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Vision- and health-related quality of life before and after vision restoration training in cerebrally damaged patients

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Abstract. *Purpose*: The aim of the study was to examine if improvements of stimulus detection performance in visual field tests after intensive visual training of the visual field border zone in patients with visual field defects are associated with changes in self-reported vision- and health-related quality of life (QoL).
Methods: We studied a clinical sample of 85 patients suffering from visual field loss after brain damage that underwent repetitive, daily light stimulation (vision restoration training, VRT) of the visual field border and the blind visual field for up to 75 hrs ($N = 16$) or 150 hrs ($N = 69$). Stimulus detection was quantified in the central visual field with a campimetric method before and after intervention. Health-related QoL was assessed by the Health-Survey SF-36 and vision-related QoL by the 39-item National Eye Institute Visual Function Questionnaire (NEI-VFQ).
Results: Both vision- and health-related QoL measures improved after VRT. Significant increases were found in 8 out of 12 NEI-VFQ and 3 out of 8 SF-36 subscales. Of the 85 participants 6% showed a decrease in stimulus detection performance, 42% showed an increase of less than 5% detected stimuli, 24% showed an increase of 5–10% detected stimuli and 28% of more than 10% detected stimuli. Changes in campimetric stimulus detection rates were related to NEI-VFQ subscales point differences general vision (3 points), difficulty with near vision activities (4 points), limitations in social functioning due to vision (4 points) and driving problems (12 points). There was no relation of visual field changes to changes in SF-36 component and subscale scores.
Conclusions: The NEI-VFQ is a valuable measure of self-reported visual impairment in patients with visual field defects. Stimulation of the visual field by training may lead to improvements of vision-related QoL which were correlated with the extent of visual field enlargements.

Keywords: Quality of life, visual field defect, National Eye Institute Visual Function Questionnaire (NEI-VFQ)

1. Introduction

Visual field defects are common in patients suffering from brain damage. They lead to impairments in activities of daily life such as reading, driving, or overall orientation. Visual field defects are often accompanied by other additional impairments such as higher perceptual or attentional deficits (e.g. Paramei & Sabel, 2008). In a

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review assessing over 450 patients with visual field defects by Kerkhoff (1999), frequent deficits were reading problems due to parafoveal field loss and/or impaired exploration.

While there are many ways to measure cerebral visual field loss there are only a few instruments to analyse daily life impairments and vision-related quality of life (QoL), respectively. It is therefore desirable to further validate existing instruments, especially in hemianopia. In a previous study (Gall et al., 2008) with the German version of the 39-item National Eye Institute-Visual function questionnaire (NEI-VFQ) we found that patients with visual field defects after cerebral damage ($N = 24$) had significantly lower vision-related QoL values than healthy subjects (see Franke, 1999) and also lower values than patients with glaucoma (Mangione et al., 1998) or optic neuritis (Cole et al., 2000). These findings are in agreement with Papageorgiou et al. (2007) who assessed vision-related QoL in 33 patients with homonymous visual field defects and also found lower scores than in reference subjects. The NEI-VFQ composite score correlated positively with the remaining visual field size in static 90° perimetry ($r = 0.67$) (Gall et al., 2008) and with the area of sparing within the affected hemifield ($r = 0.38$) (Papageorgiou et al., 2007). In contrast, no significant relationship was found between health-related QoL in general (assessed with the SF-36 Health Survey) and visual field parameters (Gall et al., 2008). To our knowledge these recent reports are the only studies that focus on vision-related QoL in patients with visual field defects after cerebral damage, while the assessment of vision-related QoL in ophthalmic patients is quite common (e.g. Gutierrez et al., 1997; Carta et al., 1998; McKean-Cowdin et al., 2007). One reason why there are so few studies of QoL assessment in cerebrally damaged patients may be that such patients frequently suffer from anosognosia (Celesia et al., 1997). Patients with anosognosia are not aware of their deficits and often do not perceive subjective restrictions in daily life. The NEI-VFQ was originally designed to measure the dimensions of self-reported vision-related QoL that are important for patients with chronic eye diseases who do not suffer from unawareness of their visual impairments. However, glaucoma patients who dominate in visual QoL data surveys are also not aware of visual field loss in the early stages of their disease (Mills, 1998; Iester & Zingirian, 2002). Therefore, anosognosia should be no counter-argument against measuring QoL in patients with visual field defects.

The impact of correctable visual impairment (e.g. refractive errors) on vision-related QoL is smaller than the impact of non-correctable visual impairment (Chia et al., 2006). Visual field defects in cerebrally damaged patients belong to non-correctable visual impairments since both compensatory as well as restorative interventions do not lead to functional improvements that reach the pre-illness status. QoL decrements due to visual field loss may motivate to train visual functions. With restorative training approaches improvements of stimulus detections were achieved in patients with post-chiasmatic lesions and with lesions of the optic nerve (Kasten et al., 1998; Julkunen et al., 2003; Sabel et al., 2004). In retrospective studies about 2/3 of the treated patients reported subjective improvements as measured in post training interviews (Mueller et al., 2003) or by analysis of pre- and post-training drawings of subjective visual field sizes (Poggel, 2002). Other studies have developed their own questionnaires and also found significant differences (Julkunen et al., 2003; Sabel et al., 2004). However, so far a systematic pre-post training assessment of vision-related QoL with a larger number of patients is still missing.

