

## Vision restoration therapy after brain damage: Subjective improvements of activities of daily life and their relationship to visual field enlargements

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**Abstract** Patients with visual field deficits following stroke or neurotrauma can use vision restoration therapy (VRT) to increase their visual field size by about 5° of visual angle.<sup>1</sup> However, little is known about whether such visual field enlargements are relevant to visually guided activities of daily life. Specifically, we wish to know (1) if VRT affects activities of daily life (ADL) measures, and (2) to what extent any subjective changes correlate with quantitative measures of visual field enlargements. A retrospective analysis was carried out with data of 69 patients that had been interviewed after 6 months of VRT. Patient testimonials were analyzed post hoc and correlated with demographic status and pre/post VRT changes as measured by perimetric testing. As previously described, VRT significantly increased detection ability and most patients (88%) reported subjective benefits in ADL. A correlation analysis of quantitative parameters of visual field enlargements with subjective patient testimonials was performed. Significant correlation was found in the categories ‘carrying out hobbies’ ( $r = 0.360$ ) and for ‘general improvement of vision’ ( $r = 0.244$ ). A trend was evident for the category ‘reading’ ( $r = 0.215$ ). No correlation was found between visual field size improvements and ‘visual confidence/mobility’ and ‘ability to avoid collisions.’ Thus, visual field size appears only to be one, surprisingly minor, factor among others (such as temporal processing) determining subjective vision in brain damaged patients.

**Key words** Vision, visual field deficits, stroke, hemianopia, training

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**Introduction** Because brain damage is often accompanied by visual field defects (VFD), patients with stroke or brain trauma can be severely limited in their ability to see the world around them and thus are seriously impaired in the ability to participate in ADL. Typically, VFD are measured by perimetric procedures, but only few attempts have been made to specifically describe visually guided activities of daily life in such patients.

A review of 450 patients with VFD revealed that most patients reported (1) reading deficits, (2) impaired exploration, or (3) visual-spatial disorders. In a standardized questionnaire, 50–90% of the patients complained of subjective reading problems and 17–70% reported visual exploration deficits in daily life.<sup>2,3</sup> During earlier experiments,<sup>4–6</sup> we have made the clinical observation that patients who benefited from VRT, as defined by perimetric or campimetric methods, reported subjective improvements in activities of daily life. For example, they felt more comfortable walking on the street because they felt safer after VRT than before. Also, they were able to read the newspaper again. Interestingly, some patients with no evidence of improved visual field size (according to diagnostic testing), still reported subjective improvements in ADL. These results suggest that besides training-induced visual field changes other factors may play an important role in subjective ADL improvements after VRT.

When considering the current literature on glaucoma patients, the relationship between VFD and subjective measurements (as studied by different quality of life instruments) appears unclear.<sup>7–13</sup> Self-reports of vision-specific quality of life questionnaires are sensitive to visual field loss, but the precise relationship between VFD and subjective reports of ADL measures is not well understood. While some authors do find such a relationship,<sup>11,12</sup> others could not find a statistical correlation between both variables.<sup>10</sup> Thus, the current literature is ambiguous as to the causal relationship of perimetric VFD measures and visually guided ADL parameters.

To be able to gain a better insight into the relationship between quantitative (perimetric) and subjective parameters of visual dysfunction we now propose to manipulate perimetric measures of vision experimentally and then study the effects of this manipulation on subjective ADL parameters of vision.

Before considering this approach, the question arises whether the size of the visual field can be altered at all. Treatments for visual field defects have been largely unknown, and the widely held model of the visual system as ‘hard wired’ suggests that visual field enlargement is not possible. However, in the last two decades a new paradigm has emerged in basic neuroscience. According to the concept of ‘neuroplasticity,’ the visual system – like other functional systems of the brain – can adapt to lesions in a process of ‘self-repair.’<sup>14</sup> Numerous studies attest to this – receptive fields, the visual systems’ basic ‘building blocks’ – have a plasticity potential, – in that they can change their size and location in response to deafferentation.<sup>15–18</sup> Another indicator of plasticity is the ability of animals and humans to spontaneously recover from an acute central nervous system (CNS)-caused visual deficit in a few weeks and months following the damage.<sup>19,20</sup> Interestingly, the

brain shows a life-long plasticity which is not restricted by the end of development or spontaneous reorganisation processes after trauma or stroke. We also have observed earlier that visual field enlargements in post-chiasmatic patients after visual therapy are not related to the age of the patients or the age of the lesion, respectively (e.g., Poggel<sup>5</sup>).

We now propose to use plasticity as an approach to manipulate visual field (VF) size and then study the consequences on ADL. The tool to achieve a visual field size increase is the 'Vision Restoration Therapy' (VRT). This method has been established during the last decade in our laboratory based on the observation that repeated perimetry and training of the visual field border can lead to a 'border shift' in hemianopic patients.<sup>21,22</sup> Kasten<sup>23</sup> has adapted this training procedure to personal computers so that patients can train at home. After an initial pilot-study<sup>3</sup> we carried out a prospective, double-blind, randomized clinical trial with 19 patients who had sustained post-chiasmatic brain injury and with 19 patients with optic nerve injuries.<sup>4</sup> In addition to a quantitative assessment of the visual field using perimetric procedures, the patients were interviewed after completing 6 months of VRT. Of the patients receiving VRT, 72.2% noticed general subjective improvements whereas in the control group (eye movement / fixation training) only 16.6% reported such improvements.<sup>4,24</sup> However, despite lively discussions about the validation of VRT in the professional field,<sup>25,26,27</sup> VRT became an established method to alter visual field size in patients with post-chiasmatic lesions. Additional studies were subsequently carried out in our laboratory<sup>5,6</sup> and it was repeatedly noted that about 70% of the patients reported subjective improvements following 6 months of VRT. This was independently confirmed by Julkunen and colleagues,<sup>28</sup> who trained the VF of five patients. In that group, four patients also experienced subjective improvements. Despite these encouraging observations, a systematic pre-post training assessment focusing on daily living skills is still required. Furthermore, none of the previous investigators has yet correlated subjective improvements with measures of quantitative perimetry in a larger patient population.

Therefore, we conducted a retrospective study, evaluating patients with visual field deficits after they had performed a six months regimen of VRT. We are well aware that retrospective studies have both advantages and disadvantages. To analyze performance of patients that have undergone routine care does not have the same power as data obtained by prospective experiments. Retrospective studies carry a risk of experimenter and subject bias, and the lack of a placebo control group amplifies this concern. Yet, retrospective studies are valuable because large patient populations can be recruited in a much more efficient way which is less costly and less time-consuming. They also typically include patients with a large variety of disorders, various backgrounds, ages, etc., thus creating a large variability which more closely resembles the clinical experience. The inherent disadvantage of such a large variability is, at the same time, an advantage: if treatment effects are still found under such variable conditions, then the treatment effect is powerful. The retrospective view is thus closer to the clinical reality than clinical trials with tightly controlled, experimental conditions. Despite this argument, it is essential to validate retrospective data to document its credibility.

