Introduction
Alexia, an acquired impairment affecting reading ability, was described in the modern era by Dejerine [1]. Although his taxonomy has been largely revised, for the layout of this article, we will respect his initial twoway subdivision. Dejerine’s simple classification depended on whether, along with impaired reading, the patient’s other main language modalities (hearing, speaking and writing) remained intact or not. He referred to the former as alexia without agraphia, now generally known as peripheral alexia, and the latter as alexia with agraphia, commonly referred to as central alexia. With the accumulation of over 100 years of patient data since Dejerine’s time, the subtypes of peripheral and central alexia have mushroomed, with the unfortunate consequence that many different terms have been used to describe the same disorder.

Although alexia can be encountered in other pathological states (a type of central alexia, surface dyslexia, can be a key presenting symptom of semantic dementia), this review is restricted to alexia caused by stroke, as this is probably the most common cause of acquired alexia in premorbidly normal readers.

It is customary in these reviews to limit comment to the last 12 months of published research, but given the paucity of publications in this difficult field, we will discuss some older relevant papers with an emphasis on those published in the last 3 years (for review of earlier studies, see [2]). Each condition will be discussed in turn along with the current best evidence on how to approach therapy.

Peripheral alexia
In these syndromes there is an isolated form of acquired reading disorder. Other language functions (writing, speech production and perception) are either normal or near normal.

Purpose of review
Reading impairments after left or right hemisphere stroke are common yet receive little attention from clinicians and therapists. In this review, we focus on the classification of acquired alexia and the current theory and practice underlying the rehabilitation of this diverse set of disorders.

Recent findings
The underlying behavioural impairments that dictate reading ability in the acquired alexias are becoming better understood; this, in turn, has led to targeted therapies being undertaken, mainly on a single subject basis. In hemianopic alexia, the most ‘peripheral’ of the acquired alexias, where text reading speed is determined largely by damage to the visual field, therapies have been directed at improving reading eye movements. In ‘pure’ alexia, techniques are usually aimed at improving whole-word recognition. In central alexic syndromes, where other language functions are also involved, the emphasis has been on strengthening connections between lexical and semantic representations, strengthening phonological representations, or both, and their association with lexical/semantic knowledge.

Summary
Despite targeted approaches to the rehabilitation of patients with alexia caused by stroke, there is still a preponderance of largely descriptive, single-case studies in the literature. In some syndromes, small trials have been attempted and the hope is that, in the future, more systematic investigations will be carried out so rehabilitation efforts can be built on a strong theoretical and empirical foundation. Well designed, single-case studies continue to play an important role in informing therapy, as these disorders are, by nature, heterogeneous.

Keywords
alexia, aphasia, hemianopia, recovery, treatment


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Hemianopic alexia

Hemianopic alexia is both the most common and most ‘peripheral’ of the alexias. It can most simply be thought of as a disorder caused by a homonymous visual field defect that encroaches within foveal or parafoveal vision (one and five degrees of radius respectively, from the fixation point), usually affecting the visual field that affords the view of upcoming text (the right visual field in left-to-right written texts). This is because information to the right of fixation is used to plan reading eye movements efficiently across text [3–5]. One obvious therapeutic target would seem to be the visual field itself. Therapies designed to restore chronically damaged visual fields exist and are still considered controversial, especially as the general dogma is that visual fields do not recover much spontaneously after the first 3 months following cerebral injury [6]. These therapies have been reviewed in two recent issues of this journal [7,8], but have not been tested in terms of their effects on reading.

