Web-based therapy for hemianopic alexia is syndrome-specific

Zoe VJ Woodhead[1,2], Yean-Hoon Ong[1,2] & Alex P. Leff[1,2,3]

Author affiliations

1. Department of Brain Repair and Rehabilitation, Institute of Neurology, University College London, Queen Square, London, UK.
2. Institute of Cognitive Neuroscience, University College London, Queen Square, London, UK.
3. National Hospital for Neurology and Neurosurgery, Queen Square, London, London, UK.

Word count (3000): 2936; abstract (300): 289.

Tables and Figures (6 max): 1 table, 4 figures.

Abstract

Rehabilitation studies rarely test the specificity of an intervention by using a control group who are matched to the therapy group in terms of baseline impairment, but who do not have the same causative syndrome. In this study we tested the specificity of an eye movement therapy for a common, acquired reading disorder called hemianopic alexia, by comparing hemianopic subjects with slow text reading, to age and reading speed matched controls without hemianopia. The study was carried out using an online therapy programme called “Read-Right” that contains validated tests of both visual field and text reading speed, as well as an eye movement therapy: laterally scrolling text. 201 self-selected subjects completed at least five hours of online therapy. After excluding those with reading speeds incompatible with hemianopic alexia and those with bilateral abnormalities on their visual field test, we were left with 105 who were then classified into one of three groups depending on their visual field: 1) right-sided hemianopia (n=47); 2) left-sided hemianopia (n=36); 3) no hemianopia (n=22, control group). All three groups’ baseline text reading speeds were significantly different to age-matched controls but not to each other. A repeated-measures ANOVA showed a significant therapy by group interaction ($p = 0.039$). Post-hoc, paired t-tests revealed that this was driven by reading speed improvements for both the right and left-sided hemianopic alexic groups but not the controls. This result demonstrates that a clinically validated therapy for hemianopic alexia improves text reading speed in hemianopic patients but not in subjects matched for slow text reading but without hemianopia. This adds weight to the hypothesis that eye movement therapies are syndrome-specific. It also demonstrates an advantage of using web-based vehicles to deliver syndrome-specific therapies that can be accessed by patients worldwide.

Introduction

Homonymous hemianopia is a loss of vision affecting the same part of both visual fields due to retrochiasmal brain injury. The main causes are stroke, traumatic brain injury and brain tumours. Persisting hemianopia complicates about 15% of strokes,[1] which is the main contributor to the estimated prevalence of ~1% in the over 50s[2]. Despite, or perhaps because of, improved management of stroke in primary and secondary care, this figure is likely to rise in the coming decades, and not just in the West.[3] Hemianopia affects a wide range of activities of daily living,[4] and, not surprisingly, is associated with poor outcomes.[5 6] Due to the one-to-one mapping of the visual field representation onto primary visual cortex,[7] established hemianopias rarely spontaneously improve in the post-acute phase.[8]

Hemianopic alexia is a specific type of reading disorder that particularly affects patients with macular-splitting hemianopias.[9] Patients with hemianopic alexia have accurate but slow text reading. Their hemianopia robs them of important upcoming visual information that normal readers depend on for planning efficient reading eye movements,[10] so they make many more fixations when reading any given line of text. While there is a directional effect,[11] which is mainly driven by the way that texts are written (either left-to-right as in English, or right-to-left in Arabic and Hebrew) homonymous damage to either visual field affects reading speeds; in readers of left-to-right scripts, a right-sided hemianopia is more disabling than a left-sided one.[9]

While restoration of high-acuity, conscious vision in the damaged field would work wonders for patients with hemainopic alexia, it seems a distant goal.[12-14] Fortunately, there have been quite a few high-quality, phase II studies of eye movement interventions that improve text reading speeds with large effect sizes ranging from 20-80%.[9 16-19] These methods almost certainly improve reading speeds by inducing changes in the patients' eye movements. A variety of methods have been tried, from inducing small-field optokinetic nystagmus (OKN),[9 15-17] to training of voluntary induced eye movements.[18-21] All training methods induce an improvement, via mass practice (many thousands of repetitions), in the pattern of small amplitude, horizontal reading saccades. Two studies have clearly shown that the nature of the eye movement practice is key,[17 18] with the most impressive evidence coming from a cross-over study where hemianopic patients practiced reading therapy in one block and visual exploration training in another. Both therapies worked in a highly specific and task-dependent way: reading speed improved in the reading therapy block, while visual search did not, and vice-versa.[18] The same group carried out another important experiment demonstrating that old (average age 77 years) and young (28 years) hemianopic patients benefited from practice to the same degree.[21]