One way of validating retrospective data is to compare certain parameters (here, perimetric performance) with those of experimental, prospective studies. A retrospective study would be considered valid if the results are somewhat comparable to prior findings. In the context of the present study the question is: are VRT-induced visual field enlargements comparable to those found in the known prospective trials, such as those reported by Kasten et al.<sup>3,4</sup> or others? If they differ markedly, then one would have to be concerned about the validity of the retrospective results. If, on the contrary, the results are comparable, then they may be considered valid.

The goals of the present paper are (1) to replicate previous findings of visual field enlargements in context of a retrospective study design, (2) to discuss if, and to what extent, VRT can help patients to regain competency in visually guided ADL, and (3) by correlating perimetric changes with subjective ADL variables we hope to gain insight into the relevance of quantitative, perimetric parameters for every day vision as probed by subjective patient testimonials.

## **Material and methods**

**STUDY DESIGN** This study is a retrospective analysis of data obtained from patients that were seen at the NovaVision Center for Visual Therapy in Magdeburg, Germany during the period of 1998–2001. None of the patients was part of a formal clinical trial or any prospective study and patients were not recruited for the purpose of this study. The large majority, about 90% of the patients, had paid privately to receive VRT from the Center. It is therefore not possible to control to what extent the data are influenced by subjective variables such as treatment expectations by the patients or bias/expectation by the attending personnel at the NovaVision Center. Also, we could not fully exclude a sampling bias or ascertain a controlled and reproducible diagnostic assessment as typically found in the formal laboratory setting of a prospective clinical trial. However, the diagnostic methods were substantially equivalent to those used in our prospective clinical trials, thus permitting a direct data comparison for this validation. None of the personnel involved in the diagnostic testing were aware of the goals or the hypotheses of the present study. Thus, despite fundamental short-comings of a retrospective data analysis approach (such as a possible sampling bias), the power of this retrospective study is adequate because of the large patient sample and the quality control procedures used to assure reproducibility. In fact, from a statistical point of view, increasing the variance by the variations within the patient population would bias the data against any hypotheses. Furthermore, we believe that a detailed analysis of this patient population would reveal important insights and, for purposes of validation, permit us to compare the results of this retrospective study directly with the results obtained by the existing data from prospective trials.

**SUBJECTS, INCLUSION AND EXCLUSION CRITERIA** A total of 90 patients were considered for inclusion in the retrospective study, but ultimately a subset of 69 subjects met inclusion criteria as defined prior

to the analysis. Patient demographic data are as follows: 23 female and 46 male patients with an average age of 51.79 ( $\pm 17.12$ ) years. The visual field defects were either the result of post-geniculate lesions (45), optic nerve lesions (3), or resulting from both (1) as shown by CT, MRI, and surgical records. In 20 patients, the cause and location of the lesion could not clearly be identified because no brain imaging or surgical record was available. Still, the homonymous character of the VFD in most of these patients indicated cerebral involvement.

The causes of visual deficits in our patient population were vascular diseases (39), head injury (13), cerebral inflammation (2), tumor (8), hypoxia (1), and other (6). The corresponding VFDs were: complete hemianopia (25), incomplete hemianopia (22), quadrant hemianopia (10), scotoma (3), tunnel vision (1), and diffuse visual field defect (8). Patients showed either homonymous (52) or heteronymous visual field deficits (17). Prior to training, all patients received an ophthalmologic examination. Patients were informed that some conditions are considered as contraindications for the VRT training (e.g., nystagmus), but they decided to train with VRT anyway (6). Patients with epilepsy or photosensitivity were generally not admitted to the therapy since these conditions were strict and standard exclusion criteria. Many of the patients in our sample had some cognitive deficits, though not all patients were assessed formally for cognitive dysfunctioning during initial screening prior to training.

Most patients performed their training binocularly; 4 patients trained monocularly, with the left and the right eye separately. In these patients results of the both eyes were averaged to one result per patient. The overriding criterion for inclusion in the study was the availability of a complete data set of perimetric and campimetric results together with the availability of a post-training interview (see below). Many patients were thus excluded from the retrospective analysis because they did not show up for the final examination. Though we can not exclude the possibility that the no-show possibly relates to lack of VRT effect in some cases, the reasons given by the patients or their care-givers were mostly related either to long travel distance, additional diseases making travel or training impossible, or death.

**DIAGNOSTIC EVALUATION** Before and 6 months after VRT the size of the visual field was assessed binocularly with High Resolution Perimetry (HRP) using the NovaVision status program ([www.novavision.info](http://www.novavision.info)). In addition, a monocular visual field evaluation was carried out with 90° perimetry using the Rodenstock Perimat 206.

### *HRP*

**Description:** HRP was carried out in a darkened room in front of 17" screen, which covered a 54° region of the visual field. To reduce head movements a chin-rest was used. As previously described,<sup>29</sup> patients had to fixate a static point located on the computer screen throughout the diagnostic session. Fixation was ascertained by requiring patients to press a button on the keyboard whenever the fixation point changed colors. Patients had to press the keyboard whenever a stimulus

appeared anywhere in their visual field. This test was repeated up to 5 times. We included patients who had a minimum of three completed tests at baseline and post VRT. Tests were superimposed in order to be able to define areas of residual vision (ARVs).<sup>4,24</sup> This method involves the presentation of visual stimuli on a computer monitor. The target stimuli are presented with a relatively high resolution. The resolution is higher because HRP presents 474 stimuli vs. only 205 stimuli are presented in the Rodenstock perimetry in a 90° area of the visual field. The visual stimuli to which patients have to respond are well above threshold. Here, no threshold testing is performed. In the HRP, repeated measures can be superimposed to specifically quantify areas of residual vision (ARVs) which are graphically represented in grey. Such areas are characterized by the fact that patients detect a minimum of one, but not all, presented stimuli at a certain position. Because the stimulus presentation is well above threshold, the task itself is usually easier than testing at near-threshold (as in conventional perimetry). The target stimulus is usually white on a black background.

**Data analysis:** The most appropriate way to analyze HRP data is to count the number of ‘hits’ (i.e., correct responses) because performance in the areas of residual vision is best represented by the counting of hits. Though absolute values can be used for data analysis, percent-values are typically used because the computer monitor covers only a portion of the visual field. If one were to use absolute number of hits as a measure, one would risk artifact because this absolute number depends on how many stimuli the program is set to present and how much of the deficit is represented on the screen (which depends on the position of the fixation point). Consequently, percentage of hits facilitates comparison between patients and is less prone to artefact. It properly represents HRP-performance and is therefore the better measure for within and between patient analyses. If only the number of absolute reactions were calculated for HRP, this would artificially induce variability between patients. HRP was chosen as the first outcome parameter, because of its high resolution character.

