THE NATURE AND PREVALENCE OF ALEXIA IN APHASIA

By

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To my parents.

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The purpose of this study was to describe the prevalence and nature of alexia in individuals with aphasia and to delineate types of errors produced by individuals with phonologic and deep alexia. Forty-one individuals with aphasia and twenty-nine controls performed an oral reading task of real word, pseudohomophone and nonword stimuli. Results showed that the prevalence of alexia associated with aphasia was found to be 80.5% and the most predominate type of alexia was phonological/deep. Predominate error type produced by alexics was phonologic ($p = 0.0004$) lending support for the simultaneous activation hypothesis. Further, regarding stimuli type, regular real words were read more accurately than irregular words which were in turn more accurate than pseudohomophones and nonwords. Finally, we found a significant covariate effect of years of formal education and reading accuracy both within and across all categories and groups ($p = 0.0085$).

CHAPTER 1
INTRODUCTION

Alexia is an acquired impairment to a premorbidly literate individual's ability to read as a result of a lesion, typically within the left hemisphere perisylvian language zone of the brain. It is commonly accepted that alexia presents concurrently with aphasia, however the incidence and prevalence of alexia within and across aphasia syndromes has not been described and reports of aphasic oral reading performance is typically limited to individual case series (Coslett, 2000; Cherney, 2004).

Alexia syndromes are typically classified according to psycholinguistic principles in terms of the pattern of reading errors revealed during oral reading of real words, pseudohomophones and nonwords and have been described using either a dual route cascade or parallel distributed processing models (Plaut et al., 1996; Coslett, 2000; Cherney, 2004). While there are inherent differences between these two models in terms of processing components, only the basic assumptions describing the alexia syndromes are reviewed here.

Surface alexia reflects impairments at the level of the lexical/semantic system and relative isolation of the phonological system. Individuals with surface alexia read real and nonwords using orthography to phonology with no or limited contribution from semantics resulting in the ability to read nonwords and difficulty reading irregular words. Phonological alexia, on the other hand, reflects impairments at the level of the phonological system and relative isolation of the lexical/semantic system. Individuals with phonological alexia read real and nonwords using an orthographic to semantics route with limited contribution from phonology resulting in the ability to read real words in the face of impaired ability to read unfamiliar words and nonwords. The mechanisms for deep alexia are similar to phonologic alexia in terms of impairment at the level of the phonological system and secondary impairment to the isolated semantic system. It has been hypothesized that phonological and deep alexia actually represent points along a continium based on observations that deep alexia often resolves towards phonologic alexia and based on symptom succession (Friedman, 1996; Glosser et al., 1990; Crisp et al., 2006). Individuals with deep alexia read words using orthography to impaired semantics with no contribution from phonology and are rendered unable to read nonwords and unfamiliar words (Plaut et al., 1996; Glosser et al., 1990; Crisp et al., 2006).

The purpose of this study was to describe the prevalence and nature of alexia in individuals with aphasia and to delineate types of errors produced by individuals with central alexia. Error analysis can provide a window into the mechanisms underlying alexic syndromes. It is hypothesized that individuals with deep or phonological alexia will produce a greater number of real word substitution errors that are not semantically related to the target item than individuals with surface alexia because they rely on an orthographic to semantics route to read with limited contribution from phonology.

Further descriptive questions will be considered; in particular we plan to describe the difference between reading performance of normal readers and individuals with aphasia both within and across word types. It is hypothesized that individuals with aphasia will be more globally impaired during the oral reading task than normal controls and that distinct patterns of aphasic reading performance both within and across word types will emerge consistent with the literature.

CHAPTER 2
METHODS

Participants

Participants were recruited through the VA RR&D Brain Rehabilitation and Research Center and surrounding community in Gainesville, Florida and consented under IRB #306-2006. Participants with aphasia (n=41) and normal control participants (n=29) were matched on the basis of age, gender, and education level. All participants were right handed, monolingual English speakers aged 21-80 years old.

