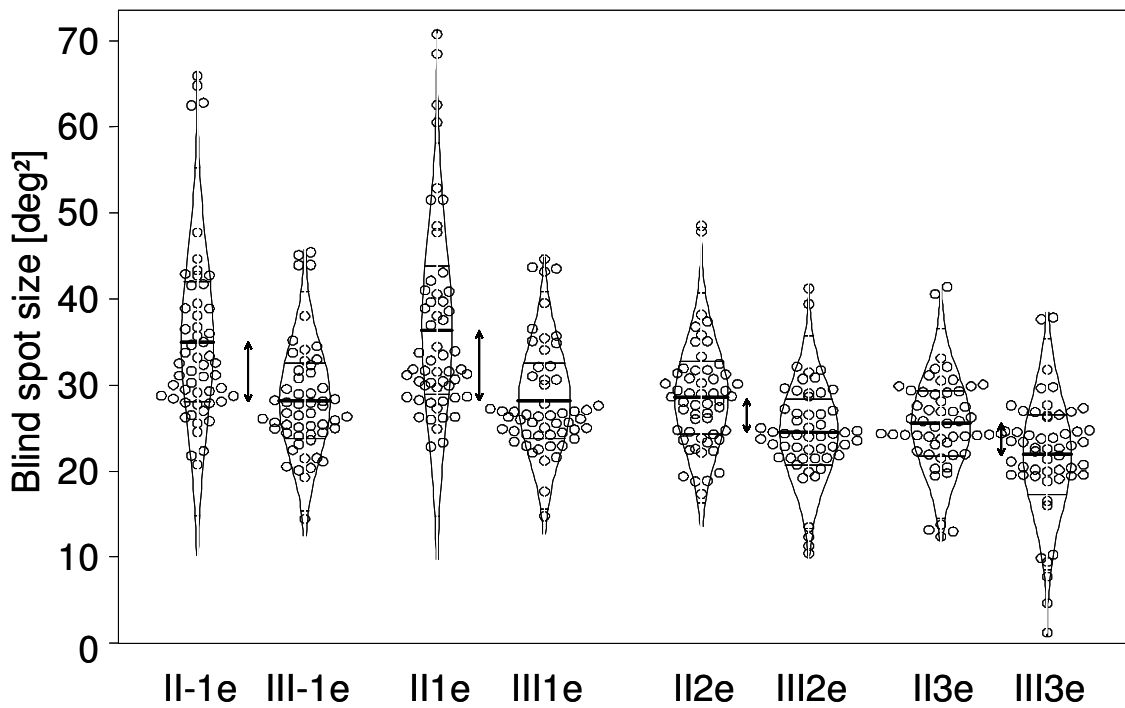


Fig. 7 Influence of stimulus size and luminance level on blind spot area. Shown are 54 observations (o) each and their estimated normal densities with mean (strong) and 50 % and 95 % reference intervals (bars) for stimuli noted in Goldmann's manner. Note the interaction effect (double arrows) and four or two replications of the extreme individuals in the bright or dark stimuli, respectively.

Appendix

Cartesian co-ordinates of the blind spot centre were calculated as follows:

$$x_{centre} = x_{left} + \frac{1}{2}w$$

where x_{centre} is the x-co-ordinate of the blind spot centre, x_{left} is the x-co-ordinate of the left limit of the blind spot and w is the width of the blind spot (all measured in degrees).

$$y_{centre} = y_{upper} - \frac{1}{2}h$$

where y_{centre} is the y-co-ordinate of the blind spot centre, y_{upper} is y-co-ordinate of the upper limit of the blind spot and h is the height of the blind spot (all measured in degrees).