#### *Conventional threshold perimetry*

**Description:** Static conventional threshold perimetry was assessed monocularly with 90° perimetry using the Rodenstock Perimat 206. This method involves the presentation of visual stimuli inside a hemispheric dome. The target stimuli are presented at a relatively low resolution (lower than in HRP, see discussion above). The stimuli are presented in different intensities to determine the near-threshold value in a staircase fashion. Thus, stimuli are usually near threshold. The near-threshold target stimuli are presented only once per location of the visual field, unless the patient does not respond to them. If the latter happens, the stimulus is presented again with greater luminance until the patient responds to it. If the patient does not respond even at the highest luminance level, the location is defined to be blind. The threshold perimetry does not permit the repeated presentation of super-threshold stimuli. The sessions with threshold perimetry do not

consistently employ identical stimuli (as does HRP). Rodenstock Perimat 206 uses a simple detection task at the fixation spot that the patient has to respond to (by pressing a button). In addition, the clinician can judge by looking at the eye-images whether the patient actually fixated or not. If the clinician notices fixation or eye movement problems, the respective region in the visual field is reevaluated.

**Data analysis:** Threshold perimetry analyses the number of hits and the number of misses. In contrast to the HRP, data analysis is based on the number of 'misses.' The advantage of the number of misses is that in areas of residual vision (ARV) the patient shows more misses depending on the integrity of the area. Areas with good function have fewer misses than areas with more impaired function. However, if one were to take number of hits as an outcome measure for threshold perimetry, areas of relative defects would always be represented by a 1 because the staircase method stops testing in this location as soon as the patient answers correctly, irrespective of the luminance of the stimulus. Consequently, unlike in HRP, the number of misses in threshold perimetry represents the 'relative defect' more adequately than the number of hits.

**TRAINING PROCEDURE** Vision Restoration Therapy (VRT) was carried out using the NovaVision program 'Progress.' Patients performed the training program at home, using a conventional PC, twice a day for about 30min for a total duration of 6 months. In VRT, visual stimuli are systematically presented in areas of residual vision which are typically located between the intact and the damaged area of the visual field. The stimulation occurs systematically within these areas. As in the diagnostic sessions, fixation is controlled via a fixation point where the patients had to respond to the color of the fixation point changing. For detailed description of the training program see Kasten et al.,<sup>4,24</sup> Poggel.<sup>5</sup>

**SUBJECTIVE MEASURES OF ACTIVITIES OF DAILY LIFE** After the 6-month training period, all patients were given a standardized post-training semi-structured interview with questions probing their subjective visual experience after training. The interview is originally based on a questionnaire for the subjective assessment of cerebral visual disorders as published by Kerkhoff.<sup>30</sup> which has been adapted and considerably expanded for posttherapy assessment of patients with visual field defects. The questions were designed to probe for any subjective changes the patients had noted in visually related tasks by comparing their subjective vision before starting the VRT training to that at the time of the interview (after VRT). The patients had therefore to rely in part on their memory and make comparisons of the two time-points with a 6-month interval between them. The questions were given orally and the oral responses were recorded.

The patient testimonials were summarized by assigning specific answers to one of 5 of the following categories: (1) general (non-specific) improvements of visual functions, (2) visual confidence and mobility, (3) reading ability, (4) collision with objects or people, and (5) improvements in individually important activities (hobbies). For each

patient we counted the number of categories where changes were noticed and subsequently analyzed how many patients named at least one category of subjective improvement. Note that the categories were designed on a content-basis and not based on a statistical factor-analysis.

**STATISTICAL ANALYSIS** We correlated the subjective ADL-scores with VRT training outcomes as defined by perimetric and campimetric measures taken at baseline and post-training. ADL was also correlated with demographics of patients from a retrospective study (in part published by Mueller et al.,<sup>31</sup> Kenkel et al.<sup>6</sup>). Results were assessed calculating Spearman's  $\rho$  with SPSS 11.0 software. Training results were calculated with t-test for paired samples, and group differences of patients who report improvement versus patients who don't report improvement with Mann-Whitney-U-Test for unpaired samples. Significant differences are shown as comparison between groups:  $p < 0.05$ ,  $p < 0.01$ ,  $p < 0.001$ , trend of  $p < 0.10$ .

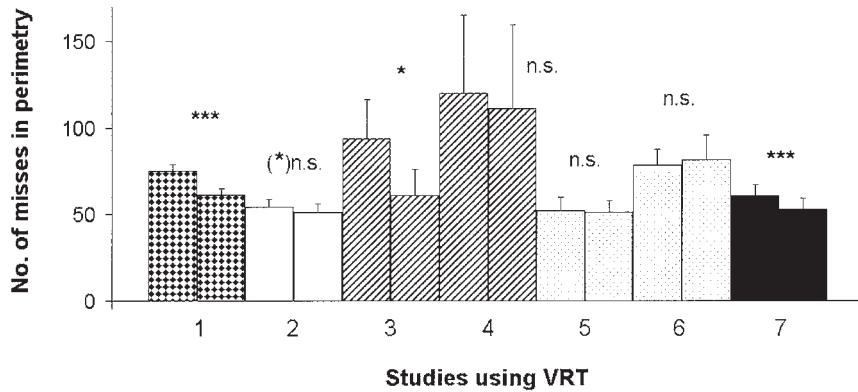
## Results

**VALIDATING RETROSPECTIVE RESULTS BY COMPARISON TO PROSPECTIVE STUDIES** In order to validate the retrospective study, we compared our campimetric findings with the data obtained by our prospective clinical trials which were essentially identical. Perimetric methods varied between the different studies. In this retrospective study the Rodenstock Perimat was used, while in previous experimental studies the Tuebinger Automatic Perimetry (TAP, Oculus) was used. The two perimetric measures vary in their luminance and threshold, but because we simply sought to document a change in the size of the VFD, a comparison between the two devices is acceptable. We reasoned that if the effects of VRT as seen in the present retrospective study were comparable with previous prospective studies, this would validate the retrospective approach.

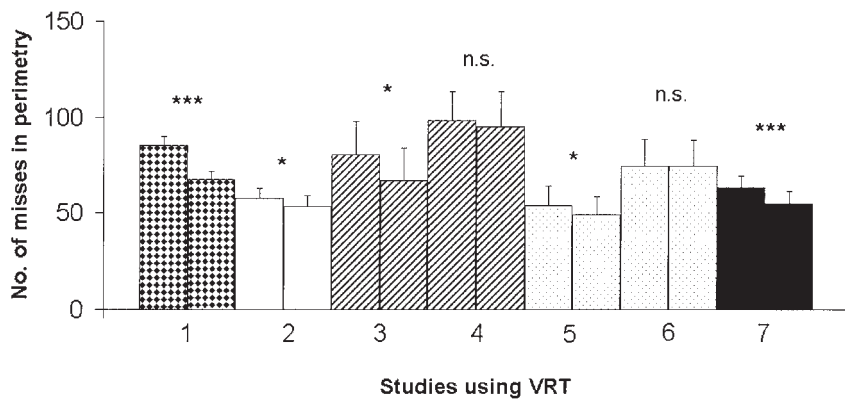
In the Rodenstock perimetric measurements the retrospective analysis revealed a decrease in the number of undetected light stimuli ('misses') from 44.64% ( $\pm 18.97$ , mean  $\pm$  SD) to 37.14% ( $\pm 17.86$ ) in the right eye ( $t = 5.68$   $p < 0.001$ ) and from 49.79% ( $\pm 21.49$ ) to 41.59% ( $\pm 20.83$ ) in the left eye ( $t = 5.27$   $p < 0.001$ ). In the HRP-tests most patients also experienced a visual-field enlargement with a mean increase in stimulus detection rate (hits) from 51.71% ( $\pm 16.08$ ) before VRT to 61.60% ( $\pm 17.58$ ) after six months of training, which was a significant increase ( $t = -6.93$ ,  $p < 0.001$ ).

