Title: ReadClear: an assistive reading tool for people living with Posterior Cortical Atrophy

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Abstract

Introduction: Progressive reading impairment is an early and debilitating symptom of posterior cortical atrophy (PCA) arising from the progressive deterioration of visual processing skills . The goal of this study was to test the effectiveness of a purpose-built reading app (ReadClear) co-produced with people living with PCA and designed to reduce the reading difficulties experienced by this population (e.g. getting lost in the page and missing words when reading). .

Method: Twenty subjects with PCA were included in a cross-over design home-based study aimed at determining whether ReadClear could 1) enhance the subjective reading experience (reading pleasantness) and 2) improve reading accuracy (reducing the number of reading errors) compared with a sham condition (a standard e-reader).

Results: Reading using ReadClear provided a better subjective reading experience than sham ($p = 0.018$, d= 0.5) and significantly reduced the percentage of reading errors ($p < 0.0001$, $r = 0.82$), particularly errors due to omissions ($p = 0.01$, r = 0.50), repeated words ($p = 0.002$, r = 0.69) and regressions in the text ($p = 0.003$, r = 0.69). We found that different kinds of reading errors were related to specific neuropsychological profiles.

Conclusions: ReadClear can assist reading in people living with PCA by reducing the number of reading errors and improving the subjective reading experience of users.

1. Introduction

Posterior cortical atrophy (PCA) is a neurodegenerative condition characterized by progressive impairment of higher visual function [1,2]. Severe dyslexia is a common characteristic of the disease, present in up to 80-95% of the individuals [3,4] and occurring early in the course of the disease [2,5,6]. While impaired reading has been reported as one of the most devastating functional limitations in the early stages of the disease, there is still no treatment to mitigate the effects of the visual impairment on reading in PCA.

The degree of reading impairment in PCA is influenced and modulated by perceptual variables. Previous investigations have provided evidence of people with PCA experiencing better recognition of single words when these are presented in smaller print and better recognition also of letters presented in isolation or flanked by stimuli of reverse contrast polarity [7,8,10]. In addition, recent studies of text reading have suggested that spatial factors are the primary determinant of reading accuracy in PCA and that reducing spatial demands may result in an increment of reading performance in this population [7,9].

The reading tool presented in this study, ReadClear, is an assistive reading app co-produced between our team and a group of people living with PCA. The app's design has been informed by previous evidence in the field [7-11] and allows customization of crucial perceptual properties of the text, intending to compensate for the following: visual disorientation (e.g. getting lost on the page), difficulties with oculomotor control (e.g. inability to follow text along the line) and excessive visual crowding (e.g. letters, words or lines cluttering up together).

We evaluated the efficacy of ReadClear compared with a sham condition in a sample of people living with PCA. The main outcome measures were: 1) subjective reading experience; and, 2) reading accuracy.

2. Methods

2. 1. Study design and randomization

An overview of the design is showed in Figure 1. In a randomized cross-over, sham-controlled study, participants were exposed to reading using ReadClear and a sham condition for 7 days each. All participants received four visits as part of the study: v0: background/baseline, v1, v2 and v3 (Figure 1). After v1, patients were randomized into either group 1 (receiving sham first and ReadClear after) or group 2 (reverse order). Since this is an assistive technology and not a restorative therapy, ReadClear works only during use and therefore washout was expected to occur immediately after app cessation.

Blocked randomization was applied (2 blocks of 4 and 2 blocks of 6) using Sealed Envelope [12] generated by one of the researchers who would have no contact with the participants (AL). The list containing each subject identifier was forwarded to a person with no further relationship to the conduct of the study and who would disclose, after v1, the allocation to group to the researchers enrolling participants (ASG, IP, DO).

2.1.1. Treatment

ReadClear was the treatment condition and consists on a software-based tool (app) designed following evidence-based principles of reading impairment and improvement in PCA [7,8,9,10] The app contains the following perceptual customizable options (settings), expected to mitigate PCA-related visual and oculomotor deficits:

1) a fixation box (Figure 2, A) aiming to limit visual disorientation and inspired by scrolling text paradigms and opposite contrast polarity, to minimize crowding risk [9,13]. This box could be fixed, minimizing the need to direct fixations vertically along the frontal plane.

2) Manipulation of width of lines/number of words per line, to reduce the 'clutter' of surrounding text and therefore minimize crowding associated with text passage reading in PCA, and the option to use a full text presentation and single line presentation.

Standard settings were those available in any kind of standard eReader: three kinds of font type (Arial, Helvetica and Times New Roman), font size and color of font and background.

2.1.2. Sham

Our control reader was selected so that it should resemble the ReadClear treatment without containing the specific perceptual manipulations built into ReadClear. Its appearance was similar to that of a standard kindle or e-Reader (Figure 2 B). The interlining space was fixed to the medium interline space for a standard kindle device. Sham contained only the standard settings described above.

Participants could access contemporaneous online news through both ReadClear and sham from the BBC, The Guardian and The Telegraph websites and a small selection of popular novels.

2.2. Procedure

The ReadClear app was set up on a Samsung Galaxy Tab A (9.7, Wi-Fi) with an admin option only accessible for the researchers and password protected. Participants were told they would be exposed to two different kinds of reading apps to see what suited better but no mention of a sham or treatment condition was made. Cognitive testing and training to use the app under both conditions was spread-out across visits. Training on how to use the app followed a rigorous harmonized protocol andwas restricted to the condition to be administered in each period (ReadClear or Sham) according to group allocation (Figure 1, v2).

At the end of v2, the app was configured to the corresponding condition depending on group allocation. and settings set to users' preferred choice (personal setting preferences were explored in each one of the previous training sessions with each participant). The tablet was then left with the participants for them to use for the next 7 days (one period). The participants were encouraged to use the app as much as they liked and in the way they preferred over the following week. No set conditions were prescribed. A sealed envelope with the subjective experience of reading questionnaire was given and the patient asked to complete it at the end of the 7 days, before the next visit and in absence of the researcher. At v3 the app's mode was switched to the alternative condition (e.g. to sham if the previous condition had been ReadClear and viceversa) and the tablet left with the participants to keep using it for 7 days.A new subjective reading experience questionnaire would be provided at this time.

2.3. Participants

Recruitment

20 people living with PCA were recruited for this study over a period of 8 months between 2016 and 2017 (mean age = 65 (SD 6.3) years, 6 female:14 male), 19 of which were randomized and completed the study protocol. Participants were identified through the Dementia Research Centre PCA database, Join Dementia Research and the Oxford Cognitive Disorders Clinic at John Radcliffe Hospital. All participants had received a diagnosis of PCA according to the current diagnosis criteria (1).