REFERENCES

- Armaly MF (1969): The size and location of the normal blind spot. Arch Ophthalmol **81**: 192-201.
- Aulhorn E & Durst W (1987): Die Bedeutung der Perimetrie des blinden Flecks für die klinische Diagnostik. Fortschr Ophthalmol **84**: 631-634.
- Bek T & Lund-Andersen H (1989): The influence of stimulus size on perimetric detection of small scotomata. Graefes Arch Clin Exp Ophthalmol **227**: 531-534.
- Fankhauser F & Haeberlin H (1980): An estimate on the falsifying effects of stray light in perimetry. Doc Ophthalmol **50**: 143-167.
- Fletcher WA, Imes RK, Goodman D, & Hoyt WF (1988): Acute idiopathic blind spot enlargement. A big blind spot syndrome without optic disc edema. Arch Ophthalmol **106**: 44-49.
- Funkhouser AT, Kwasniewska S, & Fankhauser F (1988): Clinical interest and problems related to the measurement of the blind spot and the pericoecal region by means of programs SAPRO, SAPPAR, and BSPOT. Ophthalmic Surg **19**: 485-500.
- Glück R, Bültmann S, Rohrschneider K, & Völcker HE (1999): The influence of stimulus size on fundus perimetric detection of small scotomata. Investigative Ophthalmology & Visual Science **40**, 4450. 1999.
- Gramer E, Proll M, & Krieglstein GK (1979): Die Perimetrie des Blinden Flecks. Ophthal **179**: 201-208.
- Greve EL (1973): Single and multiple stimulus static perimetry in glaucoma; the two phases of perimetry. Docum Ophthal Proc Series **49**: 593-600.
- Jonas JB, Gusek GC, & Fernández MC (1991): Correlation of the blind spot size to the area of the optic disk and parapapillary atrophy. Am J Ophthalmol **111**: 559-565.
- Lutz S, Dietrich TJ, Benda N, Selig B, Strasburger H, & Schiefer U (2001): An explicit *no* response instead of *time-out* in automated visual field testing. Graefes Arch Clin Exp Ophthalmol **239**: 173-181.
- Meyer JH, Guhlmann M, & Funk J (1997): Blind spot size depends on the optic disc topography: a study using SLO controlled scotometry and the Heidelberg retina tomograph. Br J Ophthalmol **81**: 355-359.
- Meyer JH, Guhlmann M, & Funk J (1998): Is the blind spot enlarged in early glaucoma? Eur J Ophthalmol **8**: 28-32.
- Mutlukan E (1994): A comparison of automated static dark stimuli with the Humphrey STATPAC program in glaucomatous visual field loss. Br J Ophthalmol **78**: 175-184.
- Niesel P (1970): Streuung perimetrischer Untersuchungsergebnisse. Ophthal **161**: 180-186.

Nowomiejska KE, Vonthein R, Paetzold J, Zagorski Z, Kardon RH, & Schiefer U (2005): Comparison between semi-automated kinetic perimetry (SKP) and conventional Goldmann manual kinetic perimetry (MKP) in patients with advanced visual field loss. *Ophthalmology*, accepted for publication

Olsson J, Bengtsson B, Heijl A, & Rootzén H (1997): An improved method to estimate frequency of false positive answers in computerized perimetry. *Acta Ophthalmol Scand* **75**: 181-183.

Rauscher S, Sadowski B, Vonthein R, Erdmann B, Krapp E, & Schiefer U (2003): Assessment of reaction times in order to enhance quality of semi-automated kinetic perimetry (SKP) - an age-related normative study. In: Wall M & Mills RP (eds). *Perimetry Update 2002/2003*. The Hague, The Netherlands: Kugler Publications 353-358.

Rauscher S, Vonthein R, Sadowski B, Erdmann B, Krapp E, & Schiefer U (2002): Computer-Assisted Kinetic Perimetry (CAKP) Using the Octopus 101 Perimeter: Age Related Normal Values of Local Thresholds Using Various Stimulus Conditions and Considering Individual Reaction Times. *Investigative Ophthalmology & Visual Science* **43** (12), 3810. 2002.

Rosenbach O (1903): Über monoculare Vorherrschaft beim binocularen Sehen. *Med Wochenschrift* **50**: 1290-1292.

Rouland JF & Hache JC (1991): Normal perceptual latencies during visual field measurement. *Ophthalmol* **202**: 48-52.

Safran AB, Almeida L, Mermoud C, Desangles D, de Weisse C, & Lang R (1990): Intraocular and interocular variability of blind spot surface measurements by means of automated perimetry. In: Mills RP & Heijl A (eds). *Perimetry update 1990/91*. Proceedings of the IXth International Perimetric Society Meeting. Amsterdam: Kugler 409-412.

