Rehabilitation of pure alexia

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Rehabilitation of pure alexia: A review

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Acquired reading problems caused by brain injury (alexia) are common, either as a part of an aphasic syndrome, or as an isolated symptom. In pure alexia, reading is impaired while other language functions, including writing, are spared. Being in many ways a simple syndrome, one would think that pure alexia was an easy target for rehabilitation efforts. We review the literature on rehabilitation of pure alexia from 1990 to the present, and find that patients differ widely on several dimensions, such as alexia severity and associated deficits. Many patients reported to have pure alexia in the reviewed studies, have associated deficits such as agraphia or aphasia and thus do not strictly conform to the diagnosis. Few studies report clear and generalisable effects of training, none report control data, and in many cases the reported findings are not supported by statistics. We can, however, tentatively conclude that Multiple Oral Re-reading techniques may have some effect in mild pure alexia where diminished reading speed is the main problem, while Tacile-Kinesthetic training may improve letter identification in more severe cases of alexia. There is, however, still a great need for well-designed and controlled studies of rehabilitation of pure alexia.

Keywords: Pure alexia; Letter-by-letter reading; Word recognition; Rehabilitation.

INTRODUCTION

Pure alexia refers to the selective loss of reading ability in previously literate adults, following injury to the posterior left hemisphere. Other language functions, including writing, are intact in this disorder, although slight deficits in visual perception and confrontation naming are commonly reported (Roberts et al., in press; Starrfelt, Habekost, & Leff, 2009). Reading is commonly not entirely abolished but merely deficient, and many pure alexic patients can decipher words letter-by-letter. Pure alexia is therefore, in many ways, a simple syndrome: It affects only one function, and it rarely completely destroys it, but leaves the patient with reduced function. As such, one would think that pure alexia was an easy target for rehabilitation efforts. Indeed, quite a few different approaches to treatment of pure alexia have been made, and the aim of this paper is to review these studies, and evaluate the effect of the different approaches.

Following Dejerine's (1892) seminal description of *alexia without agraphia*, many different labels have been used for this syndrome, the most common ones being, *pure alexia, global alexia, letter-by-letter (LBL) reading*, and *spelling dyslexia.* Some indicate degree of severity (global alexic patients are totally unable to read even single letters) while others focus on the compensating strategies available to patients (LBL-reading and spelling dyslexia). It is important to note, however, that a spelling strategy is just that – a strategy – and thus available to patients with acquired reading disorders other than pure alexia, and to patients with less pure conditions. It is therefore quite unfortunate that LBL-reading has been used interchangeably with pure alexia, as it refers to a mode of reading rather than a disorder or syndrome. In this review, we have aimed to differentiate between pure alexia (as defined by the absence of agraphia and aphasia), and related syndromes/compensating strategies. We also indicate the severity of deficit, where this information is available in the reviewed papers: Mild patients commonly only have deficits affecting reading speed, more severe patients also have impairments in letter identification, and the most severely impaired may be unable to identify even single letters.

METHOD

We review the literature on rehabilitation of pure alexia in languages using Latin letters, from 1990 to 2012. We searched the following databases PsychInfo, PubMed, ScienceDirect, Web of Science, and Linguistics and Language Behavior Abstracts. We used the keywords *pure alexia, letter-by-letter reading, alexia without agraphia,* and *spelling dyslexia* in any combination with *treatment, rehabilitation, training, remediation* and *intervention.* In addition, we searched the reference lists from the resulting

papers. The final search was done on 15 October 2012. Only studies of patients reading Latin scripts were included, and only papers published in English. Studies of children were excluded.

Evaluating the outcome of cognitive rehabilitation studies is not easy, as there have until recently been few guidelines for what constitutes evidence for effect of rehabilitation efforts (see e.g., Cicerone, Azulay, & Trott, 2009). It is even more difficult when it comes to relatively rare conditions such as pure alexia, as there is little if any possibility of using randomised, controlled trials (RCT) given the scarcity of patients. Case-control studies are possible for this group of patients, but as can be seen below, such studies have never been conducted for pure alexia. One reason for this may be that the patients differ in terms of severity and associated deficits, not to mention premorbid abilities, and thus it would be very difficult to match treatment and control patients satisfactorily. There are no studies in the current review that have used normal or patient controls when aiming to evaluate the effect of a given treatment. Thus it not only remains unknown if the same performance could be seen in patients not receiving therapy, or patients with other conditions (e.g., central alexia), it is also uncertain if normal controls would perform similarly on the test materials used before and after training (even if they are carefully matched on important parameters, this is not given). Given these limitations, we have adopted quite lenient criteria for what constitutes a possible effect of treatment: (1) the test and training material and procedure should be described in sufficient details so that it is possible to describe what type of treatment had an effect on which reading processes (and to replicate the study), and (2) the difference between performance before and after training should be statistically tested and found significant. Although generalisation of treatment effects is a desired goal in many cognitive rehabilitation studies, we include here studies measuring effect on trained as well as untrained items, and comment on the type of material (trained vs. untrained) used for measuring effects in the result section.

RESULTS

In all, 20 papers were found in the literature search. One was excluded, as it included no description of the training efforts (Wilson, 1994), and another (Greenwald & Rothi, 1998) because it reported a patient with central alexia with agraphia. This latter paper was retrieved in the search for LBL-reading, because it reports teaching of an LBL strategy, however, the authors do not claim that the patient has pure alexia. The 18 papers included report rehabilitation efforts with a total of 21 patients suggested to have pure alexia or LBL-reading. In addition, four other patients with other types of

reading deficits are presented in these papers, but are not commented on in the current review.

All included papers and patients are listed in Table 1. For each patient, demographic data, aetiology, time since lesion, and the diagnosis provided in the paper are listed, as well as information about alexia severity, type of reading symptoms, and associated deficits. Of the reported associated deficits, aphasia, agraphia and anomia are listed separately, as they are of particular interest, and severity or type is indicated if this information was available in the paper. Visual field defects and visual impairments are also listed separately, as are "other" associated deficits.