Patients with hemianopic alexia make many small amplitude saccades into their blind field, up to four times the number as normal readers [9]. This is a poor strategy for two reasons: firstly, each reading fixation lasts approximately 250 ms, so reading times soon increase; second, small amplitude saccades mean that most words are not fixated at their optimum viewing point (to the left of centre for most English words), but somewhere to the left of this [10]. These and previous observations have led researchers to focus on improving hemianopic alexia patients’ eye movements via an implicit behavioural therapy (reading horizontally scrolling text) that induces an involuntary pattern of eye movements called optokinetic nystagmus. For reasons that still remain unclear, practising between 7 h to 14 h of optokinetic nystagmus reading improves reading speeds on static text by approximately 20–40% [5,11]. The lower end of this effect size was recently replicated in a randomized, controlled trial on 19 patients with hemianopic alexia [12**]. The therapy can be accessed for free on a therapy website that is due to be expanded soon: http://www.readright.ucl.ac.uk/. An excellent review of the whole field of hemianopic alexia research has recently been published [13**].

Neglect alexia and attentional alexia

These rare syndromes were described in the 1980s and are usually seen as part of a general visual inattention/neglect syndrome. Neglect alexia refers to problems reading parts of words that appear contralesionally (e.g. ‘clock’ read as ‘block’), usually following right parietal pathology [14]. Prism adaptation may ameliorate the disorder: in one recent study of eight patients with neglect alexia, following adaptation, patients’ initial fixations moved towards the (neglected) left side of the word and correct reading responses improved by a third (from 45 to 60%) [15]. Unfortunately, the authors did not test for sustained after improvement; however, a review of prism adaptation for neglect alexia and generalized visuospatial neglect suggests that this may last from 24 h up to weeks [16]. Unfortunately, the authors did not test for sustained after improvement; however, a review of prism adaptation for neglect alexia and generalized visuospatial neglect suggests that this may last from 24 h up to weeks [16].

In attentional alexia, patients complain of letter crowding, sometimes blending elements of two words into one. Patients perform better when word stimuli are presented in isolation rather than flanked by other words and letters; the lesion is usually in the left parietal lobe [17]. No trials of therapy for this, or indeed any left parietal syndrome, have been published.

Pure alexia and global alexia

Pure alexia, almost certainly a misnomer, is a form of acquired alexia in which patients can recognize (and name) individual letters but have problems efficiently reading single words [18,19]. Pure alexia has received considerable scientific attention because if it were truly a ‘pure’ condition, it could inform general questions regarding the development of brain ‘modules’ that are specific to a given category of stimuli (in this case, words). Despite many well-designed studies of pure alexia, the exact deficit is still not agreed upon at either a psychological or an anatomical level, although it is clear that the dominant (left) fusiform has a key role to play [20–23]. Patients with pure alexia can read but experience difficulty as word length increases, the so-called ‘word-length effect’. This effect is taken as evidence that patients with pure alexia read by breaking words up into their constituent letters, in contrast with normal readers who process multiple letters in parallel and show little, if any, word length effect. The laborious sequential letter-by-letter reading that is sometimes encountered in pure alexia might be better thought of as a behavioural or compensatory strategy; this is because many patients evince a word length effect but still read more quickly than would be expected if they were reading each constituent letter of a word and then assembling these to spell the word in question. There is a wide spectrum of reading ability from milder cases approaching reading speeds seen in moderate hemianopic alexia (approximately 60 words per minute) to those who take many seconds to read a single word [24]. At this severe end of the spectrum pure alexia blends into global alexia, where patients either cannot recognize letters at all or make many errors naming them. It is likely that pure alexia and global alexia exist on a continuum as patients with pure alexia are slower at reading words with letters that are highly ‘confusable’ (e.g. H, M, N) [25]. Patients with global alexia tend to have more extensive lesions that include the fusiform gyrus and, usually, the deep white...
matter of the occipital lobe [20,26]. Global alexia is very disabling, and this may be why no one has reported the successful rehabilitation of a patient with this condition.

Regardless of the root cause of pure alexia, there have been many attempts to rehabilitate it over the years. A large number of case reports exist, usually single-case studies, but there have been no randomized group studies nor have attempts been made to create a control therapy. One of the controversies has been whether to focus on improving the efficiency of patients with an explicit letter-by-letter reading strategy, or to try and abolish this ‘maladaptive’ strategy. The simplest method has been to use mass practice with stimuli designed to ‘stimulate’ the damaged route; in this case asking patients to read aloud a corpus of words many times (multiple oral rereading). The most recent example of this was in a single patient treated in the postacute phase whose recovery slope continued to improve by more than would be expected due to ‘natural’ recovery alone [27]. This patient’s word length effect improved and there was no speed/accuracy trade off; therapy was relatively intensive occurring over approximately 30 weekly sessions.