Safran AB, Mermillod B, Mermoud C, de Weisse C, & Désangles D (1993): Characteristic features of blind spot size and location, when evaluated with automated perimetry. *Neuro-Ophthalmology* **13**: 309-315.

Schiefer U, Nowomiejska KE, & Paetzold J (2004): Semi-automated kinetic perimetry for assessment of advanced glaucomatous visual field loss. In: Grehn F & Stamper R (eds). *Glaucoma*. Berlin: Springer 51-61.

Schiefer U, Rauscher S, Hermann A, Nowomiejska KE, Sadowski B, Vonthein R, Paetzold J, & Schiller J (2003a): Age dependence of normative values in semi-automated kinetic perimetry (SKP) reviewing. *Investigative Ophthalmology & Visual Science* **44**, E-1957. 2003a.

Schiefer U, Rauscher S, Paetzold J, & Schiller J (2003b): Realisation of semi-automated kinetic perimetry (SKP) with Interzeag 101 instrument. In: Wall M & Mills RP (eds). *Perimetry Update 2002/2003*. The Hague, The Netherlands: Kugler Publications 233-238.

Schiefer U, Schiller J, Dietrich TJ, Besch D, Paetzold J, & Vonthein R (2001a): Evaluation of advanced visual field loss with computer-assisted kinetic perimetry. In: Wall M & Mills RP (eds). Perimetry Update 2000/2001. The Hague, The Netherlands: Kugler Publications 131-136.

Schiefer U, Strasburger H, Becker ST, Vonthein R, Schiller J, Dietrich TJ, & Hart WM (2001b): Reaction time in automated kinetic perimetry: effects of stimulus luminance, eccentricity, and movement direction. *Vision Res* **41**: 2157-2164.

Schiefer U & Witte A (1996): Patent: Perimetrisches Untersuchungsverfahren - Autokinetische Perimetrie II. Deutsches Patentamt München, DE 196 21 960 C2, Az 196 21 960 41-18.

Schiefer U & Witte A (2003c): Patent: Perimetrisches Untersuchungsverfahren - Autokinetische Perimetrie unter Berücksichtigung und Korrektur der individuellen Reaktionszeit. Deutsches Patentamt München, DE 100 13 682 C2, Az 100 13 682 6-35.

Schiller J, Selig B, Dietrich TJ, Becker S, Stumpp F, Dietz K, & Schiefer U (1999): Does direction of linear target motion influence reaction time? A campimetric study using automated kinetic stimuli. *Investigative Ophthalmology & Visual Science* **40**, 845. 1999.

Stepanik J (1986): Der blinde Fleck: Kritische Betrachtung rasterperimetrischer Aussage über ein Skotom bekannter Größe. *Klin Monatsbl Augenheilkd* **189**: 409-412.

Wabbels B, Schiefer U, Treutwein B, Benda N, & Stercken-Sorrenti G (1995): Automated perimetry with bright and dark stimuli. *German J Ophthalmol* **4**: 217-221.

Zehnder-Albrecht S (1950): Zur Standardisierung der Perimetrie. *Ophthal* **120**: 255-270.

Deutschsprachige Zusammenfassung

Ziel dieser Studie an jungen, augengesunden Probanden war es, den Einfluß verschiedener Stimulusgrößen und verschiedener Stimulushelligkeiten auf die Fläche des Blinden Flecks mittels halbautomatischer kinetischer Perimetrie zu evaluieren. Die Flächen wurden dabei bezüglich der individuellen Reaktionszeiten korrigiert. Ebenso wurde die Wiederholpräzision der Meßmethode ermittelt.