Patients and diagnoses

A first glance at Table 1 reveals that quite few patients conform to the diagnosis of pure alexia (defined as alexia in the absence of agraphia and aphasia). Six patients (HT, Tuomainen & Laine, 1991; XX (no initials given), Rothi & Moss, 1992; DM, Arguin & Bub, 1994; VT, Maher, Clayton, Barrett, Schober Peterson, & Rothi, 1998; PA1 and PA2, Lacey, Lott, Snider, Sperling, & Friedman, 2010) are considered pure alexics according to this definition, as they have alexia with no (reported) agraphia or aphasia. Of the remaining patients, one has moderate anomia (Rothi, Greenwald, Maher, & Ochipa, 1998), and another seven are reported to have aphasia (TT, Tuomainen & Laine, 1991; TL, Lott, Friedman, & Linebaugh, 1994; FD, Sage, Hesketh, & Lambon Ralph, 2005; KA, Ablinger & Domahs, 2009; LDR, DBR, IND, Lott, Carney, Glezer, & Friedman, 2010). Eleven patients are reported to have writing deficits consistent with agraphia (TT, Tuomainen & Laine, 1991; KV, Daniel, Bolter, & Long, 1992; TL, Lott et al., 1994; SI, Behrmann & McLeod, 1995; DL, Lott & Friedman, 1999; RS, Friedmann & Lott, 2000; FD, Sage et al., 2005; RB, Beeson, Magloire, & Robey, 2005; LDR, DBR, IND, Lott et al., 2010), while one had quite severe spelling difficulties premorbidly (HL, Beeson, 1998). A single patient escapes classification, as he (PA, Tuomainen & Laine, 1991) has alexia with no reported agraphia, but a range of moderate to severe "other" cognitive deficits including severe visuo-spatial and constructive problems, memory deficits, and apraxia. These "visual and memory problems hampered the reading of text severely" (Tuomainen & Laine, 1991, p. 404).

In the following, we refer to the six patients who show alexia without agraphia, aphasia, or other severe cognitive deficits as *pure alexic patients* (these are: HT, Tuomainen & Laine, 1991; XX, Rothi & Moss, 1992; DM, Arguin & Bub, 1994; VT, Maher et al., 1998; PA1 and PA2, Lacey et al., 2010). The remaining patients will be referred to simply as *alexic patients*, or as having *alexia with associated deficits*.

TABLE 1
All included studies

Author(s)	Patient	Sex	Age	Aetiology[a]	Time since lesion[b]	Lesion localisation (imaging type)	Diagnosis in article[c]	Alexia severity	Reading deficits[d]	Agraphia	Aphasia	Anomia	Visual field defect[e]	Additional impairments
Tuomainen & Laine (1991)	HT*	M	56	NR	16 m	No new lesion; old right cerebellum (CT, MRI)	PA/AWA	Moderate	Slow Read	–	–	–	Remitted	Mild visuo-spatial Mild amnesia
Tuomainen & Laine (1991)	TT	M	42	Stroke	22 m	Left parieto-occipital (CT)	PA	Moderate	Slow Read	Mild	Mild	Mild	URQ	Mild visuo-spatial
Tuomainen & Laine (1991)	PA	M	65	Stroke	19 m	Left occipital, cortical + central atrophy (CT)	PA	Severe	Slow Read	–	–	–	RH	Severe visuo-spatial apraxia Neglect Severe amnesia
Daniel et al. (1992)	KV	M	43	Stroke (h) surgery	2 m	Left temporoparietal-occipital (CT)	AWA	Moderate	LBL-reading	Mild	–	Mild	URQ, partial Lo RQ	Memory deficit; tactile, verbal, visual.
Rothi & Moss (1992)	XX*	M	59	Stroke	5 y	Left occipital + posterior left internal capsule (CT)	AWA	Moderate	Slow Read	–	–	–	LoRQ	–
Arguin & Bub (1994)	DM*	NR	24	Stroke (h)	2 y	Left PCA, no callosal damage (CT, surgical report)	PA	Severe	Let Name Let Rec WLE	–	–	–	RH	Amnesia
Lott et al. (1994)	TL	M	67	Stroke (h)	>1 y	Left post. temporal and lateral occipital (CT, 3 months), left parietal atrophy (MRI, 8 months)	PA/some agraphia	Severe	Let Name WLE	Mild	Fluent	Moderate	LRQ	Mild auditory
Behrmann & McLeod (1995)	SI	F	46	Stroke	11 m	Left parietal, occipital, temporal, incl. hippocampus, fusiform and lingual gyri (SPECT, MRI)	PA, surface dysgraphia	Severe	Let Name in word endings WLE	Severe	–	Mild	RQ	Mild amnesia
Beeson (1998)	HL	M	53	Stroke (h)	10 w	Left posterior occipito-temporal, subjacent white matter (CT)	PA	Moderate	Slow Read Let Name in words	Premorbid spelling problems	–	Mild	Remitted	–

(*Continued*)

TABLE 1
Continued

Author(s)	Patient	Sex	Age	Aetiology[a]	Time since lesion[b]	Lesion localisation (imaging type)	Diagnosis in article[c]	Alexia severity	Reading deficits[d]	Agraphia	Aphasia	Anomia	Visual field defect[e]	Additional impairments
Maher et al. (1998)	VT*	F	43	Stroke	$2\frac{1}{2}$ y	Left occipital; Brodman's 28, 31, 18, lingual and fusiform gyri, cuneus, retrosplenial area (MRI)	AWA	Severe	Let Rec WLE	–	–	–	RH	–
Rothi et al. (1998)	MC	M	72	Stroke	13 m	Left occipital / occipito-parietal junction (CT)	AWA	Severe	WLE Slow Read	–	–	Moderate	URQ, partial LoRQ	Memory problems Topographic amnesia
Lott & Friedman (1999)	DL	M	67	Stroke	10 m	Left posterior temporal-occipital + old inf. right frontal parietal lobe, lacune in right basal ganglia (CT)	PA	Severe	Let Name Let Rec WLE Slow Read	Mild	–	Moderate	NR	Mild auditory
Friedman & Lott (2000)	RS	M	46	Hemangio-pericytoma. Two surgeries	4 m	Left occipital (surgery)	PA	Mild[1]	WLE Slow Read	Spelling deficit	Mild	–	RH	–
Beeson et al. (2005)	RB	M	59	Stroke (h)	22 w	Left inferior temporal, occipital (MRI)	LBL	Moderate	WLE Slow Read	Moderate	–	Mild	URQ	–
Sage et al. (2005)	FD	M	73	Stroke (h)	NR	Left parietal, temporal, occipital, right parietal, occipital (CT)	LBL	Severe	Let Name WLE	Moderate	Mild	Moderate	RH	Moderate visual
Ablinger & Domahs (2009)	KA	M	64	Stroke	$13\frac{1}{2}$ m	Left post. Hippocampus, medial lingual and fusiform gyri (CT)	PA	Severe	Let Name Let Rec WLE	. -	Fluent	Moderate	RH	Mild visual Moderate amnesia
Lacey et al. (2010)	PA1*[2]	NR	53	Stroke (h)	2 y	Left occipital/ medial temporal (description only)	PA	Mild	Errors on word-endings in text reading	–	–	–	URQ blurred	–