An important issue for patients with hemianopic alexia is access to eye movement therapies, as they are not generally available. To address this, our group developed a web-based therapy for hemianopic alexia called "Read-Right" that includes tests of the visual field and reading speed. We reported the initial effects in a group of 33 subjects with right-sided hemianopic alexia.[16] While the results were encouraging (40% improvement in text reading speed on average, after 20 hours of therapy compared with baseline) there was no control therapy or control group, which dampened the enthusiasm of several reviewers. This was difficult to resolve as we had decided against randomizing patients into sham/treatment groups in the freely–available online therapy. However, now that the site has been running for a few years, we have managed to collect data on 22 people who have been using the therapy but have no evidence of having a visual field defect (so do not have hemianopic alexia by definition). This group forms an ideal control group to our hemianopic participants. By analysing their data we can make between-group comparisons to look for group-by-therapy effects, something that has never been done even in the previous, more traditional, phase II trials. We can also compare data from 36 patients with left-sided hemianopic alexia using the site as an additional experimental group.

Read-Right consists of two tests (a visual field test and a text reading speed test) and the therapy (laterally scrolling text). The tests are taken at the baseline time point (BL) and then again every time the subjects complete 5 hours of therapy (time spent watching the laterally scrolling text), with the exception that two text reading tests are taken at the BL time point to establish a more precise estimate of subjects' pre-therapy text reading speed.

Methods

Visual field test

We used an adaptive, automated visual field test for assessing hemianopia in patients that is bundled with the Read-Right app (http://www.readright.ucl.ac.uk/help/h_vft.php). It tests six points at 1, 2.5, 5 and 10 degree eccentricity from the fixation cross in both the left and right visual field; four of the six points are along the horizontal meridian, thus covering foveal and parafoveal vision which are key for the planning of reading eye movements.[22] This test has been validated by comparing it with a clinical 'gold standard', the automated Humphrey perimeter (10-2 sequence), and has sensitivities in the range of 0.8-1 and specificities of 0.75-1 for the affected hemifield along the horizontal meridian.[23] The test is performed at BL and again after 10 hours of therapy. Hemianopia was diagnosed if two or more points were missed in the same hemifield, at either BL or after 10 hours of therapy (for those subjects who had completed 10 hours of therapy). See Figure 1 for examples.

Text reading test

The test consisted of six standardized paragraphs of edited newspaper text, 49 words in length and spread over eight lines (Figure 2). Subjects initiated a countdown timer and then read the whole of the text, signalling when they had finished with a button press, at which point the timer recorded their reading speed for that text. Each text was followed immediately by a short, written yes/no comprehension question, which varied, to encourage patients to read the whole of the text (correct on 94% of all trials). At each time point subjects read three texts (a triplet); times were averaged over the triplet to produce their reading speed. We further averaged the two measurements taken at BL (two triplets containing all six texts between them) and used this as the pre-treatment measure of text reading speed. The order of presentation of the triplets was pseudo-randomized both within and across subjects. As reported previously, 38 age-matched controls (mean = 59.7 years), read the six texts at an average speed of 302 wpm (SD = 80).[16]

Therapy

The Read-Right therapy consisted of reading laterally scrolling text (from right-to-left), to induce small-field OKN.[9 17 24] Patients could control the speed, appearance, and content of what they read, choosing from a small library of books and ever-changing RSS text feeds from the BBC website (http://www.readright.ucl.ac.uk/help/h_vid_therapy.php). Patients could pause or stop the therapy at any time. While the text was moving, a timer measured how much therapy was being delivered, feeding this information to the secure University server. We suggested 20 minutes of therapy per day but patients could choose to do as much or as little as they wished. Thus, the subjects determined the time period between testing points.

Questionnaire data

Unfortunately, we did not imbed a way of collecting patient reported outcome measures in Read-Right as part of the main application. We were able to collect some data but this was via a post-hoc questionnaire sent to all subjects reported in this paper. The response rate was 63% so the results from this may be affected by selection bias. We asked four questions: 1) '*On which date did your visual field problem start?*'; 2) '*What caused your visual field problem?*'; 3) '*Has Read-Right helped your reading?*' (rated from 1 [no benefit] to 10 [huge benefit]); and 4) '*Compared to before starting Read-Right, every day I am reading [X] time more or less'* (rated as X = -60 minutes / -30 mins / -15 mins / the same amount / +15 mins / +30 mins / +60 mins). See Table 1.

