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25 Hz adaptation: Influence on recovery time in glaucoma

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ABSTRACT

INTRODUCTION. Normal temporal contrast sensitivity is maximally influenced by pre-adaptation with 25-Hz temporal contrast flicker. The aim of this study was to investigate the effects of 25-Hz contrast adaptation on recovery of contrast sensitivity in normals, patients with ocular hypertension, preperimetric, perimetric and advanced perimetric open-angle glaucoma.

MATERIALS AND METHODS. Temporal contrast sensitivity was examined after pre-adaptation with 25 Hz in the following: 43 normals, 14 ocular hypertension, 10 preperimetric primary open-angle glaucoma, and 33 perimetric open-angle glaucoma patients. After pre-adaptation (the time after which a test stimulus could be detected again), recovery time (RT) was measured at 3% and 5% test contrast. Additionally, 25 patients with advanced perimetric open-angle glaucoma were measured at 12%, 25%, and 35% contrast and compared to a normal group consisting of 15 subjects.

RESULTS. 1. Measurements of RT are reliable (Cronbach's $\alpha > 0.8$). 2. RT was age-dependent requiring an age-correction in further analyses. 3. $RT_{3\%}$ and $RT_{5\%}$ were significantly prolonged in perimetric primary open-angle glaucoma compared to normals (3% test contrast: $p = 0.007$; 5% test contrast: $p = 0.035$). 4. Within each group, $RT_{3\%}$ and $RT_{5\%}$ were significantly different at both test contrasts (normals, perimetric open-angle glaucoma: $p < 0.001$; ocular hypertension: $p = 0.007$; preperimetric open-angle glaucoma: $p = 0.035$). 5. $RT_{3\%}$ and $RT_{5\%}$ were significantly correlated with mean defect ($p < 0.001$) and retinal nerve fibre layer thickness ($p = 0.018$). $RT_{5\%}$ was correlated with loss variance ($p = 0.048$). 6. $RT_{12\%}$, $RT_{25\%}$ and $RT_{35\%}$ were significantly prolonged in advanced perimetric glaucoma ($p < 0.001$), and correlated with mean defect ($p < 0.001$, $p = 0.002$, $p = 0.013$) and retinal nerve fibre layer thickness ($p < 0.001$, $p = 0.003$, $p = 0.013$). $RT_{12\%}$ was also correlated with loss variance ($p = 0.016$).

CONCLUSIONS. Measurements of RT after 25-Hz pre-adaptation can be used in glaucoma diagnosis and follow-up examination, especially in monitoring glaucoma progress in advanced perimetric primary open-angle glaucoma.

KEY WORDS: glaucoma, ocular hypertension, flicker adaptation, recovery time, temporal contrast sensitivity, advanced glaucoma

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INTRODUCTION

Primary open-angle glaucoma is a progressive neurodegenerative disease. As the second most frequent cause of irreversible blindness [1–3], approximately 1100 new cases of blindness due to glaucoma were diagnosed in Germany in 2003 [4]. With a prevalence of 1.5% for persons older than 40 years, glaucoma is a disease predominantly of the elderly population [1]. However, 5% of this population are at relevant risk for developing glaucoma [5], and it is estimated that 45% of the cases are yet undiagnosed [1]. Due to demographic changes,

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the incidence of glaucoma will rise [4], therefore representing a major problem in ocular health care. Early diagnosis as well as follow-up examinations are important for a good and effective treatment. Until now perimetry has been a standard diagnostic tool, but it is limited in very early as well as advanced stages of this disease. In order to improve clinical diagnostics, temporal contrast sensitivity is investigated under different test conditions in glaucoma patients.

Temporal contrast adaptation can have retinal [6] as well as cortical origins [7]. The cortex adapts to temporal frequencies below 4 Hz [8], whereas at higher frequencies, only retinal ganglion cells of the magnocellular but not of the parvocellular pathway adapt to temporal contrast modulation [7]. Because of reduced redundancy, testing temporal contrast adaptation is of interest in glaucoma disease. After presentation of a high-contrast adaptation stimulus, a low-contrast test stimulus cannot be seen directly after presentation, only after a time [i.e. 'recovery time' (RT)]. In normals the maximal effect on temporal contrast sensitivity was seen at 25-Hz temporal contrast adaptation [9].