Study	Patient	Sex	Age	Aetiology	Time since lesion	Lesion	Diagnosis in article	Severity	Reading deficits				Visual field defect	Other deficits
Lacey et al. (2010)	PA2[*2]	NR	62	TBI	2 y	Right frontal, left temporo-occipital (description only)	PA	Mild	WLE Errors on word-endings in text reading	–	–	–	URQ	–
Lott et al. (2010)	LDR	M	61	Stroke	2 y	Left hemisphere (no scans)	PA	Severe	Let Name WLE	–	Fluent	Mild	NR	–
Lott et al. (2010)	DBR	F	84	Stroke (h)	>2 y	Left lateral occipital and post. temporal (CT)	PA	Severe	Let Name Let Rec WLE	Mild	Fluent	Severe	NR	Mild auditory impairments
Lott et al. (2010)	IND	M	68	Stroke	>1 y	Left occipital + BA 19/7 and inferior calcarine fissure (CT)	Surface alexia with agraphia / LBL-reading	Moderate	Let Name WLE	Mild	Fluent	Severe	NR	–

Patients, background variables, diagnoses provided, as well as information about the severity of the reading deficit and other cognitive or perceptual deficits given in the original publications. Studies are listed chronologically, and patients conforming to our definition of pure alexia are marked with an *.

NR = not reported; m = month; w = week; y = year.

[a]**Aetiology:** Stroke = infarction; Stroke (h) = haemorrhagic stroke; TBI = traumatic brain injury.

[b]**Time since lesion:** Number of weeks (w); months (m), or years (y) since injury.

[c]**Diagnosis in article:** Lists the label provided for the patients reading deficit in the original publications: AWA = alexia without agraphia; PA = pure alexia; LBL = letter-by-letter.

[d] **Reading deficits:** Lists the main characteristics of the patients reading performance, as provided in the original publications: LetName = deficit in letter naming; LetRec = deficit in letter recognition; SlowRead: elevated response times in word or text reading; WLE = word length effect.

[e] **Visual field defect:** L = left, R = right, U = Upper, Lo = Lower, H = hemianopia, Q = quadrantanopia.

[1] This patient is reported to have mild pure alexia, but is reported to have single word reaction times of up to 35 seconds.

[2] See main text for our concerns regarding the diagnosis of these patients.

Treatment methods and outcome

Very generally, the treatment methods used for (pure) alexia can be divided in three groups, depending on which level of the reading process they aim to ameliorate: letter identification, word reading, or text reading. This relates to the mechanism by which one aims to achieve improvement: top-down or bottom-up processing. Bottom-up treatments aim to increase or strengthen the signal extracted from the stimulus (i.e., from letters and words), for instance by using several modalities to identify individual letters. This extra input is thought to make letter identification easier by increasing the signal to noise ratio in the input (bottom-up) signal. Top-down therapies, on the other hand, aim to aid recognition by providing context information (e.g., top-down signals from semantics) to reduce the "noise". In general, one may expect different degrees of generalisation depending on what type of processing therapy is aimed at: Bottom-up treatment should improve letter identification itself, and thus improve identification of both trained and untrained words; top-down therapies rely on the presented (con)text and thus may not be expected to generalise to other texts or words to the same degree.

Under the general headings of letter, word, or text therapy hides quite a large range of different techniques, described in more detail below. Some studies employ more than one treatment method, and in these cases the task/experiments will be specified like this: (e.g., Rothi & Moss, 1992; task 2). In many of the reviewed studies, outcome is evaluated without the use of statistics. In the following, we will use the term *significant* only in relation to studies that have statistically tested the effect of training. Another issue with some of the studies is that they use the training material for testing, i.e., the patient is tested with exactly the same text or words that were used for training, or they are tested with the same material at several points during treatment. In these cases we cannot know if the patients' reading improved in general, or whether the effect was limited to the specific words or text. We will comment on whether testing was done with new or familiar material in the cases that this information is available in the original papers (this information is also listed in Tables 2–5). We will also indicate if the patient received other treatments (e.g., general language therapy) during the same period that the reading treatment was given.

Treatment targeting the letter level

Tactile/kinesthetic treatment

Patients with severe alexia often have deficits in letter naming and identification, and are thus not able to use an LBL-strategy for word reading. For

TABLE 2
Tactile-kinesthetic treatment studies

Category	Paper	Patient	Method	Treatment schedule[a]	Home Practice[b]	Improved Accuracy[c]	Improved Speed[d]	Test material familiar/ unfamiliar[e]	Statistical comparison[f]
Pure alexia	Maher et al. (1998) Task 2	VT	Kinesthetic	1 hr 4x /week $4\frac{1}{2}$ weeks	No	NR	Sentence Read	Test items – repeatedly	No
Alexia	Lott et al. (1994)	TL	Tactile-kinesthetic	1 hr 3x/week 5 months	Min. 3x/ day	Let Name Word Read Pseudo-word Read	Not tested	Pre-test – post-test Test items – repeatedly	No
	Lott & Friedman (1999)	DL	Tactile-kinesthetic	1 hr 3x/week 11 months	Yes	Let Name Let String Name Word Read	Let String Name Word Read	Pre-test – post-test	No
	Sage et al. (2005) Task 2	FD	Tactile, errorless	7 weeks	Treated at home	Word Read	Word read	Test items – repeatedly	Yes (sign)
	Lott et al. (2010)	LDR	Tactile-kinesthetic	1 hr 3x/week	Min. 3x/ day; phase 1	Let Name Word Read Sentence Read	Let Name Word Read	Pre-test – post-test Test items – repeatedly	Yes (sign)
	Lott et al. (2010)	DBR	Tactile-kinesthetic	1 hr 3x/week	Min. 3x/ day; phase 1	Let Name Word Read	Let Name Word Read	Pre-test – post-test Test items – repeatedly	Yes (sign)