Subject selection

This study was approved by the UCL Research Ethics Committee. We interrogated the database and found that 234 subjects had completed at least 5 hours of therapy. We then excluded the 33 with right-sided hemianopia and hemianopic alexia who had been reported in the previous paper, leaving 201 subjects. We rejected those subjects whose baseline reading speed was too slow (< 40 wpm) to be compatible with a diagnosis of hemianopic alexia. There were 60 subjects who read below this rate; interestingly, almost all had a right-sided hemianopia suggesting that they had a left-hemisphere lesion causing either central or pure alexia, both of which can co-exist with hemianopic alexia, but are much more disabling.[25] Finally, we rejected subjects with bilateral abnormalities on their visual field test (n = 36). This could have been a genuine reflection of their visual fields, as a single posterior circulation thromboembolic event can cause bilateral occipital damage: a recent prospective study of 915 patients has suggested an incidence as high as 13% in a stroke population reporting visual symptoms.[26] Another possibility is that certain subjects may have found the visual field test too difficult, effectively resulting in false positive visual field defects. Removing these subjects left 105 who were then classified into one of three groups depending on their visual field test: 1) right-sided hemianopia (R-HA, n=47); 2) left-sided hemianopia (L-HA, n=36); 3) no hemianopia (Control, n=22). This latter group of controls completed at least five hours of reading therapy, but do not appear to have hemianopic alexia.

Demographic data

The demographic data for all three groups is shown in Table 1. While there are differences in the central tendencies of these measures, statistical analysis did not reveal any significant differences on the following variables: age, gender or time taken to complete 5 hours of therapy (lowest p value = 0.1; chi-squared test on gender). The 76 participants who completed the post-hoc questionnaire showed no significant between-group differences on: questionnaire response rate (range from 55-68%); stroke as the stated cause of hemianopia (range 73-89%); and time from stated onset of hemianopia to taking the baseline tests. The control group had a median time post stroke four to six times higher than the hemianopia groups, but there was so much variability associated with these measures that we failed to identify any group differences (p = 0.24; independent-samples Kruskal-Wallis test).

Statistical tests

The main outcome measure was text reading speed. Reading speeds (words per minute) were entered into a repeated measures ANOVA with time as the within-subject factor (BL versus 5hr time points), and group as the between-subject factor (R-HA, L-HA and control). For the self-reported outcome measures there was only one time point, so a three-way between-subjects ANOVA was used. Both outcomes were treated as scale data: the question '*Has Read-Right helped your reading?*' was scored from 1 to 10, and the question '*Compared to before starting Read-Right, every day I am reading [X] time more or less*' was coded from 1 (one hour less) to 7 (one hour more). Lastly, one-sample t-tests were used to compare the three groups' baseline reading speeds to age-matched controls not registered on the website. Significance was set at $p < 0.05$.

For clinical interventions, it is often important to know what the effect size is as well as whether the effect is significant or not. Here we report both unstandardized ((5hr - BL/BL)*100 = % improvement in RT) and standardized (Cohen's *d*) effect sizes. Standardized methods rely on a mix of the numerical size of any difference, in this case between the two time points, as well as the variance associated with this difference. There are a variety of ways to calculate this variance, with some controversy as to how best to do this with repeated measures data.[27] Here we calculated the pooled variance using an online calculator available from Wikiversity.[28] This uses the standard deviations associated with the mean reading speeds at each of the two time points and corrects for the within-subject correlation between these measures in order to calculate Cohen's *d*.

Results

Text reading speed

All three groups' baseline text reading speeds were significantly different to age-matched controls (mean=302 wpm, SD=80 wpm; $p < 0.001$ for all comparisons); but not to each other (R-HA vs L-HA $p = 0.298$; R-HA vs Controls $p = 0.116$; L-HA vs Controls $p = 0.512$).

The repeated-measures ANOVA showed a significant time by group interaction, $F(2, 102) = 3.36$, $p = 0.039$. Post-hoc paired t-tests revealed that this was driven by reading speed improvements between the BL and 5hr time-points for both the R-HA and L-HA groups but not the Control group (Figure 3): R-HA, $t(46) = 4.65$, $p < 0.001$; L-HA, $t(35) = 4.20$, $p < 0.001$; Controls, $t(21) = 0.03$, $p = 0.977$.

The effect sizes of the improvement in the two hemianopic groups were: R-HA, 16% (Cohen's $d = 0.98$, a large effect size); L-HA, 15% (Cohen's $d = 0.99$).

Questionnaire

There were no significant group effects on the subject reported outcome measures: '*Has Read-Right helped your reading?*', $F(2, 62) = 0.46$, $p = .632$; '*Compared to before starting Read-Right, every day I am reading [X] time more or less'*, $F(2, 65) = 0.35$, $p = .704$ (Table 1).

