Author's response to reviews

Title: A technique to train new oculomotor behavior in patients with central field loss during reading related tasks using scanning laser ophthalmoscopy: immediate functional benefits and gain retention

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Author's response to reviews: see over
Dear Dr Appleford,

Thank you very much for considering our manuscript as potential publication in BMC ophthalmology. We also would like to thank both reviewers for their very useful and constructive comments on our study. We paid a careful attention to all referees’ comments and suggestions and we hope that we have adequately answered their issues.

In order to answer Gregory Goodrich requirements we rewrote the paper and put increased emphasizes on the techniques in the training procedure. For this reason we also renamed our paper.

“A technique to train new oculomotor behavior in patients with central field loss during reading related tasks using scanning laser ophthalmoscopy: immediate functional benefits and gain retention”.

We hope that the modifications made are also in accordance account Michael Stur’s opinion, which mainly emphasised the value of the results obtained.
Reviewer Michael Stur:

Firstly thank you for your interest in our paper and also thank you for your very kind comments:

This is a very interesting paper. I find the information about the results of SLO reading training with PRL and TRL very compelling, and would like to see methods like this introduced into every low vision clinic.

According to your proposition as discretionary revision:

The authors might comment the fact that the machine they have used has been out of production for many years. It could be suggested that a newer, smaller and simpler device might be introduced into the market just for the purpose of reading training.

We therefore added the following in the conclusion of our manuscript:

“The SLO has unfortunately been out of production for many years and for this reason is presently not a widespread instrument. However, our study suggested that similar and simpler devices allowing real time view of the retina and projection of chosen stimuli might be introduced into the market for the purpose of reading training.” (p.22)

Reviewer Gregory Goodrich:

Thank you so much for your interest in the paper and for the suggestion of putting an increased emphasizes on the techniques in the training procedure. We modified our manuscript accordingly and emphasized that we conducted a pilot study. We hope that stressing on the techniques solved that problem.

Major compulsory revisions:

1. I found the title to be misleading. The title states it is an “Intensive short-term reading training...”. First, given that training occurred over 10 days at an hour per day I do not feel the training is “short-term”. Others (i.e., Nilsson) have shown reading training improvement using only five sessions. Second, the authors measured aspects of reading, but not reading itself. That is, they measured change in visual acuity and “threshold character span”, which are essentially letter and word recognition respectively. They also examined eye movement which is another component of reading. However, they neglected to actually assess any measure of reading (for example, reading speed, comprehension, etc.). Absent these assessments it is not possible to transfer the results to the reading task.

As we previously mentioned, we modified the title to comply with your request. The former title was as follows: “Intensive short-term SLO training in subjects with central scotomas.
Adaptation of reading strategies, immediate benefits, and gains retention. The title now is the following: “A technique to train new oculomotor behavior in patients with central field loss during reading related tasks using scanning laser ophthalmoscopy: immediate functional benefits and gain retention“ and we hope that this new title will meet your expectations.

However, we wish to specify that we used the terms “intensive and short-term” because this naming had been previously coined by the authors who inspired our methodology (e.g. Püllvermüller et al., 2001; Nelles, 2004, taub et al., 2002). Moreover, we believe also worthwhile to mention that when compared to Nilsson et al.’s study, the number of our training sessions was more important but the overall training was conducted on a shorter period, as we performed more than one session a week.

Secondly, as you indicated we agree that we mainly measured some specific aspect of reading and not reading itself. We corrected that point. Indeed, as we also tested subjects on paragraphed text reading before, immediately after and three months following the training procedure, we added this data to our manuscript, p. 7-8 and p. 12-14, p.17, p.21, table 2 and table 3, figure 5 and figure 8. We also modified the table legends accordingly. Moreover, we did not measure reading speed on paragraphed text as the SLO is not appropriate for such a measurement because of unavoidable numerous images’ loss. Consequently, we only evaluated threshold character size and reading accuracy. Therefore our data still provided some information about patients’ ability to read pages of text before, immediately after and three months following the training.

2. The inclusion of only five subjects makes generalization of the results difficult, especially since the primary change (in visual acuity, for example) occurred in only two subjects and relatively small changes in the remaining three. Even taking all subjects together, which showed approximately a two line improvement in ETDRS acuity from pre- to post-training, the change in acuity is within the test/retest error of ETDS charts (Kiser, et al 2005) Optom and Vis Sci 82 (11), 946-54). Thus one cannot state with absolute conviction that the improvement was due to the training. The sample size is also of concern since it precludes most statistical analysis other than the descriptive analysis provided in the article (a minimum of 10 subjects is generally needed for a simple t-test).