(*Continued*)

TABLE 2
Continued

Category	Paper	Patient	Method	Treatment schedule[a]	Home Practice[b]	Improved Accuracy[c]	Improved Speed[d]	Test material familiar/ unfamiliar[e]	Statistical comparison[f]
	Lott et al. (2010)	IND	Tactile-kinesthetic	1 hr 3x/week	Min. 3x/ day; phase 1	Let Name Word Read Sentence Read	Let Name	Pre-test – post-test Test items – repeatedly	Yes (sign)

Main details of the treatment provided and the results reported in the original publications. Pure alexic patients (according to the definition provided in the introduction) are listed first, then patients with alexia and associated deficits in chronological order.

[a] **Treatment schedule:** The duration of training (number of times per week, number of weeks) as given in the original publications.

[b] **Home practice:** The "homework" the patient was to do during the training phase.

[c] **Improved accuracy:** The improvement in accuracy reported in the original publication (regardless of statistical support). Abbreviations: NR = not reported; LetName = single letter naming; Let String Name = letter string naming; Pseudoword Read = pseudoword reading, Sentence Read = sentence reading; Word Read = word reading.

[d] **Improved speed:** Improvement in reading speed or reaction times as reported in the original publications. Abbreviations as in previous column.

[e] **Test-material familiar/unfamiliar:** List whether the reported improvement was shown on material new or familiar to the patient. Pre-test – post-test: Outcome was measured by using the same test material before and after treatment. Test-items – repeatedly = progress was measured by testing the patient on the same material several times over the course of traning.

[f] **Statistical comparison:** List whether the reported improvement in speed or accuracy was tested statistically (and whether this was found significant).

TABLE 3
Other letter-based treatments – methods and results

Category	Paper	Patient	Method	Treatment schedule[a]	Home Practice[b]	Improved Accuracy[c]	Improved Speed[d]	Test material familiar/ unfamiliar[e]	Statistical comparison[f]
Pure alexia	Arguin & Bub (1994)	DM	Recognition of orthographic representations	2 weeks	Yes	Let String Name	Let Match Let String Name Word Read	Test items – repeatedly	Yes (sign)
Alexia	Daniel et al. (1992)	KV	LBL-reading	15 min 3x/ day, 3 weeks	Treated at home	Sentence Read	Not tested	Test items – repeatedly	No
	Behrmann & McLeod (1995)	SI	Ends-in	90 min 2x/ week, 9 weeks	NR	Letter report	Word Read	Pretest – posttest	Yes (sign)

Main details of the treatment provided and the results reported in the original publications. Pure alexic patients (according to the definition provided in the introduction) are listed first, then patients with alexia and associated deficits in chronological order.

[a] **Treatment schedule:** The duration of training (number of times per week, number of weeks) as given in the original publications.

[b] **Home practice:** The "homework" the patient was to do during the training phase. NR = not reported.

[c] **Improved accuracy:** The improvement in accuracy reported in the original publication (regardless of statistical support). Abbreviations: LetMatch = letter matching; Letter report = report of letters in given positions in a string; Let String Name = letter string naming; Sentence Read = sentence reading; Word Read = word reading.

[d] **Improved speed:** Improvement in reading speed or reaction times as reported in the original publications. Abbreviations as in previous column.

[e] **Test-material familiar/unfamiliar:** List whether the reported improvement was shown on material new or familiar to the patient Pre-test – post-test: Outcome was measured by using the same test material before and after treatment. Test-items – repeatedly = progress was measured by testing the patient on the same material several times over the course of traning.

[f] **Statistical comparison:** List whether the reported improvement in speed or accuracy was tested statistically (and whether this was found significant).

TABLE 4
Word level treatment methods and results

Category	Paper	Patient	Method	Treatment schedule[a]	Home Practice[b]	Improved Accuracy[c]	Improved Speed[d]	Test material familiar/ unfamiliar[e]	Statistical comparison[f]
Pure alexia	Rothi & Moss (1992) Task 1–3	XX	Reading of words (task 1), semantic categorisation (2) and lexical decision(3), limited exposure durations	1 h 2x/day, 2 weeks	No	Word Read (trained only)	Word Read	Pre-test – post-test	No
	Maher et al. (1998) Task 1	VT	Semantic categorisation, limited exposure durations	6 hr/total	No	No	No	Test items – repeatedly Training items(text)	No
Alexia	Rothi et al. (1998)	MC	Semantic categorisation, limited exposure durations	30 min 5x/ day, 2 weeks	No	No	No	Pre-test – post-test	No
	Friedman & Lott (2000)	RS	Semantic categorisation + reading of words, limited exposure durations	2 h 2x/day, 40 weeks	Yes	Word Read	Word Read	Pre-test – post-test Test items – repeatedly	No
	Sage et al. (2005) Task 1	FD	Word recognition (errorless learning)	7 weeks	Treated at home	Word Read, (trained only)	Word Read	Test items – repeatedly	Yes (sign)

| Ablinger & Domahs (2009) | KA | Reading of words, limited exposure durations | 2x/day, 4 weeks | No | Word Read Text Read | Let Name Word Read Text Read | Test items – repeatedly Training items (text) | Yes (sign) |

Main details of the treatment provided and the results reported in the original publications. Pure alexic patients (according to the definition provided in the introduction) are listed first, then patients with alexia and associated deficits in chronological order.

[a] **Treatment schedule:** The duration of training (number of times per week, number of weeks) as given in the original publications.

[v] **Home practice:** The "homework" the patient was to do during the training phase. NR = not reported.