Inclusion criteria

Patients with PCA who reported reading complaints were considered to take part in this research.

Exclusion criteria

Criteria included: 1) individuals that showed a severe global or reading impairment that impeded participation in the study; 2) individuals who lived abroad; and, 3) participants who took part on the co-design phase in which the ReadClear app was developed

Ethical approval for this study was granted by the National Research Ethics Service London-Queen Square ethics committee. All participants provided written informed consent for their inclusion in this study and all procedures were done in accord with the Helsinki Declaration of 1975.

2.4. Background assessment

All participants undertook a comprehensive neuropsychological and reading assessment that can be seen along with main demographics for group 1 and group 2 in Table 1.

2.5. Assessment of subjective experience of reading

A tailored 11-item, self-report questionnaire was developed to measure the subjective experience of reading (e.g. how easy you found it to keep your mind on reading?). Participants rated their experiences on a 3-point Likert scale (0-very little, 1-about right, 2-a lot) with a maximum possible score of 33. At the end of v2 and v3 a sealed envelope containing the assessment questionnaires was left with the participants for them to complete at the end of the week in the absence of the researcher to minimize experimenter bias.

2.6. Text reading assessment during the study

Reading assessment text materials

Fifteen assessment passages were selected to derive reading measures during the study (mean word count = 106 [92-117], SD = 7.3). Assessment passages were selected from the BBC news archive published more than 5 years before visits to reduce priming from current events, as described in Yong et al [9]. 14/15 passages were used as automatic reading assessment tasks during the study. The remaining baseline passage was presented in printed format Arial, font size 16, with an interline space of 1.5 lines, separated into 3 paragraphs and the participant was allowed to keep the text at their preferred distance.

The 14 passages used as automatic reading assessment tasks were presented in the same order across participants during the 14 days of the study. In this way it was always the condition, not the passage, that changed. This would allow group 1 to be exposed to passages from 1 to 7 under ReadClear and from 8 to 14 under sham, and group 2 vice versa. If the participant skipped days of practice during the study, this did not affect the order of the passage presented in the following session, as the order of presentation was linked to the day the app was used.

Reading assessment procedure during the study

Each day that the participants used the app they were presented with a reading task. The task was triggered after one minute into reading. The passage corresponding to that specific day appeared in the tablet's screen in the exact same format as the one being used by the participant for their daily reading. Reading performances were recorded and stored by the device in audio file format. Once the task was finished, the participants could return to use of the app as previously.

2.7. Outcome measures

Subjective reading experience was the main outcome measure in this study. Reading accuracy, defined as the number of words read both accurately and in the correct order within the text, was selected as the secondary outcome measure.

3. Analysis

Data collected through the tablets were stored in the device and transferred for processing at the end of the study. Audio files were removed from any identifier that might reveal the allocated condition under which they had been recorded, then manually transcribed and marked. Text marking to determine the reading accuracy and type of error took place using a tailored harmonization protocol that identified 9 types or reading errors. A detailed description of the steps followed in this process and access to the harmonized protocol can be found in Supplementary Material Text Marking.

Carry-over

Carry-over effect was assessed for all outcome measures by comparing the sum of values over both treatment periods between group 1 and group 2 using an unpaired t-test, with the null hypothesis being that carryover effects were equal between groups. P-values were in all cases above 0.1.

Outcome 1: Subjective experience of reading

Differences in scores between sham and ReadClear in the subjective reading experience questionnaire were calculated on 16/19 subjects of the sample due to 3 subjects (P1, P13 and P7) having provided incomplete questionnaires. Differences between sham and ReadClear for the total questionnaire score were calculated using a paired t-test and a Wilcoxon sign rank test was applied to analyze the differences between conditions at an item level. Effect size was calculated using Cohen's d using standard pooling variance method for normally distributed data [14] and r ($r = Z/\sqrt{N}$) for non-normally distributed data [15]. Confidence intervals were set at 95%.

Outcome 2: Reading accuracy

Taking order of word reading into account reflects a more sensitive and valid measure of reading accuracy, particularly given the characteristically disordered nature of reading in PCA. This variable was examined in 19/19 subjects. A Wilcoxon signed rank test assessed within-group differences. Nine exclusive categories of reading errors were identified: 1) words misread, 2) words misread and corrected, 3) omissions, 4) repetitions, 5) repetition of words misread, 6) additions, 7) approximations, 8) regressions in the text, 9) anticipations in the text. Regressions/anticipations were defined as words successfully read but in the wrong order in the text, resulting from returning/skipping forward to sections of the texts respectively. Total errors were the percentage of reading errors in each error category. Effect size was calculated using r ($r = Z/\sqrt{N}$) for non-normally distributed data [15]. Bonferroni partial correction (r = 0.5) was applied to correct for family wise error rate.

Relationship between neuropsychology profile and reading outcomes

Correlations were examined using a Spearman's rank order correlation and adjusted using a Bonferroni partial correction (r = 0.5).

4. Results

Outcome 1: Subjective experience of reading

Based on total questionnaire scores, there was evidence of overall improved subjective reading experience under ReadClear (mean = 11.6, SD = 5.6) compared to sham conditions (mean = 8.7, SD = 5.7), t = -2.650, p: 0.018, Cohen d = 0.51 (intermediate effect), 95% CI [-5.3, - 0.5](Figure 3, A). 32% of the questions were responded favorably under ReadClear relative to 10% for sham.

At an item level (Figure 3, B), observed group results showed that ReadClear was significantly associated with reduced frustration (Z= -1.5, p = 0.02). Results also suggested that the use of ReadClear might also favor better concentration (Z = -1.9, p = 0.05), reduce fatigue (Z = -1.8, p = 0.05), and facilitate quicker learning of how to use the tool (Z = -1.8, p = 0.05) relative to sham. There were trends towards ReadClear providing more sense of control (Z = -1.7, p = 0.08) and the users finding it easier to keep their mind on reading (Z = -1.7, p = 0.08) relative to sham. There was no evidence for improvements on measures regarding enjoyment of experience, ease of understanding the text, ease of remembering text, pleasure of reading or challenges involved in usage (p above 0.1 in all cases).