The aim of this study was to determine RT after 25-Hz adaptation in normal subjects, patients with ocular hypertension (OHT), preperimetric primary open-angle glaucoma (prePOAG), primary perimetric open-angle glaucoma (POAG), and advanced perimetric primary open-angle glaucoma (adPOAG).

MATERIALS AND METHODS

SUBJECTS

All subjects were recruited from the Department of Ophthalmology and Eye Hospital, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), from university staff, and from the Erlangen Glaucoma Register (ISSN 2191-5008, CS-2011. ClinicalTrials.gov Identifier: NCT00494923, Tab. 1). Forty-three normal subjects (27 female, 16 male) were measured. All had regular visual fields, defined as less than three adjoining test points with defects $p < 0.05$, no adjoining test points with defects $p < 0.01$, and mean visual field defect (MD) < 2.8 dB. A further fourteen OHT patients (7 female, 7 male) participated in the study, defined by an increased (> 21 mm Hg) IOP on several measurements, a normal optic nerve head classified after Jonas [10, 11], and a normal white-on-white perimetry. Ten preperimetric POAG patients (5 male, 5 female) were measured, presenting glaucomatous change of the optic nerve head, assessed after Jonas [10, 11] but a normal white-on-white perimetry. Thirty-three perimetric POAG patients (20 female, 13 male; 21 POAGs, 12 NTGs) were included with stage I to IV of glaucoma disease, classified after Jonas [10, 11]. All perimetric glaucoma patients had visual field defects, defined as three or more adjoining test points with defects $p < 0.05$, two or more adjoining test points with defects $p < 0.01$, or an MD > 2.8 dB. Visual field loss was diagnosed if one of the above criteria was presented in at least the latest and the previous visual field measurement at the same test locations. Additional exclusion criteria for this group were secondary glaucoma (e.g. pseudoexfoliation glaucoma) and not regulated IOP (> 21 mm Hg measured by Goldmann applanation tonometry) to avoid confounding permanent loss of function with reversible changes, caused by high IOP [12, 13]. NTG and POAG were treated as one group, as the results did not significantly differ

Table 1. Demographic data (age, visual acuity, mean defect intraocular pressure) of all subjects, divided into normal subjects, ocular hypertension (OHT), preperimetric primary open-angle glaucoma (prePOAG), and perimetric primary open-angle glaucoma (POAG). The mean ± standard deviation is given

Group	Demographic factor			
	Age (years) (min–max)	Visual acuity [decimal]	Mean defect [dB]	IOP [mm Hg]
Normals (n = 43)	50.58 ± 13.07 (21–78)	0.96 ± 0.11	1.17 ± 0.76	15.0 ± 2.65
OHT (n = 14)	49.50 ± 13.03 (23–67)	0.99 ± 0.05	0.81 ± 0.79	16.93 ± 2.46
Preperimetric POAG (n = 10)	55.40 ± 8.11 (42–65)	1.03 ± 0.08	0.67 ± 1.03	15.00 ± 3.74
Perimetric POAG (n = 33)	60.52 ± 8.53 (43–73)	0.89 ± 0.18	6.33 ± 2.86	15.24 ± 3.32

Table 2. Demographic data (age, visual acuity, mean defect intraocular pressure) of all subjects, divided into normal subjects and advanced primary open-angle glaucoma (adPOAG). The mean ± standard deviation is given

Group	Demographic factor			
	Age (years) (min–max)	Visual acuity [decimal]	Mean defect [dB]	IOP [mm Hg]
Normals (n = 15)	42.87 ± 15.83 (21–66)	0.99 ± 0.14	1.07 ± 1.09	13.08 ± 1.98
Advanced POAG (n = 25)	67.52 ± 12.49 (47–83)	0.49 ± 0.29	19.26 ± 2.80	13.70 ± 3.03

between these subgroups (see 'results'). Exclusion criteria were any eye diseases (except OHT and POAG), as well as any systemic diseases with ophthalmologic manifestations. A visual acuity < 0.6, ametropia worse than ± 6 dioptres, and any previous ophthalmological surgery, including laser treatments, were excluded. If both eyes of a subject could be included, one eye was chosen randomly.

In an additional pilot study 25 advanced POAGs (12 females, 13 male) (Tab. 2) were measured and compared to a second group of 15 normal subjects (8 female, 7 male), while the same criteria for inclusion into the study were applied as for the normal subjects and the POAGs described above. Advanced POAG was defined as an MD above 15. They were classified into Jonas stages III to V.