In a first attempt to evaluate subjective changes of daily life activities after vision restoration training in hemianopes post-training interviews were assessed in a sample of 69 clinical patients (Mueller et al., 2003). There were five main categories of activities of daily living (ADL) in which patients reported training related changes: reading (43.5%), ability to avoid collisions (31.9%), general vision improvement (47.8%), ability to perform hobby activities (29%) and confidence in own mobility (75.4%). Objective improvements of visual field parameters correlated significantly with the number of named ADL categories. However, not all patients who reported subjective improvements showed objective improvements in perimetry results, i.e. there was a "mismatch". Hence, the relevance of objective visual field enlargements for daily life is still ambiguous. This may be due to the fact that no reliable vision-related QoL questionnaire has been used so far to assess treatment-induced subjective changes of self-perceived visual functioning but it could also relate to the fact that the intact sector of the visual field has subtle deficits in temporal processing (Mueller et al., 2003) or other perceptual abilities such as contour-integration (Paramei & Sabel, 2008).

To better understand the relationship of visual field changes and QoL parameters it is therefore desirable to directly compare results of the NEI-VFQ, a common questionnaire for vision-related QoL assessment, and perimetric results. Correlations between vision-related QoL assessed by NEI-VFQ scores and visual

field size parameters were found for different patient groups (glaucoma, cataract, age-related macula degeneration) (e.g. Gutierrez et al., 1997; Carta et al., 1998; McKean-Cowdin et al., 2007). Gutierrez et al. (1997) reported correlations between the size of glaucomatous visual field loss and NEI-VFQ subscales between $r = -0.2$ and $r = -0.6$. McKean-Cowdin et al. (2007), investigating ophthalmic patients with visual field loss, demonstrated that 4- to 5-dB differences in Humphrey Automated Perimetry were associated with a five-point difference in the NEI-VFQ composite and in most subscale scores. The NEI-VFQ was shown to be sensitive to changes in visual function such as gains and losses in visual acuity (Solomon et al., 2007). The questionnaire is also sensitive to measure changes after cataract and glaucoma surgery (Lee & Wilson, 2000; Franke et al., 2003; Hymen et al., 2005) and to demonstrate the effects of low-vision rehabilitation (e.g. Stelmack et al., 2002). Weak significant correlations were also found between deteriorations of the visual field in glaucoma patients and decreases in the overall NEI-VFQ score ($r = 0.17$) and NEI-VFQ subscales *general vision* ($r = 0.19$), *role difficulties* ($r = 0.16$) and *dependency* ($r = 0.17$) (Hymen et al., 2005). In patients with advanced age-related macular degeneration changes in the NEI-VFQ composite and subscale scores of 10 points or more were associated with clinically significant changes (The Age-Related Eye Disease Study Research Group, 2005).

Health-related QoL should be considered in pre-post designs since adjustment for the physical and mental component score of the SF-36 produced changes in the estimated treatment effect when NEI-VFQ scores were compared in patients who underwent submacular surgery (Miskala et al., 2003). Furthermore, several visual-field-related factors have to be considered when interpreting visual field changes such as the extent and type of visual field deficits (site, eccentricity).

The aim of the present study was to assess if visual field enlargements after training are relevant for patients' vision- and health-related QoL.

2. Methods

2.1. QoL measures

Health-related and vision-related QoL were assessed before and after vision restoration training (VRT). The NEI-VFQ was designed to measure the dimensions of self-reported vision-related QoL that are important for patients with chronic eye diseases (Mangione et al., 2001). It was shown that the NEI-VFQ is also useful in patients with visual field loss after cerebral damage (Gall et al., 2008; Papageorgiou et al., 2007). The validated German 39-item version of the NEI-VFQ was used in self-administered format (Franke et al., 1998). It measures the influence of visual disability and visual symptoms on generic health domains. The questionnaire consists of 39 rating items with 12 subscales: The dimensions (1) to (5) assess the patient‘s visual disabilities and (6) to (12) assess difficulties that are the result of the visual impairment. The dimensions were as follows: (1) *general health* (2 items); (2) *general vision* (2 items); (3) *ocular pain* (2 items); (4) *difficulties with near vision activities* (6 items); (5) *difficulties with distance vision activities* (6 items); (6) *limitations in social functioning due to vision* (3 items); (7) *mental health symptoms due to vision problems* (5 items); (8) *role difficulties due to vision problems* (4 items); (9) *dependency on others due to vision problems* (4 items); (10) *driving problems* (3 items); (11) *color vision problems* (1 item) and (12) *peripheral vision problems* (1 item). Two composite scores were generated: one by averaging all 12 dimensions, the second by averaging 11 scales without the general health rating. Subscales and composite score ranged from 0 ("worst possible functioning") to 100 ("best possible functioning").

The Health Survey Short Form SF-36 is a standard instrument for the collection of data concerning general health-related QoL. Based on self-report, this questionnaire was used to quantify health-related QoL in patients, independent of their actual state of health or their age. In the present study the German translation of the SF-36 (Bullinger & Kirchberger, 1998) was self-administered, where patients are asked to rate the items based on the experiences during the last four weeks. The questionnaire consists of a 36 item-list which can be subdivided into eight dimensions of subjective health: *physical functioning* (10 items), *role limitations due to physical problems* (4 items), *bodily pain* (2 items), *general health perceptions* (5 items), *vitality* (4 items), *social functioning* (2 items), *role limitations due to emotional problems* (3 items), and *emotional well-being* (5 items). Additionally, there is one single item (self-reported health transition) which is not part of these eight dimensions. All items can be combined to form two summary scales: the *physical component score* (PCS) and the *mental component score* (MCS). The categories for answering the questions vary from yes-or-no-decisions to 6-point rating scales. Component scores were generated by adding the item respons-

es and including given loadings for the different dimensions. Subscale and component scores ranged from 0 ("worst possible functioning") to 100 ("best possible functioning").

For an optimal measurement of QoL in visually impaired persons, it is reasonable to use both questionnaires, the SF-36 for general health status and the NEI-VFQ for vision-targeted questions (Mangione et al., 1998b). Mangione et al. (1998b) found low correlations between the *physical component score* of the SF-36 and most NEI-VFQ subscales but high correlations with the NEI-VFQ *general health* rating scale. The *mental component score* had the highest correlation with the NEI-VFQ scale that measures vision-induced mental distress.

