Processing Lexicality across the Adult Lifespan and in Alzheimer's Disease

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“A word is the sequence of letters between two blanks.”

… Roy Byrd

“It is nothing other than words which has made us human”

… Ivan Pavlov

Dedications

In dedication to my husband Carl Evers and my children Nicholas and Megan

Carl, thank you for always believing in my ability to do this work, especially during those times when I didn't. Nicholas and Megan, thank you for being patient beyond your years.

In memory of my father Adelino Azevedo

Thank you for always encouraging me to follow my dreams and teaching me that success is the reward for hard work.

Table of Contents

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Preface

This thesis presents work carried out to investigate and describe potential changes in processing lexicality along the adult lifespan and in individuals with mild Alzheimer's disease (AD). Although memory difficulties are the hallmark of AD, impairments in language are often observed, even early in the course of the disease. Visual lexical processing is the cognitive process that allows a person to read, recognize, pronounce and extract meaning from a letter string. Most relevant to the topic of this thesis, visual lexical processing also allows a reader to determine whether a string of letters is a real word in their language or not (i.e. to process lexicality). This ability is a core component of the language processing system and is essential for the comprehension of written language. Previous studies have suggested that processing lexicality is altered in people with AD but the nature and origin of these changes are not well understood. The overarching aim of this thesis was to better understand how people perform on tasks of word recognition and how this may change across the adult lifespan and with AD. This has the potential of identifying specific difficulties that may manifest early in the course of the disease and point towards a differentiation between healthy aging and early dementia. To achieve this, we conducted a series of studies investigating lexicality judgements in young and older adults and in individuals with AD using a combination of on-line behavioural psycholinguistic methodology and electrophysiological/event-related potential (ERP) methods.

Thesis Organization and Overview

This thesis was written in manuscript format and was prepared according to the McGill Graduate and Postdoctoral studies thesis preparation guidelines. While a clear advantage of this format is that the expected contributions to the research community are quickly and easily transferable, one drawback is that the thesis can be repetitive at times.

The thesis comprises three studies, with each study presented as a separate manuscript (Chapters 4, 5 and 6) and representing original contributions to knowledge in the field of visual word recognition across the adult lifespan and in individuals with AD. All manuscripts have been submitted for publication to peer-reviewed journals.

A brief overview of the thesis is as follows:

Chapter 1 provides an overview of psycholinguistic models of word recognition and various psycholinguistic methodologies that are most pertinent to this thesis.

Chapter 2 outlines our current understanding of Alzheimer's disease including a brief overview of the linguistic abilities and deficits in this population.

Chapter 3 presents the aims and the rationale for the thesis.

Chapter 4 consists of Manuscript 1, entitled '*Lexicality judgements in healthy aging and in individuals with Alzheimer's disease: Effect of neighbourhood density*'. The study examines visual word recognition across the adult lifespan and in those with AD and explores the over-acceptance of pseudowords and nonwords in relation to words that has previously been reported in the literature for individuals with AD by investigating neighbourhood density (N) effects on lexicality judgements using on-line behavioural methodology.

Chapter 5 consists of Manuscript 2, entitled '*Electrifying the lexical decision: Examining a P3 ERP component reflecting early lexical categorization*'. The study examines visual word recognition in young adults using a novel paradigm (the ERP P3 lexical decision oddball task) to investigate whether P3 component amplitude can be used as a metric of an individuals' ability to use lexicality as a salient feature early in the course of lexical processing.

Chapter 6 consists of Manuscript 3, entitled '*Processing lexicality in healthy aging and Alzheimer's disease: P3 ERP amplitude as an index of early lexical categorization'.* The study examines visual word recognition in healthy older adults and in individuals with AD using methodologies from Manuscripts 1 and 2 to probe potential differences in processing lexicality between the two older groups.

Chapter 7 provides a summary of the results and findings obtained in the thesis. The findings are synthesized across studies and discussed in relation to psycholinguistic theory of visual word regognition and implications for future work.

Finally, the references for Chapters 1, 2, 3, 7 and the connecting text in between manuscripts are presented at the end of this thesis.

Contribution of Co-authors

For each of the three manuscripts, the candidate conceptualized the research questions, created and/or selected the stimuli for the experiments, programmed the experiments, and wrote the manuscripts with feedback provided from Dr. Eva Kehayia and Dr. Ruth Ann Atchley.

For Manuscript 1 (Chapter 4), Dr. Eva Kehayia was involved in the design of the study and, together with Dr. Ruth Ann Atchley, critically reviewed the manuscripts and provided help with revisions. Behavioural psycholinguistic data for older adults and individuals with AD were collected and processed by Nancy Azevedo while young adult data were collected at Dr. Ruth Ann Atchely's lab at the University of Kansas. Gevorg Chilingaryan provided advice regarding statistics and helped with statistical analysis. All authors read and approved the final version of the manuscript that was submitted for publication.

For Manuscript 2 (Chapter 5), Dr. Ruth Ann Atchley was involved in the design of the study and, together with Dr. Eva Kehayia, critically reviewed the manuscripts and provided help with revisions. Electrophysiological data were collected and pre-processed at Dr. Ruth Ann Atchley's lab at the University of Kansas. Statistical analyses were performed by Nancy Azevedo. All authors read and approved the final version of the manuscript that was submitted for publication.

For Manuscript 3 (Chapter 6), Drs. Eva Kehayia and Ruth Ann Atchley were involved in the design of the study, critically reviewed the manuscripts, and provided help with revisions. Behavioural psycholinguistic and attentional data, as well as electrophysiological data were all collected and pre-processed by Nancy Azevedo. Statistical analyses were performed by Nancy

Azevedo with help from Gevorg Chilingaryan. All authors read and approved the final version of the manuscript that was submitted for publication.

Statement of Originality

While there is a considerable body of research examining the abilities of young adults to process lexicality, little is known about how this basic linguistic capability may change as people age or how it may become altered by the Alzheimer's disease process. To my knowledge there have been no published studies seeking to investigate alterations in the way lexicality is processed across the adult lifespan or in individuals with Alzheimer's disease. Furthermore, I am unaware of any studies that have used the ERP P3 lexical decision oddball task with a focus on the traditional P3 analysis (i.e. the analysis between the rare/frequent conditions) to investigate word recognition in any population. Therefore, this thesis introduces novel findings to the field of psycholinguistics regarding alterations in the processing of lexicality that begin in healthy aging and become more pronounced in individuals with Alzheimer's disease. Furthermore, this thesis also makes an original contribution to the field of ERP methodology since our results have shown a clear utility in combining the P3 oddball paradigm from the ERP attention and memory literatures with the classic lexical decision task to form the lexical decision oddball task.

Results from the studies have been presented in part at the 9th International Conference on the Mental Lexicon (2014) and at the 20th Architectures and Mechanisms for Language Processing (AMLaP) Conference (2014).

Index of Tables

Index of Figures

Table of Abbreviations

Abbreviation	Meaning
AD	Alzheimer's disease
d'	D-prime (sensitivity index)
DRC	Dual-route cascaded model
EEG	Electroencephalography
ERP	Event-related potential
IA(C)	Interactive activation (competition) model
kΩ	Kilo ohm
MCI	Mild cognitive impairment
MoCA	Montreal Cognitive Assessment
MMSE	Mini Mental State Examination
MROM	Multiple read-out model
N	Neighbourhood density
Nw	Nonword
OA	Older adult
Ps	Pseudoword
µV	Microvolt
W	Word
YA	Young adult

Abstract

Alzheimer's disease (AD) is mainly characterized by memory impairments; yet, language difficulties are also often observed, even early in the course of the disease. Processing lexicality allows a reader to determine whether a string of letters is a real word in their language or not. Behavioural psycholinguistic studies have reported an alteration in processing lexicality, specifically with regard to processing pseudowords ("*filow*") and nonwords ("*knojd*") in relation to words, for those with AD; however, the nature and origin of these changes remain poorly understood.

The overarching aim of this thesis was to investigate and describe potential linguistic changes; specifically in the ability to quickly recognize words (and reject non-existent, but word-like, letter strings) by individuals along the continuum from young adulthood to healthy aging and to mild AD. We conducted a series of studies investigating lexicality judgements using two different, but complementary, approaches: 1) on-line behavioural psycholinguistic methodology (lexical decision task) and 2) electrophysiological / event-related potential (ERP) methods (lexical decision oddball tasks).

Behavioural results from the lexical decision tasks showed that individuals with AD were slower in processing lexicality than both healthy adult groups. However, surprisingly, those with AD did not show an overt deficit in over-accepting pseudowords relative to older adults as had been suggested in the literature. In contrast, ERP P3 results were instrumental in showing a difference between older adults and those with AD and highlight the usefulness of combining behavioural psycholinguistic and ERP methodologies. Across the 4 blocks of lexical decision oddball tasks, we observed that the P3 ERP component was elicited in contrasting contexts for the participant groups. ERP results suggest that the healthy adult groups are sensitive to

orthography/phonology and both appear to be more reliant on a difference in orthographic/phonological legality between stimuli types in order to correctly categorize the stimuli as either a word or not a word. On the other hand, individuals with AD showed a different pattern of P3 responses suggesting that they were no longer sensitive to the orthography/phonology of the stimuli, but rather were solely sensitive to a difference in lexical status between the stimuli types.

We propose that the observed alteration in P3 performance in those with AD, in combination with other linguistic/cognitive markers, shows promise in highlighting differences between healthy aging and early dementia that may potentially contribute to the early diagnosis of Alzheimer's disease. Furthermore, knowledge obtained regarding how the ability to process lexicality is altered in this population can then be used to help guide language therapy options that capitalize on preserved abilities and target those that are known to be susceptible to impairment in AD thus having the potential to impact on the person's quality of life.

Abrégé

La maladie d'Alzheimer (MA) se caractérise principalement par des troubles de mémoire. Toutefois, des difficultés linguistiques sont aussi fréquemment observées, même tôt dans le cours de la maladie. Le traitement lexical visuel permet au lecteur de déterminer si une chaîne de lettres est ou n'est pas un mot réel dans sa langue. Des études psycholinguistiques comportementales ont permis d'observer un changement dans le traitement de la lexicalité en langue anglaise, spécifiquement en ce qui concerne le traitement de pseudomots ("*filow*") et de non-mots ("*knojd*") comparés aux mots chez les individus avec la MA. Par contre, la nature et l'origine de ces changements sont mal compris.

L'objectif général de cette thèse est d'étudier des changements linguistiques; spécifiquement dans la capacité de reconnaître rapidement des mots (et de rejeter des chaînes de caractères ressemblant à des mots mais n'ayant aucun sens) chez un groupe de jeunes adultes, un groupe d'aînés en santé et un groupe atteint de la MA légère et de décrire les différences s'il y en a. Nous avons mené une série d'études qui examinent les décisions lexicales en utilisant deux approches différentes mais complémentaires: 1) la méthodologie psycholinguistique comportementale (tâche de décision lexicale) et 2) l'électroencéphalographie/potentiels évoqués (tâches de décision lexicale de type "oddball").

Les résultats comportementaux provenant des tâches de décision lexicale montrent que les personnes atteintes de la MA tendent à être plus lentes dans le traitement de la lexicalité que les deux groupes d'adultes en santé. Toutefois, à notre surprise, les individus avec la MA n'ont pas suraccepté les pseudomots par rapport au groupe d'aînés en santé, contrairement à ce qui avait

été suggéré dans les écrits scientifiques. Toutefois, les résultats des tâches de potentiels évoqués ont permis d'observer une différence entre les aînés en santé et ceux avec la MA, ce qui met en évidence l'utilité de combiner les méthodes psycholinguistiques comportementales avec des tâches électrophysiologiques. À travers les 4 blocs de tâches de décision lexicale de type "oddball", nous avons observé que l'onde P3 a été activée dans des contextes différents selon les groupes de participants. Les résultats P3 suggèrent que les deux groupes d'adultes en santé sont sensibles à l'orthographe/phonologie et qu'ils semblent se fier davantage à une différence de légalité orthographique/phonologique entre les types de stimuli afin de catégoriser correctement les stimuli comme étant des mots ou non. D'autre part, les personnes atteintes de la MA ont montré un profil de réponses P3 différent, qui suggère qu'ils ne sont plus sensibles à l'orthographe/phonologie des stimuli, mais sont plutôt uniquement sensibles à une différence de statut lexical entre les stimuli.