We agree that the inclusion of five patients makes generalisation of the results difficult. This issue was also one of our concerns and we are aware that additional patients would render our results more robust. We strived to overcome this issue by enrolling a larger number of subjects. We defined strong criteria of inclusion, which restricted the number of patient
recruited, but allowed to draw valuable qualitative and quantitative first results. Please let us present these criteria.

- Firstly, although age-related macular degeneration is not a rare condition, it produces macular lesions varying in size and shape. Therefore it is difficult to get a sample of patients with homogeneous lesions.

- Secondly, we enrolled only patients that had lesions stabilised for at least one year. Conditions stabilised over one year are not usual in people with age-related macular degeneration.

- Thirdly, we enrolled patients who still presented major reading difficulties despite having previously undergone a regular rehabilitation procedure. The latter requirement intended to avoid the possibility of a spontaneous recovery but was also strenuous to meet.

- Fourthly, we aimed at enrolling people with age-related macular degeneration as their only major health problem. This was also a difficult criterion to meet as these subjects are often older than 75 years of age. In fact, the sixth patient enrolled had eventually to be dropped off the study because he developed dementia, as mentioned in the paper.

- Finally, the complete training procedure for one patient extents over a period of 4 to 5 months from the first time we see him to the evaluation 3 months following the completion of the training procedure. In addition, this is a major constraint for patients of such an age to come four times a week to the clinic to be trained. Consequently few subjects accept to follow the whole procedure.

Considering these restrictive inclusion criteria the whole study needed two years and a half to be completed. It appears then unlikely that we could further the study with additional subjects within less than another two years.

Concerning the statistics used, we agree that five subjects are not enough to obtain definite results. However, instead of using T-test and to bypass the small number of subjects recruited, we strengthened our data analysis using ANOVA tests, which take into account subjects’ individual differences.

To bypass the problem of the number of patients recruited, we modified our manuscript according to your suggestion and put emphasize on the technique used. We also specified that our training study was a pilot study and that the results obtained were first results. We also
mentioned that we would need a larger group of subjects and appropriate control group to reach definite conclusions.

We added the suggested reference Kiser et al., Optom Vis Sci, 2005 to figure 6 of our manuscript and modified the figure legend accordingly:

Previously, the text was as follows:

Measures are reported for each subject. before: before SLO training; after: immediately after SLO training; three months later: three months following SLO training. Changes in ETDRS values could be considered significant when greater than 0.1 logMAR [39]. Note that ETDRS visual acuity consistently increased with the SLO training and, globally, gains were retained three months later.

We modified this figure legend for:

Measures are reported for each subject. before: before SLO training; after: immediately after SLO training; three months later: three months following SLO training. Changes in ETDRS values could be considered significant when greater than 0.2 logMAR [38, 39]. Note that ETDRS visual acuity consistently increased with the SLO training and, globally, gains were retained three months later.

We also added a sentence in the result section of our manuscript quoting these authors, p.14 under the “ETDRS acuity” section:

“Howevers when considering individual data, the majority of improvements were no greater than the test repeatability of 0.2 (34, 35).”

The change in threshold character size is also problematic since the improvement did not hold for all word lengths and the authors do not adequately explain why this should be the case if the training was effective.

We agree that the change in threshold character size is also problematic because non homogeneous for words of different lengths. However, it is also an interesting fact that such variations occur and that task, which requires the most important adaptation process and the most numerous eye movements to be performed, is also the one that is the least retained.
Indeed we did not have a proper control population and ideally we would need one to strengthen our training study. However, we enrolled subjects who had long-lasting macular degeneration and who had previously undergone rehabilitation procedure. Their condition in terms of viewing performances had reached a plateau. Therefore we could not expect spontaneous recovery from these patients. These patients had appropriate devices, which they used to read everyday, or had given up reading. We think that now that we have rewritten the manuscript and empathized on the techniques on one hand and stressed on the initial nature of the results on the other hand, this concern is not as critical as it was in our previous version of the manuscript.

We also added a section in the conclusion of the manuscript, p. 22, first and second paragraph of the discussion section:

“The first results that we obtained on five patients are definitely encouraging but to reach more definite conclusions the training of a larger group of subjects and a comparison of data with those of a control group should be considered.”

5. A less detrimental point, but one worth correcting, is that the Post-training evaluations as described on page 12 is confusing. While it does describe the contents of table 2 the reader would benefit from a clearer organization of the data rather than a simple recitation of each subject’s behavior. Was there a clear, over-all pattern? If so, it should be stated. If not, that should be stated.