2.2. Visual field diagnostics

The visual field defect was assessed before and after treatment with a campimetric method, the computer-based high-resolution perimetry (HRP; detailed description e.g. in Mueller et al., 2007). The patients were seated in a darkened room in front of a 17" monitor in a combined head-chin-rest at a distance of about 40 cm to the screen. White light stimuli were presented in a grid of 25×19 stimulus locations. The order of stimulus positions was randomized. A fixation point positioned at the center of the screen served as frame of reference to set up the screen at eye level where the fixation point was also located. The subject was instructed to keep looking at the fixation point and to press the space bar on the computer keyboard whenever either a target stimulus was detected or when an isoluminant change in the color of the fixation point occurred. Correctly detected stimuli, misses, false positives, fixation losses as well as reaction times were registered. Three measurements were performed, each with duration of about 23 minutes. Visual field areas were categorised as intact (three correctly detected stimuli per location), partially damaged (one or two stimuli detected) and absolutely impaired areas (no stimuli detection). The partially damaged area, also termed transition zone, was typically located between the intact and the completely damaged area of the visual field.

2.3. Intervention

Different approaches of outpatient visual restoration training were applied. The first approach was stimulation along the visual border with static light dots and/or kinetic (step-wise moving stimuli) for six months (150 hrs treatment during 6 months) in a clinical setting (Vision Restoration Therapy, VRT was provided by therapists of NovaVision AG, Germany, for detailed description see Mueller et al., 2007). Both approaches (static and kinetic stimulation) stimulated transition zones between intact and damaged visual fields where the probability for a response was between 20% and 80% in the diagnostic campimetric session, i.e. areas of partial function (Kasten et al., 1998). The "static training" involved a procedure of presenting stimuli with increasing brightness at random locations in the border area adjacent to the intact visual field. The brightness of these stimuli increased from dark gray (about 30 cd/m^2) to bright white (about 96 cd/m^2) on a black background (about <1 cd/m^2). Patients were instructed to press a key whenever they detected a stimulus. In the "kinetic training" condition stimuli were first presented in the intact part of the visual field. After the patient responded correctly the stimulus was moved in a step-wise mode towards the visual field defect until the patients no longer responded to the stimulus. This was then moved back towards the intact part of the visual field.

The second treatment approach was used in patients who had already received six months of static and/or kinetic stimulation (described above). This treatment lasted three months with 75 hrs of treatment (Jobke et al., 2008). During training a moving helix (10 Hz) with light and dark stripes was presented within the entire transition zone and the blind field. Further, static stimuli with increasing brightness were presented in the transition zone and the patients were asked to respond to each stimulus as well as to isoluminant color changes of the fixation point.

Both training approaches required stable fixation which was controlled in the same manner as in the campimetric diagnostic program described above. For valid measurement the program was adjusted to the size of the computer screen and the distance between eye and screen was held constant by using a head-chin-rest. The visual field covered by the training was up to about $25^\circ/40^\circ$ vertical/horizontal eccentricity. Training areas were adjusted monthly to accommodate for the performance progress, i.e. as shifts of the visual field border occurred. Treatment sessions were required two times a day for 30 min. each. One day of rest was scheduled each week. If patients did not finish 150/75 hrs of training after six/three months for any reason (such as illness), the duration of training was prolonged until 150/75 hrs of treatment were completed.

2.4. Subjects

Main inclusion criteria were visual field loss after cerebral damage indicated by standard perimetry and campimetry. Patients with epilepsy or photosensitivity were generally not included in the study. Patients were not cognitively assessed in a formal manner prior to training, but neuropsychological reports were screened for severe attentional disorders or visual neglect. All patients were able to assess the presence of their visual field defect and spontaneously reported the impairment when probed with a general question by the examiner or therapist.

The whole patient sample ($N = 85$) consisted of two sub-samples that were treated with different approaches of outpatient visual training described above. The first sub-sample consisted of 69 patients who were stimulated with static and/or kinetic (step-wise moving) stimuli in a clinical setting. Most of these patients paid privately for participating in the training while in a minority of cases the therapy was covered by health insurance. The first sample was not part of a formal study. QoL questionnaires were sent to all patients by post because answering self-administered questionnaires at home is known to result in more realistic estimates than questionnaires completed in interviews or while an investigator is present (Wolffsohn et al., 2000). A subject‘s data set was only included when NEI-VFQ questionnaires of both diagnostics (pre and post treatment) were returned till August 2007. Twenty patients of the first sample returned only NEI-VFQ but not SF-36 questionnaires.

The second sub-sample consisted of 16 patients who had already received six months of static and/or kinetic stimulation (described above) but were not part of the first sample. These patients received therapy at no charge according to a study protocol that included assessment of QoL (Jobke et al., 2008). The original sample size of this study was 18 patients. Two patients were excluded from analyses because they were already part of the first sample. There were no missing SF-36 data in this second sample.

There were no differences between both sub-samples with respect to sociodemographic (age, gender) and clinical data (etiology, age of lesion) as well as campimetric data (detetected stimuli in %) and QoL results (NEI-VFQ scores). Therefore, pooling the patients into one total sample was justified.

In this total sample of 85 patients, 58 were male and 27 female with a mean age of 53 years ($SD = 16$). The mean time from lesion onset to the beginning of the training was 33 months ($SD = 46$). In 61 cases (71.8%) the lesion was older than six months and in 42 cases (49.48%) older than twelve months. Because about 30% of the patients had their lesion less than six months ago, we can not tell for sure if some spontaneous recovery may have occurred, though we consider this unlikely because recovery in large part occurs in the fist few weeks after the lesion and the lesion age in our patients was well beyond this time (Zhang et al., 2006).