The experiments were performed in agreement with the tenets of the Declaration of Helsinki and were approved by the Local Ethics Committee (176_12B). Informed consent was obtained from all subjects after explanation of the nature and possible consequences of the study.

CLINICAL EXAMINATIONS

The subjects underwent ophthalmological examinations, including slit-lamp microscopy, Goldmann applanation tonometry and ophthalmoscopy in mydriasis, Octopus G1 perimetry (Octopus 500 program G1, Interzeag, Schlieren, Switzerland, Peridata Software; criteria see above), Spectralis OCT (Optical Coherence Tomography; Heidelberg Engineering, Heidelberg, Germany) of macula, and optic nerve papilla, delivering the overall retinal nerve fibre layer thickness (RNFL).

ERLANGEN FLICKER TEST

As described previously [14], a Ganzfeld bowl (Q450F, software: Retiport, Roland Consult, Brandenburg, Germany) with white light emitting diodes (LEDs) was used to present full-field, spatially homogeneous, sinusoidal modulating luminance stimuli.

The average luminance was 49.5 cd/m². The eye that was not included in the study was covered by an eye patch. If necessary, all measurements were conducted with the appropriate refraction correction. Fixation was centered into the bowl. Temporal Michelson contrast was used to quantify stimulus strength:

$$\text{Contrast} = (L_{max} - L_{min}) / (L_{max} + L_{min}) \times 100\%$$

L_{max} and L_{min} are the maximal and minimal luminance of the stimulus, respectively.

Temporal contrast sensitivity is defined as the reciprocal value of the threshold contrast (K): TCS = 1/K.

Prior to the main experiments, optimal conditions for measuring RT were determined in a pre experiment with eight normal subjects (2 females, 6 males; age: 21–56). The full-field adaptation stimulus had a temporal frequency of 25 Hz (100% contrast). Presentation time of the adaptation stimulus was varied: 5, 10, 15, 20, 25, and 30 seconds (s). Temporal frequency of the test stimulus was 25 Hz with different test contrasts: 3%, 4%, and 5%. Stimuli were not perceived at all when presenting lower test contrast values (data not shown here).

In the main study, a full-field adaptation stimulus (100% contrast, 25 Hz temporal frequency, 15 s) and a full-field test stimulus (either 3% and 5% contrast or 12%, 25%, and 35% contrast; 25 Hz temporal frequency) were presented alternately (Fig. 1). The subjects were instructed to press a button as soon as the test stimulus could be perceived after it had replaced the adaptation stimulus. The time between test stimulus onset and its detection was measured and defined as 'recovery time' (RT). This procedure was repeated four times and then, after a short break, repeated with the other test contrast. Mean RT was calculated using the

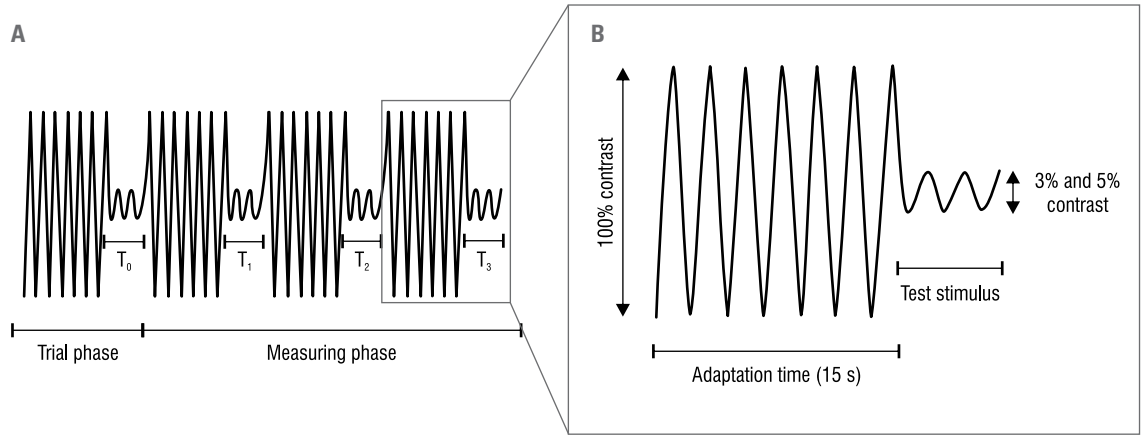

FIGURE 1. Test conditions for measurement of recovery time (RT): **A.** Schematic sketch of the presentation procedure of adaptation and test stimulus. Mean RT was calculated as average of T1–T3; **B.** Details of the presentation procedure: Preceding contrast adaptation (25 Hz, 100% contrast, 15 s) followed by the measurement of RT (25 Hz, 3% and 5% contrast)

last three measurements. The first measurement was disregarded to avoid learning effects.