Inclusion criteria for the aphasia group was a history of single left hemisphere stroke (documented by CT or MRI imaging data) at least 6 months prior to enrollment in this project resulting in aphasia as determined by standardized testing (Western Aphasia Battery). Exclusion criteria for both groups was pre-existing neurological disease or severe impairment in vision or hearing. Each participant was described using several standardized measures to assess their neurological status, word finding problems, reading competence, speech motor performance, and to screen for visual/auditory acuity. The aphasic group was a convenience sample and included 7 Broca's aphasics, 27 Anomic aphasics, 4 Conduction aphasics, 2 Transcortical Motor aphasics, and 1 Global aphasic.

Aphasic participants were profiled using the Western Aphasia Battery (WAB) (Kertesz, 1982) , the Boston Naming Test (BNT)(Kaplan et al., 1983) , the Reading Comprehension Battery for Aphasia (RCBA)(Lapointe et al., 1979), and a non-standardized speech motor performance test which was used to identify the presence or absence of apraxia of speech or dysarthria (Duffy, 2005). During the speech motor performance test participants were asked to repeat back to the investigator five increasingly longer sentences which were verbally presented to each participant one at a time. The same five sentences were then presented again verbally and the participant was instructed to repeat the sentences back to the investigator but this time "twice as fast". Participant responses were digitally recorded using a Marantz PMD671 Professional Compact Flash Recorder and Audiotechnica ATM 76 microphone. Participant responses were subjectively scored offline by the investigator to identify apraxic or dysarthric verbal errors according to the symptomology of these disorders presented within the literature. All participants completed a vision screening in which a series of symbols were presented at the top of a computer screen and were asked to identify the corresponding symbols at the bottom of the screen within a row of similar symbols by pointing. The symbols were presented in bold lowercase Arial font at 72 point centered on a white background.

The normal control participants were assessed using the same standardized measures as the aphasia group with the exception of the WAB and the RCBA and were also given the Mini-Mental Status Examination (Folstein et al., 1975) and the National Adult Reading Test (NART) (Nelson, 1982).

Item Stimuli

Stimuli were developed for this project consisting of 39 nouns (24 with regular spelling patterns, and 15 with irregular spelling patterns), 30 nonwords and 12 pseudohomophones. Item stimuli are shown in Table 2-1. Four categories were selected consisting of real words, irregular words, pseudohomophones, and nonwords. Different selection criteria were used for the selection of words for each category based on data obtained from the MRC Psycholinguistic Database (Wilson, 1988).

Real Word Stimuli

The selection criteria for hierarchy of the real words was controlled according to word type and only nouns were selected. Word length was broken down into two levels, number of syllables, and number of graphemes and phonemes which was controlled within each syllable.

For example one syllable words would have 3-4 graphemes/phonemes, two syllable words would have 4-6 graphemes/phonemes, three syllable words would have 7-9 graphemes/phonemes, four syllable words would have 9 graphemes/phonemes and a five syllable words would have 10 graphemes/phonemes. The Thorndike-Lorge written frequency was equated within and across all categories and all average values were within 1 standard deviation. The admissibility of clusters and blends was determined by word length with inclusion not permitted for short words and permitted for long words. All words were also described for the age of acquisition rating, concreteness rating, familiarity rating, imagability rating, and the number of digraphs.

Irregular Word Stimuli

Irregular words were defined as "words that violate typical letter-sound patterns in English" (Spear-Swerling et al., 2004). The selection criteria for hierarchy of the irregular words was controlled according to syllable length and all words were 1-3 syllables in length because prior test batteries typically go to 3 syllables. Selection criteria also included the Thorndike-Lorge written frequency and all words were divided into a high or low frequency subcategories with a high frequency range of 1-100 and a low frequency range of 800-2000. All words were also described for the age of acquisition rating, concreteness rating, familiarity rating, imagability rating, and the number of digraphs.

Pseudohomophone Word Stimuli

The primary criterion for the selection of the pseudohomophones was based on the Thorndike-Lorge written frequency. For this category, a 1 syllable real word was self converted into a pseudohomophone to determine the written word frequency. All words were divided into a high or low frequency subcategory with a high frequency range of 1-100 and a low frequency range of 800-2000. The pseudohomophones were also described for the age of acquisition rating, concreteness rating, familiarity rating, imagability rating, and the number of digraphs.