Outcome 2: Reading accuracy

There was a total of 14 passages assigned to 14 days of practice. Of the 7 passages assigned to each condition, participants completed 5.8 (±1.4) days for ReadClear and 5.4 (±1.7) for sham (see Table 2). Total percentage of errors was significantly lower for ReadClear (mean (SD) = 37 ± 29) than sham (mean [SD] = 62 [±33]; $Z = -3.54$, $p < 0.0001$, *effect size* r = 0.82 [large effect]). The preferred selection of settings combination for each participant is illustrated in Supplementary Material Table e-3.

There was evidence of significant reductions of the following error categories under ReadClear relative to sham: omissions, [$Z = -2.53$, $p = 0.01$, *effect size* $r = 0.58$ (large effect)], repetitions[$Z = -3.05$, $p = 0.002$, effect size r= 0.69 (large effect)], and regressions in the text, [$Z = -3.01$, $p = 0.003$, effect size r = 0.69 (large effect)] (see Table 2).

The above results survived correction for multiple comparisons after applying a partial Bonferroni correction (r=0.5) of p thresholded at 0.01.

There was no evidence of reductions for all other error categories under ReadClear compared to sham: words misread (mean(SD) = 6±4 vs 5±3), words misread and corrected (mean(SD)=1±2 vs 1±1), repetition of words misread (mean(SD) = 2±2 vs 2±2), additions (mean(SD) = 5±6 vs 5 ±3), approximations (mean(SD) = 1±2 vs 1±2), anticipations in the text (mean(SD) = 0 vs 0); all $p > 0.1$.

Relationship between neuropsychological profile and reading outcomes (exploratory analysis)

Scores in the subjective reading experience questionnaires after exposure to ReadClear showed a significant positive correlation with performances on a measure of verbal episodic memory (SRMT(w), $r=0.67$, $p=0.004$; Bonferroni partial correction with p set at 0.007). No statistically significant correlations were found between questionnaire scores after sham and the cognitive tests following Bonferroni correction.

ReadClear error rates inversely correlated with the percentage of errors made in sham, suggesting that individuals exhibiting worse reading accuracy in sham were those that benefited more from ReadClear (omissions, $r=0.73$, $p< 0.0001$; repetitions, $r=0.81$, $p<0.0001$; regressions, $r=0.85$, $p<0.0001$). Additionally, the higher the percentage of errors due to omissions in sham, the longer the disease duration and the lower the percentage of repetition (omissions, $r=0.50$, $p=0.029$; repetitions $r= -0.67$, $p = 0.002$) and this pattern is similar in ReadClear (omissions, $r=0.52$, $p=0.036$; repetitions $r= -0.58$, $p = 0.018$). No statistically significant associations were found between disease duration and regression errors following Bonferroni correction.

From a neuropsychological point of view, an increased tendency to make omission errors was associated with decreased performances in the MMSE (r= -0.63, p=0.004); digit span backwards r= -0.62, p=0.004), elevator counting task (r= -0.70, p=0.001); VOSP Dot Counting (r= -0.65, p=0.003), VOSP fragmented letters (r= -0.60, p=0.006) and activities of daily living (ADL) (r= 0.73, p < 0.0001). The analysis of repetition errors in sham found only a statistically significant association with Schonell performance following Bonferroni correction (r=0.64, p=0.003), with better performances in the reading test being associated with higher number of repetitions. Regression errors were associated with poor performance in the apraxia battery (FABERS total score right hand, r= -0.63, p=0.003) and in particular with right-hand transitive (r= -0.63, p=0.003) and left-hand intransitive praxis (r= -0.61, p=0.005) (all after Bonferroni partial correction with p set at 0.006).

5. Discussion

This constitutes the largest interventional study in PCA and first evidence-based assistive therapy to tackle the reading symptoms in this population. It provides evidence of improved subjective reading experience and text reading accuracy compared to a sham condition in a group of 19 individuals living with PCA.

The evidence indicates that ReadClear provided a less frustrating and tiring reading experience. It also suggests that it might facilitate concentration and it was easier to use than sham. This may be explained by the fact that reading with the app produced a lower percentage of reading errors and therefore fewer disruptions in reading, which may also have contributed to the reported improvements in concentration and the trends towards improvements on other self-reported measures (more sense of control;

finding it easier to keep their mind on reading). The positive correlation between subjective reading experience and verbal memory may be attributable to patients with better memory having better retention of themes in the text and ability to report their experience when using the app.

Reading errors overall were significantly reduced with ReadClear. Those participants who produced more errors on sham also obtained more benefit from ReadClear, which is explained because there is more room for improvement in those more severely affected. Reading errors due to omissions, repetitions and regressions were reduced. These error types are largely spatial in nature, in line with the commonly reported profile of acquired dyslexia in PCA, and so ReadClear might be considered a tool to tackle mainly visuospatial symptoms in this population. Interestingly, the higher the rates of errors due to omissions, the poorer the performances in the MMSE, tasks of sustained attention, working memory, visuoperceptual and spatial tasks and activities of daily living and the longer the disease duration. On the other hand, production of errors due to repetitions were inversely related to disease duration and only correlated positively with performances in the Schonell test of reading. Taken together, these results might indicate that repetitions are the most common error in the early stages of reading impairment, coinciding with the adoption of a regression strategy of checking back, in an effort of the patients to validate their reading. Omissions however are the kind of error characteristic of later stages of the disease, which might be due to the fact that, as disease severity worsens, so does visuospatial function, and consequently, omissions increase. Repetitions become less probable to happen then, since to be able to repeat a word you need to be exposed to it first. In addition, errors due to regressions correlated positively with signs of apraxia in sham, which may be due to accidental errors when handling the app's buttons. The characterization of how the reading errors related to specific cognitive impairments did not address the mechanisms underlying improvement of performance. This research question, which might inform a future cognitive marker to predict optimal usability of the tool, would be a relevant topic of future research.