Discussion

A number of eye movement-based treatments seem to be effective in treating hemianopic alexia; some induce small-field OKN,[9 15-17] while others rely on practicing small amplitude voluntary saccades along the horizontal meridian.[18-21] No studies to date have demonstrated the specificity of the training effect by comparing the therapy's efficacy with a group of control subjects. Here we show that an eye movement therapy has the predicted effect on the target patient group (hemaianopic alexia), but not on age-matched controls matched for baseline reading speed, but with no hemianopia.

Because this was an internet-based study, we have little information on those who took part and it is difficult characterise the nature of the reading deficit in the control subjects. The majority, like the hemianopic alexic readers, recorded that they had had a stroke; but they seemed less clear about when this had happened or which side of their vision had been affected (41% unsure versus 12% unsure in both hemianopic groups). Given the reasonable but not perfect sensitivity of the online visual field test, it is possible that some of the controls may have had a subtle homonymous visual field, causing hemianopic alexia that we did not pick up. Their reading was certainly slower than age-matched controls and was not significantly different to the R-HA or L-HA patients (Table 1), so they presumably did have either an acquired or developmental reading problem. Given the relatively high prevalence of developmental dyslexia (~5% of the population), we suspect that at least some of the control group had this disorder of reading, but it is impossible to be sure. Despite being a rather poorly specified control group, the lack of an effect of Read-Right training on their text reading speeds is striking (Figure 3).

Left-sided hemianopic alexia has been studied previously and is generally considered to be less disabling (at least for readers of languages written from left-to-right) than right-sided hemianopic alexia. Both patient groups respond to eye movement therapy with improved reading speeds and a reduced number of reading fixations following training with laterally scrolling text.[9] In his 1995 study, Zihl found impressive effect sizes of 81% for R-HA patients and 49% for L-HA patients. We identified smaller effects of 16% and 15% respectively (although the effect size was large on Cohen's *d* measures), with no significant between-group differences. There are two possible explanations for this discrepancy. Firstly, Zihl's patients practiced for longer – around 11 hours on average compared to 5 hours in our study. Secondly, Zihl's patients received the therapy in a rehabilitation centre where they were watched by a therapist who observed the OKN movements, corrected reading errors and controlled the speed of the scrolling text, whereas our subjects received their therapy unsupervised. While Read-Right may lose out in terms of efficacy in this regard, it offers considerable advantages in terms of convenience, as subjects can access therapy when and where it suits them, without the geographical restrictions imposed by face-to-face therapies. It is worth noting that at the point of writing Read-Right had been accessed at least once by 26,433 unique users in over 129 of the world's 196 countries (Figure 4).

With neurological rehabilitation studies, a key issue is "What is the correct control?" Because the interventions are often complex[29] there are often several reasonable options for what constitutes a good answer to this question; usually the form of the control group or intervention is dictated by the nature of the main hypothesis.[30] Rehabilitation studies rarely test the effects of an experimental intervention on a control group who do not have the disorder. On a pragmatic level this is understandable, as one could argue that there is little point providing therapy for a group of subjects who do not have the impairment; but on a scientific level this can leave open questions about the specificity of any therapeutic effect found in the impaired group. The current study takes advantage of the inclusive nature of web-based therapy platforms by gathering pre and post therapy data on a group of control subjects who are impaired on the main outcome (in this case, text reading) but not because they have the disorder that the therapy is specifically designed for (in this case, hemianopic alexia).

In summary we have demonstrated that a clinically validated therapy for hemianopic alexia improves text reading speed in hemianopic patients but not in subjects matched for slow text reading but without hemianopia. This study adds further weight to hypothesis that eye movement therapies are syndrome-specific.

Table 1

	Basic demographics					Questionnaire				
Group	N	Age (y)	Male %	BL reading speed (wpm)	Time from BL→5hr (days)	Response rate %	Cause: % stroke	Time from Ictus→BL (days)	Read-Right helpful? (1-10)	Reading more? (1-7)
R-HA	47	55 (17)	66	105 (61)	*22 [50]*	68	81	*75 [151]*	6.3	4.8
L-HA	36	60 (16)	83	119 (60)	*16 [28]*	61	89	*49 [562]*	6.2	5.2
Control	22	59 (13)	59	129 (60)	*18 [23]*	55	73	*342 [2890]*	7.0	5.2

Demographic data from the three Read-Right user groups: patients with right hemianopic alexia (R-HA), left hemianopic alexia (L-HA) and controls without hemianopia (Control). Mean age and reading speed (wpm=words per minute) are reported with standard deviations in curved brackets. Measures of the time taken from baseline (BL) to completion of 5 hours of Read-Right therapy (5hr), and the time from ictus to BL, had non-parametric distributions and therefore are reported using medians (in italics) with associated interquartile range in square brackets. Results from the self-report questions '*Has Read-Right helped your reading*' and '*Compared to before starting Read-Right, every day I am reading [X] time more or less*' are also presented.