Nonword Stimuli

Nonwords were created and controlled according to the following hierarchy: consonant and vowel frequency and frequency values from Shriberg and Kent (1982) were used in the criteria selection. The frequency of the consonants and vowels were divided into high and low frequency subcategories. For the vowels the high frequency range was greater than 7.0, the low frequency range was less than 4.0 and for the consonants the high frequency range was greater than 5.0 and the low frequency range was less than 2.0. Thus, all words in the high frequency category contained only high frequency consonants and vowels. Similarly, all words in the low frequency category contained only low frequency consonants and vowels. One syllable, two syllable, and three syllable nonwords were created using the repertoire of consonants and vowels.

Each syllable length category was also divided into low and high frequency words. All nonwords had CV word initial. The sum and average of biphone probability using the Phonetic Probability Calculator (Vitevitch & Luce, 2004) was used calculate the sum of all biphone probabilities within each nonword. The average of the biphone probability for each category (e.g. 1-syllable, high frequency words) was also calculated. The number graphemes and phonemes was controlled within each syllable with one syllable nonwords having 3-4 graphemes/phonemes, two syllable nonwords having 4-6 graphemes/phonemes and three syllable nonwords having 7-13 graphemes/phonemes

Data Collection Procedure

Stimuli within each stimulus category were randomized for presentation by computer software and were presented to the participants one at a time using a Dell Lattitude X1 Laptop. Participants were then asked to read each stimuli aloud. Stimuli were presented centered in the middle of a white screen in black, bolded, lowercase Arial font set at 72 points. The order of presentation of stimulus categories were also randomized within and across stimulus categories. Stimulus items were advanced automatically by the computer software using an inter-stimulus interval set at 8.0 seconds. Each stimulus item was advance to the next stimulus item without a transition interval.

Scoring

The inter-stimulus interval was used to ensure that test conditions were uniform across participants and participant's responses to a stimulus item beyond 8.0 seconds were scored as incorrect. Only data on correct responses were analyzed. Responses to stimuli were recorded digitally and scored offline for accuracy and error type using a Marantz PMD671 Professional Compact Flash Recorder and Audiotechnica ATM 76 microphone. A response was scored as correct if it matched the target stimulus and did not contain an omission, addition, transposition or substitution error. Close approximations and distortions due to apraxia of speech, dysarthria or phonetic differences were scored as correct since they are considered by this design to involve motor speech planning, programming or execution level errors or differences and not linguistic planning or programming level errors. Incorrect responses were defined as false starts, no response and presence of semantic and / or phonologic errors. Errors were scored as either a "phonological" error, a "verbal" error or an "other" error.

For the purposes of this design a phonological error were operationally defined as a phonologic substitution error (e.g. one phoneme subsitition), a phonologic addition error (e.g. one phoneme), a phonologic omission error (e.g. one phomeme), a transposition or exchange error, a devoicing error or a voicing, a neologistic error which was defined as a nonword involving multiple phonologic errors. A "verbal" error was operationally defined as a real word substitution error that was not semantically related to the target stimulus item, a regularization error, a pure semantic error (a real word substitution which was semantically related to the target stimulus), and a derivational error (the addition or omission of morphologic endings). An "other" error was operationally defined as a circumlocution (e.g. "the thing you open" / door), a compensatory error without correctly producing the word (e.g. c – a – t……), no vocalization, an apraxic error (e.g. /ah, ah, ah/), a false start (e.g. "d, d, d, dar, dart"), a compensatory error (E.g. "c – a – t" spells cat), a distortion (e.g. consonant and vowel imprecision, or prolongation) or a stress error (e.g. "**A**lly vs all**Y**).