The whole sample consisted of 77 patients with homonymous visual field defects, three patients with heteronymous defects and five patients with monocular defects. Different topographies of visual field defects were observed. 35 patients showed an incomplete and 17 a complete hemianopia. Quadrantanopia was found in ten patients, two suffered from tunnel vision and two from paracentral scotomata. Six patients had altitudinal visual field deficits, seven patients showed diffuse losses of the visual field and in five patients the visual field defect affected three quadrants (hemianopic plus quadrantanopic visual field defect). One patient showed severe bitemporal losses of the visual field.

35 patients had left-sided visual field defects, 26 patients right sided and 24 patients binocular visual field loss where damage affected both sides. In the majority of cases the etiology of the visual field defect was ischemic infarction ($N = 50$), the remaining 35 patients had either non-progressive or extirpated brain tumors ($N = 15$), traumatic brain injury ($N = 7$), hemorrhagic infarctions ($N = 6$) or encephalitis ($N = 1$). Non-arteritic anterior ischemic optic neuropathy was found in five patients and one patient had arteritic optic nerve infarction.

2.5. Statistical analyses

Main outcome measures were NEI-VFQ and SF-36 composite and subscale scores. These were correlated with the number of stimulus detections (%) in the campimetric visual field test (Spearman rank correlations). Secondary measures were reaction times (ms) and reliability parameters (fixation rate, false positives) in campimetry. Pre vs. post comparisons for NEI-VFQ, SF-36, and visual field test results were calculated with Wilcoxon-Z-Tests. The sample was divided into four groups according to changes in the stimulus detection rate in the campimetric visual field test (I: decrease in stimulus detection performance, II: increase of less than 5% detected stimuli, III: increase of 5–10% and IV: increase of more than 10%). Differences between

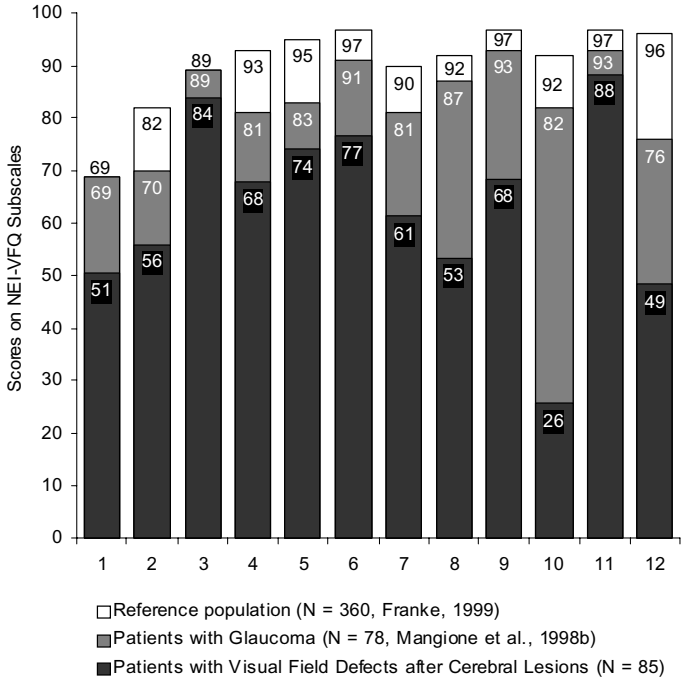

Fig. 1. Comparison of patients with visual field defects after cerebral lesions with glaucoma patients and a healthy reference group on mean NEI-VFQ 39 item subscale scores (Scale 1: general health rating, Scale 2: general vision rating, Scale 3: ocular pain, Scale 4: difficulty with near vision activities, Scale 5: difficulty with distance vision activities, Scale 6: limitations in social functioning due to vision, Scale 7: mental health symptoms due to vision, Scale 8: role difficulties due to vision, Scale 9: dependency on others due to vision, Scale 10: driving problems, Scale 11: color vision, Scale 12: peripheral vision).

these groups in their changes in NEI-VFQ and SF-36 results were calculated with the Kruskal Wallis H-Test. The level of significance was set at 0.05. Results are displayed as mean $\pm$ standard deviation ($M \pm SD$). Statistical analyses were carried out with SPSS 15.0.

3. Results

3.1. Vision-related QoL in patients with visual field defects after cerebral damage

NEI-VFQ scores of the whole sample of patients with visual field loss due to cerebral lesions were generally lower than scores of a disease-free comparison group (Franke, 1999). In clinical studies, between-group differences of 10 points are defined to be "clinically relevant" (Mangione et al., 1998a; 1998b). A mean difference of 10 points in comparison to the reference group (Franke, 1999) and to the glaucoma group (Mangione et al., 1998b) was found in all scales except for *ocular pain, color vision* and *distance vision activities*. There were more than 20 points difference when compared to the reference group and glaucoma patients for the scales *role difficulties due to vision, dependency on others due to vision, driving problems* and *peripheral vision*.

When patient groups with incomplete hemianopia ($N = 35$), complete hemianopia ($N = 17$), quadrantanopia ($N = 10$) and diffuse visual field loss ($N = 7$) were compared with regard to their mean pre-training NEI-VFQ results, only the subscale *peripheral vision* significantly differed between groups, $\chi^2(4) = 8.33$; $p < 0.05$. Patients with complete hemianopia showed the lowest peripheral vision score (45.59). In patients with incomplete hemianopia (52.86) and diffuse losses of the visual field (53.71) subjective peripheral vision was slightly better. Patients with quadrantanopia (75.00) reported highest subjective peripheral vision which was comparable to the values found in glaucoma subjects (Mangione et al., 1998b) (see Fig. 1). There were no differences between male vs. female patients, monocular vs. binocular visual field defects and between patient groups of different etiologies. Pre- as well as post-training ratings of NEI-VFQ and SF-36 subscales were lower in patients with higher age (NEI VFQ mean score, $r = -0.30$; $p < 0.01$, SF-36 *physical*