Study limitations and strengths

The sample size is relatively small but still this constitutes the largest interventional study in PCA to date. We intended to reduce unconscious bias by: 1) randomization taking place after v1 to delay the time researchers learned the group allocation and a harmonized protocol of training administered across conditions, 2) avoiding the researchers also being raters by having participants complete questionnaires in the absence of researcher and 3) capitalizing on technology to enable a home-based study and get the app to automatically record the participants reading their passages out aloud. Despite this effort, it is possible that participants might have appreciated differences when exposed to different conditions, noticing the facilitation provided by ReadClear which would consequently influence their subjective rating. If this were the case, the resulting bias should have remained restricted to the subjective experience of reading but in fact we also observe benefits of ReadClear on objective measures of reading accuracy. Carry-over effects were not detected, although we acknowledge that, in small series, a lack of power may lead to Type II errors. In addition, the self-administration of the questionnaires avoided the potential bias arising from the influence of the research team on the feedback given by the participants. This method, however, can also increase the risk of missing data. In fact, although we made sure that a close relative was available to support the participants during their participation in the study, and with the completion of the questionnaire in particular, still three participants returned blank or uncomplete questionnaires. Another potential concern is the arbitrary selection of what we called standard settings and the definition of the sham condition. Smaller font size might have a therapeutic effect on PCA's reading speed and accuracy according to previous studies [10]. Yong et al. [10] found that increasing font size significantly reduced accuracy and speed of reading in half the sample of participants explored, a finding that has been termed as 'reverse size effect' as have been well-documented in the literature [16,17]. We however decided to keep it as a standard setting present both in sham and ReadClear because customization of font size is already an in-built feature in all e-readers on the market and eliminating this option might have incurred more bias than conserving it. Similar arguments serve to justify the customization of font and background color under sham which might, again, be seen as introducing a therapeutic element into the placebo condition since words presented in negative polarity have proved to increase the reading speed in some populations of patients e.g. those with retinitis pigmentosa [18]. Regarding color adjustments, a recent systematic review by Griffiths et al. [19] has confirmed the lack of evidence of the utility of color overlays to improve reading so its value remains controversial in different dyslexic populations. Furthermore, if font size and color customization options were actually having an effect on our results, the direction of such an effect would have been to reduce the magnitude of the benefit obtained with ReadClear which we have, nevertheless, proved strong. In the future, including a more multidimensional assessment of the reading deficits of each participant may contribute to further characterized the relationship between specific deficits and the utility of specific characteristics of the reader.

ReadClear can effectively support reading in PCA and has the potential to improve reading in patients with neurological conditions exhibiting visuospatial and eye-movements limitations.

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Tables and figures titles and legends

Table 1. Demographics and background assessment of the 20 participants recruited

Table 2. Number of days of usage and percentage of errors between condition.

Figure 1. Diagram of study design.

Timeline shows corresponding timepoints and time windows for the following: BL = background/baseline visit, V1 to V3 = timepoint of visits to the participant. The treatment blocks were either sham or ReadClear. Training = indicate when training on how to use the app was provided.

Figure 2. ReadClear full page mode versus sham.

A) Shows ReadClear in full page mode, with background text in the lowest level of opacity and mobile fixation box (user can move the box up and down with the arrows on the right). B) sham format used during the study.

Figure 3. Responses to questionnaire about the subjective reading experience.

Red bars correspond to questionnaire scores given by the participants after using ReadClear. Blue bars correspond to questionnaires' scores after sham. Figure A) shows global scores on the questionnaire after using ReadClear and sham (error bars correspond to between-person SD). Figure B) shows scores in each one of the 11 individual questions of the questionnaire. ** means $p < 0.05$, * means $p = 0.05$, + means trend toward significance, $p = 0.08$.

Supplementary Material Text Marking. Description of the marking method for the classification of reading errors and the protocol to harmonize text marking across different raters.

Supplementary Material Table e-3. Settings choice under ReadClear

Table 1. Demographics and background assessment of the 20 participants recruited ordered from less to more impairment of ADL

Participant	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	P16	P17	P18	P19	P20	Mean (SD)
Allocation group	1	2	1	2	2	2	2	2	2	1	1	1	1	1	1	2	1	1	2	2	
Demographics																					
Disease duration (m)	37	49	37	37	25	61	25	32	39	39	37	61	42	62	39	86	37	61	50	60	45 (15.2)
Age	64	63	72	57	57	70	63	58	59	65	63	58	68	62	68	59	74	78	73	71	65 (6.3)
Education	1	1	1	2	1	2	2	1	1	1	3	2	2	1	1	2	1	1	1	1	-
Years from retirement	0.5	1	6	3	1	na	0	9	3	5	2	0	5	5	0	2	10	13	4	8	4 (3.8)
Dominance	R	R	R	R	L	R	R	R	R	L	R	R	R	R	R	R	R	R	R	R	-
MMSE	25	29	24	26	15	22	24	22	29	23	20	20	16	14	23	9	14	18	19	14	20 (5.4)
Attention/working memory																					
Digit span forwards	9	11	8	12	5	6	9	6	6	5	6	7	5	2	4	3	6	3	6	2	6 (2.7)
Digit span backwards	5	4	4	3	3	3	4	3	3	3	0	3	0	0	3	1	2	3	0	2	2 (1.5)
Elevator counting TEA (/7)	7	7	7	6	5	7	6	7	7	5	5	4	2	0	4	6	6	5	1	0	4 (2.3)
Memory and Naming																					
Short RMT (/25)	25	24	24	24	16	20	18	21	25	23	22	21	21	20	13	21	17	11	11	22	19 (4.3)
Naming (verbal description)	15	17	19	17	7	16	19	17	19	18	14	18	7	14	8	5	19	12	7	13	14 (4.7)
Limb praxis FABERS																					
Transitive R	20	20	20	20	19	20	18	16	20	17	20	18	17	19	14	7	9	20	4	0	15 (6)
Transitive L	15	20	20	20	18	20	18	7	20	14	14	17	16	16	4	2	1	19	20	0	14 (7)
Intransitive R	10	10	10	10	10	10	10	10	10	9	10	10	10	10	8	8	10	10	3	6	9 (1.7)
Intransitive L	10	10	10	10	10	10	10	7	10	8	7	10	9	10	6	2	1	10	10	4	8 (2.8)
Total R	30	30	30	30	29	30	28	26	30	26	30	28	27	29	22	15	19	30	7	6	25 (7.5)
Total L	25	30	30	30	28	30	28	14	30	22	21	27	25	26	10	4	2	29	30	4	22 (9.7)
Visual processing																					
Visual acuity CORVIST	6/9	6/19	6/9	6/12	6/9	6/12	6/9	6/12	6/9	6/18	6/9	6/9	6/12	6/12	6/9	6/24	6/12	6/12	6/24	6/9	
Figure-ground VOSP (/20)	20	13	16	19	18	20	20	12	16	17	16	17	20	12	16	16	16	13	13	12	16 (2.8)