Table 2-1. Item stimuli

Real Words	Irregular Words	Pseudohomophones	Nonwords
lot	chance	fyte	nis
job	laugh	rhed	reat
red	suit	phine	kes
bin	pew	traine	nush
fib	coup	kupp	thaun
itch	heir	pset	yane
body	office	phinn	dessy
baby	promise	clinck	simite
city	service	jirm	leedle
melon	ally	rhigg	junooge
vigil	nausea	troall	choithane
boxer	bodice	kaud	shounooth
afternoon	ratio		tisadel
president	tentative		sedeatin
family	rhapsody		nysimin
caramel			shoinaejouth
promoter			chaythoinooth
meteorite			jounaethawn
ultimatum			
diplomacy			
regulator			
disability			
imbecility			
generosity			

CHAPTER 3
DATA ANALYSIS

Research Question One

To answer research question one and to determine the prevalence and type of alexia within the aphasic group simple descriptive statistics including means, standard deviations, and percentages for variables within normal, aphasic, and phonological/deep alexia subjects were used. The normal control group's mean and standard deviation was calculated for overall accuracy across word types. Any participant within the aphasia group whose overall accuracy score fell below two standard deviations of the normal control group's mean was profiled by this analysis as having alexia. For each participant, accuracy across each word type was calculated. Each participant within the aphasia group identified with alexia was further profiled as having either surface, phonological or deep alexia based on the following criteria: If the participant's nonword accuracy exceeded their regular word accuracy they were classified as having surface alexia. If the participant's regular word accuracy exceeds their nonword accuracy or was equal to their nonword accuracy they were classified as having phonological/deep alexia.

Research Question Two

To compare the amount of verbal errors and the amount of phonological errors among subjects with phonological/deep alexia, one-way repeated measures ANCOVA was used with the error type as the factor while controlling for age, gender, education, months post onset, and history of speech therapy using the Mixed procedure in SAS.

To determine if there was a difference in reading performance and moreover if there was a difference in reading performance across word types between normal subjects and aphasic subjects, a multivariate linear regression was used to account for the correlation due to simultaneous measurements on several dependent variables on a same subject. The dependent variables, total score, regular word, irregular word, pseudohomophone, and nonword sub total scores, were simultaneously related with the factor group (normal or aphasic) while controlling for covariates age, gender, education, and history of speech therapy in one model using the GLM procedure in SAS.

Scoring Reliability

To examine the intra-rater scoring reliability and inter-rater scoring reliability, Kappa coefficients were calculated to describe the agreement in identifying correct responses to items and classifying error responses to items between two ratings by the same rater and the agreement between two different raters, respectively.

CHAPTER 4
RESULTS

Research Question One

Most individuals (33 out of 41) with aphasia (80.49%) fell below 2 standard deviations of the normal reading group total mean (56.93, s.d. 6.16) and were classified as presenting with alexia. Descriptive statistics for variables among normal subjects are shown in Table 4-1 and normal total score distribution is shown in Figure 4-1. A number of individuals (8 out of 41) with aphasia (19.51%) fell within 2 standard deviations of the normal reading group mean and were classified as not presenting with alexia. Prevalence of alexia within aphasia is shown in Figure 4-2. Of those individuals with alexia and aphasia, all (33 out of 33 or 100%) were determined to read regular words more accurately than nonwords and were subsequently classified as presenting with alexia of the phonological/deep type and no individual with alexia and aphasia (0 out of 33 or 0%) presented with an alexia of the surface type.

Research Question Two

The results of comparing the amount of verbal errors and the amount of phonological errors among subjects with phonological/deep alexia are shown in Table 4-2. Subjects with Phonological/Deep Alexia made significantly more phonological errors ($p= 0.0004$) than verbal errors after controlling for age, gender, months post onset, education, history of speech language therapy. Distribution of alexic reading error types are shown in Figure 4-3.

There is a significant difference in total score between the normal reading group and the subjects with aphasia after controlling for gender, age, education and history of speech therapy. The effect of variables on reading performance are shown in Table 4-3. The subjects with aphasia had significant lower mean total score (26.117 less) than the normal reading group after controlling for covariates. Education is also significantly positively associated with total scores

(p= 0.005). MANOVA tests show that there is significant overall group (aphasic versus normal) effect ($p < 0.0001$) and overall education effect (p= 0.0085) on total scores.