Methoden: Die Fläche des Blinden Flecks von 18 jungen (Alter 20 bis 34 Jahre), augengesunden Probanden wurde mit Hilfe des Tübingen Computer Campimeters (TCC) ermittelt und bezüglich individuellen Reaktionszeiten korrigiert. Die Stimuli wurden rechnergestützt mit einer konstanten Winkelgeschwindigkeit von 2 Grad/s auf einem kalibrierten Bildschirm mit einer konstanten Hintergrundleuchtdichte von 10 cd/m² bewegt. Sie wiesen einen Durchmesser von entweder 13´ oder 26´ auf (entsprechend Goldmann II oder III), die Leuchtdichte des Stimulus betrug entweder 110 cd/m², 41.62 cd/m², 20 cd/m² (inkrement, entsprechend Goldmann 3e, 2e, 1e) oder 0 cd/m² (dekrement). Der Untersuchungsabstand betrug 50 cm. 25% aller Stimulusdarbietungen dienten der Reaktionszeiterfassung. Die Untersuchungen wurden an einem zweiten Tag innerhalb von höchstens zwei Wochen exakt wiederholt.

Ergebnisse: Die Fläche des Blinden Flecks unterliegt beträchtlichen inter- und auch intra-individuellen Schwankungen (individuelle Fläche [Least Square Means, LSM] zwischen 17 und 49 Quadratgrad, Standardabweichung 6.8 Quadratgrad). Die Fläche des Blinden Flecks wird mit abnehmendem Kontrast des Stimulus größer (LSM 32, 31, 27 und 24 Quadratgrad für Stimulusleuchtdichten 20, 0, 41.62 und 110 cd/m²), der kleinere Stimulusdurchmesser ist mit größerer Fläche vergesellschaftet (LSM 31 gegenüber 26 Quadratgrad bei 13´ gegenüber 26´).

Die Korrektur mit den individuellen Reaktionszeiten konnte die Varianzen der Flächen erheblich vermindern: Ohne Reaktionszeitkorrektur (die korrespondierenden Werte *mit* Korrektur finden sich in Klammern) betrug die Standardabweichung des Residuums 4.8 (3.6) Quadratgrad, die inter-individuelle Standardabweichung 9.1 (6.8) Quadratgrad.

Die Untersuchungsabfolge oder der Untersuchungstag hatten keinen Einfluß auf die Fläche des Blinden Flecks, die Wiederholstandardabweichung betrug 0,1 Quadratgrad.

Schlußfolgerung: Die halbautomatische kinetische Perimetrie, in diesem Fall das TCC, ist eine zuverlässige Methode, um die Größe kleiner, scharf begrenzter Skotome - wie am Beispiel des Blinden Fleck exemplarisch dargestellt - zu bestimmen. Die Wiederholpräzision ist gut, die Korrektur mit der individuellen Reaktionszeit verringert die Streuung der Ergebnisse nochmals beträchtlich. Die Studie konnte hohe inter-individuelle Unterschiede in der Größe des Blinden Flecks zeigen.

Interessant sind auch die unterschiedlichen Ergebnisse des Dekrement-Stimulus (0 cd/m^2) und des Inkrement-Stimulus (20 cd/m^2) mit demselben Leuchtdichteunterschied von jeweils 10 cd/m^2 zum Hintergrund, welche vermuten lassen, daß zumindest bei kinetischer Perimetrie die angenommene (und auch in Studien bestätigte) Äquivalenz von Inkrement- und Dekrement-Stimuli mit gleichem Leuchtdichteunterschied nicht besteht.