Another approach is to use cross-modal therapy such as kinaesthetic or motor cross-cuing therapy initially described by Lott [28]. Patients trace out the letters of the word they are trying to read. There have been several, broadly positive, case reports of this treatment with the most recent one using a small pool of words [29]. This approach may be best suited for patients at the slower end of the pure alexia spectrum.

Another popular strategy, although there has been little on it in recent years, has been to try and suppress overt letter-by-letter reading in patients with pure alexia and force them to read via the ‘direct’ route, utilizing the ‘Saffran Effect’; this means presenting words at brief exposure durations to facilitate implicit comprehension. The theory is based on the observation that patients with pure alexia reveal semantic knowledge about a word that is presented too briefly to allow explicit reading [30,31]. Although this effect exists in most patients with pure alexia, it is not clear how this approach will help improve reading ability which relies on correctly identifying a given word form, rather than promoting an implicit awareness of which superordinate category of words it belongs to.

Central alexia
In central alexia, the perceptual processing of letter strings is preserved and the disorder is attributable to problems ‘downstream’ of the early visual areas which interact with more general language regions processing lexical, phonological, and/or semantic information. There are three major forms of central alexia: surface, phonological and deep (‘dyslexia’ is also used interchangeably with alexia in these terms; for comparison of developmental and acquired forms of dyslexia, see [32]).

Surface alexia
In surface alexia, associated with damage to the left temporoparietal region, words that contain regular grapheme–phoneme correspondences (such as ‘save’ = regular) are read correctly whereas those that violate these correspondences (such as ‘have’ = irregular) usually result in regularization errors (‘have’ read to rhyme with ‘save’). Given this, treatments typically retrain orthographic knowledge of specific words, with some emphasis on those that are maximally problematic such as homophones (words that sound the same but have different orthographic forms, for example: too and two) and homographs (words that have the same orthographic form but are pronounced differently, e.g. close, meaning ‘shut’ or ‘near’ depending on the context). Therapy usually involves pairing the specific orthographic representation with semantics (picture or definition of word) to enhance the use of the lexical–semantic form of reading [33,34]. Also, as in pure alexia described earlier, some studies induce the patients to rely on a lexical strategy for word recognition by presenting stimuli for very brief exposure durations [35]. Because generalization to untrained items is unlikely given the word-specific focus, words of relevance to the patient are usually selected as training targets.

Phonological alexia
Patients with phonological alexia can often read familiar words (both regular and irregular) by virtue of preserved lexical–semantic representations, but fail to read nonwords [36•]. This failure arises from the inability to transform graphemes into phonemes, and, thus, nonwords are often read as real words they resemble (‘mave’ may be read as ‘save’). Within the class of real words, factors such as concreteness and frequency affect performance (better reading of concrete than abstract words, and of high compared with low frequency words). Nouns are read better than verbs that are read better than function words (pronouns, prepositions, determiners). Treatment can be directed at the sublexical or lexical process (or both). Letter-to-sound correspondences can strengthen phonological reading and these can be applied to a whole host of words, even untrained words. This is usually achieved by training a ‘key word’ which instantiates the grapheme–phoneme correspondence and then example words are used to reinforce this association. One approach has been to pair difficult words such as function words and verbs with homophones (e.g. ‘be’; with ‘bee’ [37]) or with words that share an initial phoneme (‘much’ with ‘mud’ [38••]) to establish a phonological association or relay for the difficult items; this approach has met with
some success. Lexical reading treatments usually include simultaneous spoken production of orthographic stimuli either at a single word or supraword level. In a recent study with one phonological alexic patient, multiple oral rereading treatment gave rise to substantial improvement both of known and novel text, with the reading speed for the latter up from 34 to 44 words per minute [2]. Interestingly, comprehension of text also showed some gains.