The comparison of these results with other studies is displayed in Figures 1-3. Figures 1 and 2 show the percentage of misses in the left and the right eye in perimetric measurements and Figure 3 shows the change of detection in HRP in several different experiments before and after VRT. It demonstrates that the original size of the deficits are roughly comparable between all studies. Poppel's studying the effects of attention in patients after brain damage, as well as the 'Tuebingen trial,' examining 16 hemianopic patients before and after VRT,<sup>32,33</sup> showed a significant gain of visual field size after VRT. The study with post-

### Perimetric results right eye



### Perimetric results left eye



### VRT outcome in HRP

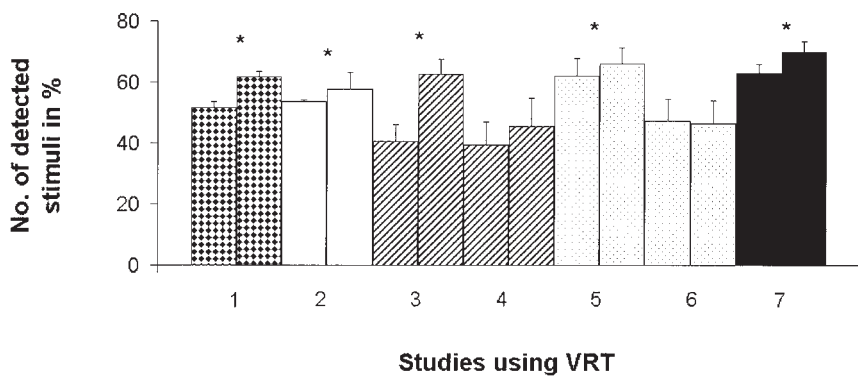


Fig. 1. Perimetric results pre- and post-VRT of patients as obtained in different, independent studies. These studies were: 1 = present study, 2 = Attention trial (Poggel 2002<sup>3</sup>), 3 & 4 = Optic nerve patients; with treatment group (3) and placebo group (4; Wuest, 1997,<sup>34</sup> Kasten et al. 1998a<sup>4</sup>), 5 & 6 Post-chiasmatic patients; with treatment group (5) and placebo group (6; Kasten et al., 1998a<sup>4</sup>), 7 = Tuebinger trial with patients with post-chiasmatic lesions (Kasten et al., 2002,<sup>33</sup> Sabel et al., 2002<sup>32</sup>). The graphs display number of misses in Tuebingen Automatic Perimetry in the right eye only. Note that the right eye was always tested first.

Fig. 2. Same as in Fig. 1, but for the left eye only.

Fig. 3. Summary of prior studies with regard to performance in HRP before and after a 6-month VRT training period. The number refer to the same studies as described in Fig. 1.

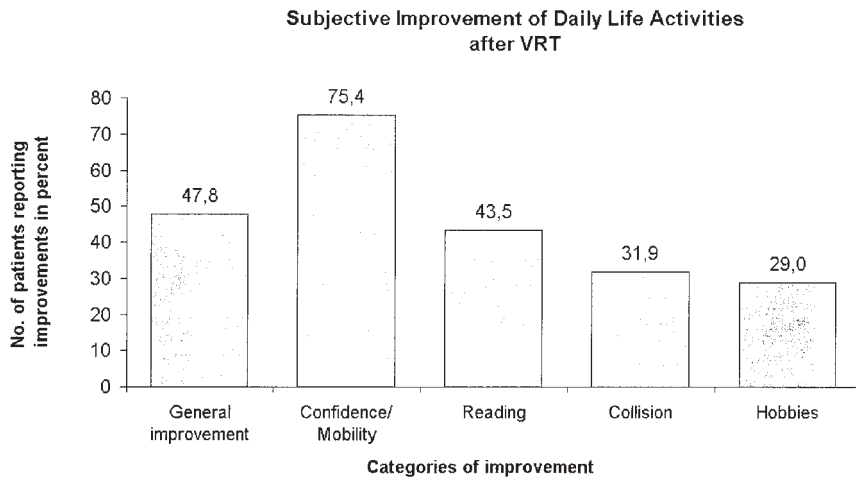
chiasmatic patients, however, failed significance, but a trend exists for enlarged VF after VRT.<sup>4</sup> Optic nerve patients have generally been shown to benefit more dramatically from VRT than patients with post-chiasmatic injury.<sup>34</sup>

**DISTRIBUTION OF SUBJECTIVE ADL IMPROVEMENTS** As one would expect, the subjective reports vary considerably between sub-

TABLE I. Individual testimonials of subjective improvements by patients after Vision Restoration Therapy.

- 
1. *Category 'General Improvement'*
    - 'I perceive much more light in my lower visual field.'
    - 'Visual ability of left eye improved by 30 percent, said eye doctor.'
    - 'Spatial vision is better.'
    - 'I have gained visual field, where I can see colours and contours just like in healthy times.'
    - 'I am able to see in the central visual field again.'
    - 'Perceives a little more in the defect visual field.'
    - 'The pictures have become less distorted, are calmer now.'
    - 'Left side has become brighter.'
    - 'I am able to see in the upper left quadrant, still problems in lower left.'
  2. *Category 'Confidence and mobility ability'*
    - 'During daytime I can drive my car again.'
    - 'Better orientation in new environments.'
    - 'More overview outside.'
    - 'I feel more self reliant, therefore I can walk around much more.'
    - 'Better orientation.'
    - 'Visual defect has no impact on daily life activities any more.'
    - 'Feel more confident in cycling.'
    - 'Orientation is better.'
  3. *Category 'Reading'*
    - 'I can read better.'
    - 'I can read and write again.'
    - 'I can find the beginning of the line much easier.'
    - 'Nearly no problems with finding the end of the line any more.'
    - 'I do not write beyond the edge of the paper any more.'
    - 'Much better reading, had nearly given up reading at all before training.'
    - 'No difficulties with reading any more, finding of beginning of line is easy now, very seldom missing of next line.'
  4. *Category 'Collisions with objects or people'*
    - 'Less collisions with objects or people.'
    - 'Less collisions with people.'
    - 'Does not bump into obstacles left side, does not get caught on the left side any more.'
    - 'No collisions with doors and walls any more.'
  5. *Category 'Hobbies or improvements in individually important activities'*
    - 'I can work in the garden again, I can differentiate my garden plants from weeds.'
    - 'Being an accountant, I can fill in a tax declaration or an application form again and help my wife with this.'
    - 'While watching TV, I do not miss the upper right quadrant any more.'
    - 'Before training I did not dare to go skiing and I found I am able to do it again.'
    - 'Does not avoid eating in the restaurant any more, before he used to push the food from the plate (spouses comment).'
    - 'I am able to shave on my own again.'
- 

jects. Table 1 displays a list of different examples of patient testimonials. There is a large variety of different ways in which patients have experienced changes in the visual abilities in every day life. Because of the very specific details of most examples it is not likely that patients



*Fig. 4.* Analysis of subjective ADL improvements. Patients were asked in the postVRT interview if they noted any improvements in the due to VRT. The graph displays the number of patients in percent that did notice improvements in the various response categories.

were trying to impress the interviewer with enthusiastic reports. Rather, the nature of the changes and their corresponding visual field enlargements match in many cases and are highly specific. This argues for the credibility of their testimonials.