Nicht eingereichte Abbildungen

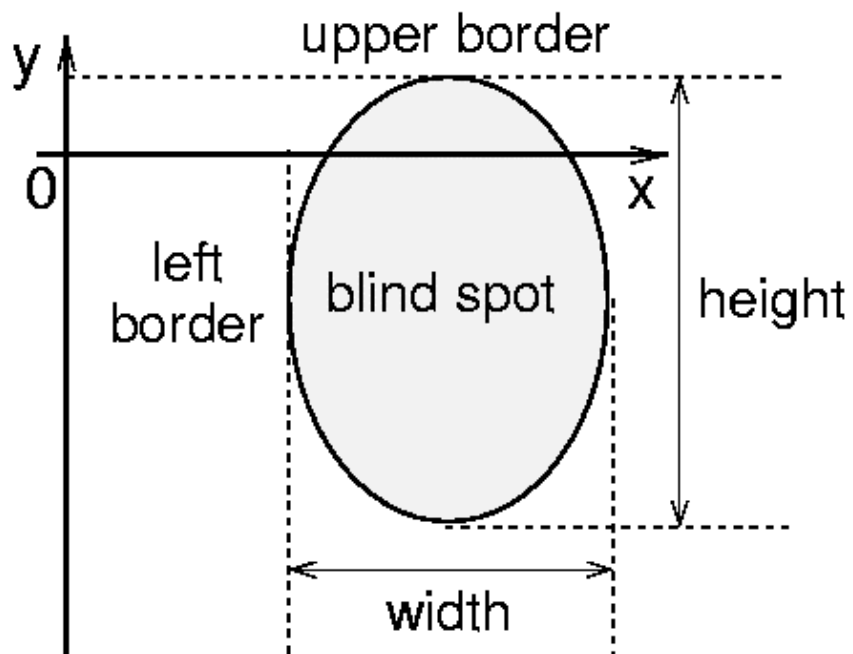


Fig. A1 Measuring values determined for detection of the blind spot centre. The upper and left border of the blind spot are used together with its width and height for calculation of its centre.

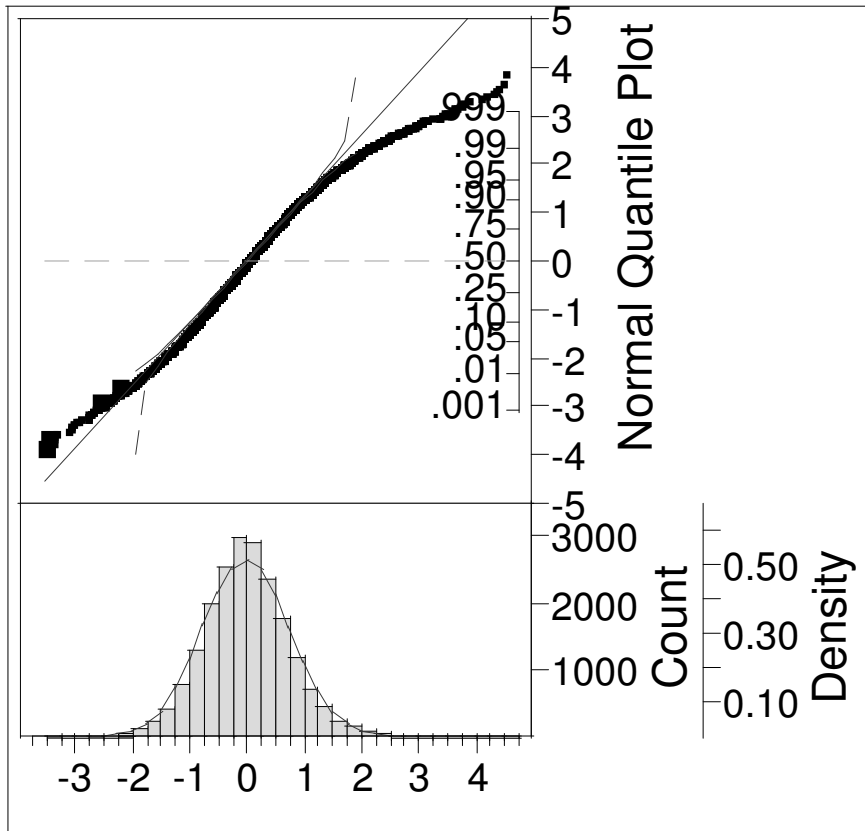


Fig. A2 Distribution of the blind spot eccentricities, corrected by reaction times. Residuals of the model resemble a normal distribution.