Figures

Figure 2

Three examples of the visual field test results from representative participants from each patient group: top = a participant with right hemianopic alexia (R-HA); middle = a participant with left hemianopic alexia (L-HA); bottom = a participant without hemianopia (Cont).

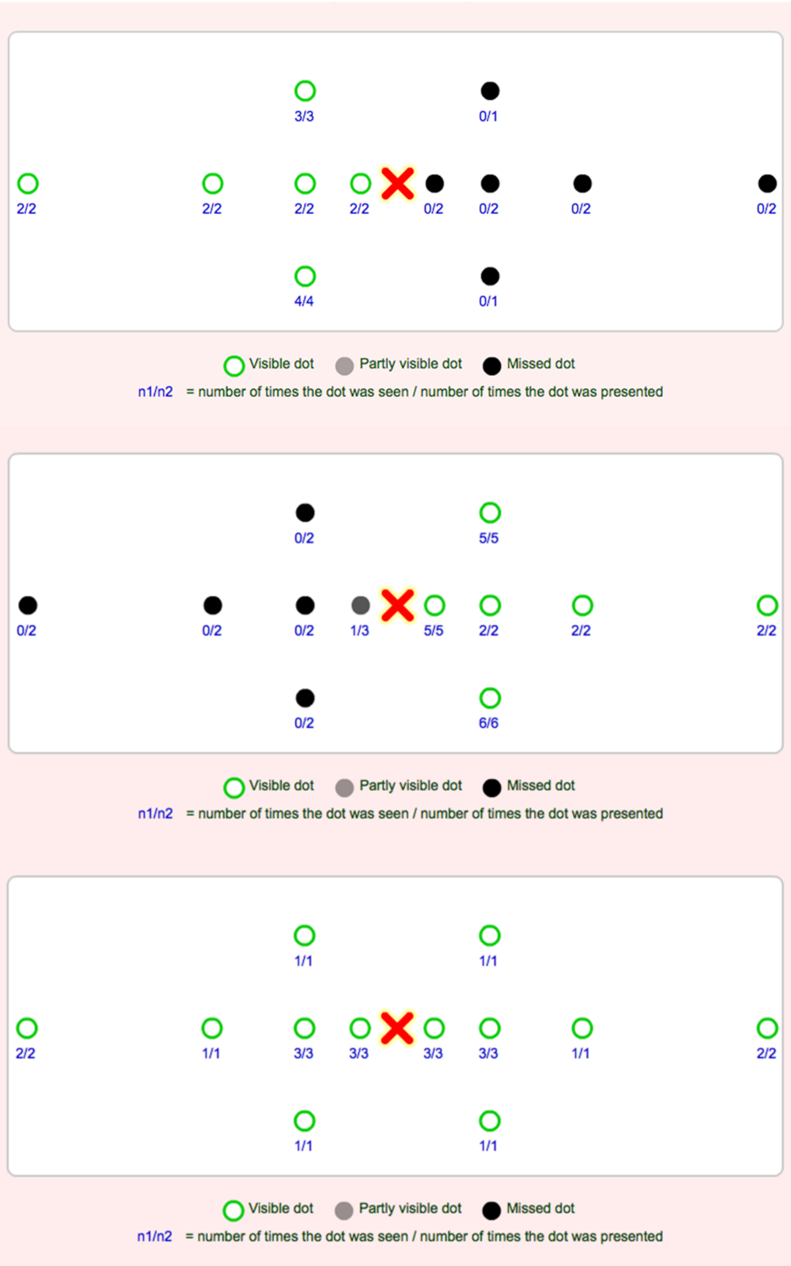


Figure 2

An example of one of the text reading tests used to measure reading speed.