[c] **Improved accuracy:** The improvement in accuracy reported in the original publication (regardless of statistical support). Abbreviations: LetName = letter naming; Text Read = text reading; Word Read = word reading.

[d] **Improved speed:** Improvement in reading speed or reaction times as reported in the original publications. Abbreviations as in previous column.

[e] **Test-material familiar/unfamiliar:** List whether the reported improvement was shown on material new or familiar to the patient. Pre-test – post-test: Outcome was measured by using the same test material before and after treatment. Test-items – repeatedly = Progress was measured by testing the patient on the same material several times over the course of traning. Training items = Outcome measured on the same material as used during training.

[f] **Statistical comparison:** List whether the reported improvement in speed or accuracy was tested statistically (and whether this was found significant).

TABLE 5
Multiple oral re-reading: Methods and results

Category	Paper	Patient	Method	Treatment schedule[a]	Home practice[b]	Improved accuracy[c]	Improved speed[d]	Test material familiar/unfamiliar	Statistical comparison
Pure alexia	Tuomainen & Laine (1991)	HT	MOR	1x/week, 2x3 months	Min. 2x/ day	NR	Word Read Text Read Non-words	Test items – repeatedly	Yes (words, sign)
	Lacey et al. (2010)	PA1	MOR	2 hrs, 1x/week 8 weeks	Read text 5x/day	Remained high	Text Read (trained texts + texts with trained words)	Training items	Yes (sign)
	Lacey et al. (2010)	PA2	MOR	2 hrs 1x/week 8 weeks	Read text 5x/day	Remained high	Text Read (trained texts + texts with trained words)	Training items	Yes (sign)
Alexia	Tuomainen & Laine (1991)	TT	MOR	1x/week 2x3 months	Min. 2x/ day	NR	Text Read	Test items – repeatedly	Yes (words, nonsign)
	Tuomainen & Laine (1991)	PA	MOR	1x/week 3 months	Min. 2x/ day	NR	No	Test items – repeatedly	Yes (words, nonsign)
	Beeson (1998)	HL	MOR	1 hr 2x/week 5 months then: 1x/week, 1 month	Min. 3x/ day	NR	Text Read	Unfamiliar	Yes (words, nonsign) No (text reading)
	Beeson et al. (2005)	RB	MOR	1x/week 32 weeks	Min. 30 min/day	Word Read	Text Read Word Read (slightly)	Unfamiliar	Yes (text, sign) No (words)

Lists the main details of the treatment provided and the results reported in the original publications. Pure alexic patients (according to the definition provided in the introduction) are listed first, then patients with alexia and associated deficits in chronological order.

[a] **Treatment schedule:** The duration of training (number of times per week, number of weeks) as given in the original publications.

[b] **Home practice:** The "homework" the patient was to do during the training phase. NR = not reported.

[c] **Improved accuracy:** The improvement in accuracy reported in the original publication (regardless of statistical support). Abbreviations: NR = not reported; Text Read = text reading; Word Read = word reading.

[d] **Improved speed:** Improvement in reading speed or reaction times as reported in the original publications. Abbreviations as in previous column.

[e] **Test-material familiar/unfamiliar:** List whether the reported improvement was shown on material new or familiar to the patient. Pre-test – post-test: Outcome was measured by using the same test material before and after treatment. Test-items – repeatedly = Progress was measured by testing the patient on the same material several times over the course of traning. Training items = Outcome measured on the same material as used during training.

[f] **Statistical comparison:** List whether the reported improvement in speed or accuracy was tested statistically (and whether this was found significant).

such patients, improvement of letter identification and naming has been a target for rehabilitation efforts, with the higher aim of enabling patients to read letter-by-letter. Tactile and kinesthetic treatments aim to provide the patient with alternatives to the impaired visual recognition of letters using other input-modalities than vision. *Tactile* treatment uses the sense of touch, typically by tracing the outline of letters on the patient's skin, and asking the patient to name the letter. *Kinesthetic* treatment utilises the patient's sense of the movements of the muscles to aid letter recognition, and is administered by having the patient write or trace letters with a finger before naming them. Combining the two treatments into *tactile-kinesthetic* training is done by instructing the patients to trace the letters onto their own skin. Tactile-kinesthetic treatment combined was used in three studies (Lott et al., 1994; Lott & Friedmann, 1999; Lott et al., 2010), one study used the tactile method alone (Sage et al., 2005; task 2), and one study used the kinesthetic method only (Maher et al., 1998, task 2). An overview of these studies, with a brief summary of the particular methods and results are presented in Table 2.

In the only study using this type of method on a patient with pure alexia (according to our definition) Maher et al. (1998; task 2) report improved reading speed for untrained sentences, following kinesthetic treatment. These sentences were, however, used repeatedly over the training sessions to test the patient's progress. No statistical comparisons are reported. In another, quite severely impaired patient with alexia and associated deficits, Sage et al. (2005) found significantly improved accuracy in word reading following treatment using errorless learning principles with simultaneous oral and tactile letter presentation. The changes were significant for both trained and untrained items (note though, that the untrained control list was presented to the patient several times during the course of training). In five patients with moderate to severe alexia with associated deficits, Lott and colleagues (Lott et al., 1994; 2010; Lott & Friedman, 1999) have reported improvements in speed and accuracy of letter naming and word reading, as well as improved accuracy in sentence reading following tactile-kinesthetic training. For three patients, the improvement was analysed statistically and found significant (LDR, DBR, IND; Lott et al., 2010). These three patients were also able to recognise letters in the repeatedly used test materials, without overt use of the tactile-kinesthetic technique, following training (Lott et al., 2010).

In sum, tactile and/or kinesthetic training seem to have some effect for patients with quite severe alexia, and, at least for some patients, the effect seems to carry over to relatively novel/untrained words. This possible generalisation effect is perhaps to be expected, as the therapy targets word reading through identification of single letters. However, studies of tactile/kinesthetic training testing the patients on completely novel material are needed to fully document the generalisability of this type of treatment. Also, as only one

study presented a pure alexic patient (Maher et al., 1998), and this study did not present any statistical tests of the reported effect, further studies on such patients are much needed.