Table 1
Changes in vision-related QoL - Thirty-nine-Item National Eye Institute-Visual Function Questionnaire Subscale Scores before and after VRT

NEI-VFQ Subscale	N	Baseline	Post-VRT	Wilcoxon-Z	Level of significance
NEI-VFQ mean score of 12 subscales	85	63.68 ± 15.51	68.01 ± 14.59	-4.41	$p < 0.0001$
NEI-VFQ mean score of 11 subscales without general health	85	64.93 ± 16.01	69.78 ± 15.13	-4.65	$p < 0.0001$
1. General health	85	50.06 ± 18.74	49.44 ± 18.42	-0.24	ns
2. General vision	83	55.96 ± 17.12	58.64 ± 15.68	-1.67	$p < 0.10$
3. Ocular pain	83	84.04 ± 17.28	84.04 ± 16.14	-0.12	ns
4. Near activities	85	67.94 ± 20.83	71.73 ± 19.70	-2.17	$p < 0.05$
5. Distance activities	83	73.99 ± 19.64	77.26 ± 18.26	-2.14	$p < 0.05$
6. Social functioning	84	76.74 ± 20.35	81.15 ± 19.14	-2.39	$p < 0.05$
7. Mental health	83	61.43 ± 23.28	69.20 ± 22.96	-3.95	$p < 0.0001$
8. Role difficulties	81	53.42 ± 21.59	58.92 ± 23.42	-2.57	$p < 0.01$
9. Dependency	83	68.27 ± 30.49	76.73 ± 26.91	-3.08	$p < 0.01$
10. Driving	64	25.65 ± 35.71	38.09 ± 36.66	-3.16	$p < 0.01$
11. Color vision	80	88.44 ± 19.05	90.63 ± 15.60	-1.29	ns
12. Peripheral vision	84	48.51 ± 22.75	53.27 ± 22.22	-2.18	$p < 0.05$

All results are Mean $\pm$ SD. Subscales are scored on a 0–100 range.

Table 2
Changes in health-related QoL – SF-36 Subscale Scores before and after intervention

SF-36 Subscale	N	Baseline	Postintervention	Wilcoxon-Z	Level of significance
Physical Component Score	61	45.00 ± 9.65	46.46 ± 9.20	-1.10	ns
Mental Component Score	61	47.12 ± 10.84	49.42 ± 9.55	-1.55	ns
1. Physical Functioning	63	73.72 ± 24.42	77.21 ± 23.51	-2.17	$p < 0.05$
2. Role Limitations due to Physical Problems	65	49.62 ± 43.41	61.67 ± 43.27	-2.04	$p < 0.05$
3. Bodily Pain	63	81.37 ± 24.71	82.05 ± 22.22	-0.36	ns
4. General Health Perceptions	61	56.89 ± 19.94	60.37 ± 17.99	-1.44	ns
5. Vitality	65	54.08 ± 19.16	57.62 ± 18.65	-1.60	ns
6. Social Functioning	65	74.04 ± 25.42	82.12 ± 23.28	-2.59	$p < 0.01$
7. Role Limitations due to Emotional Problems	61	72.68 ± 42.82	78.69 ± 38.98	-1.05	ns
8. Emotional Well-being	65	67.95 ± 17.69	69.69 ± 16.86	-1.19	ns
Self-reported health transition[†]	65	3.29 ± 1.20	2.34 ± 1.08	-4.30	$p < 0.0001$

All results are Mean$\pm$SD. Subscales are scored on 0–100 range except for subjective change of health status (†) which was a single Likert item scored from 1 (enhanced) to 5 (declined).

component score $r = -0.28$; $p < 0.05$; SF-36 *mental component score*, $r = 0.18$, ns).

3.2. Changes of vision- and health-related QoL after visual stimulation

The comparison of pre- and post-training NEI-VFQ and SF-36 data is shown in Tables 1 and 2. Both questionnaires revealed significant pre-post differences. Significant increases in subjective vision-related QoL were observed in 8 of 12 NEI-VFQ subscales. Less than five point differences were found for *difficulty with near vision activities*, *difficulty with distance vision activities*, *limitations in social functioning due to vision* and *peripheral vision*. Differences of more than five points were found for *mental health symptoms due to vision*, *role difficulties* and *dependency on others due to vision* as well as *driving problems*. The subscale *driving problems* had the worst score prior to VRT and improved by more than 10 points. The patients' willingness to answer driving items was considerably lower than for the other subscales, 75% of the patients answered the driving questions. Of the remaining 25% about 9% stopped driving because of reasons other than vision problems and 14% gave no answers.

Significant increases in subjective health-related QoL were observed in 3 of 8 SF-36 subscales and for the single-item self-reported health transition. Subscales with more than 5 point differences were *physical functioning* and *social functioning*. For *role limitations due to physical problems* a difference of more than 10 points was found.

On average there was a significant increase of stimulus detection performance from 53.47% ($SD = 15.43$) before to 62.98% ($SD = 18.11$) after treatment ($Z = -6.92$; $p < 0.001$) with a reduction of the field defect size in the campimetric visual field test from 39.6% to 29.1% ($Z = -6.07$; $p < 0.001$) and a slight increase of positions with inconsistent stimulus detections from 12.5% to 15.7% ($Z = -2.00$; $p < 0.05$). The size of the