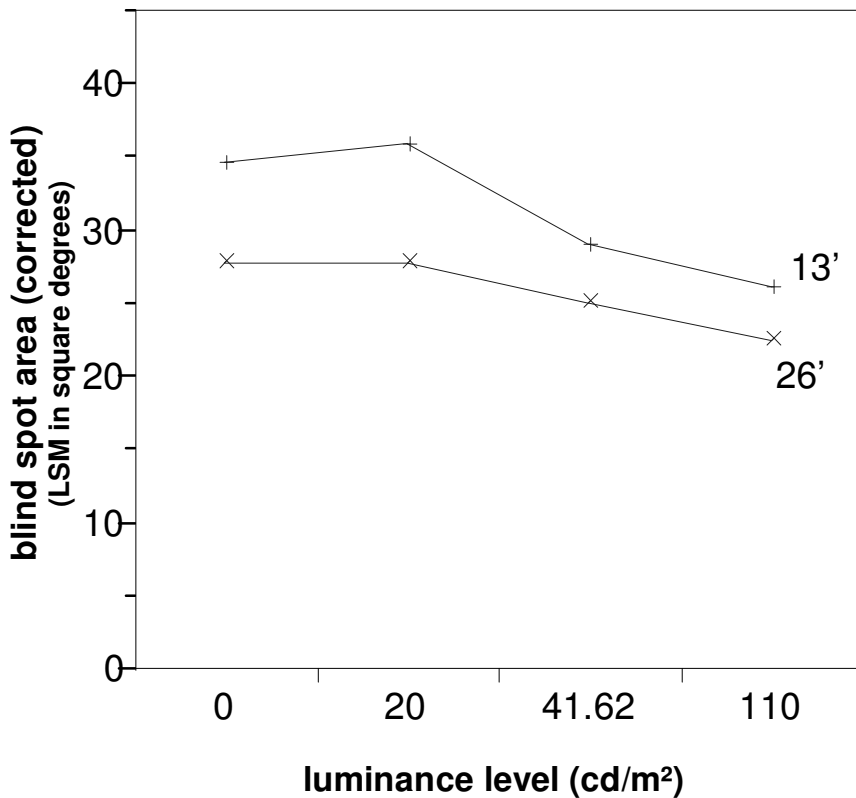


Fig. A3 Influence of stimulus luminance and stimulus size(13' upper line, 26' lower line) on the area of the blind spot, **corrected** by individual reaction times (in square degrees).

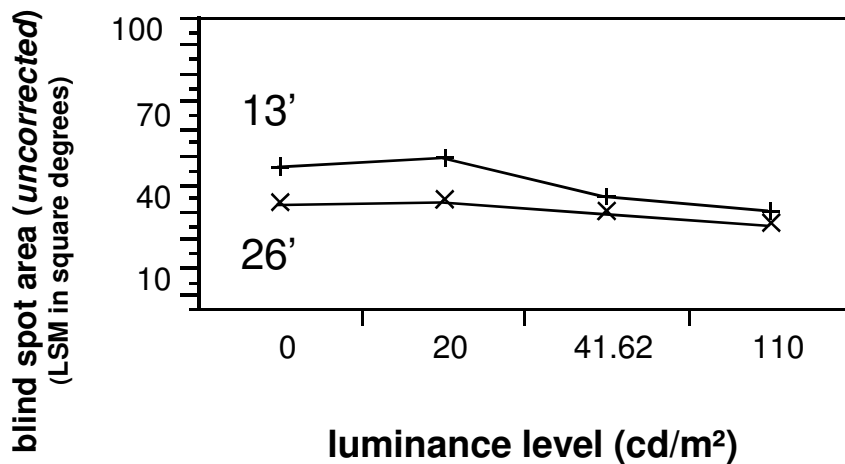


Fig. A4 Influence of stimulus luminance and stimulus size(13' upper line, 26' lower line) on the area of the blind spot, **not corrected** by individual reaction times (in square degrees). Please remark the other scale of the x- and y-axis in comparison to Fig. A3.