In the pilot study with advanced POAGs, however, patients were unable to perceive a contrast as low as 3 or 5% (data not shown here). Therefore, this group was measured using 12%, 25%, and 35% contrast, and a second normal group was measured applying the same method.

In addition, all subjects underwent measurements of TCS without adaptation. A method of adjustment was used for measurement of TCS. Starting off at 0%, first contrast was manually increased in 0.05% steps until detection of the stimulus. Second, contrast was decreased in 0.05% contrast steps until disappearance of the stimulus, starting 1% above the previously found threshold. This procedure was performed three times.

RELIABILITY

Testing reliability of this test set-up, 5 normal subjects were measured twice on two subsequent days. Several weeks later, the measurements were repeated three times in a row. Hence short term and long term reliability were examined.

STATISTICAL ANALYSIS

Statistical analysis was done using SPSS (v. 21) software. For statistical analysis of RTs with 3% contrast stimuli ($RT_{3\%}$), 31 data points of perimetric POAG patients and 42 data points of normal subjects were analysed, because three individuals were not able to detect the test stimulus after 60 seconds. To compare RTs between the different groups non-parametric testing was performed. In addition, the difference between $RT_{5\%}$ and $RT_{3\%}$ was calculated: $\Delta RT = RT_{3\%} - RT_{5\%}$. All RTs, except $RT_{35\%}$, and TCSs, were age corrected by means of linear regression. As $RT_{35\%}$ showed a ceiling effect in normals, this data could not be age corrected. For analysis, the decimal logarithms of TCSs were calculated. Correlation analysis was performed using correlation coefficients after Pearson, using data of the perimetric glaucoma group only. Comparing the diagnostic value of the two test conditions, receiver operating characteristic (ROC) analyses were performed. The area under the curve (AUC) values were used as a measure of the ability to distinguish between normals and patients. Reliability was analysed by calculating the Cronbach's α coefficient, which is a marker for internal consistency. The more consistent the data, the more it approximates to 1. Results were Bonferroni-corrected for multiple testing.

RESULTS

RELIABILITY

Data of $RT_{3\%}$ and $RT_{5\%}$ were reliable with Cronbach's $\alpha > 0.9$, the short-term (three measurements in one day) reliability with $\alpha = 0.924$ ($RT_{3\%}$) and $\alpha = 0.964$ ($RT_{5\%}$), the long-term (measurements on different days) reliability with $\alpha = 0.976$ and $\alpha = 0.949$, respectively.

PRE EXPERIMENT: INFLUENCE OF FLICKER ADAPTATION TIME AND TEST CONTRAST ON RT

In the pre experiment, the influence of adaptation time on RT was measured. In Figure 2 the mean RTs (± standard deviations; n = 8) are plotted as a function of adaptation time separately for the

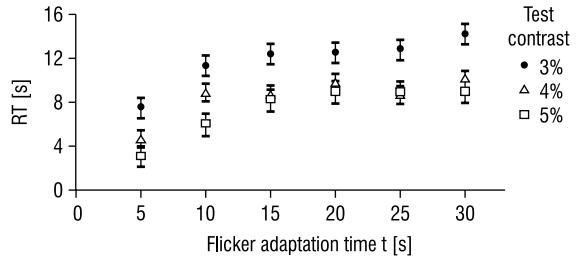

FIGURE 2. Recovery time (RT) vs flicker adaptation time given for three test contrasts (3%, 4%, 5%): RT increased with increasing adaptation time up to 15 seconds, at which a plateau was reached. RT decreases with increasing test contrast

three used test contrasts (3%, 4%, 5%). RT increased with decreasing contrast of the test stimulus and with increasing adaptation time. However, RT reached a plateau at 15 s adaptation time. Further increase of adaptation time had only little additional effect on RT. On basis of these data, we used 3% and 5% contrast for the test stimulus and 15 s adaptation time in the subsequent experiments, excluding the pilot study with advanced POAGs.