We have summarized the subjective reports of all patients and found the following results: 47.8% (n = 33) reported general improvements of vision, 75.4 (n = 52) reported increased visual confidence and mobility after VRT, 43.5% (n = 30) mentioned that they could read better after training, 31.9% (n = 22) improved in avoidance of collisions with people or objects, and 29.0% (n = 20) resumed old hobbies again (Fig. 4). Of all patients, only 11.6% did not notice any change in subjective vision, 15.9% noticed improvement in one category of visual improvements, 31.9% in two categories, 23.2% in three categories, 8.7% in four categories, and 8.7% in all five categories (see Fig. 5). Thus, 88.4% (n = 61) of all patients reported improvements in at least one category.

**DEMOGRAPHICS AND ADL IMPROVEMENTS** By performing a correlation analysis of ADL improvements and demographic data we wished to determine to what degree factors such as age, type of lesion, and gender influence the extent of subjective improvements following VRT. Hardly any correlation was found between categories of ADL-improvements and demographics. Only age demonstrated a relationship with hobbies ( $r = 0.292^*$ ). This would suggest that older patients mentioned an improvement in hobbies more often than younger patients. This was surprising taking into consideration that age has little influence on perimetric improvements and, if any, such improvements decrease slightly with age. Thus, there is some mismatch between perimetric and subjective measures. Time since lesion correlated with reading ( $r = 0.255^*$ ) and hobbies ( $r = 0.272^*$ ), and a trend was evident for number of named ADL categories ( $r = 0.230^*$ ). The unexpected finding that the older the lesion the greater the subjectively reported improvements indicates that patients with older lesions might be more sensitive to VF changes due to VRT. There was no correlation between the parameters 'type of lesion' and 'number of ADL categories named.'

Fig. 5. This graph shows the extent of subjective improvement following VRT in terms of the number of ADL categories where the patients noticed changes. 11.6% of the patients did not notice any change. Most patients (31.9%) reported subjective improvements in 2 categories and 8.7% benefited from VRT in all categories.

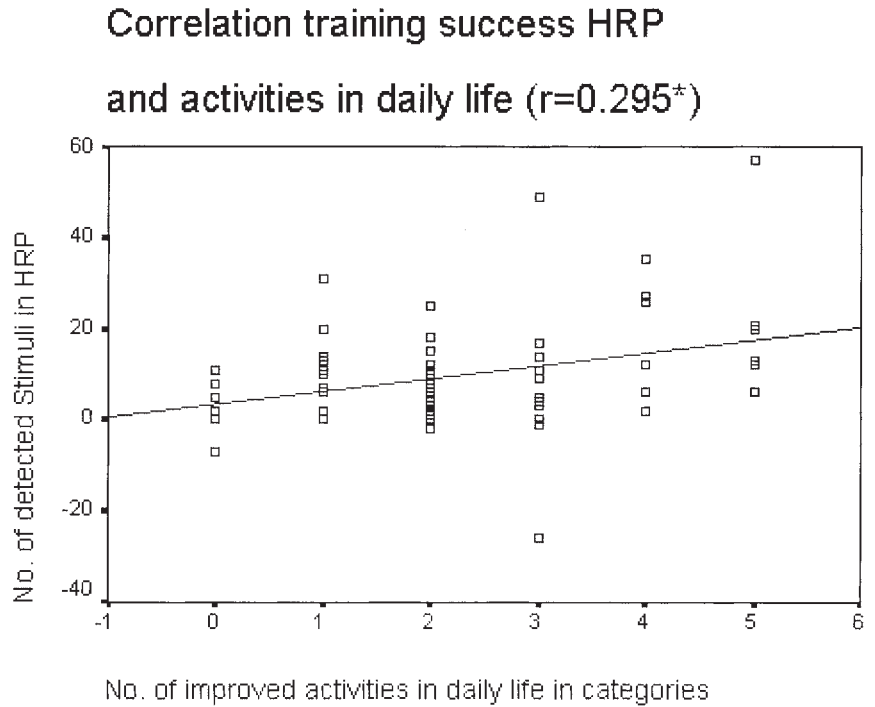
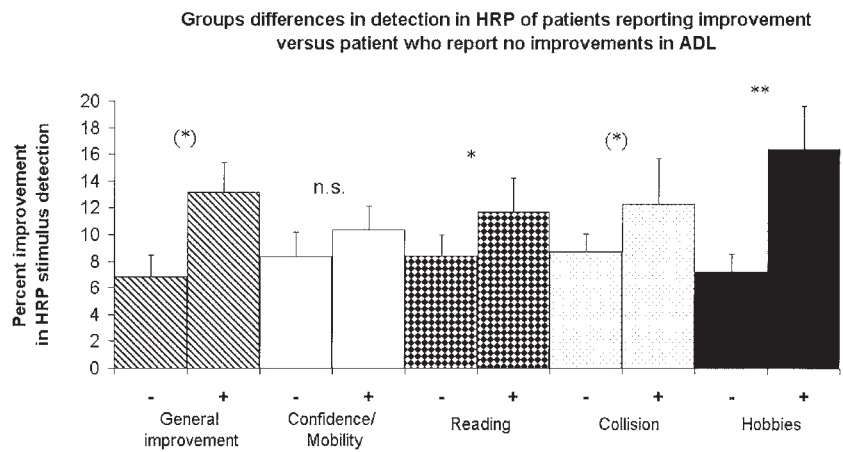
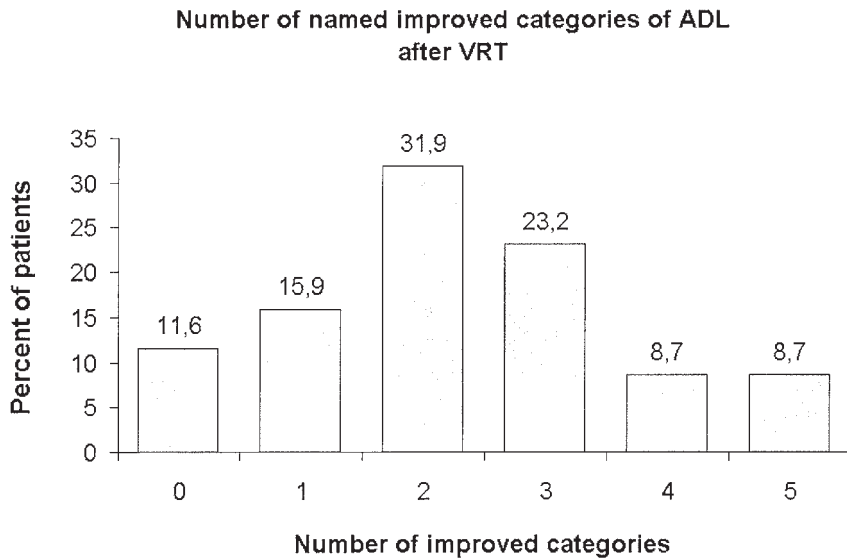


Fig. 6. Training success as measured in number of more detected stimuli in HRP after VRT is significantly correlated ( $r = 0.295^*$ ) with activities in daily life (in number of categories) as assessed in patients report.