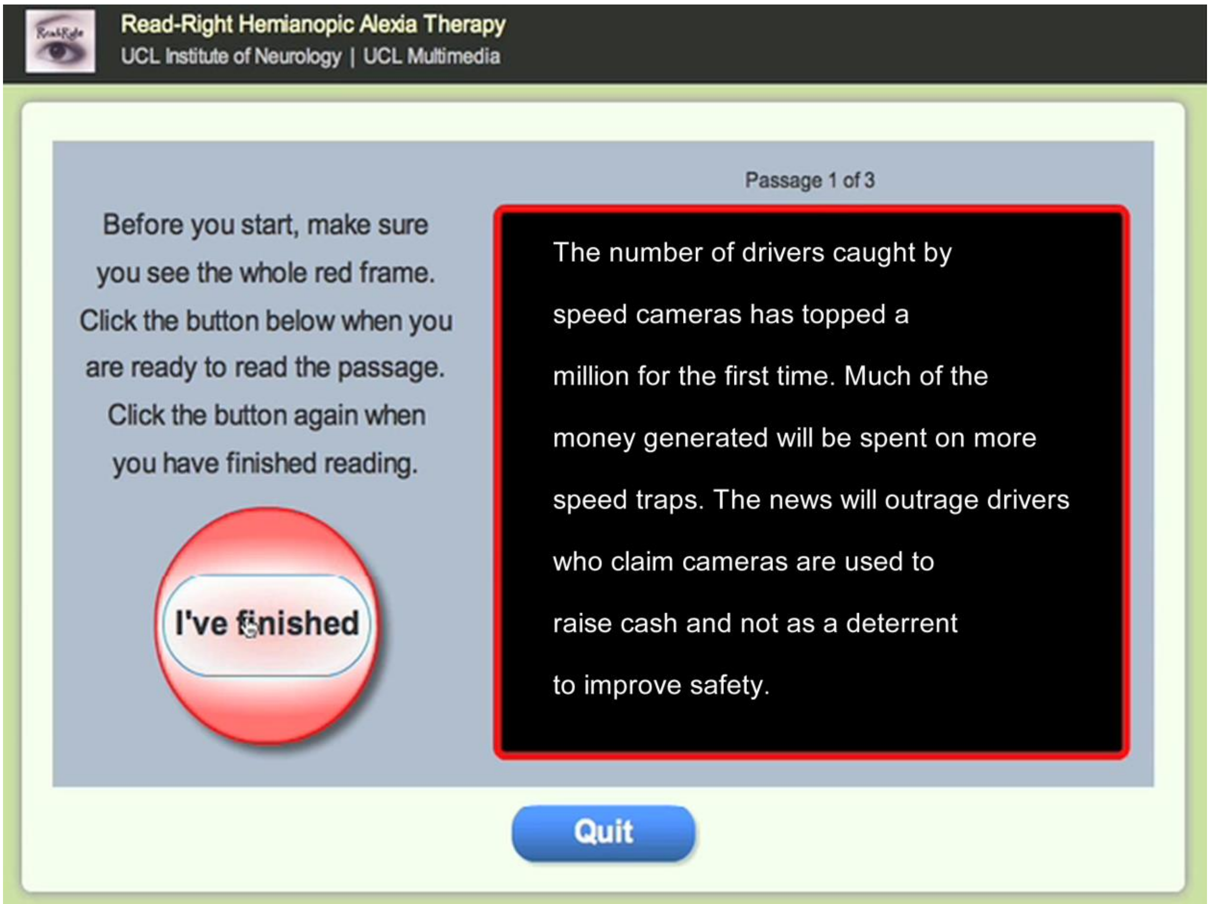


Figure 3

Text reading speeds (words per minute) at baseline (BL) and after five hours of Read-Right therapy (5hr) are reported for three experimental groups: participants with right hemianopic alexia (R-HA, red), participants with left hemianopic alexia (L-HA, green) and the control group without hemianopia (Cont, blue). A repeated measures ANOVA revealed a significant time by group interaction, driven by the specificity of the therapy effect to the R-HA and L-HA groups.