Nous concluons que l'altération observée dans la performance P3 chez les aînés avec MA, en combinaison avec d'autres marqueurs linguistiques ou cognitifs, pourraient mettre en évidence des différences entre le vieillissement en santé et les premiers signes de démence et ainsi contribuer à un diagnostic plus hâtif de la MA. Ces résultats pourront également être utilisés pour aider à guider les choix de thérapies de langage qui misent sur les capacités langagières préservées et qui ciblent celles qui sont affectées par la MA, ce qui pourrait affecter considérablement la qualité de vie des personnes concernées.

CHAPTER 1: *Introduction to Visual Word Recognition and Lexicality*

1.1 Preface

The field of visual word recognition has greatly expanded over the last 50 years. Currently there exist numerous models of word recognition and many distinct methodologies (behavioural, electrophysiological, hemodynamic, etc.) that have been employed to both guide the creation of and test predictions made by these models. The overarching aim of this thesis was to better understand how people process lexicality and how this may change across the adult lifespan and with the onset of Alzheimer's disease. To do this, we studied performance on tasks of word recognition using a combination of on-line behavioural psycholinguistic methodology and electrophysiological/event-related potential (ERP) methods. With this goal in mind, the motivation for this introductory chapter is to provide a brief overview of those models of word recognition and psycholinguistic methodologies that will be relevant to this thesis.

1.2 Visual Word Recognition

Visual lexical processing is the cognitive process that allows a person to read, recognize, pronounce and extract meaning from a letter string. Most relevant to the topic of this thesis, visual lexical processing also allows a reader to determine whether a string of letters is a real word in their language or not (i.e. to make a lexicality judgement). The term lexicality refers to the status of a string of letters or sounds as being a word in a particular language. For example, the string of letters "*cat*" has a lexical status in English while "*jof*" does not. An integral part of knowing a language is having the capacity to recognize words in one's language. The ability to process lexicality, i.e. to reliably differentiate between words and word-like stimuli, is considered to be a core component underlying language comprehension. In order to be able to properly process lexicality, and thus make a lexicality judgement, a person must be able to process strings of sounds presented in the auditory modality and strings of letters presented in the visual modality. It is believed that these two processes are subserved by different cognitive systems. While both types of lexical processing are important components of the language processing system, the focus of this thesis will be only on processing in the visual modality.

The processing of visually presented words is complex, involves various cognitive operations, and forms a subset of the reading system. The time needed to access a word is influenced by various features associated with the word such as its frequency of use, familiarity, length or regularity. Another important feature that is also the focus of Manuscript 1, is the number of lexical neighbours (N) a stimulus has.

1.3 Models of Visual Lexical Processing: Word Recognition and Reading

The study of word recognition (and reading) involves investigating the processes involved in the extraction of sensory, orthographic (letters or graphemes), phonological (sounds or phonemes), and semantic (meaning) information from patterns in printed text. For example, readers of languages like English that use an alphabetic system, i.e. that have a set of graphemes that are linked to phonemes, do not perceive words as discrete objects, but rather as being composed of constituent letters. One major aim of psycholinguistic research is to understand how these representations are organized and how they interact with higher and lower level processes depending on the language context and the task (Jacobs, Rey, Ziegler, & Grainger, 1998). Many models of reading and/or word recognition propose that in order for a word to be recognized and have its meaning accessed, a number of steps must be undertaken. When processing a string of letters, the brain must initially process the physical characteristics of the stimulus before progressively accessing orthographic, phonological, and semantic representations of the word, which must be stored in memory (Hauk Davis, Ford, Pulvermüller, & Marslen-Wilson, 2006; Holcomb & Grainger, 2006; Liu & Perfetti, 2003).

Although current models of word recognition and reading have limitations, they have vastly improved since their introduction in the 1960s (Norris, 2013). Some of these models only describe the processes involved in the recognition of a written word, while other models describe the processes that allow a word to be pronounced (i.e. reading aloud). While the following models are often referred to as "models of reading," they can more accurately be described as models of reading a word aloud (or the process underlying the identification of a single word presented in isolation) (Rayner & Reichle, 2010).

Models can be categorized as being either descriptive or computational. Furthermore, models can vary in their approach to how information is represented within the network. In models using a localist representation, information (letter features, letters, and words) are represented as units (sometimes referred to as nodes) in a network while in models using distributed representations, information is represented as a pattern of activations over a set of units. While localist models posit that a higher number of words in a person's vocabulary will result in a higher number of individual word units (one per word), distributed models propose that there are no individual word units for known words but rather that words are represented as patterns of learned distributed patterns of activation across many units (Norris, 2013; Rastle, 2007). Models can also vary based on the method used to access words: via a serial search through a list of representations or directly via activation of units linked to a particular representation. In this thesis, a focus on computational models that posit a localist representation and access word representations via activation of units has been been opted for due to the breadth of the behavioral phenomena that they address and to their fidelity to behavioral data (Coltheart et al., 2001).

1.4 Descriptive Models

Descriptive models, often referred to as a boxes-and-arrows diagram, are expressed verbally or graphically without making use of closed-form or algorithmic formulations and are used to explain how theories and observations fit together (Jacobs and Grainger, 1994). Descriptive models allowed for the development of accounts of the types of procedures and knowledge representations that led to the performance of an overt behaviour.

Descriptive boxes-and-arrows models of cognitive processes have been criticized on the grounds that they are too ambiguous and imprecise. Specifically, these types of models had little to say about exactly what processes occur within the boxes or what type of information flows along the arrows (Norris, 2013). Furthermore, their qualitative descriptions are not falsifiable or distinguishable from other qualitative descriptions. Another criticism of descriptive models is that researchers can assume considerable resources are available for their model and, therefore, have the freedom to introduce types of representation, and processing mechanisms (by adding boxes and/or arrows to the model) in response to behavioural data (Seidenberg & Plaut, 2006).These criticisms have led many researchers to favor models that are computationally explicit.

1.5 Computational Models

Of all the cognitive domains, reading/visual word processing is the domain that has most extensively used computational modeling (Coltheart, 2005). Computational modeling is a "formal technique that is designed to instantiate a proposed computational description of the processes that underlie a specific set of behaviours" (Lambon Ralph, 2001). This is done by specifying a network architecture (arrangement of simple processing units) that describes how simulated activation can be exchanged between the units.

Computational models have increased in popularity because they contain several desirable characteristics that are not provided by descriptive boxes-and-arrows models. Since implementing a computational model requires completeness, the ambiguity inherent in a descriptive model's specification is avoided. That is, researchers must explicitly spell out all components of a theory for the computer program to execute and this can reveal areas in a theory which are incomplete or underspecified. Furthermore, once an executable program has been created, the adequacy of the model (and underlying theory) can be assessed by simulation and comparison of the model's performance with human data (Coltheart, Rastle, Perry, Langdon, & Ziegler, 2001). These principles guide models (and the theory that underlies them) to undergo various modifications to better address limitations in fit with empirical data (Andrews, 2006). In the case where mismatches are so fundamental that there is no way of making minor modifications, modeling can lead to theory refutation (Coltheart et al., 2001). However, even when a computational model's output closely resembles human behaviour, it is possible that the theory from which the model was generated is not the only one capable of explaining this behaviour. The possibility remains that an alternate computational model, generated from a different theory, could perform equally well (Coltheart, 2005). Another limitation of computational modeling is that, despite increases in computational power available for large-scale modeling, it is still not possible to implement the massively parallel processing that is assumed by many current theoretical frameworks. As a result, current computational models, while vastly improved over earlier ones, remain relatively impoverished implementations of the theories that they are designed to simulate (Andrews, 2006).

Each computational model described below attempts to simulate visual word processing and/or reading aloud. Moreover, each postulates a localist approach with all words which have been learned in past experience being stored in memory. Their development was guided by an evidence-based (data-driven) approach which relies on empirical findings to guide the development of a model. From this approach, a model's success is evaluated by its descriptive adequacy, or how well it can simulate those findings.

Interactive activation (IA) model (McClelland & Rumelhart, 1981; Rumelhart & McClelland, 1982). The IA model is one of the earliest, and most influential, computational model of visual word recognition (Plaut, 1997). The IA model is purely a model of visual word recognition and is not concerned with semantics or phonology. In developing the IA model, McClelland and Rumelhart made several important assumptions.

First, they assumed that processing is organized into at least three levels of representation: the visual feature level, the letter level, and the word level. The word level is accessed by way of the letter level and the letter level is accessed via the visual feature level. Each level is composed of units and when a unit is activated it will send activation in parallel to all other units to which it is linked. The model also assumes that processing can occur both from bottom-up and top-down; i.e. readers can use their knowledge (top-down) of words to help identify letter sequences from visual input (bottom-up). The visual feature and letter levels are linked by pools of units for each of four possible letter positions (all words in the model are four letters in length). Feature units have excitatory connections to all of the letter units in the same spatial position that have those features and inhibitory connections to those that do not have those features. Hence, an active feature unit excites letters which contain that feature and inhibits letters that do not.

The letter level is comprised of four sets of letters, one for each letter position. Each letter unit in a given position has excitatory connections to the word units that contain that letter in that position and inhibitory connections to all of the word units that do not have that letter in that position. The feature-to-letter and letter-to-word connections represent the bottom-up knowledge of the network. The word level is made up of word units for each word in the tested data set. The original IA model (1981) included 1179 four-letter words taken from the word list of Kučera and Francis (1967). Each word unit also has excitatory connections to all of the letter units which compose that word. The word-to-letter weights represent the top-down knowledge of the network. Connections between units do not skip levels (i.e. feature level units are connected upward to letter level units not to letter level units and, conversely, word level units are connected downward to letter level units but not to feature level units). In addition to between-level connections, the IA model also posits within-level connections. All of the word units are mutually inhibitory; i.e. each word unit has negative connections to every other word unit. Unlike other models that preceded it, the IA model does not assume that information between levels must reach a threshold before passing on to another level but rather that information flows in cascade or continuously through the levels of representation.

Processing begins with a visual input (a written word) which activates appropriate feature level units. Activation then flows upstream to activate appropriate letter level units, then to the appropriate word level unit. Activation also flows downstream from word level units to lower level units via a process called feedback activation. Lexical selection (and recognition) is achieved once the activation of a lexical representation reaches a threshold.

One criticism of the IA model is that connection strengths between units have to be coded by hand and the system does not have the ability to learn (Norris, 2013). Also, while the model did not address either phonology or semantics, these domains have been introduced in a more extensive computational model, often referred to as SM89, which was proposed by Seidenberg and McClelland (1989). The IA model also serves as the core inspiration for the multiple read-out model (MROM) and for the dual-route cascaded model (DRC) (Lupker, 2005). These two models are the most relevant to this thesis and we will repeatedly refer to them in each of the three manuscripts (Chapters 4, 5, and 6).