Other treatments at the letter level

An overview of studies using other techniques for letter-level training are listed in Table 3. Daniel et al. (1992) aimed at improving the efficiency of their patient's LBL-reading, asking their patient to spell out words overtly, and then use the auditory output to identify the word. Later on, covert spelling was encouraged. The treatment started two months post-injury and lasted for three weeks until the patient's reading had reached a functional level and the patient felt confident about returning to work. No statistical tests are reported. It seems likely, given the short time since the injury, that spontaneous recovery may have contributed significantly to the improved reading in this patient. In addition, general language training was administered at the same time as the reading therapy.

Other treatments have attempted to strengthen the damaged parallel letter processing (as opposed to LBL-reading, which, at least in the overt form, is based on serial letter processing). A pure alexic patient studied by Arguin and Bub (1994) had difficulties encoding letters as abstract orthographic units, and this was hypothesised to be the cause of his LBL-reading pattern. This comprehensive study controlled testing and training material by using separate letter sets for training and testing (test words also consisted of untrained letters only). First, the patient was trained on a cross-case matching task using pairs of single letters of varying physical similarity, i.e. V-v (similar), A-a (different). The patient's task was to decide if the letters were the same or different. Subsequently the patient was trained in reading pronounceable strings of letters under time pressure in order to encourage him to abandon LBL-reading and rather encode several orthographic units in parallel. A significant improvement in reaction times in cross-case (v – V) and same-case (V - V) matching both for trained and untrained letters was evident following training. Accuracy and speed of letter string naming also improved significantly. More generally, the speed with which the patient could recognise letters, name letters in letter strings, and read words also improved with training. Note, however, that the patient was tested repeatedly with the same materials over the training sessions, so at least part of the improvement may be due to repetition of the test materials.

Using an *ends-in* strategy, where subjects are asked to report the first and last letter of a briefly presented word, Behrmann and McLeod (1995) aimed to improve their patient's (SI) ability to process letters in parallel rather than in a left–right sequence. SI also had quite severe surface agraphia and mild anomia. Words were presented at a set, short exposure duration, and SI was

instructed to report the first and last letter of every word. The exposure duration and length of words were adjusted as the patient's accuracy improved. While SI's ability to identify the final letter in a word improved significantly following this treatment, there was little effect on word reading. Using the same stimuli as in the pre-treatment testing, Behrmann and McLeod (1995) did find that the patient's mean reaction times were significantly faster post-treatment, while the word length effect was unchanged. It is possible that this drop in mean reaction time can at least partly be explained by the repetition of the stimuli, but as the data (means and stand deviations) are not reported, this is impossible for us to evaluate.

Treatments at the word level

Treatments at the word level generally target parallel processing of letters in words. Five of the six studies reviewed in this section (see Table 4 for an overview of studies, methods and main findings) used limited exposure durations in order to discourage LBL-reading and capitalise on the patients' implicit reading skills. Implicit reading refers to the ability shown by some alexic patients to evaluate the meaning or lexicality of words they cannot explicitly identify (Saffran & Coslett, 1998; Roberts, Lambon Ralph, & Woollams, 2010).

Semantic and lexical decision tasks

In this type of treatment, a single word is presented for a limited exposure duration (commonly 250 ms; too short for overt LBL-reading). The patient is then asked to assess the meaning (e.g., "animal or not", "edible or not") or lexicality (word or nonword) of the word in a two-alternative forced choice paradigm. These methods were employed in four studies (Rothi & Moss, 1992; task 2 & 3; Rothi et al., 1998; Maher et al., 1998; task 1; Friedmann & Lott, 2000). In a study using implicit reading in the treatment of a patient with moderate pure alexia, Rothi and Moss (1992) used a reading task, a semantic categorisation task, and a lexical decision task, all with limited exposure durations. They report an effect on the word reading speed of their patient following treatment. However, the effect on the patient's reading was only tested after all three treatments had been implemented, which makes it impossible to discern the effect of each task, and no statistical analyses are reported. In another pure alexic patient, Maher et al. (1998) found no effect of training with semantic categorisation at brief exposure durations.

In a study of an alexic patient with concomitant moderate anomia, Rothi et al. (1998) report a slight *deterioration* in their patient's reading skills following training with semantic categorisation. Friedman and Lott (2000; task 1), on the other hand, studying a patient with quite severe alexia and problems in spelling, report improvements in the patient's word length effect, word

reading speed and accuracy following treatment with semantic categorisation tasks at very brief exposures (30 ms). The patient's accuracy improved for trained words, also when presented in a different font than the training stimuli. In this study, the same word lists were used for pre- and post-treatment testing, and no statistical comparisons were reported. In sum, no studies of lexical or semantic categorisation of briefly presented words have reported improvement supported by statistical analyses.

Reading briefly presented words out loud

Ablinger and Domahs (2009) targeted word reading in their treatment of patient KA, who suffered from severe alexia, fluent aphasia and impaired visuospatial memory span. Language training was administered concurrently with the reading treatment. KA showed very long reaction times in reading (before training it took him on average 9 seconds to read 3–4 letter words), and he also made many reading errors (40/64 words of 3–4 letters were read correctly before training). "Limited exposure durations" for this patient were set at between 800 and 1300 ms, much less than his reaction times, but longer than in most other studies. KA was familiarised with the material in a auditory-visual verification task, where visually presented training words were presented "briefly" (800–1300 ms), and he was asked to decide if a spoken word was the same as the visually presented one. Following this familiarisation, he was trained in reading words presented for 800–1000 ms out loud. Feedback was provided on errors, and if the patient did not respond, the correct word was provided. In this study, the authors took great care to control the training and testing materials. However, outcome was measured both with trained and untrained words three times during the treatment period. Significant changes in word reading speed (from 9 to about 5 seconds) and accuracy were observed following the first intervention, both on trained and untrained words, but further training on another subset of words did not produce more improvement on either set. KA still used an overt LBL-strategy following treatment. Although not directly targeted, reaction times in letter naming, but not accuracy, also improved significantly following the first treatment period. Reading of (the same) text also improved, but was still severely impaired following treatment: KA used 14 minutes reading a text that normal subjects read in about a minute.