Dot counting VOSP (/10)	9	9	7	3	10	7	7	4	10	8	5	3	8	5	4	8	3	7	0	na	6 (2.7)
Fragmented letters VOSP (/20)	14	16	12	18	7	3	0	0	19	0	12	6	8	0	0	0	4	0	4	0	6 (6.7)
Flanked letters (/48)*	48	48	48	48	48	42	48	39	48	30	48	32	48	44	48	na	43	22	45	na	43 (7.6)
Cookie theft	1	0	1	1	0	1	1	1	1	0	1	1	1	0	0	0	0	0	0	0	-
Schonell (/100)	96	95	100	99	97	97	98	97	95	88	95	94	67	35	100	0	97	78	96	90	85 (25.2)
BL text reading (% errors)	14	4	13	15	15	10	9	75	na	13	60	48	19	101	26	na	16	105	110	136	43 (42.8)
ADLQ																					
Selfcare	0	6	0	6	6	17	6	6	6	6	7	6	6	6	0	33	44	61	33	61	15 (45.2)
Household care	0	0	17	28	39	22	33	22	8	33	11	87	27	87	44	80	100	67	100	100	45 (35.2)
Employment and recreation	22	17	17	14	27	33	22	22	44	39	62	56	67	52	56	57	72	86	86	81	46 (24.2)
Shopping and money	17	0	22	11	17	33	50	33	44	67	100	100	89	89	83	100	100	100	100	100	62 (37.1)
Travel	0	33	33	42	17	33	25	44	42	42	75	50	83	58	92	42	67	92	100	100	53 (28.7)
Communication	20	7	33	27	20	7	20	0	33	13	13	47	27	40	53	53	67	60	60	80	34 (22.5)
Technology	0	0	17	20	20	7	0	33	20	27	80	20	87	60	73	93	100	100	100	100	47 (39.4)
average total ADLQ	8	9	20	21	21	22	22	23	28	32	50	52	55	56	57	66	79	81	83	89	43 (26.2)

Allocation group 1 (ReadClear-Sham), group 2 (Sham-ReadClear). No differences between group in main demographic variables: age (group 1 = 67 ±6, group 2 = 63±6; χ^2 (13)=15.3, p=0.28); MMSE (group 1 = 20 ±4, group 2 = 21 ±7; χ^2 (12) = 15.3, p=0.22) and disease duration (group 1 = 45 ±11, group 2 = 46 ±19; χ^2 (10) = 11.4, p=0.32).

*Disease duration = months from symptoms onset; Education : 1 = University, 2= A-levels/equivalent, 3 = uncompleted A-levels; R = right hand, L = left hand; MMSE: Minimental state examination; Digit span forward and backward; TEA = Test of Everyday Attention; Short RMT (w) = Short Recognition Memory Test for Words; FABERS = Florida Apraxia Battery-Extended and Revised Sydney; CORVIST = Cortical Vision Screening Test; VOSP = Visual Object and Space Perception Battery; Crowding task (Yong et al.2014; Yong et al., 2013) *all errors resulting from the non-spaced condition. Cookie theft sheet from the Boston Aphasia Battery was used to test the presence of simultagnosia, 1 indicates good performance, 0 indicates impaired performance. Schonell = Schonell Reading Test.*

BL= baseline

ADLQ = Activities of Daily Living Questionnaire; ADLQ: 0-33= impairment, 34-66= moderate impairment, 67+= severe impairment. Na = not applicable due to floor effect. P16 was excluded from the analysis due to severity of reading impairment.

Table 2. Number of days of app usage and differences in the percentage of errors between condition

	N	N	Omissions			Repetitions			Regressions		
	Sham	ReadClear	ReadClear	Sham	*discrepancy*	ReadClear	Sham	*discrepancy*	ReadClear	Sham	*discrepancy*
P1	7	7	1	2	1	1	7	6	0	0	0
P2	7	7	1	1	0	5	26	21	1	3	2
P3	7	7	5	9	4	6	25	19	1	1	0
P4	5	6	1	3	2	3	38	35	0	0	0
P5	7	6	4	3	-1	3	60	57	0	0	0
P6	6	7	6	17	11	2	2	0	0	0	0
P7	5	6	6	10	4	5	26	21	0	2	2
P8	4	4	7	7	0	17	49	32	1	3	2
P9	7	7	1	1	0	4	12	8	1	0	-1
P10	2	5	12	11	-1	2	10	8	0	2	2
P11	1	2	10	42	32	30	25	-5	1	3	2
P12	7	7	13	32	19	1	4	3	0	1	1
P13	6	7	8	6	-2	4	16	12	0	1	1
P14	6	6	41	92	51	21	1	-20	1	1	0
P15	5	6	23	27	4	4	69	65	0	7	7
P17	5	6	18	14	-4	7	27	20	0	5	5
P18	6	6	17	20	3	22	24	2	0	2	2
P19	3	3	62	84	22	3	24	21	1	9	8
P20	6	6	16	34	18	18	16	-2	3	3	0
Total mean(SD)	5.4±1.7	5.8 ±1.4	13.3±15.3	21.8±26.2		8.3±8.6	24.3±18.7		0.5±0.7	2.2±2.4	

N = equivalent to number of passages read, which also corresponds to the number of days the participant used the tablet, in total, 102 passages were read under sham and 111 under ReadClear, 5 participants completed the 14 tasks (100% of the passages), 3 completed 13 (92%), 3 completed 12 (85%), 4 completed 11 (78%) and 4 participants completed 8 (57%), 7 (50%), 6 (42%) and 3 (21%) passages respectively. % of discrepancy between conditions = the difference between the percentage of errors with sham minus ReadClear for each of the three error categories.

Figure 1. Diagram of study design.