TCS THRESHOLDS

TCS without adaptation showed decreased values for perimetric POAGs (1.71 ± 0.18) in comparison to normals (1.82 ± 0.12; p = 0.024). No significant difference was found for OHTs (1.83 ± 0.13) and preperimetric POAGs (1.84 ± 0.10) compared to normals (p > 0.05).

AGE DEPENDENCY OF RT

RT increased with age in normals (Fig. 3). $RT_{3\%}$ increased 1.62 s per decade, $RT_{5\%}$ showed an increase of 1.38 s per decade. Correlation analysis yielded a significance between age and $RT_{3\%}$ (p = 0.032) as well as between age and $RT_{5\%}$ (p = 0.022) in normals. Because of this age dependency an age-correction was performed by means of linear regression before comparing data of the different groups (see 'Erlangen Flicker Test').

RT AFTER 25-HZ ADAPTATION IN PERIMETRIC POAGS

RT after 25-Hz adaptation (100% contrast, 15 s) was significantly prolonged in perimetric OAGs in comparison with normal subjects. This could be seen for both test contrasts ($RT_{3\%}$: p = 0.007; $RT_{5\%}$: p = 0.035) (Fig. 4). RT was not significantly prolonged in OHTs and preperimetric POAGs. Preperimetric POAGs showed significantly different $RT_{5\%}$ values than perimetric POAGs (p = 0.008). $RT_{3\%}$ data were not significantly different between perimetric POAGs and preperimetric POAGs. In addition, the difference between $RT_{3\%}$ and $RT_{5\%}$ (ΔRT) was found to be significantly different between normals and perimetric POAGs (p = 0.014). Data of the two test conditions were significantly different within each group (normals, perimetric POAGs: p < 0.001; OHT: p = 0.007; preperimetric POAGs: p = 0.035) (Fig. 4). Between NTGs and POAGs no significant difference was found, hence they were combined in one group.

ROC-ANALYSIS OF RT

To compare the diagnostic value of measurements of $RT_{3\%}$ and $RT_{5\%}$, an ROC analysis was done (Fig. 5). $RT_{3\%}$ yielded an area under the

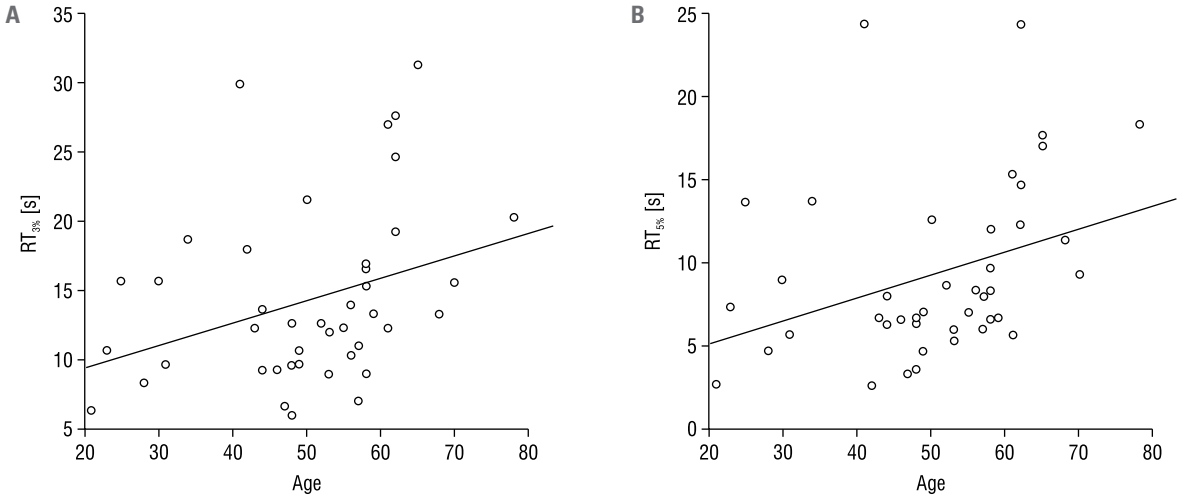

FIGURE 3. Recovery time (RT) plotted for age; **A.** 3% contrast ($RT_{3\%}$); **B.** 5% contrast ($RT_{5\%}$). Per decade increase by 1.62 s (**A**) and 1.38 (**B**) of RT was observed