There is a significant difference in Regular word, Irregular word, Pseudohomophone, and Nonword subtotal scores between the normal reading group and the subjects with aphasia after controlling for gender, age, education, and history of speech therapy. The subjects with aphasia had significant lower Regular word (7.765 less), Irregular word (6.787 less), Pseudohomophone (5.285 less), and Nonword (6.280 less) subtotal scores than the normal reading group after controlling for covariates. Education is also significantly positively associated with Regular word (p= 0.015), Irregular word (p= 0.019), and Nonword (p= 0.0003) subtotal scores, and marginally significantly associated with Pseudohomophone (p= 0.059) subtotal scores. MANOVA tests show that there is significant overall group (aphasic versus normal) effect ($p < 0.0001$) and overall education effect (p= 0.0085) on all subtotal scores.

Scoring Reliability

Kappa coefficient (95% confidence interval) is 0.9764 (0.9702, 0.9825) and 0.9603 (0.9531, 0.9674) for the agreement between ratings by the same rater at different time on identifying correct responses to items and on classifying error responses to items, respectively, and is 0.9024 (0.8779, 0.9269) and 0.8462 (0.8197, 0.8727) for the agreement between ratings by different raters on identifying correct responses to items and on classifying error responses to items, respectively. These high kappa coefficients indicate strong agreement between ratings by the same rater at different time and between ratings by different raters.

Table 4-1. Statistical profile of normal subjects

Variable	N	Mean ± SD	% yes
Age	29	61.66 ± 9.72	
Education	29	15.45 ± 2.58	
Female	29		62.07
SLP-history (yes)	29		6.90
Total score	29	56.93 ± 6.16	