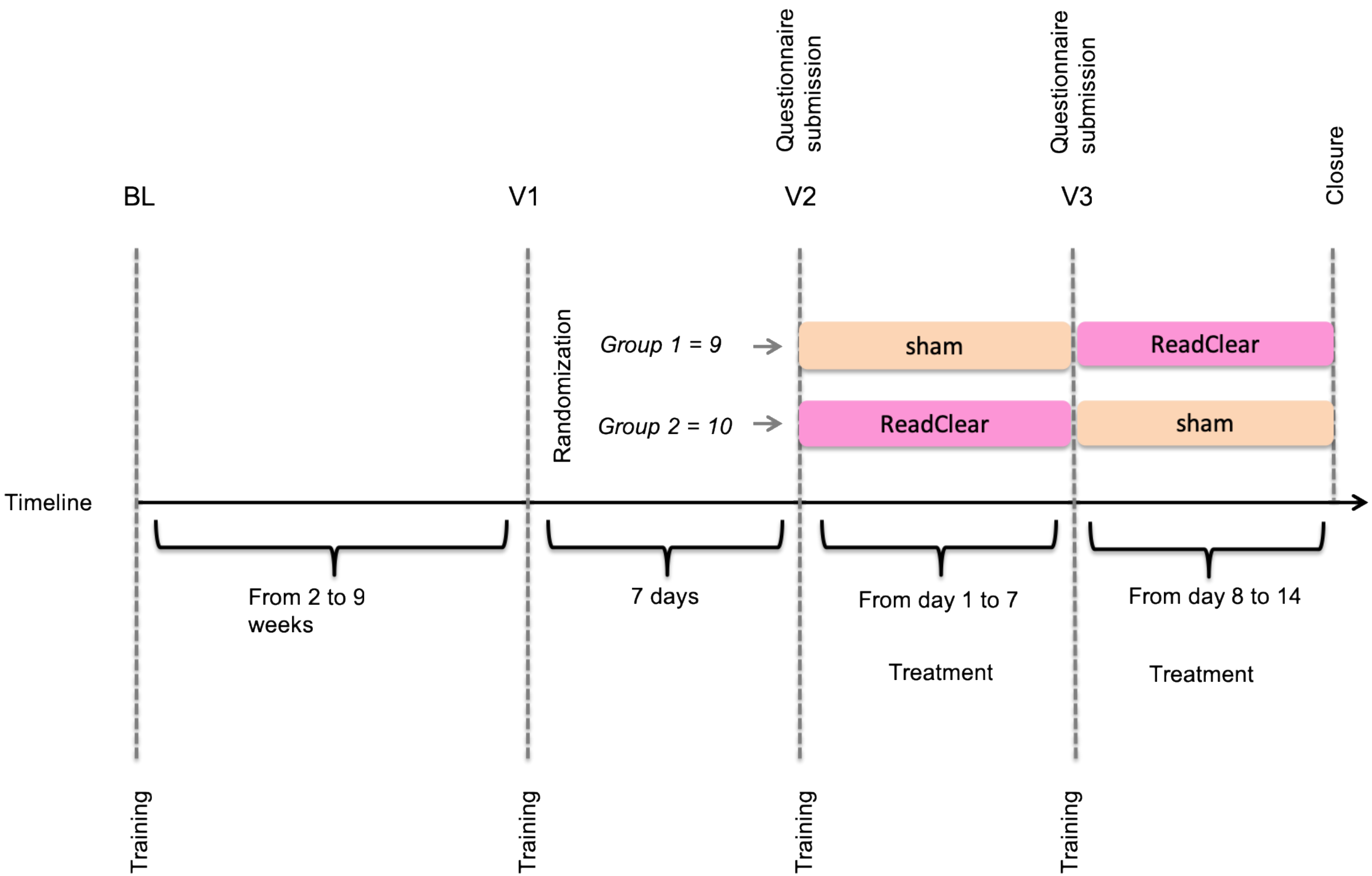


Figure 2. ReadClear full page mode versus sham.