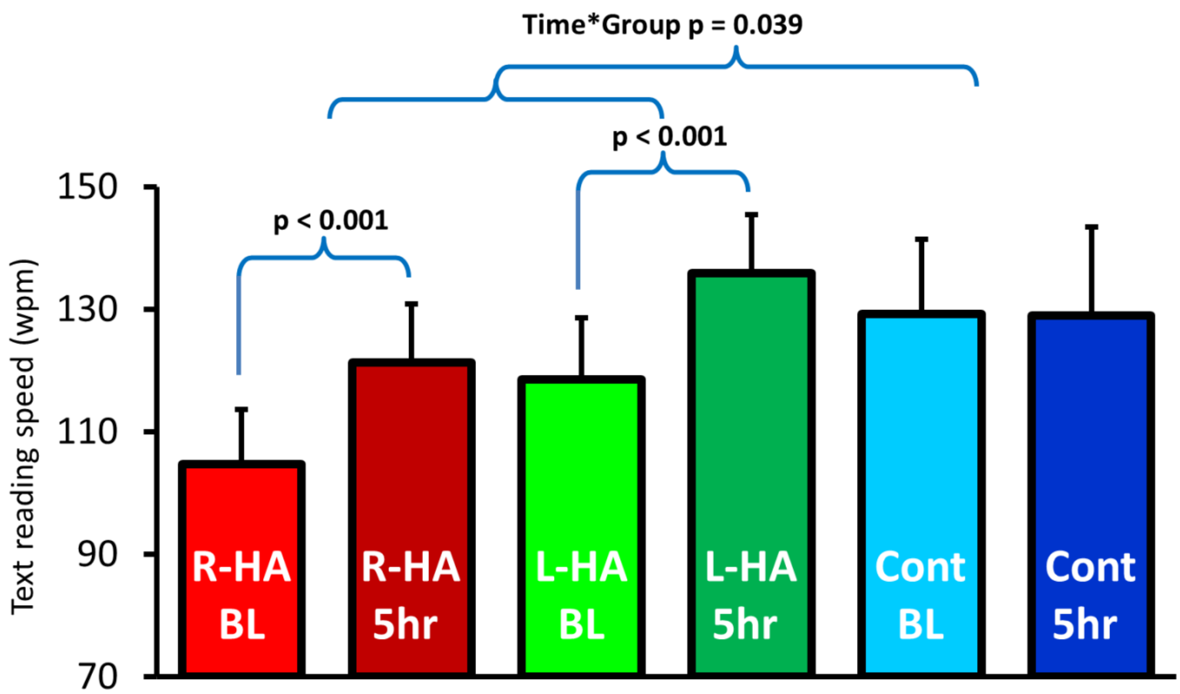
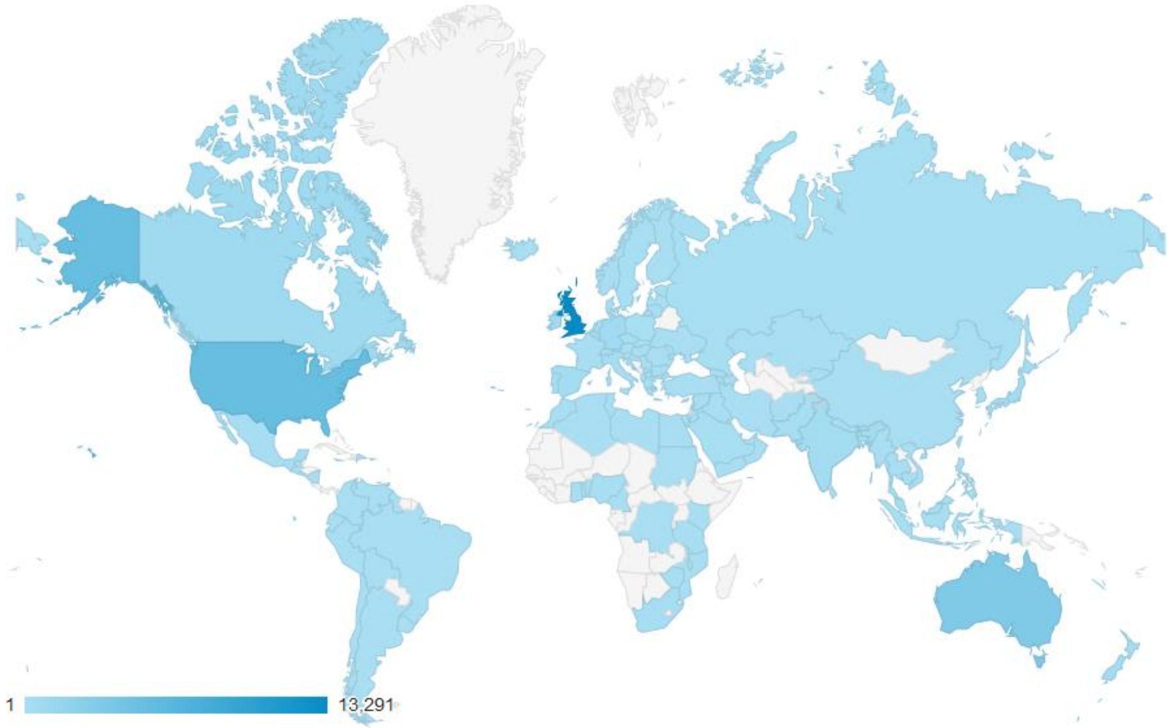


Figure 4

Infographic showing the number of Read-Right user sessions per country between February 2012 and December 2014. Data from Google Analytics©.