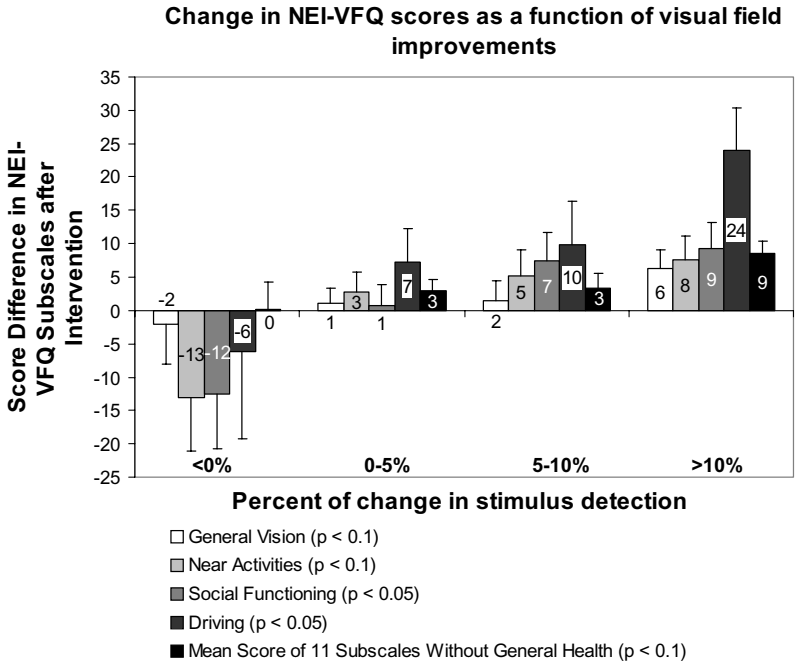

Fig. 2. Number of point differences in NEI-VFQ subscales according to changes in stimulus detection performance in the campimetric visual field test.

intact visual field increased from 47.9% to 54.9% ($Z = -3.74$; $p < 0.05$). Reaction times decreased from 468 ms ($SD = 65$) to 456 ms ($SD = 62$) after treatment ($Z = -1.91$; $p = 0.06$). The number of detected color changes of the fixation point did not differ between 93.89% ($SD = 7.75$) before and 94.13% ($SD = 7.06$) detected fixation controls after treatment ($Z = -0.13$; ns). The false positives rate increased from 1.53% to 2.58% ($Z = -3.14$; $p < 0.01$). Improvements of stimulus detection performance were significantly related to the increase of false positives ($r = 0.41$; $p < 0.0001$).

In order to test the hypothesis that changes in NEI-VFQ subscales reflect training-induced visual field improvements the sample was divided into four groups according to how much the stimulus detection rate changed in the campimetric visual field test. Of 85 participants included in this study, 6% showed a decrease in stimulus detection performance, 42% showed an increase of less than 5% detected stimuli, 24% showed an increase of 5–10% detected stimuli and 28% of more than 10% detected stimuli. The Kruskal Wallis H-Test revealed significant differences between the four groups according to changes in NEI-VFQ subscales *social functioning*, *driving* ($p < 0.05$) and *general vision*, *near activities* as well as *both composite scores* ($p < 0.10$) (Fig. 2). There were no group differences for SF-36 subscales.

Spearman rank correlations between changes in NEI-VFQ subscales and changes in visual field size (stimulus detection increase/decrease in campimetry) were significant for *general vision*, $r = 0.24$, *near activities*, $r = 0.22$, *distance activities* $r = 0.24$ and *driving* $r = 0.27$ ($p < 0.05$). Spearman coefficients of correlations between SF-36 subscales and changes in visual field size did not reach significance.

When relating subgroups of different visual field defect topographies to NEI-VFQ changes after treatment a descriptive non-significant trend was found for patients with complete hemianopia showing decreases of vision-related QoL in subscales *distance activities*, *social functioning* and *role difficulties* or small increases in the remaining subscales (Fig. 3). In contrast, patients with incomplete hemianopia, quadrantanopia or diffuse visual field loss reported considerable changes in NEI-VFQ subscales.

Spearman rank correlations between responses on the NEI-VFQ and results of the campimetric visual field test at baseline and after intervention are shown in Table 3. Significant correlations were found for all subscales. *Color vision* correlated significantly only with fixation accuracy, i.e. the number of isoluminant color changes of the fixation point. Increased *ocular pain* was significantly associated with increases in reac-

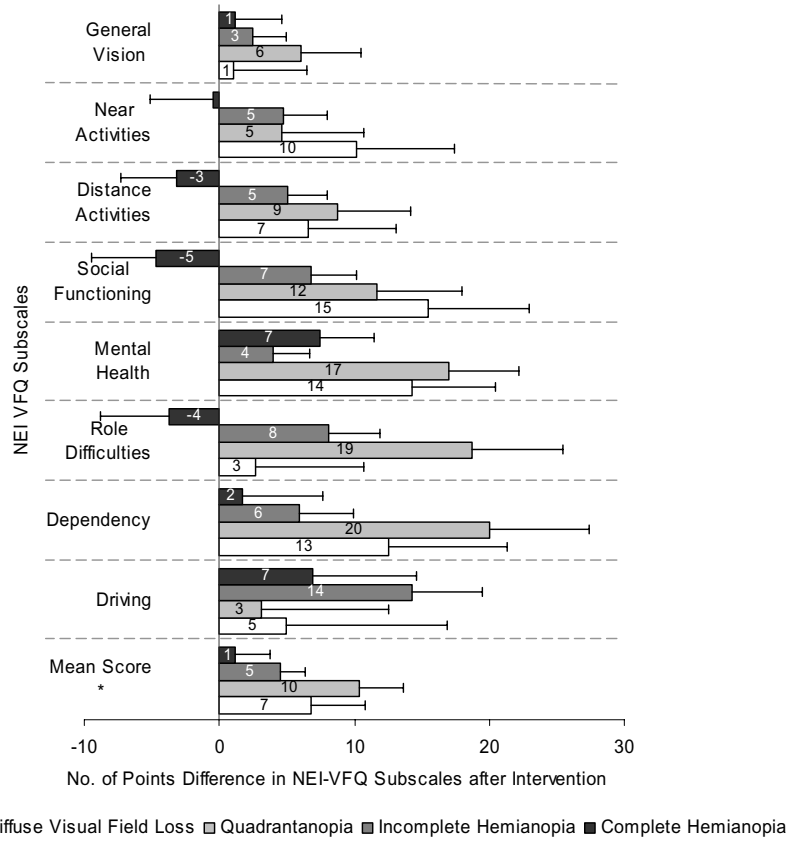

Fig. 3. Number of point differences in NEI-VFQ subscales according to the topography of the visual field defect. *The mean NEI VFQ score is based on 11 subscales without the general health rating.

tion time, while there was no significant correlation of *ocular pain* and reaction time prior to the intervention.