Also, no correlation was found between number of named ADL categories and gender; however, we found a small correlation of gender with certain ADL categories: males had greater benefits in visual confidence and mobility ( $r = 0.262^*$ ) and females were more likely to profit from VRT by being better able to avoid collisions with objects or people ( $r = -0.220^*$ ).

RELATIONSHIP OF TRAINING OUTCOME AND ADL CATEGORIES  
A significant correlation was found between HRP improvement after VRT (number of hits in HRP) with hobbies ( $r = 0.360^{**}$ ), general improvement of vision ( $r = 0.244^*$ ) and number of named improved categories of ADL ( $r = 0.295^*$ ). A trend was evident for reading ( $r = 0.215^*$ ) (Fig. 6). However, we did not find any correlation between number of hits in HRP with the category visual confidence/mobility or



*Fig. 7.* Group differences in stimulus detection in HRP of patients who did or did not report subjective improvements. Except in the category “confidence/mobility” and the category “collision” the group of patients with subjective improvements also had significantly more detections. This indicates that visual field enlargements (improvements) do contribute in part to the subjective changes noted by the patients.

the ability to avoid collisions. Apparently, visual field size changes and visual confidence/mobility and ability to avoid collisions are unrelated. We also compared the number of hits in HRP after VRT with patients who reported improvements versus patients who did not report improvements (Fig. 7). Significant correlation between improved and not improved patients was found in the categories hobbies ( $Z = -2.96$ ,  $p < 0.003^{**}$ ), general improvement of vision ( $Z = -2.01$ ,  $p < 0.044^*$ ) and general improvement of vision ( $Z = -2.01$ ,  $p < 0.044^*$ ). A trend between improved and not improved patients was evident in reading ( $Z = -1.77$ ,  $p < 0.076^*$ ). No group differences were found between groups in the categories confidence/mobility and collision.

When correlating the monocular perimetric measures with ADL outcome, only the number of reduced misses (in %) in the left eye correlated significantly with improvements in the category hobby ( $r = 0.317^*$ ). Hence, ADL improvements seem to become more visible in correlation with binocular visual field measures, for example, HRP than in monocular measures.

We have previously reported that VRT may also reduce reaction time of stimuli detection in campimetric measures.<sup>5,31,35</sup> We therefore also compared the improvements in reaction time in HRP after VRT to ADL and related that to whether patients reported improvements or not in the ADL categories. The differences in response time improvements between groups in the category ‘general improvement’ was on average about 40ms, results are highly significant ( $t = -2.72$ ,  $p < 0.008^{**}$ ). In the other ADL categories the calculation of group differences was not significant.

**CORRELATION OF ADL CATEGORIES WITH MONOCULAR 90° PERIMETRIC AND BINOCULAR HRP RESULTS AT BASELINE AND POST VRT**  
 The number of detected stimuli in binocular perimetry at baseline and ADL categories were not correlated at all. Performance in monocular perimetry was calculated by counting the number of detected stimuli and relative defects found in 90° perimetry testing (as

TABLE 2. Perimetric results in number of detected stimuli and relative defects in absolute numbers at baseline and post training correlated with ADL improvements. OD = Right Eye, OS = Left Eye.

	<i>General improvement</i>	<i>Confidence/Mobility</i>	<i>Reading</i>	<i>Collision</i>	<i>Hobbies</i>
Baseline	No. hits OS $r = 0.282^*$	No. hits OS, $r = -0.308^*$	n.s.	n.s.	n.s.
Post	n.s.	No. hits OD, $r = -0.350^*$  No. hits OS, $r = -0.323^{**}$	n.s.	n.s.	No. hits OS, $r = 0.278^*$

stated in absolute numbers). As Table 2 shows, subjective improvements after VRT in the category ‘visual confidence/mobility’ showed a negative relationship with the VFD size before training. That is to say, patients with greater amounts of field loss before training reported less improvement in visual confidence after training. On the contrary, intact visual field size before VRT correlated positively with improvements in the category ‘general improvement.’ However, this was just the case for results for the left eye, but not for the right eye.

After training, the size of the baseline field loss correlated negatively with confidence/mobility but positively with hobbies. Correlation between monocular perimetry, and binocular campimetry and ADL categories was not significant.

**ANALYSIS OF SINGLE CASES** We carried out a single case analysis to evaluate whether or not HRP results and ADL measures match. Theoretically, different scenarios are conceivable: a patient with HRP-improvement should notice changes in ADL while a patient without perimetric change should have no ADL change. However, if both parameters do not strictly relate to each other, then it would be conceivable that a mismatch occurs with positive HRP results and negative subjective results after VRT or vice versa. As the following single case analysis revealed there are many ‘matching’ cases where the campimetric result and the subjective results covary. Surprisingly, there is also a considerable number of mismatch cases as Figure 8 shows the superimposed results in HRP before and after VRT of four selected single cases.

*Matching cases* Patient B.D. is an example of a case where VRT training produced visual field enlargements and corresponding ADL improvements. This patient suffered from homonymous hemianopia to the left after stroke (infarction of anterior communicating artery one year prior training). B.D. was 66 years-old when starting VRT. After stroke and before training he reported that he would bump into objects once in a while. After VRT he reported that his visual field was enlarged, that he would see better, and that he felt more secure in daily life. He reported that he bumped into objects (e.g., into door frames) less frequently and that his reading had improved.

Patient S.F. is a 36-year-old male with a VFD in the upper left quadrant. He started training 8 months after stroke. S.F. is a case with no

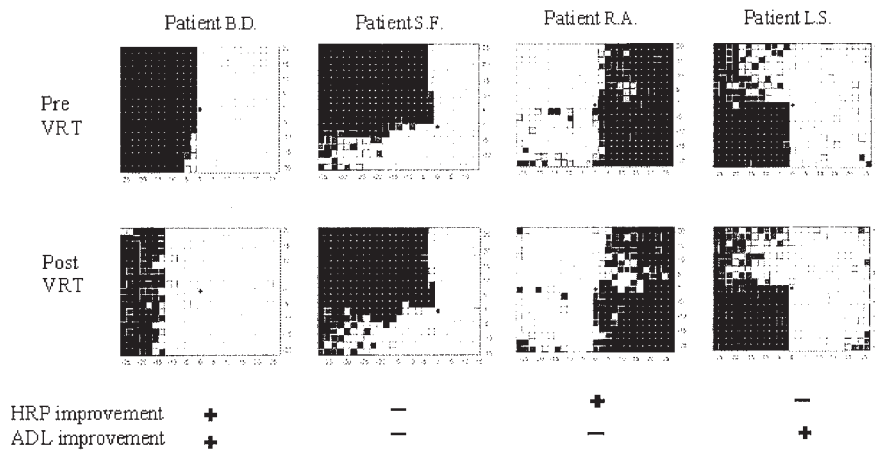


Fig. 8. Superimposed results in HRP before and after VRT and references regarding training success (HRP +) or no training success (HRP -) and improvements in ADL (ADL +) or no improvements (ADL -). Results are shown from the four single cases; Patient B.D. and L.S. are matching cases, whereas patient S.F. and patient L.S. report of subjective improvement of ADL and HRP results don't match.

improvement in HRP and also no improvement in ADL after VRT. Therefore, both parameters match.