Friedman and Lott (2000; task 2) trained their patient, who had alexia with mild aphasia and spelling difficulties, in reading briefly (30 ms) presented words out loud, with feedback including the correct response. For nouns and function words, they report increased accuracy for trained words in particular, but also to a lesser degree for untrained words. In pseudoword reading, only accuracy for trained items improved. In this study, the same

word lists were used for pre- and post-treatment testing, and no statistical comparisons are reported.

Repeated presentation of words with feedback (errorless learning)

The basic assumption behind errorless learning is that the production of errors can lead to the encoding of incorrect representations. The therapist therefore aims to help the patient avoid errors by providing feedback and immediate correction (see Middleton & Schwartz, 2012 for a critical review of errorless learning interventions). This method was used to treat a patient with severe alexia and associated deficits in a study by Sage et al. (2005; task 1). Words were initially visually presented and read aloud to the patient, who was to look at and concentrate on the word. In a second presentation, the word was again read aloud and the patient would subsequently repeat it 5 times. If errors were made, the procedure was repeated with the same word. After a four-week period, the treatment was altered to draw additional attention to the visual features of the words (such as length and double letters) as well as reading it aloud. This was done by tracing the outline of words and printing the final letters of visually similar words in red ink. This treatment improved the patient's word reading speed significantly for untrained words, while accuracy only improved significantly on trained items (Sage et al., 2005; task 1).

Treatments targeting text reading

Multiple Oral Re-reading

In Multiple Oral Re-reading (MOR), patients are asked to read the same text aloud over and over. The main hypothesis about effects of such a treatment is that familiarisation with the text, namely the context of the sentences (syntax and semantics) will promote top-down processing rather than bottom-up LBL-reading, and that increased reliance on top-down processing should lead to a generalisation to untrained texts (Tuomainen & Laine, 1991). This interpretation has, however, recently been challenged (Lacey et al., 2010).

In this training paradigm, the patient reads out the same text either a certain number of times (Beeson,1998; Lacey et al., 2010; Tuomainen & Laine,1991) or at a certain time a day (Beeson et al, 2005) for either a predetermined period (e.g., a week; Lacey et al., 2010; Tuomainen & Laine, 1991) or until reading speed had reached a certain level (e.g., 100 words per minute; Beeson, 1998; Beeson et al., 2005). Following this, a new text is provided, and the procedure starts again. Feedback on the reading and the patient's progress is administered regularly. An overview of patients, methods and main results from the studies of MOR-treatment (Tuomainen & Laine, 1991;

Beeson, 1998; Beeson et al., 2005; Lacey et al., 2010) are presented in Table 5.

Following MOR-treatment, Tuomainen and Laine (1991) found significant improvements in the reading speed for text, words, and nonwords in their pure alexic patient (HT). In this study, the follow-up tests (words, nonwords and texts) were re-administered to the patients "three to five times during their recovery phase. Thus the patients were to a certain extent familiar with the material" (Tuomainen & Laine, 1991; p. 405). It is thus unclear how much of the observed improvement can be attributed to the MOR-training. Lacey et al. (2010), carefully controlling the content of texts for training and testing, show that MOR-treatment significantly improved the text reading speed for two mildly affected pure alexic patients, but only when these texts had a degree of word overlap with the training material (and when reading the trained text itself). The reading speed for novel texts did not improve. They interpreted this as reflecting a bottom-up effect that strengthens visual-orthographic connections, because the effects were found on practised material only. They go on to suggest, however, that a combination of bottom-up and top-down processing may be the best explanation for the treatment effects. We are concerned by the relative mildness of the deficit in the pure alexic patients reported by Lacey et al. (2010). Both patients mainly had difficiulties with word endings in text reading, and "read faster than the mildest patient reported by Behrmann, Nelson, and Sekuler (1998)" (p. 604), but few details of how word reading speed was measured are given. It is notable though, that the mildest patient from Behrmann et al.'s (1998) study has been suggested to suffer from hemianopic rather than pure alexia, given her relatively fast reaction times in reading, and small word length effect (Leff et al., 2001), and this makes us suspect that Lacey et al's (2010) patients may have suffered from hemianopic rather than pure alexia.

For their patients with alexia and associated deficits, Tuomainen and Laine (1991) report mixed findings: For patient TT, an improvement in text reading is noted, but no statistical analysis is reported. TT's single word reading speed did not significantly improve following MOR-training. For patient PA, the patient with the most severe cognitive deficits reviewed here, no improvement was noted in either single word or text reading. Beeson (1998) reports increased reading speed for untrained texts, following MOR-treatment in the alexic patient, HL, and describe a steady increase in reading rate over the six months the training lasted. No statistical comparisons are reported. Reaction times in single word reading did not improve significantly. Patient RB (Beeson et al., 2005) showed improvements in text reading over the course of MOR-training, with words per minute increasing from 37 to 57 for new text over a training period of 30 weeks. These results are not directly compared statistically, but the authors report effect-sizes for the improvement

observed in an untreated phase compared to the treatment phase, and results post-treatment. In the non-treated phase, the "index of change" effect-size was 2.69, while following the treatment, this index had an effect-size of 9.28, indicating significant improvement. RB's speed and accuracy in single word reading, as measured repeatedly with the same word lists, improved over the course of treatment, and the patient's word length effect diminished and ultimately disappeared when measured on these lists. Even with this repetition of stimuli, RB's mean reaction times for single words were still markedly elevated following treatment (mean reaction time was about 3 seconds per word).

DISCUSSION

Based on our review of the literature, we have little "evidence" to build conclusions on, or even to recommend one type of treatment over another with any degree of certainty. Studies are few, and they are mostly based on investigations of single patients that differ quite widely with regard to the severity of their reading deficit, time since onset, and associated deficits. Well-designed studies of single patients can of course be highly informative with regard to both the cognitive mechanisms affected, and effects of a given treatment method. However, the lack of similarity between studies makes it very difficult to compare patients and treatments, and thus drawing conclusions about "what works for whom" . Several papers include insufficient details for us to evaluate the training procedures and/or the outcome. There is little if any data from control participants (normal or patients), and statistical analyses of pre- and post-training tests are in many instances not reported. That said, are there any tentative conclusions we can make, or can we at least point to some interesting avenues for further research?

Are some therapies for (pure) alexia a better bet than others?