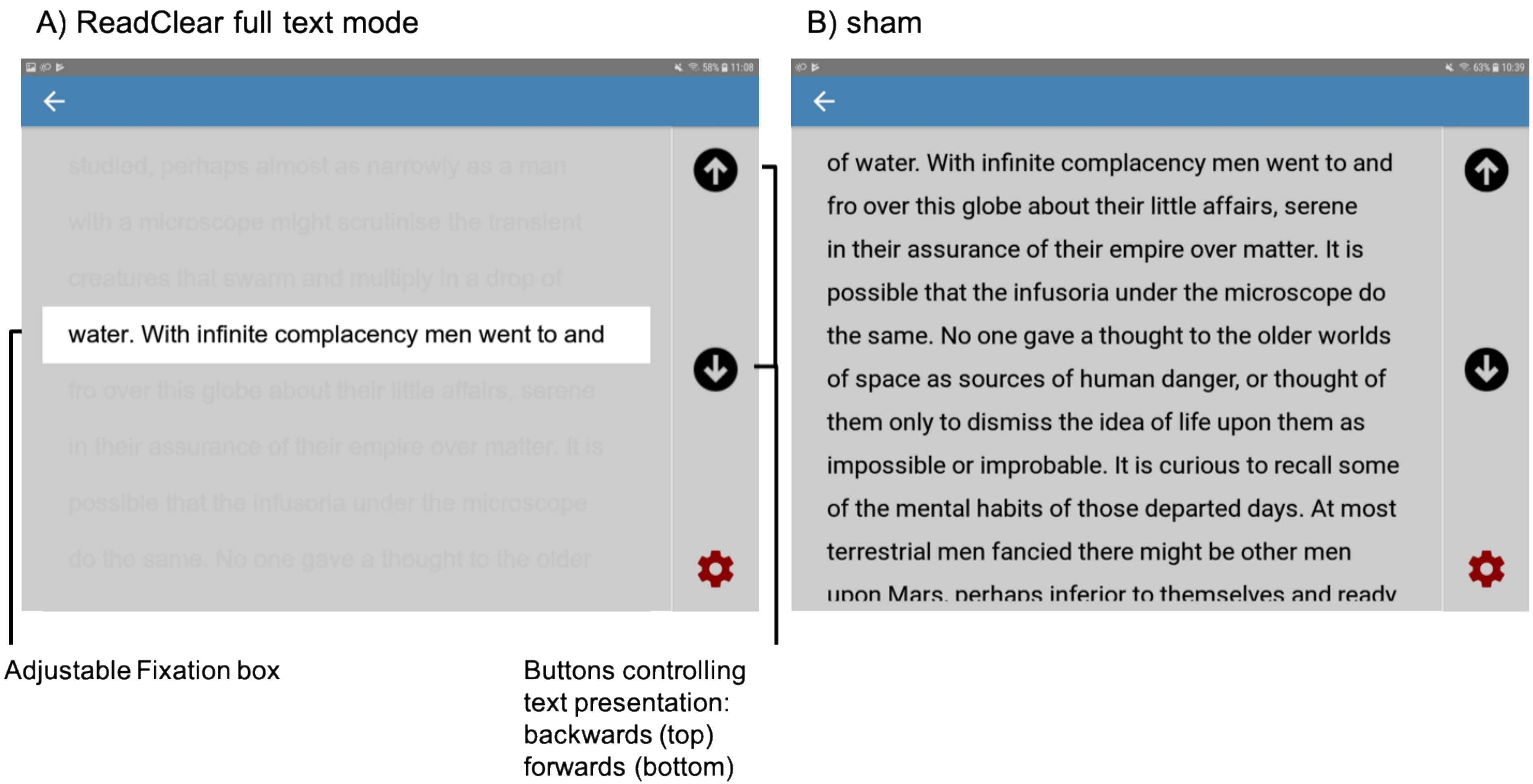
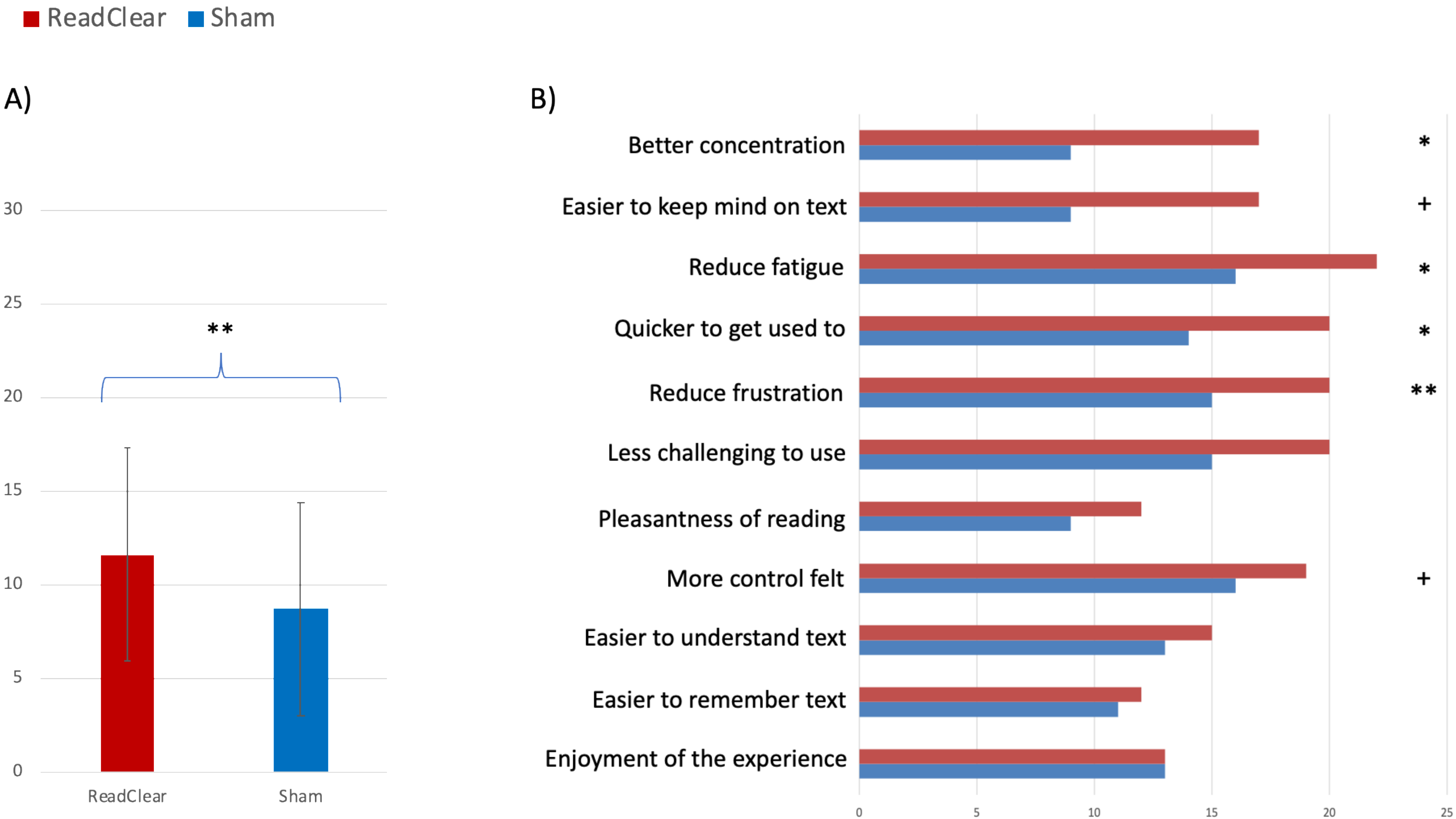


Figure 3. Responses to questionnaire about the subjective reading experience



Supplementary Material Text Marking

Description of the marking method for the classification of reading errors:

The audio files were transcribed verbatim by four members of the research team (ASG, MN, DO and IV). The full content of the audio files was transcribed, including hesitations and approximations.

The next step was marking the texts. This was conducted by ASG and MN following the below steps:

- Each word of the original audio was placed in order in cells along the column of a spreadsheet (column 1). In the immediate parallel column, the same would be done for the transcribed audio (column 2).

- A simple excel formula in the third column would identify whether the word in the first cell of column 1 would correspond to the word in the first cell of column 2 and so on until finishing the comparison between the original and the transcribed text. Score 1 would be assigned to every accurate correspondence (the word "moon" in the original text being read accurately and therefore transcribed faithfully as "moon" in the transcribed text) and score 0 to the rest.

- The outcomes from running this formula would be checked manually and corrections applied.

- Those cells scoring 0 and therefore corresponding to errors would be consequently classified as one of 9 kinds of reading errors. Error classification was informed by previous reports of acquired dyslexia in PCA (e.g. omissions, repeats and skipping lines; Yong et al., 2015) in addition to errors that were apparent during error classification (e.g. approximations)

On the purpose of harmonising the marking system for intra and interrater consistency, a protocol was developed (enclosed below). Three iterations to the entire dataset were needed to guarantee consistency and quality of marking, two of them completed by the same rater (ASG).

ReadClear's protocol to harmonise text marking across different raters

Error classification (9 categories)

Error 1: Misread (no replace)

Example:

OrigText	*Transcript*
represents	presents

This includes when a whole sentence is being read again and one of the words that was correctly read in the first attempt becomes an error during the repetition (see below).

OrigText	*Transcript*	Error
emergency	emergency	
services	services	
would	would	
carry	carry	
out	out	
a	a	
search	search	
on	on	
Saturday	Saturday	
to	to	
confirm	confirm	
they	they	
	they	Repeat
are	are	
empty	empty	
or	or	
	ooor	Repeat
	in	Added
	in	Repeat misread
	emergency	Repeat
	services	Repeat
	would	Repeat
	would	Repeat
	carry	Repeat
	out	Repeat
	a	Repeat
	search	Repeat
	on	Repeat
	Saturday	Repeat
	to	Repeat
	confirm	Repeat
	they	Repeat
	area	Misread

	they	Repeat
	are	Repeat
	empty	Repeat
	and	Repeat

It is also considered a misread error (and no *Addition* error (error 6)) when the two words flanking the target receive a point as correct response:

OrigText	*Transcript*	*Error*
example	example	
of	of	
our	the	Misread
drive	drive	
to	to	

Error 2: Misread error (then replaced)

Includes words that have been misread in the first attempt but corrected in consequent attempts.