*Mismatch cases* Patient R.A. is a 32-year-old mechanic, who suffered a polytrauma with head injury and underwent surgery for removal of an epidural hematoma. He was blind in his left eye afterwards and suffered from an incomplete hemianopia to the right in the right eye. One year after the lesion, R.A. commenced with VRT (monocular training with the right eye) and achieved a >5% VF increase in HRP but did not notice any subjective improvements in ADL. At post-diagnostics, he was not aware of any subjective improvement even when prompted.

Patient L.S. is a 38-year-old accountant who suffered from a homonymous incomplete hemianopia after a car accident 14 years earlier. Here, VRT produced no perimetric improvement but she noticed clear subjective improvement of ADL. She reported that VRT had improved her 'general vision' in the upper left quadrant and that her reading had improved, (e.g., that she finds the beginning of a line right away). Statistically she showed no improvement in HRP after VRT. Thus, perimetric and subjective results do not match; quite the opposite of patient R.A.

Thus, as in previous studies, we found cases in our patient sample from the following categories: patients benefiting from VRT perimetrically, but not reporting subjective improvements in ADL and patients not showing visual field improvements but still reporting improvements in activities of daily life. To get a better understanding on the number of such matches vs. mismatches, we counted the number of patients (A) reporting improvements in both perimetry and ADL or (B) no improvements in either one of these parameters (matches), (C) patients with perimetric improvements but no ADL change, or (D) patients without perimetric improvements but with ADL improvements.

Table 3 shows the number of matches and mismatches in relation to whether or not patients experience ADL improvements. It is evident that the match/mismatch ratio varies if one chooses different criteria for HRP-improvement. For patients with ADL improvements a more 'liberal' criterion for perimetric success (>1% or >3% improvement)

TABLE 3a-c. Number of patients reporting improvements of ADL in relation to training outcome in HRP.

<i>1% criterion No. patients</i>	<i>ADL+</i>	<i>ADL-</i>	<i>Sum</i>
HRP +	54	5	59
HRP -	7	3	10
Sum	61	8	69
<i>3% criterion No. patients</i>	<i>ADL+</i>	<i>ADL-</i>	<i>Sum</i>
HRP +	49	4	53
HRP -	12	4	16
Sum	61	8	69
<i>5% criterion No. patients</i>	<i>ADL+</i>	<i>ADL-</i>	<i>Sum</i>
HRP +	44	4	48
HRP -	17	4	21
Sum	61	8	69

produces fewer mismatches (match/mismatch ratio is 7/1 and 3/1, respectively) whereas the stricter criterion (>5%) has relatively more mismatches (match/mismatch ratio 2/1). For patients without ADL improvements the match/mismatch ratio is about 1/1 (i.e. chance), irrespective of the criterion.

**Discussion** In the present study we first wished to replicate previous observations that patients with VFDs benefit from VRT as assessed perimetrically in the context of a retrospective study design. We also wanted to determine if VRT improves ADL-competency in visually-guided tasks. By correlating perimetric changes with subjective ADL variables we hoped to gain insight into the relevance of quantitative, perimetric parameters for every day vision as probed by subjective patient testimonials.

COMPARING OUR RESULTS WITH PROSPECTIVE STUDIES The perimetric results of this retrospective study are very similar to the percentage values of the double-blind study of patients containing post-chiasmatic and optic nerve lesions,<sup>4,24,34</sup> the 'Tuebingen trial'<sup>32,33</sup> and the attention trial,<sup>5,36</sup> though the percent change in the present study was slightly better (Figure 1–Figure 3). This difference may be explained by any one of the following possibilities: (1) the perimetric procedures of the retrospective study were somewhat different, (2) we included patients with lesion age of under one year (n = 27) who still might have been in the spontaneous recovery phase with some spontaneous improvements independent of the VRT, and (3) patients who did not benefit from VRT might have skipped the post therapy assessment, whereas in the experimental studies all subjects were evaluated after training, and (4) patients performing VRT in this retrospective study might be a selected group because they have paid for their therapy. This might have introduced a small sampling bias. Regarding subjective improvements of ADL parameters; nine out of ten patients

in our study reported improvements of some kind. This rate is also higher than in our previous placebo-controlled double-blind study, where about 70% of the treated patients noticed subjective improvements. In that study a forced choice question was asked: 'Have you benefited from VRT in daily life' with a yes/no answer choice.<sup>4</sup> Thus, on both quantitative and subjective measures, the benefits of VRT are more pronounced in the retrospective study compared to the prospective, experimental studies.

**SUBJECTIVE IMPROVEMENTS OF ADL AFTER VRT** The major question addressed by our study was whether VRT has an influence on visually-related ADL-measures. Particularly, it is clinically important to know whether any change in perimetric measures due to VRT is of functional use to the patients. We therefore categorized the statements given by the patients into five categories.

Our first category 'general improvement of vision' is rather vague, containing testimonials to general visual functions after VRT such as 'I can see better' or 'left side becomes brighter,' which are rather unspecific. However, this category is obviously a very valuable source to better understand our patients. Patients who reported improvements in this category have a significantly better detection rate in HRP as well as response time improvements after VRT compared to patients who didn't improve in this category.

About two-thirds of our patients reported an improvement in the category 'visual confidence and mobility.' While this is a factor clearly influenced by vision itself, we should keep in mind that such types of ADL statements are also influenced by non-visual factors such as motor problems (e.g., due to hemiplegia after stroke). Indeed, this category showed no significant relation to training outcome. Additionally, our clinical observations reveal that many patients hope to drive a car again after VRT. By German law, an intact visual field in at least one eye is necessary to drive a car. Patients may have had high expectations in hoping to drive again after VRT (a wish that has been fulfilled only for a few patients). About one third of our patients reported subjective improvements in the categories concerning collisions, hobbies, and reading, respectively, and a relationship between visual field enlargement and these categories, albeit small, were found after VRT. The relationship between visual field enlargements and reading was significant, suggesting that even minor VF enlargements have an impact on reading abilities. The category concerning hobbies contains diverse activities ranging from skiing to handy crafting and we assume that patients are most motivated to resume activities that they like most or which are most important to them. It would therefore be reasonable to expect that visual improvements might become apparent first in this category. Because hobbies are important to people, reporting changed performances in this category is of high subjective relevance and is also a solid testimonial. We found some correlation between visual field enlargements and subjective improvements of daily life activities with respect to both reading and hobbies. These two categories seem to be most sensitive to an increase of visual field size of an average of about 10% (as measured by the increased number of detected stimuli in

HRP). Thus, visual field size does influence reading and performance of hobbies. In addition, the gain of intact visual field size after VRT may lead also to improvements in the ability of patients to avoid collisions.