When rewriting our manuscript we paid a particular attention to this page and rephrased the whole section:

Our previous version was as follows:

“Post-training evaluations
Immediately after SLO training, analyses of reading strategies for single letters and isolated words revealed that subjects used the examiner’s selected TRL, as well as additional newly
self-selected PRLs (figure 3B). Four subjects (SL, LG, AA, GM) consistently used the examiner’s selected TRL. Three of them (SL, LG, AA) (table 2) used the examiner’s selected TRL most often in combination with their initial PRL. However, under specific conditions (namely single letter deciphering and 1.5 logMAR word reading), one subject (SL) persisted to use exclusively the initial PRL. One subject (AA) used additional newly self-selected PRLs in combination with the initial PRL and the examiner’s selected TRL for reading isolated words. Another subject (GM) used the examiner’s selected TRL alone.

Three months following SLO training, four subjects (SL, LG, AA, GM) consistently used the examiner’s selected TRL either in isolation (GM), or in combination with the initial PRL (LG, AA, SL) (table 2, figures 3C, 4C). The use of newly developed self-selected PRLs was observed in three subjects (SL, AA, GM).

The remaining subject (MT) showed an improved ability to scan the word, only using the initial PRL (figure 4B). This ability was apparently lost three months following SLO training (figure 4C).”

Our new version reads as follows:

Post-training evaluations
Immediately after SLO training, analyses of reading strategies revealed that four subjects (SL, LG, AA, GM) used the examiner’s selected TRL, or additional newly self-selected PRLs (figure 3B and 5B) alone or in combination with their initial PRL for reading isolated words and paragraphed text. One of these subjects (GM) (no defined PRL before SLO training) used the examiner’s selected TRL alone. The remaining fifth subject (MT) showed an improved ability to scan the word but only used the initial PRL (figure 4B).

Three months following SLO training, four subjects (SL, LG, AA, GM) consistently used the examiner’s selected TRL either in isolation (GM), or in combination with the initial PRL (LG, AA, SL) for reading both isolated words and paragraphed texts (table 2, figures 3C, and 5C). The use of newly developed self-selected PRLs was observed in three subjects (SL, AA, GM) to read isolated words and in two subjects to read paragraphed text (MT, SL). Interestingly, one subject (MT) lost the ability to perform eye movement to scan the entire words, but kept some adaptation, i.e. used newly self-selected PRLs, during text reading (table 2). (p. 13, Paragraph 3, p.14 Paragraph 1).
1. Is the question posed by the authors new and well defined?

The methodology employed is novel and interesting. The paper could be presented as a methodology for the study of component behaviors in reading with the cases presented as examples.

We did our best to rewrite the paper according to this comment.

2. Are the methods appropriate and well described, and are sufficient details provided to replicate the work?

The work could be replicated, however the research design lacks a control population and too few subjects were studied to allow the reader to generalize the results. And, as stated above, the study examined components of the reading task, but did not examine reading per se.

3. Are the data sound and well controlled?

No, the study lacks the appropriate control group. The data are interesting, but limited by too few cases.

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?

In general yes, however, there are several limitations to the study that are not reported by the authors; small sample size, lack of a control group, limited measures of "reading" to mention a few.

Please refer to our previous comments, here above, where we considered these points (#2 and #4).

5. Are the discussion and conclusions well balanced and adequately supported by the data?

The primary effects of the training appear to be large in two individuals, moderate in two, and absent in one. While discussing each case in the results the discussion tends to focus on the over-all trend which is heavily influenced by the two cases. This may lead to an inaccurate conclusion. On the other hand, with more cases and a control population the conclusions may prove to be valid.

Please also refer to our previous comments, here above, where we considered these points (e.g. #2, #3, #4).

Major Compulsory Revisions Summary: I would like to see this manuscript re-written as a proposed methodology to study reading related behaviors in cases of central field loss and as a possible training technique. I found the study very interesting in that regard and it stimulated a number of additional questions for me. For example, would this technique reveal differences in behavior between newly diagnosed cases of central field loss versus those with a long-standing history? Does SLO training as described result in faster reading speeds, greater fluency, less difficulty, longer durations, and/or greater comprehension in reading? I think the methodology and use of the SLO as described would be an excellent methods paper (Please see numbered comments above). As a results oriented paper it suffers from too few subjects, lack of a control population, and an incomplete assessment of reading.

We greatly appreciate your effort for the major compulsory revisions summary and for your suggestion about reforming our manuscript as a methods paper. If we did not consider this
possibility before, we reckon that it improves the overall paper, as it nicely highlights the main concern for which this study was devised.

We look forward to hearing from you in the near future.

Sincerely yours,

Dr Anouk Déruaz