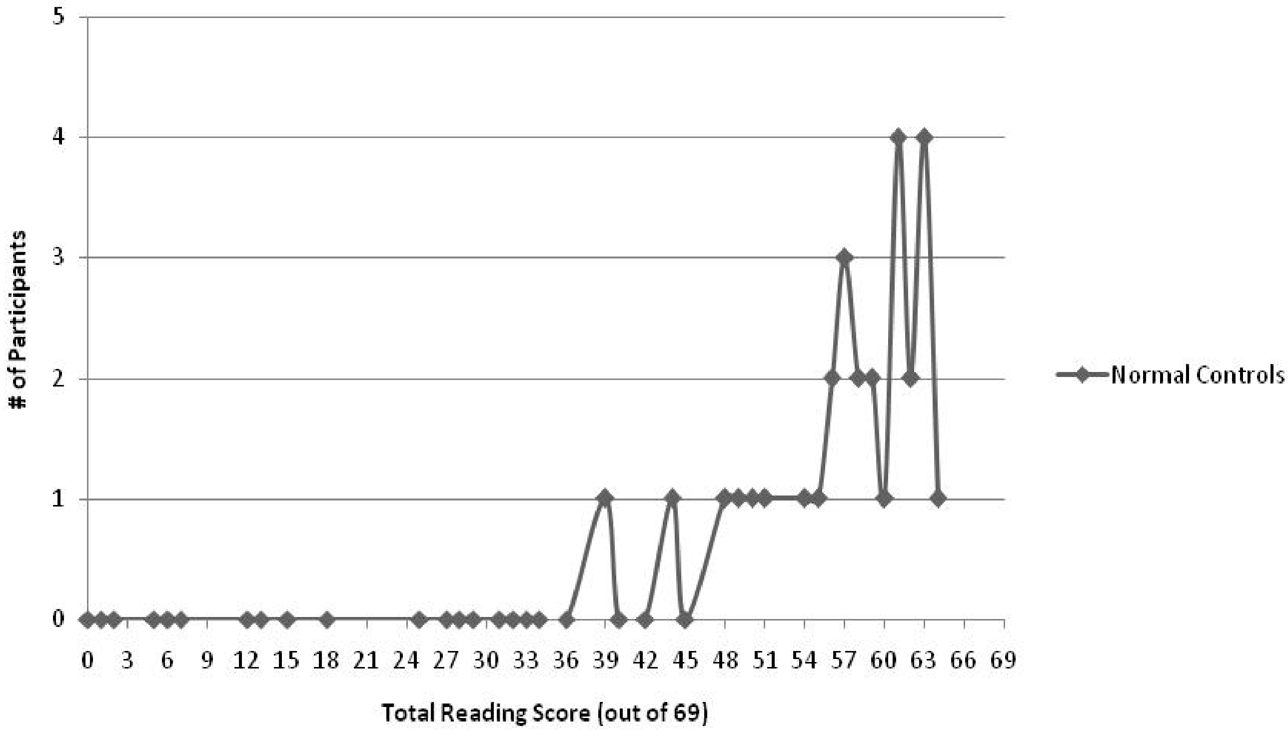

Figure 4-1. Distribution of total scores among the normal group

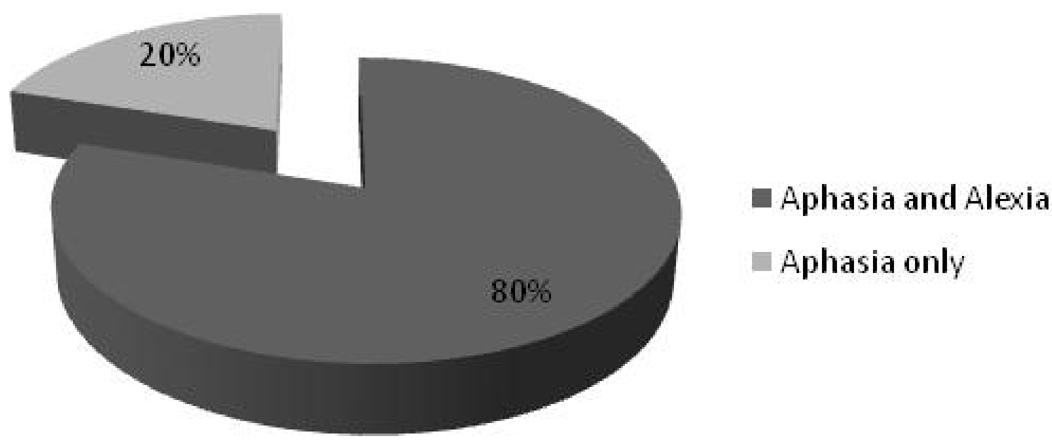

Figure 4-2. Prevalence of alexia within aphasia

Table 4-2. Covariate effects in phonological/deep alexia

Variable	Coefficient ± SE	P-value
Intercept	-1.940 ± 9.704	0.843
Error Type (phonological)	15.000 ± 3.790	0.0004
Gender (female)	-3.883 ± 3.003	0.207
Age	0.238 ± 0.155	0.137
Education	-0.188 ± 0.481	0.699
SLP - history (no)	-0.272 ± 3.323	0.935
Months post onset	-0.011 ± 0.022	0.612

Table 4-3. Variable effects on reading accuracy

Variable	Coefficient ± SE	P-value
Intercept	17.709 ± 13.669	0.200
Group* (ref: normal) Aphasic	-26.117 ± 4.663	<.0001
Gender (ref: male) Female	2.265 ± 3.584	0.530
Age	0.151 ± 0.182	0.408
Education*	1.728 ± 0.596	0.005
SLP - history (ref: yes) no	1.916 ± 4.260	0.655

* MANOVA tests show significant overall group effect (P-value < 0.0001) and education effect (P-value = 0.0085) on total and all subtotal scores.