If we consider first the treatments tried on several patients and reported in more than one paper, two types of intervention stand out: Tactile and/or kinesthetic training is reported to have an effect on speed and/or accuracy in all the seven patients presented in the five studies reviewed (Lott et al., 1994; 2010; Lott & Friedmann, 1999; Maher et al., 1998, task 2; Sage et al., 2005; task 2). Lott et al. (2010) report significant statistical differences in letter naming and word reading following the combined tactile-kinesthetic training, while Sage et al. (2005) report significant improvement in word reading using combined tactile and oral letter presentation and errorless learning principles. The remaining studies of these methods do not report any statistical comparisons. For the only *pure* alexic patient treated with this method (Maher et al., Task 2), improvement is reported but not supported by

statistical analysis. Thus, as a tentative conclusion, tactile-kinesthetic training seems to have some effect when aimed at patients with poor letter recognitions skills (be they pure alexics or alexics with associated deficits), and for these patients, some generalisation to untrained words seems to occur.

For relatively mildly impaired patients (pure alexic or LBL-readers) improvement in reading speed for words and /or text is reported in six out of seven patients following multiple oral re-reading treatment (MOR). In four patients, the improvement is found to be statistically significant (Beeson et al., 2005; Lacey et al., 2010; Tuomainen & Laine, 1991), and in another two patients, effects on word reading speed are reported but not supported by statistics (Beeson, 1998; TT, Tuomainen & Laine, 1991). The effect is strongest on trained text, but significant effects on unfamiliar material have been reported in one patient (Beeson et al., 2005). For one patient, no effect of MOR-training was observed (PA, Tuomainen & Laine, 1991). PA suffered from severe associated deficits such as neglect and severe amnesia, which may be at least part of the reason for the lack of treatment effect in this patient. Again, as a very tentative conclusion, MOR may be said to have some effect on text reading in mildly affected patients.

Many of the specific treatment methods reviewed have only been tried on a single patient, making conclusions difficult regarding the effects of these treatments. We mention here only those methods where there is at least some statistical support for an effect in the single case: Training recognition of orthographic representations (Arguin & Bub, 1994); using errorless learning principles in word identification (Sage et al., 2005; Task 1.); reading out loud words presented for a limited duration (i.e., shorter than the patient's reaction times in reading; Ablinger & Domahs, 2009). Finally, a significant effect on overall reading times has been reported following training with the "ends-in" strategy (Behrmann & McLeod, 1995), but the authors themselves put more weight on the fact that the word length effect remained unchanged following treatment. These methods need to be investigated further, in order to evaluate their effect.

As a final note, the use of limited exposure duration and forced choice tasks such as semantic or lexical decision (implicit reading) does not seem to have the desired effect in treating pure alexia or LBL-reading. Indeed, two of the three studies reporting no effect, or even negative effect of treatment, have used semantic categorisation tasks with limited exposure (Maher et al., 1998; task 1; Rothi et al., 1998). These studies do have theoretical interest with regard to questions of implicit reading, which may have contributed to their publication. One can suspect that a significant number of studies of the other reviewed methods may also have had negative results, but being less theoretically interesting (and allowing for publication bias), these may never be published. This means that even if there seems to be at least some effect of some of the reviewed treatments, these results should be treated

with much caution, and further studies of both tactile-kinesthetic and MOR-training, as well as other less practised methods, are greatly needed. In fairness it should also be noted that some intervention studies have not only aimed to treat the patient(s) in question, but also to shed light on the underlying deficit(s) in pure alexia. Indeed all the studies reviewed are theoretically interesting with regard to the cognitive or perceptual mechanisms that may be at stake in reading disorders. Future studies may aid both in the understanding of the underlying deficit(s) as well as in delineating which treatments are most valuable for which patients, as defined by the locus of their particular impairment(s) as well as their associated deficits.

Should pure alexia training generalise to untrained material?

In attempts to rehabilitate cognitive deficits following brain injury, generalisation is often an explicit goal; we want patients not only to get better with the trained material, but also to improve the function itself, be it reading, attention, memory or speech. Looking at the outcome of the studies reviewed here, the effect on trained items is by far the most impressive, with little or no clear generalisation to untrained items, or at least items to which the patient has not previously been exposed. Particularly regarding the training of letter identification and naming, this seems disappointing, as one should think that training the identification of the parts of words should be more prone to have an effect on untrained items (if you can recognise the C in COW, you should be able to recognise the C in CAN). As mentioned above, the letter-based treatments seem to show the greatest degree of generalisation, although patients do not improve sufficiently to have any fluency in reading. But perhaps we should not despair: In the words of Friedman and Lott (2000, p. 236): "Improvement in accuracy resulting from the present treatment is seen, for the most part, in trained words. At first glance, this may seem to make this approach to remediation of reading in pure alexia overly daunting. Are we to retrain all words of the language? In fact, if one considers that a large proportion of most sentences is composed of a small number of very high frequency words, the task seems far more manageable. If patients could be trained to rapidly recognise the 125 or 150 most frequent words of the language, it is likely that overall reading could improve substantially." Thus, our clearest recommendation to clinicians aiming to improve reading in (pure) alexic patients would be to target words important to the patient. Our recommendations to researchers interested in (pure) alexia rehabilitation is to use controlled material for training and testing, compare performance to normal and/or patient control subjects, and analyse results using statistical tests. And importantly, to describe everything in detail when reporting the treatment attempt, be it successful or not.

Conclusion

Based on a review of the literature on rehabilitation of pure alexia, we find that no treatments have yet been discovered that can help these patients read normally or even relatively fluently, but there are some indications that therapy can improve reading speed or letter identification accuracy. The picture is complicated by the fact that most patients reported to have pure alexia in the reviewed papers have deficits other than their reading problems. As a tentative clinical recommendation, tactile-kinesthetic training may be chosen for treatment of patients with severe letter identification deficits, while the multiple oral re-reading technique may help more mildly impaired patients whose deficits are mainly reflected in reading speed. Further studies, preferably reporting control data and using statistical methods to evaluate change, are very much needed, and one may hope that new treatment methods can be developed and investigated. Also, a systematic evaluation of the effect of associated deficits on treatment for (pure) alexia would be very informative.

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