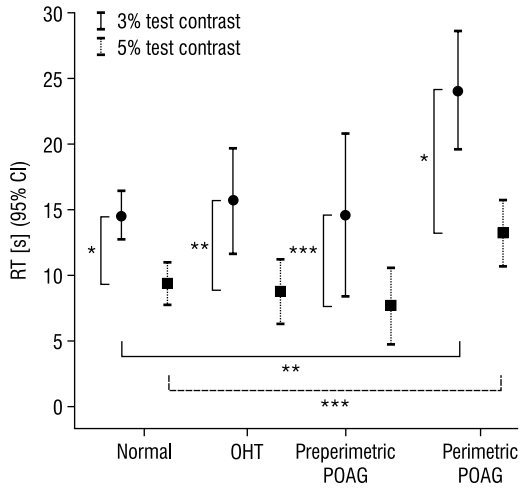

FIGURE 4. Recovery time at 3% contrast ($RT_{3\%}$) and 5% contrast ($RT_{5\%}$; dotted line) in normals, ocular hypertensions (OHT), preperimetric primary open-angle glaucomas (POAG), and perimetric primary open-angle glaucomas (POAGs). Error bars are shown, 95% confidence interval (CI): Significant difference between normals and perimetric glaucoma group was found with both testing methods. $RT_{3\%}$: p = 0.007(**); $RT_{5\%}$: p = 0.035(***). Additionally, significant differences between the two test conditions within each group were found: Normals, perimetric POAGs: p < 0.001 (*); OHT p = 0.007 (**); preperimetric POAGs: p = 0.035 (***)

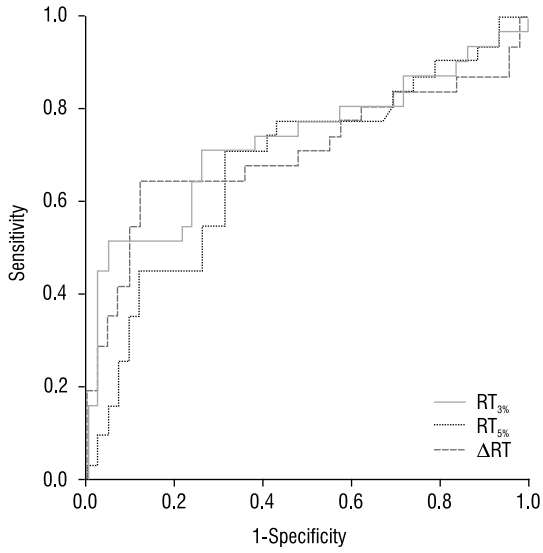

FIGURE 5. Receiver-operating-characteristic (ROC) analysis for recovery time at 3% contrast ($RT_{3\%}$) and at 5 % contrast ($RT_{5\%}$; N (normals) = 42; N (perimetric primary open-angle glaucoma, prePOAG) = 31): Sensitivity is shown for 1-specificity; AUC $RT_{3\%}$: 0.734, AUC $RT_{5\%}$: 0.684, AUC ΔRT: 0.710

curve (AUC) of 0.734, and the AUC of $RT_{5\%}$ was 0.684. ΔRT resulted in an AUC of 0.710.

PILOT STUDY: RT AFTER 25-HZ ADAPTATION IN ADVANCED PERIMETRIC POAGS

Reliability analysis showed reliable Cronbach's α with a short-term (three measurements in one day) reliability of α = 0.852 ($RT_{12\%}$), α = 0.943 ($RT_{25\%}$), and α = 0.838 ($RT_{35\%}$). RT after 25-Hz adaptation (100% contrast, 15 s) was also significantly prolonged in advanced perimetric POAGs compared to normal subjects for all three test contrasts ($RT_{12,\ 25,\ 35\%}$: p < 0.001) (Fig. 6). Advanced POAGs showed significantly different data of $RT_{25\%}$ than of $RT_{35\%}$ (p = 0.002); $RT_{12\%}$ differed significantly from $RT_{35\%}$(p = 0.004). TCSs were significantly different between normals (1.8663 ± 0.13) and advanced POAG (1.3416 ± 0.38; p < 0.001).