OrigText	*Transcript*
represents	presents
	represents

This also applies to the correction following an approximation errors: "al" "alcohol"

Error 3: Omissions

The word was not read in the place where it should have been read

OrigText	*Transcript*
represents	

Error 4: Repeat

Words read correctly and repeated.

OrigText	*Transcript*
Which	Which
	Which

This includes repetitions of words coming from the error category "**Go back and read correctly"** and "**Jump ahead and read correctly".** Also including repetitions coming from **"Misread (then replace)"**

It does not include repetitions from errors categorised as **"Added"** or **"Misread (no replaced)"**
In order to be considered a *repeat error* and to avoid confusion with *Addition error (error 6)*, there will only be considered a *repeat error* a) single words like nouns and verbs that are unlikely to be additions like "equipment" and "inflatable" in opposition to function words like "when" or "to" b) two words that are repeated exactly in the same order as they have appeared before even if one of the words is a function word like "to be" or "to send".

5. Error 5: Repeat (misread)

These are words that 1) have been misread and are incorrectly read again and 2) words that had been correctly read but misread when repeated

1)

OrigText	*Transcript*
represents	presents
	presents

2)

OrigText	*Transcript*	*Error kind*
initiative	in	Approximation
	Initiative	Repeat
	ive	Repeat (misread)

Also applies to repetition of *Addition errors (error 6)*.

OrigText	*Transcript*	*Error kind*
	that	Added
they	they	I
are	are	I
	coming	Added
	that	**Repeat (misread)**
	they	Repeat
	are	Repeat

Also applies to repetitions of *Approximation errors (error 7)*.

OrigText	*Transcript*	*Error kind*
record	rec	Approximation
	record	Misread (then corrected)
attempt	attempt	I
	is	added
	a	added
	rec	**Repeat (misread)**
	record	repeat
	attempt	repeat

Error 6: Addition

Additions always correspond to an empty space in the column "Original text". Otherwise they are considered **"Misread".**

OrigText	*Transcript*
	that

This is a non-repeated, new word - These are real words but that you cannot see around in the text (otherwise they would be repetitions (error 4)).

The repetition of an addition is marked as a "Repeat (misread)" (error 5)

OrigText	*Transcript*	*Error kind*
	that	addition
	that	Repeat (misread)

Error 7: Approximation

Attempts to say a word that ends up in subject saying something that may be a word or a nonword.

For instance, if subject says:

OrigText	*Transcript*
disrupting	Dis..rup..ting

We mark it as an accurately read word (no error).

If subject says "dis …. [full stop] [attempt from scratch] dis…rupting" we count the first "dis…" as an approximation.

OrigText	*Transcript*	*Error kind*
disrupting	dis	approximation
	Dis …rupting	Misread (then replace)

If subject says "dis …. [full stop] [attempt from scratch] dis…ruptabily" we count "dis…" as an approximation.

OrigText	*Transcript*	*Error kind*
disrupting	dis	approximation
	Dis…ruptability	misread

If the subject says:

OrigText	*Transcript*	*Error kind*
week	Wo	misread
	week	Misread (then replaced)

We don't count it as an approximation and score it as a misread instead

If the subject says:

OrigText	*Transcript*	*Error kind*
attempt	a	approximation
	att	misread

If the approximation behaviour ends with "att", this is marked as misread. If it continues to another attempt it is marked as approximation

OrigText	*Transcript*	*Error kind*
attempt	a	Approximation
	att	Approximation
	attempt	Misread (then corrected)

in If the approximation behaviour happened during the repetition or a word previously read it scores as *repeat (misread) error*.

If the approximation arises from going back into the text and try reading a word previously skipped, then it is scored as Approximation *error*.

Sometimes it is necessary to go back to the audio to take the decision of whether the word is an approximation or an addition.

<u>Error 8: Go back and read correctly.</u>

Goes back and read a part of the text that has been previously skipped. E.g. a whole line or set of words or a single word.

<u>Error 9: Jump ahead and read correctly.</u>

Jumps ahead in the text by skipping a portion of it and landing in a later section that is read correctly. E.g. a whole line, or a set of words or a single word.

Supplementary Material Table e-3. Setting choice under ReadClear

	Font type	Font size	Font colour	Background colour	**Full text[a]**	Fixed box	Box colour	Column width*	**Single line[b]**	Number words
P1	Arial	39	dark red	gray	+	fixed	white	8	–	–
P2	Helvetica	32	black	gray	+	fixed	white	12	–	–
P3	Arial	24	black	gray	–	–	–	–	+	7
P4	Arial	34	dark blue	gray	+	fixed	white	12	–	–
P5	Arial	29	black	gray	+	fixed	white	7	–	–
P6	Helvetica	38	Black	gray	+	mobile	white	9	–	–
P7	Helvetica	20	black	gray	–	–	–	–	+	8
P8	Arial	27	dark red	gray	+	fixed	white	6	–	–
P9	Arial	48	black	gray	–	–	–	–	+	6
P10	Arial	28	black	white	+	fixed	white	11	–	–
P11	Arial	50	Black	white	+	fixed	white	12	–	–
P12	Arial	50	black	gray	+	mobile	gray	12	–	–
P13	Arial	50	Black	white	–	–	–	–	+	10
P14	Helvetica	43	black	gray	+	mobile	white	7	–	–
P15	Helvetica	38	black	gray	+	mobile	white	8	–	–
P17	Arial	34	black	gray	+	mobile	white	12	–	–
P18	Arial	50	black	gray	+	mobile	white	8	–	–
P19	Helvetica	31	black	gray	+	fixed	white	8	–	–
P20	Times new roman	50	black	gray	+	fixed	white	5	–	–

Fixed box: refers to fixation box; when in fixed mode, the box remains stationary in a certain location of the page and when mobile, the user can control the box moving across lines in the text. Box colour: refers to the background colour of the fixation box. *Measured in ems (ration of the letter size adjusted to the size of the fixation box). Number of words refers to the number of words occupying the width of a line. a) Full page mode, which displays a full page with text partially vanished in the background and a line at a time highlighted by a customizable fixation box controlled by the user and that can be set mobile or fixed. b) Single line mode fixation box displays only one line at a time and the possibility to modify the number of words (similar to described in Yong et al., 2015 Neurology).