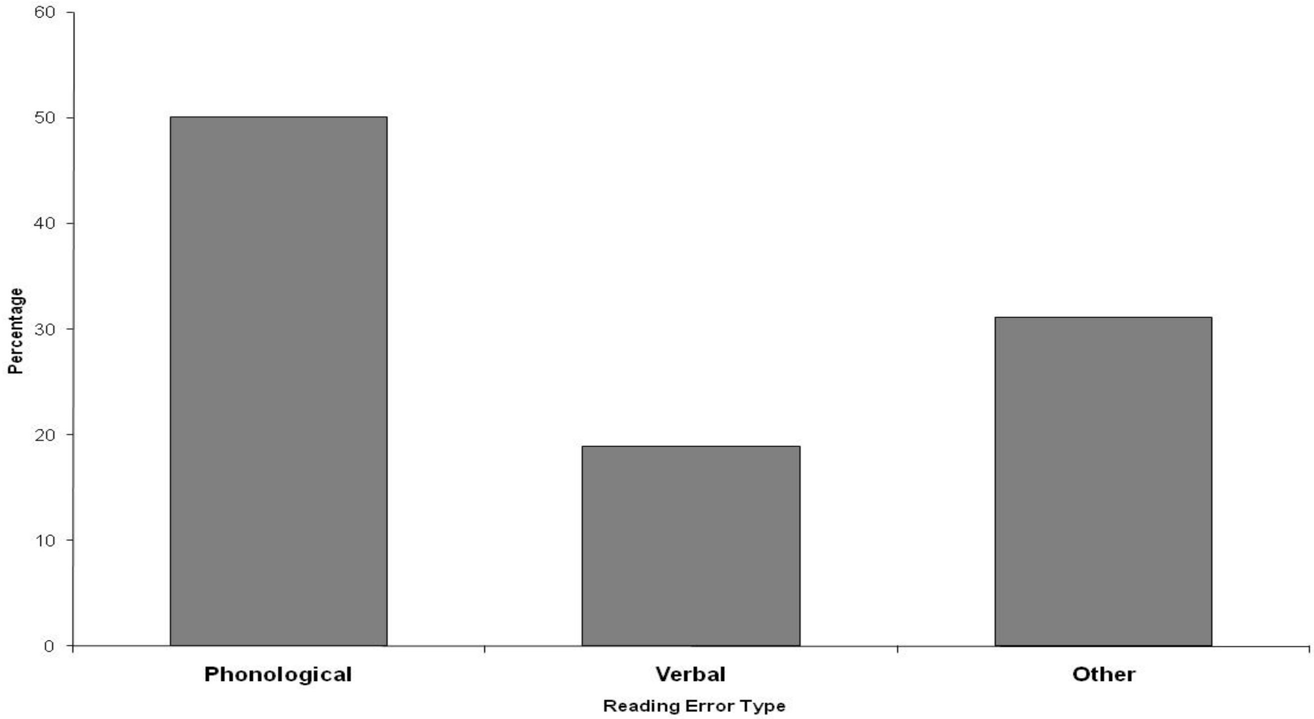

Figure 4-3. Distribution by error type among the group of aphasics with alexia

CHAPTER 5
DISCUSSION

The purpose of this study was to describe the nature and prevalence of alexia in aphasia. Our finding that alexia is common both within and across aphasic syndromes is supported by the literature (Webb et al., 1983). We found that the reading performance of individuals with aphasia is typically impaired, and that the severity but not the nature of this impairment is highly variable and associated with an individual's educational experience. This finding is novel and will be discussed in further detail below. We found that phonological/deep alexia is the only central alexia associated with the aphasia group and that the predominant reading error is phonological in nature.

Research Question One: Prevalence and nature of alexia

While a significant majority of individuals with aphasia had alexia we note that a number of individual's with aphasia scored well within two standard deviations of the normal range. While it is generally accepted that alexia can present either as an isolated symptom or within the context of an aphasic syndrome we conclude on the basis of this study that no dependent relationship exists. We find that aphasia can present without significant impairment to the reading modality. In contrast a number of early group studies found that alexia always occurs within aphasia (Webb et al., 1983; Duffy et al., 1976), but this finding is controversial (Hoffmann et al., 1997; Nance et al., 1981). We speculate that the close association of alexia both within across aphasic syndromes and the finding that severity of aphasia is not significantly correlated with severity of alexia is suggestive either of a highly vulnerable or of a distributed cortical network for reading. This account is well supported by recent radiographic and neuroimaging studies of normal readers elsewhere (Church et al., 2008; Mechelli et al., 2005).

The finding that both the aphasic and normal groups read real words better than nonwords and that the aphasic group was generally impaired suggests a graceful degradation of the reading system. This aphasic pattern of reading performance together with reading error analysis is consistent with earlier descriptions of phonological and deep alexia and is inconsistent with descriptions of surface alexia (Cherney, 2004; Plaut et al., 1996). We account for this finding on the basis of the right hemisphere hypothesis (Coltheart, 2000; Hildebrandt, 1994). Phonological alexia is prevalent because the right hemisphere usually lacks the substrate of phonological sequence knowledge that could compensate for the results of the left hemisphere lesion, whereas it is better equipped to support whole word reading to some degree and thereby compensate surface alexia (Coltheart, 2000; Hildebrandt, 1994).