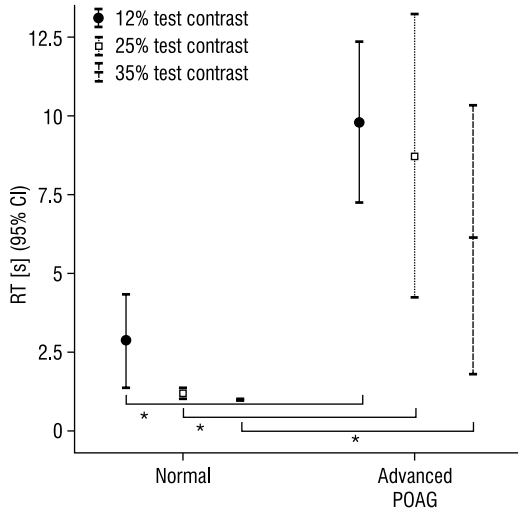

FIGURE 6. Recovery time at 12 ($RT_{12\%}$), 25 ($RT_{25\%}$, small dotted line), and 35% contrast ($RT_{35\%}$, big dotted line) in normals and advanced primary open-angle glaucoma (POAGs). Error bars are shown, 95% confidence interval (CI): Significant difference between the two groups was found with all three testing methods: p < 0.001(*)

CORRELATIONS OF STANDARD PERIMETRIC PARAMETERS AND SPECTRALIS OCT PARAMETERS WITH RT

Correlation analysis of RT with standard perimetric and Spectralis OCT parameters were performed for all test contrasts (3%, 5%, 12%, 25%, and 35%) (Tab. 3). $RT_{3\%}$ and $RT_{5\%}$ were positively correlated with MD (p < 0.001) and negatively correlated with the overall RNFL obtained with Spectralis OCT (p = 0.018). Furthermore, $RT_{5\%}$ was also positively correlated with loss variance (LV; p = 0.048). $RT_{12,\ 25,\ 35\%}$ were positively correlated with MD (p < 0.001, p = 0.002, p = 0.013) and negatively correlated with RNFL (p < 0.001, p = 0.003, p = 0.013). $RT_{12\%}$ was positively correlated with LV (p = 0.016).

Table 3. Correlations between recovery time at 3%, 5%, 12%, 25%, and 35% contrast ($RT_{3\%, 5\%, 12\%, 25\%, 35\%}$) and standard perimetric (mean defect — MD, loss variance — LV) and optical coherence tomography parameters (retinal nerve fibre layer thickness — RNFL)

Strategy		Parameter		
		MD	LV	RNFL
$RT_{3\%}$	Significance p	< 0.001	0.060	0.018
	Pearson Coefficient	0.420	0.261	–0.299
$RT_{5\%}$	Significance p	< 0.001	0.048	0.018
	Pearson Coefficient	0.408	0.264	–0.292
$RT_{12\%}$	Significance p	< 0.001	0.016	< 0.001
	Pearson Coefficient	0.652	0.404	–0.642
$RT_{25\%}$	Significance p	0.002	0.204	0.003
	Pearson Coefficient	0.500	0.220	–0.496
$RT_{35\%}$	Significance p	0.013	0.567	0.013
	Pearson Coefficient	0.405	0.097	–0.408

DISCUSSION

The aim of this study was to investigate the effect of a 25-Hz adaptation, previously found to have maximal effect on TCS in normals [9], on recovery time in patients with OHT, preperimetric POAG, perimetric POAGs, and advanced perimetric POAG. Alterations in early glaucoma patients or suspects can refer to a potential diagnostic value of this test set-up. Changes in RT of perimetric glaucoma patients can potentially be used in follow-up diagnosis.

Perimetric POAGs showed significantly longer $RT_{3\%}$ and $RT_{5\%}$ after an adaptation of 25 Hz than normals. However, no significant difference was found for OHT and preperimetric POAG patients. $RT_{12\%}$, $RT_{25\%}$, and $RT_{35\%}$ in advanced perimetric POAG were significantly elongated compared to normals. Significant correlations of $RT_{3\%}$ and $RT_{5\%}$ with age could be observed in normals. This is in agreement with data of Cursiefen et al. [15], showing a discreet non-significant increase of RT with rising age (0.55 s per decade). However, the age-dependent increase of RT was higher than Cursiefens. The different light source, flicker rate, or measured contrast might be responsible.