References

1. Rathore SS, Hinn AR, Cooper LS, et al. Characterization of incident stroke signs and symptoms: findings from the atherosclerosis risk in communities study. Stroke 2002;**33**(11):2718-21.
2. Gilhotra JS, Mitchell P, Healey PR, et al. Homonymous visual field defects and stroke in an older population. Stroke 2002;**33**(10):2417-20.
3. Feigin VL, Forouzanfar MH, Krishnamurthi R, et al. Global and regional burden of stroke during 1990-2010: findings from the Global Burden of Disease Study 2010. Lancet 2014;**383**(9913):245-54.
4. Warren M. Pilot study on activities of daily living limitations in adults with hemianopsia. Am J Occup Ther 2009;**63**(5):626-33.
5. Friedman PJ. Stroke outcome in elderly people living alone. Disabil Rehabil 1995;**17**(2):90-3.
6. Gray CS, French JM, Bates D, et al. Recovery of visual fields in acute stroke: homonymous hemianopia associated with adverse prognosis. Age Ageing 1989;**18**(6):419-21.
7. Leff A. A historical review of the representation of the visual field in primary visual cortex with special reference to the neural mechanisms underlying macular sparing. Brain Lang 2004;**88**(3):268-78.
8. Zhang X, Kedar S, Lynn MJ, et al. Natural history of homonymous hemianopia. Neurology 2006;**66**(6):901-5.
9. Zihl J. Eye movement patterns in hemianopic dyslexia. Brain 1995;**118**:891-912.
10. McConkie G, Rayner K. Asymmetry of the perceptual span in reading. Bulletin of the Psychonomic Society 1976;**8**:365-68.
11. Pollatsek A, Bolozky S, Well AD, et al. Asymmetries in the perceptual span for Israeli readers. Brain Lang 1981;**14**(1):174-80.
12. Kasten E, Wust S, Behrens-Baumann W, et al. Computer-based training for the treatment of partial blindness. Nat Med 1998;**4**(9):1083-7.
13. Reinhard J, Schreiber A, Schiefer U, et al. Does visual restitution training change absolute homonymous visual field defects? A fundus controlled study. Br J Ophthalmol 2005;**89**(1):30-5.
14. Plant GT. A work out for hemianopia. Br J Ophthalmol 2005;**89**(1):2.
15. Kerkhoff G, Munssinger U, Haaf E, et al. Rehabilitation of homonymous scotomas in patients with postgeniculate damage of the visual-system. saccadic compensation training. Restorative Neurology and Neuroscience 1992;**4**(4):245-54.
16. Ong YH, Brown MM, Robinson P, et al. Read-Right: a "web app" that improves reading speeds in patients with hemianopia. J Neurol 2012.
17. Spitzyna GA, Wise RJ, McDonald SA, et al. Optokinetic therapy improves text reading in patients with hemianopic alexia: a controlled trial. Neurology 2007;**68**(22):1922-30.
18. Schuett S, Heywood CA, Kentridge RW, et al. Rehabilitation of reading and visual exploration in visual field disorders: transfer or specificity? Brain 2012;**135**(Pt 3):912-21.
19. Schuett S, Heywood CA, Kentridge RW, et al. Rehabilitation of hemianopic dyslexia: are words necessary for re-learning oculomotor control? Brain 2008;**131**(Pt 12):3156-68.
20. Schuett S, Kentridge RW, Zihl J, et al. Adaptation of eye-movements to simulated hemianopia in reading and visual exploration: Transfer or specificity? Neuropsychologia 2009;**47**(7):1712-20.
21. Schuett S, Zihl J. Does age matter? Age and rehabilitation of visual field disorders after brain injury. Cortex 2013;**49**(4):1001-12.
22. Rayner K. Eye movements in reading and information processing: 20 years of research. Psychol Bull 1998;**124**(3):372-422.
23. Koiava N, Ong YH, Brown MM, et al. A 'web app' for diagnosing hemianopia. Journal of Neurology Neurosurgery and Psychiatry 2012;**83**(12):1222-24.

24. Kerkhoff G, Munsinger U, Eberle-Strauss G, et al. Rehabilitation of hemianopic alexia in patients with postgeniculate visual field disorders. Neuropsychological Rehabilitation 1992;**2**(1):21-41.
25. Leff Aa, Starrfelt Ra. *Alexia : diagnosis, treatment and theory*. 1st ed: Springer, 2014.
26. Rowe FJ, Wright D, Brand D, et al. A prospective profile of visual field loss following stroke: prevalence, type, rehabilitation, and outcome. BioMed research international 2013;**2013**:719096.
27. Dunlap WP, Cortina JM, Vaslow JB, et al. Meta-analysis of experiments with matched groups or repeated measures designs. Psychol Methods 1996;**1**(2):170-77.
28. Secondary 21 July 2011. http://en.wikiversity.org/wiki/Effect_size/Data_analysis_tutorial.
29. MRC. *Developing and evaluating complex interventions:new guidance*. London: Medical Research Council, 2008.
30. Leff AP, Howard D. Stroke: Has speech and language therapy been shown not to work? Nat Rev Neurol 2012;**8**(11):600-1.