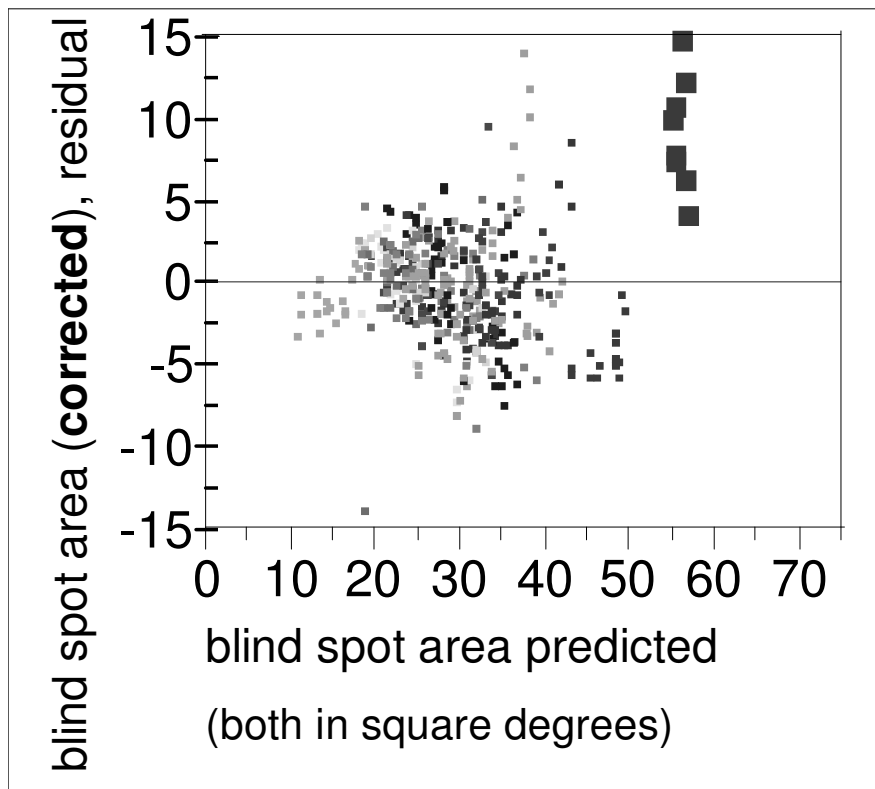


Fig. A5 Scatterplot for blind spot area, **corrected** by individual reaction times, and predicted area in the fitted model; marked results (large squares) from examinations with small (13'), 0 and 20 cd/m² stimuli in one subject (subject number 20). Other subjects show similar deviations.

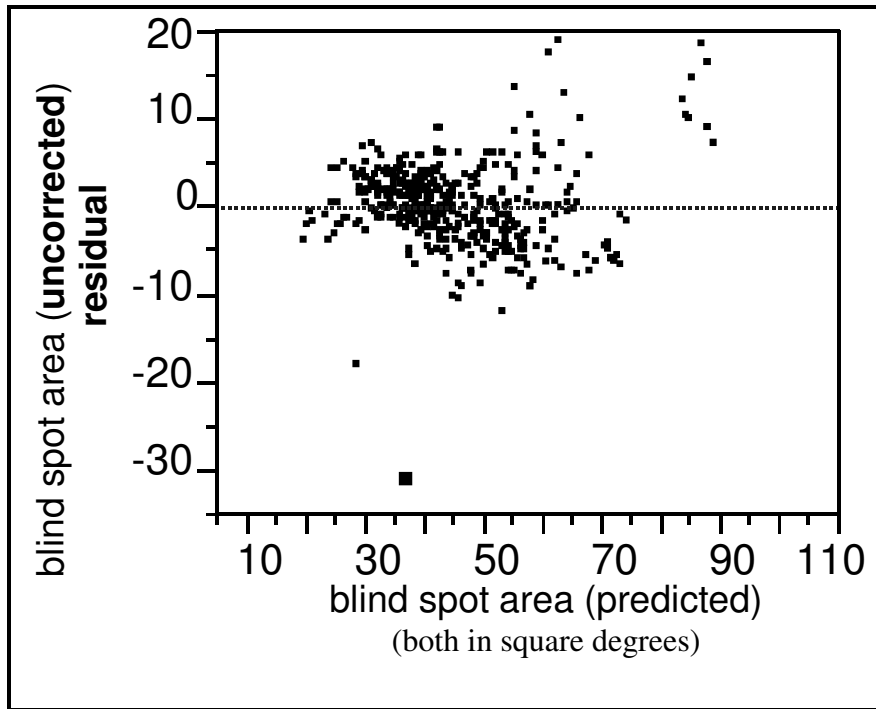


Fig. A6 Scatterplot for blind spot area, **not corrected** by individual reaction times, and predicted area in the fitted model. Please pay attention to the changes in the scaling of the x- and y-axis in comparison to Fig. A5.

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