Flicker perception can be examined by different methods. Various test set-ups were described, using either circumscribed stimuli that were presented centrally [16–20] or both centrally and peripherally [21–26] or full-field stimuli [14, 15, 27–32] as we used in the present study. Additionally, different light sources can be used, such as Xenon high-pressure arc lamp [15, 27–29, 31] or LEDs [14, 19, 22, 25, 26] as well as different contrast values and adaptation times. Horn et al. [14], Cursiefen et al. [15], and Smith et al. [33] proposed a 30-s adaptation time to give a maximal or near-maximal adaptation. In our experimental set-up a 15-s adaptation seems to be sufficient to reach a maximal effect. This may substantially improve the feasibility of this test in elderly subjects.

The observed prolonged RT after flicker adaptation in glaucoma patients is in agreement with previous data [14, 15]. In addition, we could confirm the significant difference of RT between perimetric POAGs and preperimetric POAGs as shown by Horn et al. [14] at 5% test contrast. $RT_{3\%}$ data showed no difference between perimetric POAGs and preperimetric POAGs. Horn et al. [14] measured RT after flicker adaptation of 37.1 Hz (adaptation time: 30 s, contrast: 100%, luminance: 17.3 cd/m^2) with 12% test contrast, while we used 3% and 5% and 12, 25, and 35%, respectively. Horn et al.'s [14] ROC analysis yielded an AUC value of 0.95 for RT. Their preperimetric group showed AUC values of 0.86 for RT. In contrast, we found lower AUC values for $RT_{3\%}$ (0.734) and $RT_{5\%}$ (0.684). Possibly, the amount of patients included in the study of Horn et al. [14] could lead to higher AUC values. Furthermore, in the perimetric group of Horn et al. [14] patients with secondary open-angle glaucoma were also included, hampering a direct comparison to the present study, including strictly primary POAGs. Another aspect that might be considered is the different MD values obtained for normal patients (our normal group: MD: 1.17 ± 0.76; Horn et al.'s [14] normal group: MD –0.29 ± 1.2). The different luminances used in the two studies

(Horn: 10 cd/m^2 vs ours: 49.5 cd/m^2) may be another reason for the difference in results. Measurements of RT under mesopic conditions could potentially offer an option for improvement of the diagnostic value of this test set-up in early glaucoma diagnosis.

Correlation of RT data with perimetric parameters yielded a significant correlation between $RT_{3\%}$, $RT_{5\%}$, $RT_{12\%}$, $RT_{25\%}$, $RT_{35\%}$, and MD, in agreement with previous studies [15]. LV was significantly correlated with $RT_{5\%}$ and $RT_{12\%}$, a correlation not previously described in literature. As perimetric parameters have been shown to be potential predictors of glaucoma onset or progression [34], correlation of RT with MD or LV might be a hint for the potential benefit of RT measurements as an additional diagnostic tool. Further analysis of RNFL showed a significant correlation with all RTs, also not previously described in literature. The only study on correlation of RT with morphologic parameters of the optic nerve based on papillometric measurements (neuroretinal rim area [35]) is that by Cursiefen et al. [15]. The observed correlations with RNFL, a further parameter for indicating conversion of glaucoma suspect into glaucoma or progression of this disease [36], strengthen the evidence for RT as a diagnostic method in glaucoma follow-up. Additionally, this test set-up might be helpful in assessing advanced glaucoma with reduced fixation ability, which limits the diagnostic value of perimetry, as fixation is not necessary in measurements of RT using the Erlangen Flicker Test [37]. Significant differences between the advanced perimetric POAGs and the normals at all test contrasts ($RT_{12\%}$, $RT_{25\%}$, $RT_{35\%}$ — $p < 0.001$) as well as the correlations of RTs with MD and RNFL hint at a potential benefit in long-term follow-up. In addition cataract, a further factor influencing perimetric data, does not influence the present method [38].

CONCLUSIONS

Measurement of RT after an adaptation of 25 Hz is prolonged in perimetric primary open-angle glaucoma patients. Hence, it may be a potentially useful additional technique in glaucoma diagnosis. Further studies are needed to investigate if modulating luminance (e.g. mesopic conditions) could potentially increase the diagnostic value in early glaucoma diagnosis. Additionally, it may be a sensitive tool for monitoring glaucoma progress. As advanced POAGs show reliable and significantly different data from normals, additional long-term studies are necessary to evaluate the diagnostic value of this test set-up, especially when perimetric follow-up is limited.

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Conflict of interest and source of funding

None declared.

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