Multiple read-out model (MROM, Grainger & Jacobs, 1996; Jacobs et al., 1998). MROM is an extension of the IA model with processing also being organized into at least three levels of representation: the visual feature level, the letter level, and the word level, with activation flowing in parallel via bi-directional excitatory or inhibitory connections between levels. However, the model also incorporated the design principle of multiple read-out (i.e., a response is generated, or read out, to a task once at least one of the appropriate codes for responding in that particular task reaches an activation threshold). The main goal of the MROM was to explain neighborhood (N) effects in both lexical decision and perceptual identification tasks. The authors posit that a lexicality judgement requires a source of information that quickly and reliably allows the participant to make a decision about the "word-likeliness" of a stimulus and propose three criteria that could reliably determine the lexicality of a given stimulus. While two of these criteria use intralexicon information in order to make a "YES" response to a word, a "NO" response to a pseudoword relies on extralexicon information.

A time-based mechanism (called T) is proposed in order to explain how participants make negative lexicality judgements to pseudowords. A "NO" response is given if, after a pre-specified time (T), no representation is sufficiently activated to meet a threshold. Second, the assumption is made that positive lexicality judgement to words can be made based on two different criteria, M and ∑. A "YES" response can be made when a specific word level unit reaches an activation threshold (called M) or based on a "fast guess" criterion of global activation (called ∑) that uses a heuristic of "if there is a high overall level of activation at the word level then make a positive lexicality judgement" (i.e. if that activity level exceeds a criterion, it provides sufficient evidence that a word has been presented). Therefore, a lexicality judgement can be made before lexical identification has been completed. The M criterion is assumed to be fixed and not under strategic control, i.e. a participant cannot voluntarily speed or slow this process by shifting a response criterion. However, both the ∑ and T criteria are adjustable with either stimulus driven, or task related factors influencing these criteria.

A more recent version of the model, the MROM-p (Jacobs et al., 1998) has also incorporated phonological processing into the model and proposes that when letters activate word units in the orthographic lexicon, they also activate a parallel set of nodes in the phonological lexicon.

Dual-route cascaded (DRC) model (Coltheart, Rastle, Perry, Langdon, & Ziegler, 2001). The DRC model originated from a descriptive boxes-and-arrows model, the dual-route model of reading aloud (Coltheart, 1978; Coltheart, 1985; Coltheart, Curtis, Atkins, & Haller, 1993). Like its predecessor, the computational realization of this model (the DRC, Coltheart, et al., 2001) posits that there are two procedures that are used to access and verbalize letter strings: a nonlexical route and a lexical route.

The lexical procedure operates by (a) accessing a word's representation in the orthographic lexicon followed by (b) the retrieval of that word's spoken form from the phonological lexicon (either directly or via the semantic system). The process starts with the visual analysis and identification of written letters and the translation of the letters' shapes into a sequence of orthographic patterns (coding of visual word form information). This perceptual analysis is believed to be performed automatically, quickly and in parallel for each of the letters in the presented letter string. Next, processing proceeds to the orthographic input lexicon which is made up of the stored representations of previously encountered word forms. The letter string is compared to stored spelling patterns in the orthographic input lexicon and selection occurs when the letter string is matched to a previously stored representation.

There are two routes that can be taken that will allow a skilled reader to read a word (or string of letters) aloud. The lexical route will proceed from the phonological output lexicon which consists of the stored phonological representations (sound pattern) for each word in the system. Alternatively, a string of letters can be read aloud by a non-lexical route that operates by applying a set of letter-to-sound (grapheme-to-phoneme) correspondence rules to a string of letters; this procedure is nonlexical in that it requires neither access to the orthographic input lexicon nor retrieval from the phonological output lexicon (Coltheart & Rastle, 1994). While the lexical route can only be used to read a real word that a person has previously encountered and has been entered as a lexical representation, the non-lexical route can be employed to read novel words and pseudowords and can also act as a backup for the lexical system. Furthermore, the model posits that both routes operate in parallel in the model, thus the pronunciation of any given word is jointly determined by the products of both routes. Although simulation with the DRC model has been used more extensively for reading aloud than for the lexical decision task, the model can simulate a lexicality judgement by using the following operations: 1- Decide "YES" if any entry in the orthographic lexicon has reached a certain pre-set activation level. 2- Decide "YES" if the sum of the activations of all of the entries in the orthographic lexicon has reached a pre-set value (similar to the global activation criterion in MROM). 3- Decide "NO" if a pre-determined number of processing cycles (i.e. time) have passed without a "YES" decision having yet been made.

1.6 Psycholinguistic Methodologies

To date, a large amount of empirical data has been gathered on how various properties of a written word influence the speed and accuracy with which it is recognized and pronounced by skilled readers and by people with selective reading impairments due to a developmental or neurodegenerative disorder or following an injury to the brain (Plaut, 1997) . This has been accomplished by using a wide assortment of psycholinguistic methodologies. Results from psycholinguistic studies have been used to both inform models and to test a model's ability to accurately model patterns of performance exhibited by people.

A major distinction between different psycholinguistic methodologies involves the nature of the dependent variables that they seek to measure. Whereas behavioural methodologies measure variables associated with an overt response such as latency or accuracy of a button-press in response to a task, electrophysiological methodologies measure variables associated with electrical brain activity in response to the performance of a task in real time. One important variable that will eventually have to become an intrinsic part of any viable computational model of word recognition is the time course within which different types of information become available and are used in the process allowing a letter string to recognized (or not) as a word (Barber & Kutas, 2007). The spatial and/or temporal dynamics of visual lexical processing and visual word recognition have been investigated using both behavioural methodologies such as lexical decision and naming as well as with electrophysiological techniques including electroencephalography (EEG) and magnetoencephalography (MEG). In this thesis we have chosen to use a combination of behavioural and electrophysiological methodologies in order to capitalize on the strengths that each has to offer.

1.7 Behavioural Methods

While numerous behavioural psycholinguistic methods exist, most are based on a common basic assumption. Regardless of task specifics, the complexity of mental process(es) involved in performing the task is assumed to be reflected in response latency and accuracy (Garrod, 2006). Thus, in visual word recognition, differences in response latency and/or accuracy as detected on-line can be interpreted as an unbiased measure of the relative processing difficulty among different types of stimuli.

Although many on-line behavioural psycholinguistic methodologies exist, two in particular have been extensively employed to study visual word recognition: the naming task and the lexical decision task. In each of these tasks, behavioural responses, error rate and the time taken to make a response (response time (RT) measured in milliseconds) are recorded. Furthermore, since participants are asked to make a speeded response in both tasks, it is thought that the processes involved are automatic, and therefore are assumed to be similar to the word recognition process observed in natural reading (Katz, Brancazio, Irwin, Katz, Magnuson, et al., 2012). To date, studies employing one or both of these methodologies have been used to examine various psycholinguistic characteristics that influence word recognition (frequency, length, spelling regularity, and neighborhood density (N)) with findings obtained from these studies being used to inform and test models of word recognition.

Naming. This is a timed task where participants are asked to read a string of letters, either a word or a pseudoword (a nonsense string of letters that respects the orthographic/phonological rules of a language but carries no meaning, i.e. "*filow"*), aloud. Words presented can vary based on their regularity of spelling (words that have regular orthographic-to-phonological correspondences, such as "*dig*" versus exception words with irregular correspondences, such as "*sew*"), on their frequency of occurrence in a language, on their familiarity, as well as on other psycholinguistic characteristics.

Lexical decision task. Performing a lexicality judgement is often considered to be one of the most elementary skills that can be performed by a reader (Rastle, 2007). The lexical decision task, one the most frequently used paradigms psycholinguistics, is commonly employed to investigate visual word recognition (Ratcliff, Gomez, & McKoon, 2004). The basic aim of the task is to measure how quickly and accurately people can identify stimuli as being a word or not. In a visual lexical decision task, participants are presented with a mix of words and pseudowords (i.e. "*filow"*) or words and nonwords (nonsense strings of letters that do not respect the orthographic/phonological rules of a language nor carry any meaning, i.e. "*knojd"*) on a computer screen. For each stimulus, the participant is asked to indicate, via a button-press response, whether the presented letter string is a word or not. One important observation is that when seeing pseudowords, participants cannot use orthography or phonology alone to make the lexicality judgement while nonwords may be excluded from being words quickly and simply by using orthography or phonology constraints imposed by the language of the individual.

Lexical decision tasks can also be combined with priming, in which the participant is 'primed' with a stimulus (usually a written or spoken word) presented immediately before the performance of the actual lexicality judgement on a second stimulus. Priming is the implicit memory effect in which exposure to a stimulus influences the response to a stimulus that follows it. Primed lexical decision tasks can be semantic (the prime and target are from the same semantic category, such as *apple-pear* versus *apple-mouse*), morphological (the prime and target share a morphological relation, such as *bake-baker* versus *bake- painter*), or phonological in nature (the prime and target share phonological characteristics, such as *bullet-bull* versus *bullet-tick*). Although priming is most efficient when the two stimuli are in the same modality, priming also occurs across modalities.

Given that participants are not explicitly required to access the word's meaning nor are they asked to say the stimulus aloud in order to correctly perform a lexical decision task, it is possible to use this task with a wide variety of people with acquired or degenerative language conditions. However, while this task has provided valuable information regarding how visually presented stimuli are processed, one drawback is that error rate and RT reflect the conclusion of a complex series of processes, including the time taken to make a behavioural response (Stemmer & Connolly, 2011).

With this limitation in mind, instead of relying solely on results from behavioural lexical decision tasks, electrophysiological tasks were also included in this thesis since they permit a more in-depth investigation of processing of lexicality in our populations of interest. Because they offer the possibility of describing the process of making a lexicality judgement as it unfolds over time, electrophysiological data is expected to complement the behavioural data and allow for a better understanding of potential changes in processing lexicality.

1.8 Electroencephalography (EEG)

In the past twenty years, the addition of electrophysiological techniques such as electroencephalography (EEG) has contributed supplementary information regarding the cognitive processes underlying word recognition that would not be possible to obtain using traditional behavioural methodologies alone. EEG measures electrical activity that occurs in neural cell assemblies and the principle that underlies itis that as groups of neurons fire, they produce changes in the local electrical field. Clusters of thousands of synchronously activated pyramidal cortical neurons are believed to be the main generators of EEG signals.

EEG measures electric potentials which are produced by electrical brain activity on the scalp. The technique is considered to be non-invasive as it does not require the injection of isotopes or exposure to magnetic fields and therefore allow for repeated testing to be performed. Moreover, EEG can be used to investigate the brain's response to a specific stimulus (as opposed to measuring naturally-occurring activation over long intervals) by measuring event-related potentials (ERP). ERPs are a measure of the electrical activity of the brain that is generated by the execution of a specific cognitive task, such as reading.They are produced by averaging over both stimuli and subjects and are usually time-locked to the presentation of a stimulus. The averaging process cancels out spuriouselectrical activity that is not related to the cognitive task being performed by the participant (Démonet, Thierry & Cardebat, 2005).

ERP data have been used successfully to understand the timing of cognitive processes with a high degree of precision and to localize active brain regions in sensory and perceptual processing, selective attention and discrimination, memory storage and retrieval, as well as language comprehension (Hillyard 1993).

One disadvantage of EEG is that, although it provides outstanding temporal resolution, the exact nature of brain mechanisms generating the electrical signals is not known since these signals are measured far from where they were generated. This limitation is referred to as the inverse problem. In theory there are infinite possible correct answers to source localization and the task of finding the best solution has become the subject of intensive research. Despite this limitation, ERPs have been especially useful in the study of various aspects of human cognition, including word comprehension. Furthermore, since any viable and correct account of word recognition will need to reflect temporal and anatomical constraints associated with the fact that reading is a human brain function, both techniques may be essential to the development of biologically realistic models of visual word recognition (Barber & Kutas. 2007).

To date, some of the most influential psycholinguistic research has frequently used EEG because it is relatively inexpensive to run ERP experiments and also because the technique offers similar temporal resolution (at the level of milliseconds) to that of behavioural methods and, therefore, corresponds to the rate at which processes of word recognition occur (Garrod, 2006). As a result, ERPs are now often used in combination with behavioural methods to investigate various cognitive processes (Barber & Kutas, 2006).