In summary, a large majority of VRT patients report ADL-specific improvements by using this semistructured interview. It is now of interest to determine whether visual field enlargements are linked to ADL-improvements or if both parameters are unrelated, that is, mediated by different factors of visual function. One way of addressing this problem is to correlate changes as measured perimetrically with subjective ADL improvements as expressed in patient testimonials.

RELATIONSHIP OF VISUAL FIELD TOPOGRAPHY AND SUBJECTIVE IMPROVEMENTS IN ADL The relationship of size of VFD and subjective improvements was found to be rather complex in our study. While no relationship of size of VFD and subjective improvements of ADL was found in binocular assessments at baseline, a negative correlation was found between the number of detected stimuli in monocular perimetry and the category 'visual confidence and mobility.' This relationship was also evident after VRT. Patients suffering from a greater VFD before training seem, on average, to less frequently experience subjective improvement in the category confidence and mobility even after successful therapy. We can conclude that even after gaining an average of VF size of about  $5^\circ$  after VRT their visual field still remains defective and that the achieved VF gain does not help them to function better, for example, to ride a train or to drive a car (see above). In contrast, there is some indication that smaller VFD post training correlates significantly with subjective improvement in performing hobbies.

We should also consider that patients with smaller VF loss at the beginning have, statistically speaking, a greater relative chance to achieve a VF enlargement after VRT, that is, patients with minor visual field deficits prior to VRT may thus experience more subjective improvement in ADL. In patients suffering from retinal lesions, especially in glaucoma patients, the relationship of size of scotomas and ADL has been investigated and some authors found a significant correlation of size of VFD and subjective report of daily life activities<sup>11,12</sup> while others could not find a statistical correlation between these variables.<sup>10</sup> From experiments with artificial scotoma we have learned that the degree of filling-in possibly depends on the size of VFD defect<sup>37</sup> and that there is probably an upper limit of VFD that can be compensated for by this phenomenon. Although little is known about the 'filling-in' processes in patients with cortical lesions, one could conceive that smaller visual field deficits can be compensated more easily by perceptual completion than larger VFD. We can speculate that in addition to increasing the visual field size by VRT perceptual completion due to filling-in phenomena may add some degree of subjective improvements,<sup>37,38</sup> but this proposal needs experimental verification.

Due to the complexity of visual field defects observed in the sample of our study, we could not analyze the relationship between the subjective importance of a specific visual field area (e.g., the center of the

visual field vs. the peripheral regions for coping with everyday life) and the evaluation of the treatment program by patients who had vs. had not recovered intact visual functions in those areas. Preliminary results show, however, that the subjective ‘weighting’ of a visual field region is crucial for the perception of a visual border shift induced by VRT.<sup>5,36</sup>

**DEMOGRAPHIC FACTORS** As we have previously shown, training outcome does not depend on age, sex, age or type of lesion.<sup>31</sup> As the present study confirms our previous observations<sup>5</sup> that older patients benefit from VRT as much as younger patients do, but, as we now show for the first time, older patients are more likely to name subjective improvements after VRT, especially in the category hobby. We assume that hobbies of older patients may be different in nature and of a different significance to them. It is conceivable that younger people have more sporting activities involving speed and action, which are more difficult to perform after severe visual impairments despite VRT. In addition, the more time that had passed since the lesion occurred, the more likely patients state that hobbies had improved or that they named at least one category of subjective improvement. As observed previously, in our retrospective study, ‘type of lesion’ does not play a role in subjective improvements after VRT. With regard to gender we noted some interesting differences: while males are more likely to name subjective improvements in the category visual confidence/mobility, females state more frequently that they are significantly more able to avoid collisions with objects and people after VRT.

**NON-VF-SIZE FACTORS RESPONSIBLE FOR ADL IMPROVEMENT** The correlation analysis and the match/mismatch comparison lead us to the following conclusions. When the visual field size is increasing (which occurs frequently following VRT), nearly all patients benefit subjectively in daily life. The more the visual field increases after VRT the more likely patients are to report improvements. The extent of this change is related to the number of improved categories named by the patients. Thus, VF size enlargements appear to be a sufficient but not an exclusive or necessary condition for subjective improvements of vision.

We can not exclude that therapy expectation (placebo-effect) plays a role in our post-therapy interview. About 9% of our patients who had only a minimal improvement of VF size reported subjective improvement. However 16% of patients of the placebo-group in the double-blind study by Kasten et al.<sup>4</sup> also reported of improvements in daily life. This suggests that our data simply reflects the type of placebo effect inherent with any therapy. Another explanation for the mismatch may be that temporal processing of visual stimuli in the brain is a major contributing factor in the subjective visual experience, but this has not yet been evaluated. Indeed, we feel that this additional factor, namely the temporal processing of visual information is of great relevance in the context of interpreting subjective improvements. Specifically, a currently ongoing investigation shows that VRT can improve reaction times in the detection of visual stimuli.<sup>5,31,32,35</sup> This suggests that improved temporal visual processing may contribute to the effects of

VRT. It would not be surprising if subjective improvements in visual confidence and general mobility depend more on proper (or improved) temporal processing of visual information and not just on VF size, in the intact visual field region and/or the area of residual vision. This is an issue worthy of study in future investigations.

Yet, another possibility is that patients may become more aware of their VFD and that they pay more attention to their visual functions in general. It is conceivable that improvement of awareness of visual field defects may also contribute to overall subjective improvements, though currently we have no indication whether this is actually the case. Perhaps, in a speculative spirit one may conceive that patients suffering from hemianopia anosognosia<sup>40</sup> could perhaps gain some awareness of their deficit by daily VRT training.

**Conclusion** Patient testimonials indicate that VRT leads to subjective improvements of vision guided activities in everyday life. Interestingly, even patients with small VF enlargements noted subjective improvements in daily life. Most patients reported subjective improvements from VRT in at least one category of daily life as assessed here. The number of improved categories increases with the size of visual field enlargements from visual training. It is interesting, however, that subjective improvements of most activities can not be predicted with the size of VFD alone as assessed with perimetric measures before or after therapy. As described, the glaucoma literature is controversial with respect to this point, but our study, the first investigation of a larger population of post-chiasmatic and optic nerve injury patients, clearly shows that the size of the surviving visual field and subjective visual impairments are not associated in a one-to-one fashion. Rather, other factors like temporal processing or awareness of visual deficits are important, contributing in a significant way to subjective vision. Ideally, our investigation should be followed by a study using a systematic questionnaire with a pre/post design. Such a study is currently underway. This would then also give us a better understanding why VRT is not only subjectively beneficial to patients with major visual field enlargements (matched cases), but even in those patients with minor or no objective changes in visual field size (mismatched cases). By further studying this question, we will learn more about the mechanisms of vision restoration.

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