4. Discussion

This study was carried out to determine if "objective" changes of the visual field (perimetry results) after vision training result in subjective improvements measurable with the NEI-VFQ. We furthermore wished to learn whether the NEI-VFQ is a valuable measure of self-reported visual impairment in patients with visual field defects after cerebral damage because the questionnaire is not commonly used in this kind of patients.

Confirming previous observations it was found that NEI-VFQ scores were considerably lower in patients with visual field defects after cerebral damage than in patients with glaucoma or a reference population without visual field loss (Papageorgiou et al., 2007). In the present study poor functioning scores (<60) were found for *general health*, *general vision*, *role difficulties*, *driving* and *peripheral vision.* All of these scales (except *general health*) were significantly related to stimulus detection performance in the campimetric visual field test (Table 3). Scores indicating higher levels of functioning (>80) were found for *ocular pain* and *color vision* and were unrelated to stimulus detection rates. These unrelated subscales showed less differences to the scores of a disease-free comparison group (Fig. 1) than subscales related to visual field results (Mangione et al., 1998b). From these observations we conclude that (severe) visual field loss as measured by stimulus detection performance in campimetry is associated with diminished vision-related QoL which is in agreement with previous findings (Gall et al., 2008; Papageorgiou et al., 2007).

Both subjective QoL measures implemented in our study (vision-related NEI-VFQ and health-related SF-36) improved significantly after VRT. When QoL estimates were compared to objective changes in campimetric stimulus detection performance only differences in NEI-VFQ subscales were significantly related to

Table 3
Spearman Rank Correlations between results of the campimetric visual field test and NEI-VFQ Subscales

NEI-VFQ	Detected stimuli in %			Fixation accuracy in %			Reaction time in ms		
	Pre	Post	Diff	Pre	Post	**Diff**	Pre	Post	**Diff**
NEI-VFQ mean score of 12 subscales	0.22*	0.32**	**0.18**#	0.17	0.26*	**0.01**	−0.25*	−0.21#	**0.16**
NEI-VFQ mean score of 11 subscales without general health	0.23*	0.32**	**0.20**#	0.16	0.22*	**−0.03**	−0.24*	−0.24*	**0.14**
1. General health	0.02	0.13	**−0.06**	0.03	0.27*	**0.24***	−0.08	−0.17	**0.08**
2. General vision	0.27*	0.20#	**0.24***	0.24*	0.21#	**0.17**	−0.16	−0.17	**−0.06**
3. Ocular pain	0.09	0.07	**0.07**	−0.08	0.18	**0.00**	−0.04	−0.20#	**0.30****
4. Near activities	0.19#	0.28*	**0.22***	0.18#	0.36**	**0.14**	−0.07	−0.17	**0.14**
5. Distance activities	0.23*	0.31**	**0.24***	0.24*	0.27*	**0.02**	−0.17	−0.13	**0.00**
6. Social functioning	0.13	0.24*	**0.21**#	0.21#	0.24#	**−0.15**	−0.17	−0.10	**0.03**
7. Mental health	0.15	0.21#	**−0.08**	0.21#	0.14#	**−0.03**	−0.19#	−0.04	**0.11**
8. Role difficulties	0.13	0.28*	**0.15**	0.13	0.20#	**−0.00**	−0.25*	−0.27*	**0.13**
9. Dependency	0.26*	0.21#	**−0.05**	0.22*	0.20#	**0.03**	−0.29**	−0.04	**0.11**
10. Driving	0.33**	0.25*	**0.22***	0.03	0.07	**−0.15**	−0.25*	−0.24*	**−0.09**
11. Color vision	0.06	0.06	**0.02**	0.23*	0.38**	**−0.05**	−0.09	−0.13	**0.09**
12. Peripheral vision	0.17	0.30**	**0.20**#	0.01	−0.06	**−0.13**	−0.22*	−0.23*	**−0.09**

Correlations were performed separately for the pre and post data sets (NEI-VFQ results at baseline/after treatment correlated with campimetric results at baseline/after treatment) and for the post minus pre data set (Difference of post minus pre data sets for NEI-VFQ and campimetric results were correlated). Significance levels of two-tailed spearman rank correlations as follows: $^{*}p < 0.05$, $^{**}p < 0.01$, $^{\#}p < 0.10$.

such detection changes: the greater the improvements of detection ability, the higher the score differences in the NEI-VFQ (i.e. subjective improvements in vision-related QoL). However, correlations between areas of unimpaired vision in the affected hemifield and NEI-VFQ scales were found to be slightly stronger using kinetic perimetry results (Papageorgiou et al., 2007). This indicates that correlations of NEI-VFQ results with perimetric information may depend on the perimetric strategy. Therefore, also the ability of the questionnaire to detect changes in objective visual field results may be influenced by the kind of visual field test (e.g. campimetry vs. perimetry, supra-threshold vs. super-threshold strategy, static vs. kinetic testing). In contrast to the NEI-VFQ, the SF-36 which is commonly used in stroke patients (e.g. Almkvist Muren et al., 2008) may reveal improvements in general health estimates but was not sensitive to changes in the degree of visual impairments.