1.9 Combination of Event-related potentials (ERPs) with Psycholinguistic Behavioural Methods

Whereas behavioural methodologies measure variables associated with an overt response such as the latency or accuracy of a button-press response to a task and thus reflect the conclusion of a complex series of processes (Stemmer & Connolly, 2011), ERPs measure variables associated with electrical brain activity in response to the performance of a task in real time. Furthermore, ERPs also allow the investigation of automatic processes, in contrast to behavioural responses which can be influenced by more conscious decisions or strategies from participants (Kaan, 2007).

Behavioural tasks that require stimuli to be read aloud do not lend themselves well to ERP studies because the waveforms related to the production of speech overlap with the waveforms associated with the word processing (Picton, Bentin, Berg, Donchin, Hillyard et al., 2000). However, the passive reading task lends itself well to ERP studies. Since ERPs reflect the processing associated with a cognitive task and word reading is assumed to be both automatic and irrepressible, there is no need for an overt response to be made by the participant in the passive reading tasks.

Lexical decision tasks have also been employed to elicit ERPs (Bentin, McCarthy, & Wood, 1985; Braun, Jacobs, Hahne, Ricker, Hofmann, & Hutzler, 2006; Sereno, Rayner, & Posner, 1998; Simon, Bernard, Largy, Lalonde, & Rebai, 2004). ERP lexical decision tasks allow for more flexibility when investigating the time course of word recognition than traditional lexical decision tasks because ERP results can provide insight into what is occurring during the stages of lexical processing and have the potential to identify some component(s) which may prove to be sensitive to one or more of the processes involved in lexical processing.

One way that ERP methodology has been combined with lexicality judgements has been to ask participants to perform lexical decisions on strings of letters presented within an oddball task. In a traditional oddball task, two stimulus types are presented in random order, with one type occurring more frequently (usually 80% of the trials) than the other. Participants are asked to discriminate between infrequently-occurring targets and frequently-occurring stimuli by responding, either covertly (by counting) or overtly (by making a button-press response) to the rare targets.

The oddball paradigm described above is known to elicit the P3 ERP (sometimes called the P300) component for the rare event trials while the frequent stimulus solely reflects components of sensory processing (Polich & Corey-Bloom, 2005). P3 is an umbrella term that encompasses two distinct subcomponents; the P3a and P3b where each index separate attentional processes (O'Connell, Balsters, Kilcullen, Campbell, Bokde, et al., 2012; Polich, 2007). The P3b has a central parietal scalp distribution and is elicited 300–600 ms after the presentation of a rare target presented within a set of frequent but different stimuli (i.e. in the oddball task described above) and is believed to reflect the top-down allocation of attentional resources (Polich, 2007). In contrast, the P3a (or novelty P3) has an earlier latency (250-280 ms) and a more anterior distribution (frontal/central sites) and is elicited by a rare deviant non-target stimulus (i.e. the 3-stimulus oddball task). The P3a is believed to reflect a bottom-up (stimulus-driven) orientation of attention to a salient but irrelevant stimulus (Polich, 2007). In this thesis, unless otherwise specified, we have used the term P3 to refer to the P3b.

The P3 represents the brain's electrophysiological response to a stimulus that is unexpected or "surprising" and thus can be elicited by "low-probability task-relevant stimuli during stimulus classification tasks in auditory, visual, and somatosensory modalities" (Olichney, Yang, Taylor, & Kutas, 2011). P3 component amplitude is sensitive to the allocation of attentional resources during task processing and has been documented as an index of attentional resources associated with context updating, updating of the neural representation of a stimulus in memory, stimulus-categorization, and processing capacity (Ashford, Coburn, Rose, & Bayley, 2011; Juckel, Karch, Kawohl, Kirsch, Jäger, et al., 2012; Polich, 2007). The presence of a P3, if elicited, can be interpreted as indicative of an allocation of attentional resources to a stimulus (Brandeis, Banaschewski, Baving, Georgiewa, Blanz, et al., 2002), normally as a precursor to more complex processing (Ilardi, Atchley, Enloe, Kwasny, & Garratt, 2007) while a reduction in P3 amplitude can be interpreted as indicative of a significant change in the individual's ability to selectively attend to the task-critical stimulus type or effectively create categories that can be used to distinguish between different stimuli types.

While the oddball task has more traditionally been used with non-linguistic stimuli, in this thesis we have chosen to employ it as part of a modified lexical decision task (i.e. the lexical decision oddball task) (Bentin et al, 1999) where the rare stimuli are written words presented among frequently occurring written nonwords or pseudowords (or vice versa). Given that P3 amplitude is significantly larger when an individual encounters a stimulus that differs in a salient fashion from its antecedent context, this paradigm can be particularly interesting when investigating word recognition since it can be used as a metric of an individuals' ability to use lexicality as a salient feature when performing lexical decision oddball tasks.

CHAPTER 2: *Alzheimer's Disease (AD)*

2.1 Preface

Given that there is a substantial focus on individuals with Alzheimer's disease in this thesis, the motivation for this introductory chapter is to provide a brief overview of this neurodegenerative disease.

2.2 Alzheimer's Disease (AD)

Alzheimer's disease (AD) is a progressive and irreversible neurodegenerative disease with an insidious onset. While there is variability between individuals regarding the timeline of the disease, its course is characterized by a progressive pattern of cognitive and functional impairment and is ultimately fatal.

2.3 Prevalence

Demographic aging is resulting in a worldwide increase in the proportion of older individuals and has been associated with an increase in the number of people with dementia. It is estimated that 35.6 million people worldwide are currently living with AD or a related dementia and this figure is expected to double every 20 years to reach 115.4 million people by 2050 (Ferri, Sousa, Albanese, Ribeiro, & Honyashiki, 2009). In Canada, approximately 1 125 000 people (2.8% of all Canadians or 9% of those over the age of 60) will be living with a form of dementia by 2038. AD, a fatal progressive neurodegenerative disease, is the most prevalent form of dementia affecting the elderly. In 2008, approximately 304 000 Canadians were suffering from AD. The disease accounted for 63% of all cases of dementia in Canada and this number is expected to rise to 69% of cases in the next 30 years (Rising Tide: The Impact of Dementia on Canadian Society, 2010). The prevalence of AD is markedly higher in women than in men with women representing 72% of all cases (compared to 62% of cases of overall dementia) (Rising Tide: The Impact of Dementia on Canadian Society, 2010).

2.4 Etiology

Since the disease is heterogeneous, its cause still remains unknown. However, onset of AD is known to be affected by the ageing process acting in concert with a complex interaction of environmental and genetic risk factors (Blennow, de Leon, & Zetterberg, 2006). A traumatic brain injury, family history of AD, history of clinical depression, and vascular risk factors including stroke, high cholesterol, hypertension, atherosclerosis, coronary heart disease, smoking, obesity, and type 2 diabetes, have all been associated with AD (Rising Tide: The Impact of Dementia on Canadian Society, 2010; Jellinger, 2004; Mayeux, 2003). In terms of genetic risk factors, a strong association has been found between the apolipoprotein E (APOE) ε4 allele and AD. The APOE ε4 allele is believed to operate primarily by modifying the age of onset of the disease, with each copy of the allele lowering onset by almost 10 years (Corder, Saunders, Strittmatter, Schmechel, Gaskell, et al., 1993). The lifetime risk for AD in individuals with the APOE ε4/ε4 genotype is high, estimated to be approximately 33 % by age 75, and the risk climbs to 52 % for men and 68 % for women by age 85 (Genin, Hannequin, Wallon, Sleegers, Hiltunen, et al., 2011; Schellenberg & Montine, 2012).

2.5 Effects

The effects of the disease on the individuals are threefold. The disease process causes deficits in cognitive function such as loss of memory and language impairments; psychiatric symptoms and/or behavioural disturbances, including depression, anxiety, and personality changes; and difficulties in performing activities of daily living, with instrumental activities such as handling money and driving being affected early in the course of the disease and with basic activities such as dressing and feeding becoming impaired later in the disease progression (Burns, Byrne & Maurer, 2002). Limitations in activities of daily living (ADLs) along with participation restrictions result from these impairments and lead to an increase in need of care (Anderson, Wittrup-Jensen, Lolk, Andersen, & Kragh-Sorensen, 2004). The course of AD varies from person to person, while symptoms tend to develop over the same three general stages (Thies & Bleiler, 2013). In mild AD, memory loss becomes apparent and changes in other cognitive abilities are also present. Individuals show symptoms that include repeating questions, becoming disoriented and getting lost, and having word-finding difficulties. Changes in personality or mood can also begin in this early stage. In moderate AD, damage occurs in brain areas that are responsible for language, reasoning, sensory processing, and conscious thought. Individuals may experience an increase in confusion and memory loss, difficulties in recognizing family members and friends, and problems in carrying out complex tasks such as dressing themselves. They may become more impulsive in this stage and hallucinations, delusions, and paranoia may be present. In severe AD, individuals can no longer communicate and are completely dependent on others for their care.

In addition to the actual consequences to the individuals with AD, there are also numerous components of care that are required by those suffering from AD and that contribute to the societal and financial burden of AD. These include nursing home care, medications, and community based health and social services over and above the resource costs of unpaid informal caregiving services that are offered by family, friends and volunteers. It has been estimated that the number of hours of care, provided by unpaid Canadian family members for individuals with all forms of dementia, including AD, will more than triple by 2038, increasing from 231 million hours in 2008 to 756 million hours. Furthermore, the current economic burden of care for all forms of dementia, being $15 billion (CDN) per year, is expected to rise to $153 billion (future CDN $) by 2038 (Rising Tide: The Impact of Dementia on Canadian Society, 2010).

Having AD leads to a decrease in the rate of survival when compared to rates for individuals who do not suffer from dementia (Knopman, Boeve & Petersen, 2003; Larson Shadlen, Wang, McCormick, Bowen, et al., 2004). Although rates of survival vary across individuals, death usually occurs within 4 to 7 years following diagnosis (Larson et al., 2004; Wolfson, Wolfson, Asgharian, M'Lan, Østbye, et al., 2001). While a definite diagnosis of AD requires confirmation at autopsy, individuals may be diagnosed with probable AD based on clinical criteria specified by the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA criteria, McKhann, G. M., Knopman, D. S., Chertkow, H., Hyman, B. T., Jack Jr, et al., 2011).

2.6 Diagnosis

In order to make a definitive diagnosis, a histological examination of a brain specimen at autopsy must be performed. Diagnosis is based on the observation and identification of morphological abnormalities that are distributed in a somewhat fixed pattern (Perl, 2010). AD is defined by a specific neuropathology with two primary cardinal lesions: neocortical neurofibrillary tangles and neuritic amyloid plaques (Nelson, Head, Schmitt, Davis, Neltner, et al., 2011). Neurofibrillary tangles consist of atypical accumulations of abnormally phosphorylated tau within certain neurons while plaques are composed of a central core of beta-amyloid that is surrounded by abnormally configured neuronal processes or neurites (Perl, 2010). Neurofibrillary tangles are thought to impair the transport of nutrients and other essential molecules within the affected neuron and are also believed to contribute to cell death. On the other hand, the accumulation of beta-amyloid plaques is believed to interfere with the neuron-to-neuron communication at the level of the synapse (Thies & Bleiler, 2013). While these are the hallmarks of the disease, any of the neuropathological alterations of AD can be observed, to some degree, in the brains of older adults who showed normal cognitive function during life. (Nelson, Braak, & Markesbery, 2009; Perl, 2010; Schneider, Aggarwal, Barnes, Boyle, & Bennett, 2009).