Deep dyslexia

Deep dyslexia has all the features of phonological dyslexia, but, in addition, patients make numerous semantic errors (e.g., reading ‘peach’ as ‘apricot’) [39], suggesting that these patients have additional damage that prevents intact semantic representations from being activated by letter strings. Some authors consider deep dyslexia to be a more severe version of phonological dyslexia, the two forms of alexia existing on a continuum. Similar treatment approaches are often used for both disorders, but some studies focus more on the deep dyslexia aspect. In one recent treatment study a patient was trained using a bigraph–syllable pairing method (e.g. pa–/pae/), and demonstrated better performance especially with abstract words, perhaps because of the substantial phonemic cues when little semantic information is available [40]. Also, pairing the words with pictures to enable semantic access has yielded an improvement of 80% for trained versus untrained items in a single patient with deep dyslexia [41].

The oral reading for language in aphasia method was used in another study, which utilizes repetitive multimodal stimulation to elicit a response [2]; improvements in oral reading, as well as comprehension, were observed. Other treatment strategies pair words with semantic content using word–picture matches to reinforce the link between the words and their meaning.

There have also been recent intervention studies that pair multiple outputs or inputs (cross-modal therapy). In one recent study the patient repeatedly read sentences of personally relevant scripts and, at the same time, practiced writing a subset of the words from the same scripts [42]. Compared with the 23 words per minute pretreatment baseline, they improved to 60 words per minute with some generalization on untreated material. A similar treatment approach combined written and spoken words with two patients who were given repeated training using a set of 40 words. Both made significant gains on the treated material but showed little generalization to untrained items [27].

Future directions

Important hypotheses that need to be further pursued include: generalizability; can improvements on one item transfer to similar or even distant items? Does therapy come at a price? If patients improve on a trained set of items, is there a loss of function on other items from the same or different class of visual objects? Should undamaged, or less damaged sensory/motor routes be used to circumvent problems occurring in the visual inputs to the language system? These questions can be framed even using single-case studies, if they are appropriately designed. The use of functional imaging to document the neural substrate of observed changes will also be important in shedding light on the potential for plasticity in the reading system.

Conclusion

The treatment of acquired alexia is often idiosyncratic and highly individualized, tailored to the patient’s unique combination of strengths and weaknesses. Consequently, there are few rigorous and systematic studies that carefully evaluate the efficacy of the different approaches. The field is sorely lacking a systematic evaluation of possible intervention procedures.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:
++ of special interest
* of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 763).

1. Dejerine J. A contribution to the pathoanatomical and clinical study of different types of word blindness. Memes Societe Biologique 1892; 4:41–90.

A study of optokinetic nystagmus inducing therapy for hemianopic alexia that largely recapitulated previous findings, but in the context of a controlled trial. Changes in eye-movement parameters, including increased amplitude of reading saccades into the damaged but not the undamaged hemifield, correlated with improvements in (oral) text reading speed.


36 Tree JJ. Two types of phonological dyslexia: a contemporary review. Cortex 2008; 44:696–706. A detailed analysis of 38 cases of phonological dyslexia suggests, in contrast to current views, that an effect of grammatical class (i.e. poor reading of function words) is rather uncommon. A relationship between nonword reading impairment and function word impairment, as well as nonword repetition, is seen and these are taken as evidence confirming that a ‘generalized’ phonological deficit is the root cause of phonological dyslexia.


38 Lott SN, Sample DM, Oliver RT, et al. A patient with phonologic alexia can learn to read ‘much’ from ‘mud pies’. Neuropsychologia 2008; 46:2515–2523. This study used a paired association approach in which treated items, consisting of especially problematic grammatical words (such as function words or verbs), were paired with phonological relays (words which shared the same initial letter such as ‘much’ with ‘mud’) to facilitate reading in a patient with phonological alexia. Reading performance improved considerably for trained over untrained items, but only in the phonological relay condition. Maintenance of gains over time was low but considerable saving in relearning was evident.