Subjective treatment effects were already shown with vision-related QoL measures for different ophthalmic diseases. Franke et al. (2003) compared the NEI-VFQ scores in 102 cataract patients with impaired visual acuity before vs. after surgery. They found significant improvements of more than five points in 9 out of 12 NEI-VFQ subscales, i.e. *dependency*, *ocular pain*, *social functioning* and *color vision*. More than 10 points differences were observed for the *general vision* score, *near activities*, *distance activities*, *mental health* and *peripheral vision*. In the present study NEI-VFQ differences exceeding ten points were found only for the *driving problems* subscale. More than five point differences were documented for *vision-related mental health symptoms*, *vision-related role difficulties* and *dependency on others* as well as *driving problems*.

Our results should be interpreted with some caution because the present data were mostly collected from a clinical sample. Only a small number of patients were part of a formal study with rigorous experimental design. The study protocol included only one treatment group with no control group. The patients were highly motivated to do well in the tests after having committed a lot of effort and time into the training. It is therefore difficult to distinguish between placebo effects and intervention-based changes. All visual function questionnaires are susceptible to such placebo effects. In future research, a control group would certainly provide more reliable information about the underlying character of the observed vision-related changes of QoL. Furthermore, most researchers and clinicians would agree that patients may overestimate their visual abilities immediately after completion of therapy, no matter what the nature of the treatment was. However, since visual fields were trained for longer periods of time in an outpatient setting it may be assumed that patients were able to adapt their QoL constructs during the course of treatment.

Observed vision-related QoL changes and their relationship to treatment-induced visual field changes also have to be interpreted carefully as the study sample was quite heterogeneous in terms of their medical history. Correlations of stimulus detection increases and NEI-

VQ scales suggest that both are related and not the mere result of an experimental bias. Nevertheless, it should be kept in mind that several factors may have influenced the kind of relationship between QoL and visual field defects which have not been studied in detail. For example, the time since lesion of about one-third of the patients was below six months. It is known that most of the spontaneous recovery in patients with acute visual field defects occurs in the first few weeks or months (Zhang et al., 2006) and most of our patients were well outside this time window. Still, we can not determine the influence of spontaneous recovery effects but the likelihood is very small that they alone would explain the therapy outcome. In fact, in a previous study it was shown that results of vision restoration training did not differ between groups with lesion ages under vs. above 12 months (Mueller et al., 2006). Secondly, the etiology of the patients was quite variable, and it is very likely that patients with cerebral lesions suffered from additional cognitive impairments besides visual field defects. These could have interfered with their rating behavior. In summary, while a clinical sample clearly has experimental flaws, a clinical observational sample still has a scientific value in its own right. Despite the limitations of study design, our results indicate that VRT not only improved visual field sizes but also improved associated subjective visual functions.

The finding that the general health score in patients with visual field defects after cerebral damage was lower than in patients with glaucoma or healthy subjects indicates that this patient group may have suffered from non-visual conditions that have limited their subjective general health ratings. Anosognosia which limits the self-rating reliability of QoL-questionnaires can be excluded to some extent in the studied sample because each treated patient was highly motivated to complete the treatment and most likely well aware of the visual field defect.

It was shown previously that the relationship between visual field defects and subjective improvement after intervention is rather complex, with one important factor to approach this topic being the topography of the visual field defect (Mueller et al., 2003). Descriptive differences in changes of NEI-VFQ subscales were found between visual field defects of different topographies. In patients with complete hemianopia who show an abrupt transition between intact and defect parts of the visual field decreases or only small increases of self-evaluated vision-related QoL were found in some scales. In contrast, patients with incomplete hemianopia and gradual transitions between the intact and defective part of the visual field showed larger subjective improvements. When the sample was divided into these subgroups the number of patients remaining in each group was limited. Therefore, these results could only be descriptive to show some trends (Fig. 3).

Whether vision is disturbed in one eye or in both eyes has a major influence on subjective vision (Varma et al., 2006). However, in the present study patients with binocular visual field defects did not show worse NEI-VFQ scores compared to the small number of patients with monocular visual field defects.

To study further the relationship of the impact of vision-related changes after intervention into the patient's daily life, and for validation of our findings, other functions such as driving skills, orientation or mobility (e.g. navigation in a labyrinth) should be evaluated using objective performance tests. Another potential limitation of the study is that analyses were not adjusted for other measures of visual function such as visual acuity which is probably the most important one (Franke et al., 2001). Other uncontrolled factors were intraocular pressure, contrast sensitivity, glare sensitivity and stereo acuity.

Increases in self-evaluated ocular pain were positively correlated with increases in reaction time indicating a possible side effect of intensive visual training but since there is no proven causal relationship the correlation may also indicate the occurrence of ocular pain unrelated to the treatment (Table 3).

Many studies focus on change sensitivity of QoL measures after (ophthalmologic) interventions (e.g. Stelmack et al., 2002; Stelmack & Massof, 2007). To our knowledge the present study is the first one that systematically assessed QoL before and after intervention in patients with visual field defects that result from cerebral damage. The findings generally confirm previous observations of subjective improvements after visual stimulation but where no standardized questionnaire was given to the patients (Kasten et al., 1998; Julkunen et al., 2003; Sabel et al., 2004; Mueller et al., 2003).

The assessment of vision-related QoL provides a meaningful complement to objective visual field data. Findings from this study may help both patients and clinicians to be better informed about the impact of visual field loss on vision-related QoL. NEI-VFQ assessment may also help to weigh the risks (effort/cost) and benefits of interventions for specific conditions considering not only the psychophysical impairment but also its impact on vision-related QoL.

In summary, stimulation of the visual field by training led to improvements of vision-related QoL in pa-

tients with cerebral visual field loss. These subjective improvements were correlated with objective campimetry results. Changes of health- and especially vision-related QoL should be addressed in future vision rehabilitation studies since most previously published outcome studies have not included this information (Bouwmeester et al., 2007). Pre and post QoL measurement will enhance understanding of the clinical relevance of functional improvements after interventions such as vision training and may also help to predict subjective benefits that patients might expect from visual field restoration.

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