Criteria for the clinical diagnosis of AD were established in 1984 by the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's Disease and Related Disorders Association (ADRDA). While the criteria were universally adopted and have been successfully used for over 25 years, advances in the understanding of AD, a better ability to detect the pathophysiological process that underlies AD, and changes in the conceptualization of the disease's clinical spectrum have all led to the re-evaluation and update of the criteria used to diagnose AD in 2011(Jack Jr, Albert, Knopman, McKhann, Sperling, et al., 2011). In order to meet the current NINCDS-ADRDA diagnostic criteria (McKhann, et al., 2011) for probable AD, an individual must meet criteria for dementia. These are cognitive or behavioural symptoms that: 1) interfere with the individual's ability to function at work or during usual activities, 2) show a decline from one's previous levels of function, and 3) cannot be attributed to delirium or a major psychiatric disorder. Also, cognitive or behavioural impairment must involve a minimum of two of the following domains: memory (impaired ability to acquire and remember new information); executive function (deficit in reasoning or the completion of complex or sequential tasks); agnosia and apraxia (impaired visuospatial abilities including difficulty in operating simple implements); aphasia (impairment in language function such as speaking, reading, or writing); and personality (changes in personality or behaviour like social withdrawal or agitation). Furthermore a diagnosis of probable AD requires that symptoms have an insidious onset, over the span of months or years, and show a clear history of worsening with time. Presentation of the initial and most prominent cognitive deficit in AD can take several forms. The most common syndromic presentation of AD is amnestic, i.e. individuals show deficits in memory such as an inability to learn or to recall recently learned information. However, it is also possible, but more rare, to have a nonamnestic presentation, a visuospatial presentation, or an executive function deficit presentation. In order to make a diagnosis of probable AD, a clinical assessment that includes a detailed history (review of medical and medication history as well as symptoms) a cognitive evaluation and a physical examination must be performed.

While the progression and clinical course of AD is currently better understood than that of other forms of dementia, individuals with AD can present with diverse clinical symptoms at the time of evaluation. This heterogeneous presentation can sometimes complicate diagnosis and may be a reflection of differences in pathology that can only be confirmed at autopsy (Karantzoulis & Galvin, 2011). An early and accurate diagnosis is essential in order to provide a proper plan of treatment as well as to allow prognostic information and counselling to individuals with AD and their family members (Camicioli, 2006). Additional benefits of early recognition include the possibility of early medication intervention which has shown to be most effective when begun early, as well the involvement of patients in decision making and planning for their future care (Forster, 2006).

2.7 Treatment

Research indicates that the AD disease process may start many years or decades before the first clinical symptoms are recognized and a diagnosis is made (Beason-Held, Goh, An, Kraut, O'Brien, et al., 2013; Carrillo, Saunders, Strittmatter, Schmechel, Gaskell, et al., 2009; Sperling, Aisen, Beckett, Bennett, Craft, et al., 2011; Morris, 2005). Presently, pharmacological interventions that have been approved to treat AD only address symptoms which are generally manifested after the disease is already well-established. Although current medications offer modest improvements in memory impairments and other cognitive symptoms caused by AD, to date no treatment has been proven to slow the disease's underlying neurodegeneration. However, there are medications currently being developed and evaluated that aim to alter the AD underlying pathology thereby slowing or even halting the progression of the disease. Current experimental treatments for AD are concerned with reversing existing pathology in the brains of people who already have a diagnosis, with the primarily focus being placed on the removal of beta-amyloid (Callaway, 2012). Nonetheless, to date, participants in these trials do not show any significant cognitive benefits that are related to the removal of beta-amyloid (Beason-Held et al., 2013). As a result, a priority has been placed on the need to identify early markers of brain changes that occur before the onset of cognitive impairment and an intense research focus has been directed towards the early identification of elderly individuals who will develop AD (Taler & Phillips, 2008).

2.8 Language

While memory impairment is commonly considered to be the primary symptom of AD, language deficits are observed as a primary symptom in approximately 10% of patients with AD early in the course of the disease (Emery, 2000). Moreover, it has been observed that patients who presented with prominent language impairments early in the course of AD had developed cognitive impairments at a younger age and progressed to the severe stage of dementia at a faster pace than those with AD who did not present with aphasia early in the course of the disease (Faber-Langendoen, Morris, Knesevich, Labarge, Miller et al., 1988). Estimates of the prevalence of language disturbances in AD range from 30% to 100% of patients (Farcnik, Persyko, & Bassel 2002). The prevalence of language disturbances depends on the stage of severity of the illness. In a study of 150 patients with AD and 83 elderly healthy individuals (Faber-Langendoen et al., 1988), aphasia (as measured by the Aphasia Battery) was reported in 36% of patients with mild AD, in 82% of patients with moderate AD and in 100% of patients with severe AD. In contrast, 83% of the healthy elderly control participants attained perfect scores of 0 while the other 17% scored 1 or 2 (a score of 3 or above on the Aphasia Battery was considered indicative of aphasia). Furthermore, none of the control participants progressed to a clinical diagnosis of aphasia during the four year study

Impairments in processing lexical and semantic knowledge are regularly observed in those with AD even early in the course of the disease (Karantzoulis & Galvin, 2011; Taler & Phillips, 2008). Impairments in language tasks that require intentional processing such as confrontational-naming and verbal fluency and tasks that rely on more automatic processing such as lexical decision and word naming have been observed in individuals with AD. However, the order in which these impairments appear is currently poorly understood (Taler & Phillips, 2008).

The presence of word-finding difficulties is well documented (Appell, Kertesz & Fisman, 1982; Bayles & Kaszniak, 1987; Joubert, Joncas, Barbeau, Joanette, & Ska, 2006) and individuals with AD are also often impaired across various measures of semantic memory including visual confrontation naming and verbal fluency (Taler & Phillips, 2008). A meta-analysis of 153 studies that examined semantic and letter fluency in individuals with AD found that, although their performance was impaired relative to healthy older adults on tests of semantic and letter fluency, the effect was more pronounced for semantic fluency (Henry, Crawford, & Phillips, 2004). Impairment on one but not both types of fluency tasks suggests that the observed deficits in verbal fluency are not the result of executive or inhibitory dysfunction. Instead, impairment in the category fluency task is generally believed to be due to a breakdown in semantic representations (Taler & Phillips, 2008). As the disease progresses, agrammatism, paraphasic errors, impoverished speech content, and impaired comprehension become apparent With more time, prosody will commonly also become affected and global aphasia or muteness is common in the late stages of the disease (Karantzoulis & Galvin, 2011).

2.9 Visual Word Recognition in AD

The recognition of one of the many thousands of written words that adults know is a complex, multi-step process (Hauk, Davis, Ford, Pulvermuller, & Marslen-Wilson, 2006). However, despite this complexity, this process is accomplished rapidly in young adults with word-specific information beginning to be accessed in the first 200 milliseconds (ms) after presentation (Sereno & Rayner, 2003). When asked to perform lexicality judgements, healthy adults show a difference in performance to pseudowords versus nonwords by being both faster and more accurate when rejecting non-pronounceable letter strings than pronounceable letter strings (Ratcliff, Gomez, & McKoon, 2004).

As we age many types of cognitive processes begin to slow down. While tasks in some non-lexical cognitive domains tend to show more age-related slowing than lexical tasks (Lima, Hale, & Myerson, 1991), even with many years of exposure to words over a lifetime, the time taken to make lexicality judgements increases with age. Moreover, numerous studies have shown that those with AD are consistently slower when compared to older adults across different languages and across a range of words with different lexical properties such as frequency, regularity, neighbourhood density, and number of semantic associates (Caza & Moscovitch, 2005; Duñabeitia, Marín, & Carreiras, 2009; Duong, Whitehead, Hanratty, & Chertkow, 2006;

Madden, Welsh-Bohmer, & Tupler, 1999). In addition to having longer RTs, individuals with AD also appear to show a decrease in accuracy when compared to older adults when making lexicality judgements. A decline in the ability to accurately process lexicality has been reported in some studies and suggests the presence of a selective deficit in the ability of individuals with AD to process pseudowords (i.e. "*filow*"). While healthy adults have been shown to be both faster and more accurate when rejecting nonwords than pseudowords in lexical decision tasks, individuals with AD appear to be having comparatively more difficulty in rejecting pseudoword stimuli. (Cuetos, Herrera, & Ellis, 2010; Glosser, Kohn, Friedman, Sands, & Grugan, 1997; Madden, Welsh-Bohmer, & Tupler, 1999).

In an off-line auditory lexical decision task probing words and pseudowords, Glosser and colleagues (1997) found that individuals with AD and healthy older adults performed at comparable rates of accuracy for the word stimuli, but individuals with AD performed significantly worse than older adults on pseudoword stimuli (incorrectly responding) "YES" to many pseudowords. Furthermore, in a modified lexical decision task requiring participants to indicate the real word presented among three legal pseudoword foils, those with AD made significantly more errors than healthy aging adults, choosing a pseudoword foil (Cuetos, Herrera, & Ellis, 2010). This over-acceptance of pseudowords has also been observed in an on-line lexical decision task (Madden, Welsh-Bohmer, & Tupler, 1999), while young and older adults both performed at similar rates of accuracy for words and pseudowords, those with AD made significantly more errors to pseudowords. However, they showed similar accuracy for words when compared to young and to older adults.

Taken together, these studies suggest that processing lexicality may be vulnerable to disruption by the AD disease process in a manner that may only become apparent when pseudoword stimuli are used. However, since many language screening tests use words (and not pseudowords) to evaluate linguistic abilities, there is a possibility that deficits in processing lexicality are being missed and that the language abilities of individuals with AD may actually be over-estimated.

CHAPTER 3: *Aims and Rationale of the Thesis*

3.1 Aims of the Thesis

Although memory impairments are the hallmark of Alzheimer's disease (AD), disturbances in language are often seen, even early in the course of the disease. Behavioural psycholinguistic studies investigating visual word recognition have reported an alteration in processing lexicality, specifically with regard to processing pseudowords and nonwords in relation to words, for the Alzheimer population, in both off-line and on-line tasks.

The overarching aim of this study was to investigate and describe potential changes in the ability to quickly recognize words (and reject non-existent, but word-like letter strings like "*filow*" or "*knojd*") along the adult lifespan and in individuals with mild AD. To do this we conducted a series of studies investigating lexicality judgements in young and older adults and in individuals with AD using: 1) on-line behavioural psycholinguistic methodology (lexical decision task probing words, pseudowords, and nonwords) and 2) electrophysiological / event-related potential (ERP) methods (lexical decision oddball tasks probing four comparisons: words among nonwords (W-Nw); words among pseudowords (W-Ps); nonwords among words (Nw-W); pseudowords among words (Ps-W)). Furthermore, since the oddball tasks are known to rely on mechanisms of selective attention we also conducted a brief evaluation of this cognitive ability. Non-verbal tasks of selective attention were included in order to rule out any overt deficits in this area that could potentially be affecting performance on the lexical decision oddball tasks in the older adult groups.

3.2 Rationale

While behavioural findings from the lexical decision task can provide general information regarding the end stage of word recognition, i.e. differences between groups in speed and accuracy when performing lexicality judgements, the ERP tasks can provide insight into differences in how the groups are processing the stimuli types while making lexicality judgements.