We account for our finding that years of formal education is inversely associated with severity of alexia on the basis that literate adults with greater educational experience may rely more on whole word reading routes than literate adults with less educational experience. This account is supported by a number of aphasia group studies which found that severity of aphasia is inversely associated with years of formal education (Smith, 1971; Conor, 2000). Recent neuroimaging studies of children and adults have also shown that literate adults rely less on phonological and auditory processes to read than children (Church et al., 2008; Bitan et al., 2007). We speculate that decreased activation of phonological and auditory pathways during reading is due to increased reliance on whole word reading routes supported by semantics. It follows that adults with greater educational experience may have richer semantic support systems used for reading and will therefore be better protected from the effects of a neurological insult that interferes with phonological route processing. The finding that individuals with greater levels of educational experience make less reading errors under stimulus conditions that preclude whole word reading (nonwords) suggests that whole word readers also have fully mature phonological sequence knowledge. The use of whole word reading routes may be entirely conditional on underlying phonological efficiency (Church et al., 2008; Bitan et al., 2007). It may be that degraded phonological efficiency also implicates a degraded semantic system leading to phonologically based reading errors and at it's furthest extreme semantically based reading errors (Southwood et al., 2000). This point will be discussed in further detail below.

Research Question Two: Predominant Error Type

Our finding that individuals with phonological and deep alexia predominantly made phonological errors and not whole word substitutions is unexpected. Earlier descriptions of phonological/deep alexia describe word substitutions as the defining characteristic of this form of alexia (Southwood et al., 2000; Cherney, 2004; Coslett, 2000). Phonological and deep alexics have impaired phonological systems and only relatively spared semantic systems. The finding that phonological errors are more prevalent during oral reading is in line with the simultaneous activation hypothesis which hypothesizes that simultaneous activation of competing impaired primary reading routes will overide the lexical/semantic reading route sufficiently to activate a visually based or neologistic phonological error (Southwood et al., 2000). According to this hypothesis stimulus conditions which prohibit whole word reading (nonwords and unfamiliar word stimuli) will increase the probability of phonological errors and semantic errors will only occur with severe damage to direct and indirect reading routes. At the furthest extreme nonword reading will be entirely abolished. This is the case in deep alexia (Southwood et al., 2000). It may also be that phonological errors are more prevalent than whole word substitutions because the right hemisphere usually lacks the substrate of phonological sequence knowledge that could compensate for the results of the left hemisphere lesion, whereas it is better equipped to support whole word reading to some degree (Coltheart, 2000; Hildebrandt, 1994).

Implication of Findings

These findings can inform clinical practice in several ways. Since the majority of aphasics have alexia, it is suggested that initial testing in the clinical environment should incorporate a reading evaluation in addition to traditional aphasia tests. While oral reading and reading for comprehension share neural mechanisms, at present, there is insufficient clinical data to support any conclusion that a significantly positive correlation exists within this population. Since all individuals with alexia have phonologic alexia, treatment should be directed at the level of the phonologic processor. There is evidence in aphasic literature that by treating the phonologic system, reading as well as speech production improves (Kendall et al., 2003; Kendall et al., 2006).

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BIOGRAPHICAL SKETCH

Jonathan Paul Wilson was born in 1971, in Bangor, Northern Ireland. He is the eldest son of two children and grew up in Bangor, a seaside town on the east coast of Ireland. He attended primary school in Bangor and graduated from his grammar school, the Royal Belfast Academical Institution, in Belfast in 1989. He graduated from the Queen's University of Belfast in 1992 with an honors degree in English language and literature. He went on to study computing and information systems at the University of Ulster where he received his post graduate diploma in computing and information systems in 1998.

Upon graduating he joined the Royal Bank of Scotland (UK) where he worked as a computer systems engineer and later as an account executive. In 2005 he relocated to Florida, USA where he joined the University of Florida's masters program in the Department of Communication Sciences and Disorders, majoring in speech-language pathology. Upon completion of the master's program Jonathan intends to pursue clinical certification as a speech-language pathologist and will continue his clinical research into the PhD program at the University of Florida starting in Fall 2008. His current research interests include adult neurogenic communication disorders and the study of anomia.