The ERP paradigm that we have chosen, the oddball task, is known to elicit the P3 component for the rare event trials in healthy adults. Because P3 amplitude is significantly larger when an individual encounters a stimulus that differs in a salient fashion from its antecedent context, we investigated whether P3 amplitude can be used as a metric of an individuals' ability to use lexicality as a salient feature early in the course of lexical processing, while performing the lexical decision oddball tasks. While the presence of a P3 can be interpreted as indicative of an allocation of attentional resources to a stimulus, a reduction in P3 amplitude can be interpreted as indicative of a significant change in the individual's ability to selectively attend to the task-critical stimulus type or effectively create categories that can be used to distinguish between the different stimuli types. In a recent review of P3 research with individuals with AD (Polich & Corey-Bloom, 2005), two important observations about AD patients' P3 components were made. First, despite the generalized neurocognitive decline, which is the hallmark of AD, a reliable P3 can be observed in individuals with AD. This is highly noteworthy given that some other patient populations do not readily show a reliable P3 (for example, research by Bruder, Tenke, Stewart, Towey, Leite, et al.,1995 and Röeschke, Wagner, Mann, Fell, Grözinger, et al., 1996 has demonstrated a significant attenuation of the P3 component in individuals with depression). Secondly, the review suggests that AD individuals' ERP data can differ from the data of age-matched controls in two distinct ways: in P3 amplitude as well as latency. Although there have been a number of P3 oddball studies conducted with individuals with AD (Ally, Jones, Cole, & Budson, 2006; Chapman, Nowlis, McCrary, Chapman, Sandoval, et al., 2007; Katada, Sato, Ojika, & Ueda, 2004; Polich & Corey-Bloom, 2005), we are not aware of any research that has employed the P3 oddball task to specifically examine changes in the ability to process lexicality in individuals with AD. In this way, though the P3 task has been established as a clearly viable task to use with individuals with AD, the current research is innovative in that it uses this established task to study deficits in the processing of lexicality in this patient population.

The combination of ERP and psycholinguistic methodologies was chosen because it permits a more in-depth investigation of the lexicality processing deficits that have been observed in the AD population by using tasks that are simple enough to administer with individuals with AD while likely to yield vital information regarding language breakdown in this vulnerable population. By combining results from both methods we anticipate to obtain a better understanding of how people perform on tasks of word recognition and in what ways this may change across the adult lifespan. This may potentially allow the identification of specific deficits that begin to appear early in the course of AD and that can act as linguistic pointers that differentiate healthy from pathological aging long before overt manifestations are evident thus contributing to an earlier diagnosis. Moreover, this information can then be used to inform and to test models of word recognition by providing information regarding how lexicality is processed as people age and how this process can become impaired with the onset and progression of AD.

CHAPTER 4: ***Manuscript 1.*** *Lexicality judgements in healthy aging and in individuals with Alzheimer's disease: Effect of neighbourhood density*

Preface to Manuscript 1

The aim of the following manuscript was to examine one particular lexical parameter and its influence on visual word recognition across the adult lifespan and in those with AD. Using a classic lexical decision task, we explored the over-acceptance of pseudowords and nonwords in relation to words that has previously been reported in the literature for individuals with AD by investigating neighbourhood density (N) effects on lexicality judgements. While the effects of N on word recognition in young adults are fairly well understood, understanding these effects across the adult lifespan and, more specifically, in neurodegenerative conditions such as AD, remains impoverished. In particular, we sought to examine whether having a large N (i.e. having many real word lexical neighbours) versus having a small N (i.e. having few or no lexical neighbours) could be influencing an over-acceptance of pseudowords in any of the three participant groups. We chose to begin this thesis by exploring N effects in word recognition because high-N pseudowords are perceived as being highly word-like (since they partially activate the mental representations of many real words) and sensitivity to N could thus provide an interesting parameter with which to compare the three groups.

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Title Page

Lexicality judgements in healthy aging and in individuals with Alzheimer's disease: Effect of neighbourhood density

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Abstract

Neighbourhood density (N) has been shown to influence how lexical stimuli are accessed. In young adults, a large N is facilitatory for words but inhibitory for pseudowords in English. While there is a paucity of studies probing N as people age, results to date point towards changes in lexical processing that occur with aging. We are not aware of any studies that have sought to investigate N in Alzheimer's disease (AD) in English. Results from the lexical decision task reported here support previous N findings for young adults. However, older adults and those with AD showed a different pattern of performance. Both were slower to respond to and made more errors to high versus low N pseudowords but, unlike young adults, older adult groups showed a decrease in sensitivity to N for words. Results suggest that the aging process may change how N is processed; older individuals are no longer as sensitive to N and this appears to be further altered by AD. In the context of the multiple read-out model of lexical processing, this change may be due to a longer time required to activate lexical neighbours which, in turn, results in differential N effects for words and pseudowords.

Keywords: neighbourhood density (N); orthographic neighbourhood; lexical processing; lexicality; lexical decision; lexicality judgement; healthy aging; Alzheimer's disease (AD)

The processing of visually presented strings of letters is a complex cognitive activity that requires the selection of the target representation from alternative lexical candidates. Since all words are composed of a limited set of features and letters, a target word will frequently be similar to many other lexical representations. Consequently, the retrieval of a target word requires accessing the target representation from alternative lexical candidates that have been previously stored in memory and the investigation of how various features influence how a target representation is selected from lexical memory has provided crucial information for models of visual word recognition (Andrews, 1997).

The time needed to access a word is influenced by various features such as frequency, familiarity, length or regularity. Another important feature, that is also the focus of this paper, is the number of lexical neighbours (N) a stimulus has. The notion of an orthographic similarity metric that denotes the number of close neighbours a stimulus (either a word or a pseudoword) possesses, called "N", was originally proposed in 1973 by Landauer and Streeter. Specifically, N refers to the number of words that can be generated by substituting one letter of a target stimulus while preserving letter positions (Coltheart, Davelaar, Jonasson, & Besner, 1977; Pollatsek, Perea, & Binder, 1999). While some words have many lexical neighbours (e.g. butter) others may only have only one (e.g. motor) or even none (e.g. robot). Neighbourhood density is believed to interact with the mechanisms underlying both the speed at which a word can be accessed and the speed and accuracy at which a judgement of lexicality can be made to a visually presented stimulus. N effects occur due to the graded, parallel activation of multiple similar representations; lexical candidates that are visually similar to a target become partially activated via spreading or shared activation that results in either facilitatory or inhibitory N effects depending on the task and modality.

N effects are consistently observed in different modalities of lexical processing. However, in different lexical processing tasks (lexical decision, repetition, oral reading (word naming), picture naming, word-picture matching), N can elicit differential effects. While repetition and oral reading tasks show a density facilitation effect for both younger and older adults (Taler, Aaron, Steinmetz, & Pisoni, 2010; Spieler & Balota, 2000), picture naming tasks show a density facilitation effect in young adults but this effect disappears with aging (Gordon & Kurczek, 2014) and word-picture matching tasks show a density inhibition effect in young adults (Garlock, Walley, & Metsala, 2001). However, why and how lexical neighbors can exert facilitatory effects in some contexts and inhibitory effects in others and how this can be affected with age remains poorly understood (Chen & Mirman, 2012, Gordon & Kurczek, 2014). In this paper we seek to explore and better understand how N affects one aspect of lexical processing, namely in making lexicality judgements, with a focus on potential differences that occur with age and with the onset of Alzheimer's disease.

Neighbourhood Effects in Young Adults

In 1977, Coltheart, Davelaar, Jonasson, and Besner were the first to manipulate N as part of a study on lexical access. They found that, in a lexical decision task, although neighbourhood density had no effect on participants' performance on the word stimuli, pseudowords with a high neighbourhood density (i.e. high-N pseudowords) took longer to be classified than pseudowords with few lexical neighbours. Andrews (1989) replicated this pseudoword neighbourhood density effect and also reported a neighbourhood effect for real words (but only for words with a relatively low frequency). However, the author also found that neighbourhood density had a paradoxical influence depending on the lexical status of the stimulus; while a large lexical neighbourhood was found to facilitate word access (fast reaction times (RTs) and low error rate) it was inhibitory for pseudowords (slower RTs and higher error rate). Conversely, Grainger (1990) found that words that had at least one higher- frequency neighbour slowed lexical decision latencies to the stimulus word.

In an attempt to resolve these conflicting results observed for words, Andrews (1997) conducted a review of the effect of lexical neighbourhood density (and of neighbourhood frequency) on lexical access and investigated the role of orthographic neighbours during word-recognition process in young adults. The results of 16 published papers investigating the effects of neighbourhood density (N) or frequency were reviewed. The studies included were selected based on the fact that they had all used single presentations of words that had been systematically selected to manipulate neighbourhood density and/or frequency in tasks that yielded measures of reaction time (RT) and/or accuracy.

In her review, Andrews found a facilitatory effect of N for English words when using lexical decision tasks. Two studies in particular, Sears, Hino, and Lupker (1995) and Forster and Shen (1996), provided robust evidence for this claim. Both studies independently manipulated N and neighbour frequency. Sears and colleagues (1995) found facilitatory effects of N in four lexical decision tasks using high- and low-N words with and without a higher frequency neighbour. They did not, however, find any effect of neighbour frequency. These findings were replicated by an additional series of three experiments carried out by Forster and Shen (1996). Once again, effects of N (but not neighbour frequency) were observed for the words.

Andrews concluded that, for all the languages that have been studied, in lexical decision tasks where words must be discriminated from stimuli that are the least word-like (i.e. illegal nonwords or pseudowords that are not very word-like) there is a clear and robust advantage for words that have a large neighbourhood density. In the case where words and legal pseudowords that varied in neighbourhood density were randomly intermixed, the effects were still facilitatory but somewhat smaller than in the easier decision environment (Andrews, 1989; Forster & Shen, 1996). Moreover, Andrews also concluded that, as a whole, data for English suggest that word identification is more consistently influenced by neighbourhood density than by neighbour frequency. In addition, effects of this variable, neighbourhood density, are almost always facilitatory for words except in the case of perceptual identification tasks. Since Andrews' review, this pattern of effects (a large lexical neighbourhood facilitating word access but inhibiting pseudowords access) has been replicated in several (although not all) additional studies in English (Huntsman & Lima, 2002; Holcomb, Grainger & O'Rourke, 2002).

In a series of two lexical decision tasks, Huntsman and Lima (2002) also found that when word frequency, average neighbourhood frequency, word length, and number of syllables were held constant, words that have many lexical neighbours were responded to more quickly than those from a small lexical neighbourhood. Furthermore, Holcomb, Grainger and O'Rourke (2002) conducted an event-related potential (ERP) study that looked at two tasks (lexical decision and go-no-go) with written words and pseudowords. The authors found that, for both tasks, words and pseudowords produced a consistent pattern of ERP effects. Specifically, stimuli that had many lexical neighbours elicited larger N400 components than similar items with relatively smaller neighbourhood density. However, the RT data for the lexical decision task showed a different pattern that was consistent with previously published behavioural studies: words with higher neighbourhood density tended to have faster RTs while pseudowords with a higher number of lexical neighbours showed an inhibition effect.

In their multiple read-out model (MROM) based on the interactive activation and competition (IAC) framework, Grainger and Jacobs (1996) have proposed that the influence of N on the time needed to make a lexicality judgement occurs due to enhanced lexical activity, i.e. many partially-activated word representations when neighbourhood density is large (Holcomb, Grainger & O'Rourke, 2002; Braun, 2006). According to the model, a speeded lexicality judgement can be made using either a standard criterion based on activity in the target word representation or a criterion set on global lexical activity. A "YES" response is given if either the local target word criterion (called M) or the global lexical activity criterion (called sigma (∑)) is reached before the time criterion (called T) elapses, otherwise a "NO" response is given. As a result, errors to words happen when the T criterion is set too low and/or both the M and ∑ response criteria are set too high. Errors to nonwords occur in exactly the opposite circumstances (i.e. high T criterion and/or low M criterion or low ∑ criterion). The M criterion is assumed to be fixed, i.e. word recognition is not under strategic control that individuals can speed up or slow down by shifting a response criterion. However, the ∑ and T criteria are both adjustable depending on the stimuli that are being processed, and the model assumes that in an environment that has many high N stimuli, a longer deadline, (higher T criterion) and a lower ∑ criterion will be set.

Having a lower ∑ global lexical activity criterion, i.e. using a heuristic of "respond 'word' if many similar word representations are activated", will facilitate the processing of words with a large N (that generate more global lexical activity) relative to words that only have a few or no neighbours. However, for pseudowords, this increase in global activation can delay the correct "not a word" decision or even lead to an incorrect "word" decision if the ∑ global lexical activity criterion to reaches threshold. While the MROM model can simulate and explain

N effects in the lexical decision task, Chen and Mirman (2012) have recently proposed a general model, also based on the IAC framework, which can be applied across various tasks and modalities with the goal of uncovering the computational principles underlying the differential N effects that have been observed in the literature. To date, the model only simulates N effects for words but these simulations showed that strongly active neighbors have a net inhibitory effect (i.e. their inhibitory effect outweighs their facilitatory effect) but weakly active neighbors have a net facilitatory effect (their facilitatory effect outweighs their inhibitory effect). As with the MROM model, Chen and Mirman's model was successful in simulating the facilitatory N effects for words (i.e., representations of words with a high N were activated more quickly that those with a low N) but currently the model does not simulate accuracy. Furthermore, in order to be able to use the model across different tasks, Chen and Mirman do not attempt to capture all of the details of any one task. Consequently, to date no pseudowords or nonwords have been tested and the model cannot simulate the lexical decision task. While both models predict and simulate the facilitatory effect of N on activation of the target word's representation, a lexicality judgement can be made prior to or without a word target being activated. The MROM model invokes the $\sum$ global lexical activity criterion only when simulating a lexicality judgement so it is still unclear whether Chen &Mirman's model can simulate N effects, especially for pseudowords as well as the MROM.

Neighbourhood Effects in Aging

It has been observed that older adults consistently take longer to make a response in lexical decision tasks when compared to young adults (Balota, Cortese, Sergent-Marshall, Spieler, & Yap, 2004; Ratcliff, Thapar, Gomez, & McKoon, 2004; Stadtlander, 1995). A meta-analysis of 22 lexical decision experiments showed that although error rates did not differ significantly between young and older adults, the older adults' RTs were 250 to 300 ms longer than those of the young adults (Myerson, Hale, Chen, & Lawrence, 1997). To our knowledge there are only three studies that have addressed the effects of neighbourhood density on lexical access in healthy aging. Stadtlander (1995) investigated the effects of both neighbourhood size and frequency on lexical access. Balota and colleagues (2004) looked only at neighbourhood density and Robert and Mathey (2007) focused only on the neighbourhood frequency effect.

Stadtlander (1995) explored the effects of orthographic neighbourhood and frequency on lexical decision in young and older adults. Stimuli varied on three dimensions: target frequency, neighbourhood frequency, and neighbourhood density. With regard to neighbourhood density, Stadtlander found that, as has been observed for young adults, N did indeed influence the time taken to respond to words. However, the older individuals showed an opposite RT pattern to what had been observed for young adults, i.e. they had faster RTs to words with a low neighbourhood density. In addition, while the younger adults made many errors to pseudowords with a high neighbourhood density, older individuals showed little difference in error rate to low versus high density pseudowords (results did not reach statistical significance for the RT data).

Balota and colleagues (2004) examined how various psycholinguistic variables, including neighbourhood density, affected lexical decision and naming performance on a very large set of stimuli (2,906 monosyllabic words and 2,906 pseudowords). They observed that N facilitated response latencies for lexicality judgements only for low frequency words in young adults. In contrast, the older adults showed a consistent inhibitory effect of N for all words. For pseudowords, a large inhibitory effect of N on RTs was found for both the young and older adults.

Robert and Mathey (2007) only investigated the effects of neighbourhood frequency on lexical decision in young and older adults. However, they also found a difference in performance between young and older participants. While an inhibitory effect of neighbourhood frequency was observed in young adults, older adults did not show a neighbourhood frequency effect. Instead, older participants showed no difference in RT to words with or without high frequency orthographic neighbours.

Neighbourhood Effects in Alzheimer's Disease

Episodic memory loss is commonly considered to be the earliest and most severe deficit associated with AD (Henry, Crawford & Phillips, 2004). However, a general slowing in processing speed is also a hallmark of the disease (Nebes & Brady, 1992; Pate & Margolin, 1994) and estimates of the prevalence of language disturbances in AD range from 30% to 100% of patients with this prevalence depending on the stage of severity of the illness (Farcnik, Persyko, & Bassel, 2002).

Impairments in language tasks requiring intentional processing (such as confrontational-naming and verbal fluency) and tasks that rely on more automatic processing (such as lexical decision and word naming) have been observed in individuals with AD. However, the order in which these impairments appear is not well understood (Taler & Phillips, 2008).The majority of individuals with AD exhibit word-finding difficulties from the onset of the disease (Appell, Kertesz & Fisman, 1982; Bayles & Kaszniak, 1987; Joubert, Joncas, Barbeau, Joanette, & Ska, 2006) with impairments in confrontational naming and verbal fluency often being reported. A meta-analysis of 153 studies that examined semantic and letter fluency in individuals with AD found that, although their performance was impaired relative to healthy older adults on tests of semantic and letter fluency, the effect was more pronounced for semantic fluency (Henry, Crawford, &Phillips, 2004).

When it comes to making lexicality judgements, on-line lexical processing studies have reported slower response times when compared to older adults (Caza, & Moscovitch, 2005-experiment 2; Duong, Whitehead, Hanratty, & Chertkow, 2006). Two lexical decision tasks, one probing words with high and low frequency trajectories and high and low cumulative frequency and legal pseudowords (Caza & Moscovitch, 2005) and the other probing regular and irregular high- and low frequency words and legal pseudowords (Duong et al., 2006) both reported longer response times for individuals with AD. Furthermore, those with AD may also have lower accuracy rates than age-matched controls, with a particular propensity to over-accept pseudowords and nonwords while correctly accepting words, in off-line (Snyder, Holland, & Forbes, 1996; Glosser, Kohn, Friedman, Sands, & Grugan, 1997) and on-line (Madden, Welsh-Bohmer, & Tupler, 1999) lexical decision tasks. Snyder and colleagues (1996) found that, in an off-line visual lexical decision task, individuals with AD and healthy older adults performed at comparable rates of accuracy for the word stimuli while those with AD performed significantly worse compared to older adults, on both pseudoword and nonword stimuli (incorrectly responding "YES" to many of the nonwords and pseudowords) while the same pattern was observed in an off-line auditory lexical decision task using probing words and pseudowords (Glosser et al., 1997). An over-acceptance of pseudowords has also been reported in an on-line lexical decision task (Madden, Welsh-Bohmer, & Tupler, 1999). Although young and older adults and those with AD all performed at similar rates of accuracy for words, those with AD made significantly more errors to pseudowords than either the young or older adults.

While there has been some research conducted addressing how neighbourhood density is processed as people age, we are unaware of any studies that have investigated this issue in individuals with Alzheimer's disease (AD) in English. One study, employing a lexical decision task in Spanish, investigated the effects of both neighbourhood density and of the number of semantic associates on lexical access in older adults and individuals with AD (Duñabeitia, Marín, & Carreiras, 2009). With regards to N, the authors found that although those with AD had significantly longer response latencies than older adults, both groups showed a clear N facilitatory effect for words for both RTs and error rate. However, the authors did not perform an analysis of the pseudowords in the task, so it is unclear whether either group showed an inhibitory N effect for the pseudoword stimuli.

Aims of the Current Study

Although the effects of N on lexical processing in young adults are believed to be fairly well understood, our understanding of these effects across the adult lifespan and, more specifically, in neurodegenerative conditions, such as AD, is much poorer. The current study presents a first attempt to address this gap by investigating N effects in lexical processing in young adults, as well as in older adults and also in individuals with AD. A closer examination of how N affects lexical processing in healthy aging and in AD may provide insight into potential changes in organization or timing within the mental lexicon, thus enhancing our understanding of lexical processing across the lifespan. Furthermore, by investigating specific word features, such as N, we hope to obtain information regarding subtle alterations in lexical processing that may be present early in the disease and may potentially help distinguish pathological from healthy aging before gross and overt manifestations of decline become apparent. While, N effects are the main focus of the study, a secondary goal was to explore whether individuals with AD show an over-acceptance to nonword stimuli (i.e. higher error rate to pseudowords and/or nonwords), but not to words, when compared to older adults as has previously been reported in the literature.

Methods

Participants

A total of 77 adults participated in this study: 42 healthy young adults (24 women), 19 healthy older adults (13 women) and 16 individuals with AD (9 women). All were dominant English speakers and had normal or corrected-to-normal vision. Young adults were undergraduate students taking an Introductory Psychology course at the University of Kansas and were typically aged university freshman and sophomores who ranged in age from 18-21 years and had an average of 13.5 years of education. Older adults and individuals with AD were recruited primarily through the Memory Clinic of the Douglas Mental Health University Institute in Montréal, Québec. Individuals with neurological (other than AD) or psychiatric disorders, epilepsy, or those who had a history of alcohol abuse, psychosis or major depression were not included in the study. Individuals in the older adult group had a mean age of 68 years (range: 53-88) and they averaged 15 years of education (range: 10-19). In order to rule out the possibility of any cognitive deficits in the older control group, only individuals who scored 26/30 or above on the Montreal Cognitive Assessment (MoCA, Nasreddine, Phillips, Bédirian, Charbonneau, Whitehead, et al., 2005) were included. The MoCA was chosen because it has very good sensitivity and specificity in differentiating normal aging from mild cognitive impairment (MCI).

Individuals from the AD group had a mean age of 75 years (range: 57-83) and they averaged 16 years of education (range: 7-21). Diagnosis of probable AD was made in accordance with the criteria specified by the National Institute of Neurological and Communicative

Disorders and Stroke-Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA; McKhann, Drachman, Folstein, Katzman, Price, et al., 1984). The diagnosis of probable AD was performed by a psychiatrist with extensive experience with this population and attests that each individual met the criteria for dementia (by history and neuropsychological testing) and had had progressive deficits in memory and one other area of cognition. While efforts were made to include individuals with AD who were not taking psychoactive medications at the time of recruitment, individuals who were taking psychoactive medications, including cholinesterase inhibitors, were included in the study as long as the dosage had been stable for three months prior to study entry and throughout the study. In order to specify Alzheimer's disease severity, the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975; Folstein, Robins, & Helzer, 1983) was administered. The MMSE is extensively employed to measure dementia severity in individuals with AD due to the fact that it is brief to administer and is applicable across the mild and moderate stages of AD (Mendiondo, Ashford, Kryscio, & Schmitt, 2000). Patients whose score on the MMSE ranged from 20 to 29 (mild severity, Feldman & Woodward, 2005; Feldman, Van Baelen, Kavanagh, & Torfs, 2005) were included in this study. All participants were carefully assessed by study staff to ensure that they were capable of complying with the requirements of cognitive testing. Written informed consent was obtained from all participants.

Stimuli and Task

A standard visual lexical decision task, composed of 320 trials, was run using E-Prime experiment software (Psychological Software Tools, Pittsburgh, PA). Three types of stimuli were examined: words (80 nouns, PENCIL and 80 filler verbs, CANCEL), pseudowords (80 legal and pronounceable strings of letters that do not carry meaning, GLONET), and nonwords (80 illegal and unpronounceable string of letters, TLKMP) While traditional lexical decision tasks only probe words and pseudowords or words and nonwords, we included all three stimuli types within the same task to explore whether the individuals with AD would show an over-acceptance to either of the two "not a word" stimuli types that has previously been reported in the literature. In order to maintain an equal number of stimuli in each of the 3 stimuli groups of interest (i.e. words, pseudowords, and nonwords) but still have a 1:1 ratio of word and "not a word" stimuli (i.e. nonwords and pseudowords) that is required in a lexical decision task, we added 80 filler words (verbs) that were not included in any analyses.

All word and pseudoword stimuli were controlled in terms of frequency, length (letters and number of syllables), and number of lexical neighbours (see Table 4.1). Experimental words were concrete monomorphemic nouns with a low frequency of use (between 3 and 32 occurrences per million) according to the USENET database (Shaoul & Westbury, 2006) while filler words were verbs of low frequency (between 2 and 50 occurrences per million). Pseudowords were pronounceable letter strings and nonwords were unpronounceable letter strings. All stimuli were 4-6 letters in length (1-2 syllables). Experimental word and pseudoword stimuli were each divided into a high and low neighbourhood density group (40 stimuli per group). High neighbourhood density stimuli had between 5 and 18 lexical neighbours and the low neighbourhood density stimuli had 0, 1 or 2 lexical neighbours. All nonwords had 0 lexical neighbours (see Appendix A for a full list of stimuli). Two sample t-tests indicate that there was no significant difference in frequency of occurrence between High-N and Low-N words (t = 0.30, p = 0.76). Also, there was no variability in the number of neighbours within the Low-N stimuli or within the High-N but there was a difference between the High- and Low- stimuli. There was no significant difference in the number of neighbours between High-N words and

High-N pseudowords ($t = -0.37$, $p = 0.71$) nor between Low-N words and Low-N pseudowords ($t = -0.96$, $p = 0.34$). However, there was a significant difference in number of neighbours between High-N words and Low-N words ($t = 13.05$, $p = <0.0001$) and also between High-N pseudowords and Low-N pseudowords ($p = <0.0001$) with High-N stimuli having more lexical neighbours than the Low-N stimuli.

In terms of stimulus length (number of letters), there was a significant difference in length between High-N and Low-N pseudowords ($t = -3.15$, $p = 0.002$), between High-N pseudowords and High-N words ($t = -3.86$, $p = 0.002$), between High-N pseudowords and nonwords ($t = 2.64$, $p = 0.01$) and between Low-N words and nonwords ($t = -2.45$, $p = 0.02$). No other comparisons reached significance. It is worth noting that these differences in mean length, while statistically significant, were very small (the largest difference (0.7 letters, occurred between High- N pseudowords and Low-N words) and appear to be driven by the overall relatively shorter length of the High-N pseudowords (mean 4.5 letters). Given the small range of letters that made up all the stimuli (4-6) and that the pseudowords were carefully matched in N to the words, we believe that this difference in length is minor and does not affect the overall results of the study.

--*Insert Table 4.1 here*--

Stimuli were presented in random order and participants were given a short break half way through the experiment. For each trial, a fixation cross was presented for 500 ms and was followed by a stimulus, presented in lowercase letters, that remained on the screen until the participant made a response. The interstimulus interval (ISI) was set at 500ms. Participants were asked to decide as quickly and as accurately as possible whether the stimulus was a word or not by pressing one of two buttons on a keyboard. We conducted 10 practice trials before beginning the experiment. Response time (RT, in ms, measured from stimulus onset until a response was made) and accuracy were collected for each trial.

Statistical Analysis

Mean correct lexical decision latencies and percent error for each stimulus type are presented in Table 4.2. Participants who made 50% or more errors in any of the stimuli types were excluded from all analyses. This cut-off led to seven (7) young adults and one (1) individual with AD to be excluded and resulted in a final total of 69 participants (35 young adults- 21 women; 19 older adults- 13 women; and 15 individuals with AD- 8 women). For the young and older adults, trials with incorrect responses or with lexical decision latencies above 2 standard deviations from the group mean (for each stimulus type) were removed from the RT analysis and resulted in an average of 3% of data for the young adults and 4% of data for older adults to be discarded. For the AD participants, trials with incorrect responses and latencies above 2 standard deviations from their individual mean (for each stimulus type) were not included in the RT analysis and led to an average of 5% of data to be discarded. Data for the filler trials (the verbs) were not included in the analyses for any participant group.

Response latencies were submitted to separate mixed-model analyses of variance (ANOVA). Differences between the three participant groups on the lexical status of the stimuli were investigated using a 3 (Group: young adults, older adults, and individuals with AD) x 3 (Stimulus type: words, pseudowords and nonwords) mixed-model ANOVA. Neighbourhood density effects in the three (3) participant groups were investigated using a 3 (Group: young adults, older adults, and individuals with AD) x 2 (Lexicality: word, pseudoword) x 2 (Density: high, low) mixed model ANOVA. Three types of covariance structure were considered for the mixed-model ANOVAs: compound symmetry, heterogeneous compound symmetry, and unstructured. Based on the fit statistics for each of the 3 models we chose the unstructured covariance structure because this model has the best fit (see Table 4.3). We used an alpha level of .05 for all statistical tests.

--Insert Table 4.3 here--

The error rates did not follow a normal pattern of distribution and, therefore, were analysed using nonparametric tests. Kruskal-Wallis & Wilcoxon-Mann-Whitney tests and Wilcoxon Signed-rank tests were used to investigate the effects of lexical status of the stimuli and of neighbourhood density on error rate between the three groups.

Results

Effects of Stimulus Type (Words, Pseudowords, and Nonwords)

Before investigating N effects we first looked at each group's overall performance on each of the three stimuli types.

Reaction times. The 3 (Group: young adults, older adults, and individuals with AD) x 3 (Stimulus type: words, pseudowords and nonwords) mixed-model ANOVA showed a significant interaction of Group x Stimulus Type ($F(4, 77) = 5.51$; $p < 0.001$). Planned t-tests showed than individuals with AD were significantly slower than the older adults for all three stimulus types ($p < 0.001$ for the 3 stimulus types). Individuals with AD were also significantly slower than the young adults ($p < 0.001$ for the 3 stimulus types). The older adults were significantly slower than the young adults for the pseudowords ($p = 0.03$) and for the words ($p = 0.01$), but the difference did not reach significance for nonwords ($p = 0.06$).

--Insert Figure 4.1 here--

Furthermore, the three participant groups showed a significant difference in RT between nonwords and pseudowords ($p < 0.001$ for the each of the 3 groups) and between words and pseudowords (also $p < 0.001$ for the each of the 3 groups). As expected, each group responded faster to nonwords when compared to pseudowords and faster to words when compared to pseudowords. However, when comparing words to nonwords the individuals with AD and the young adults did not show a difference in RT (AD: $p = 0.39$; young adults: $p = 0.22$) while the older adults were significantly faster to the nonwords than to the words ($p = 0.03$) (See Figure 4.1).

Error rates. When comparing the three groups on error rates across the three stimulus types the Kruskal-Wallis & Wilcoxon-Mann-Whitney test showed an overall significant effect for pseudowords ($H = 11.59$, $p < 0.01$) but not for nonwords or words ($H = 3.10$, $p = 0.21$ and $H = 4.74$, $p = 0.09$ respectively). While the 3 groups did not a show a difference in error rates for nonwords or words, planned post-hoc Wilcoxon Two-Sample tests showed that the young adults made significantly more errors to pseudowords than either the older adults ($p < 0.01$) or the individuals with AD ($p = 0.04$). There was no significant difference in error rate to pseudowords between the older adults and individuals with AD ($p = 0.26$) (See Figure 4.2).

--Insert Figure 4.2 here--

Effects of N (Words and Pseudowords)

Reaction times. The 3 (Group: young adults, older adults, and individuals with AD) x 2 (Lexicality: word, pseudoword) x 2 (Density: high, low) mixed model ANOVA showed significant main effects of Group ($F(2,66) = 35.07$, $p < 0.0001$), of Lexicality ($F(1,66) = 189.098$, $p < 0.0001$) and of Density ($F(1,66) = 43.47$, $p < 0.0001$). Furthermore, there was a significant Group x Lexicality interaction ($F(2,66) = 9.95$, $p = 0.0002$), a significant Group x Density interaction ($F(2,66) = 9.62$, $p = 0.0002$), a significant Lexicality x Density interaction ($F(1,66) = 85.45$, $p < 0.0001$) as well as a significant Group x Lexicality x Density interaction ($F(2,66) = 4.42$, $p = 0.02$). Planned t-tests showed that individuals with AD were significantly slower than the older adults for each of the 4 stimulus types ($p < 0.001$ for the 4 stimulus types). Individuals with AD were also significantly slower than the young adults ($p < 0.001$ for the 4 stimulus types). The older adults were significantly slower than the young adults for the high N pseudowords ($p = 0.03$) and for both the high and low N words ($p < 0.01$ and $p = 0.02$ respectively) but the difference just failed to reach significance for the low N pseudowords ($p = 0.05$).

Additional planned t-tests revealed that although all 3 groups showed an N effect for the pseudoword stimuli (AD: $p < 0.001$; older adults: $p < 0.01$; young adults: $p < 0.01$) only the older and younger adults showed an N effect for words ($p = 0.04$ and $p < 0.001$ respectively) while the individuals with AD did not ($p = 0.98$).

A large N was inhibitory for the pseudoword stimuli for each of the three groups; on average, the young adults were 73 ms slower when responding to high density pseudowords than to low density pseudowords, the older controls were 117 ms slower when responding to high density pseudowords than to low density pseudowords, and the individuals with AD were 232 ms slower to high density pseudowords. In contrast, high density words were responded to an average of 37 ms faster for the young adults, 19 ms faster for the older individuals, but there was less than a 1 ms difference in RT between the high and low density words for the individuals with AD (See Table 4.2).

--Insert Table 4.2 here--

Error rates. When comparing the participant groups' error rates across the 4 neighbourhood density stimuli types the Kruskall-Wallis & Wilcoxon-Mann-Whitney tests showed no overall significant effect for the high N words ($H = 2.75$, 1 d.f., $P = 0.25$) or for the low N words ($H = 4.41$, 1 d.f., $P = 0,11$). However we did observe an overall significant effect for both high and low N pseudowords ($H = 13.51$,1 d.f., $P = 0.001$ and $H = 8.41$, 1 d.f., $P = 0.02$ respectively). Planned post-hoc tests revealed that individuals with AD and older adults both made significantly fewer errors than the young adults for high N pseudowords ($p = 0.01$ and $p <$

0.001 respectively). Error rates for older adults and those with AD did not differ for high N pseudowords ($p = 0.47$).

When we examine how error rates for each group differed with respect to the 4 neighbourhood density stimuli types, Wilcoxon signed rank sum tests showed that young adults made significantly more errors to high versus low N pseudowords ($t = 8.95$, $p < 0.001$) but they had the opposite pattern for words, i.e. more errors to low versus high N words ($t = -4.15$, $p < 0.001$). Individuals with AD and older adults also showed higher error rates to high versus low N pseudowords ($t = 3.90$, $p = 0.001$ and $t = 2.48$, $p < 0.01$ respectively). Conversely, they did not show a difference between high and low N words (AD: $t = -1.47$, $p = 0.10$; and older adults: $t = -1.89$, $p = 0.13$).

Discussion

In the current study we observed a progressive slowing of reaction times that occurred with age and that becomes more prominent with the onset of AD. As had previously been reported in the literature (Stadtlander, 1995; Ratcliff et al., 2004), we observed that older adults were significantly slower than young adults for words and pseudowords but while they were also slower to nonwords this difference failed to reach statistical significance. Furthermore, individuals with AD were even slower than healthy older adults across all three types of lexical stimuli. While a general slowing in processing speed occurring with aging has been reported in the literature, this reduction appears to be further aggravated by the neurodegenerative process associated with Alzheimer's disease. At the same time, there appears to be an improvement in accuracy in the two aging groups, particularly for the more challenging pseudowords.

In the current study, the individuals with AD were older (mean = 75) than the older adults (mean = 68). This difference in age may be a confounding variable since progressing age and the presence of the disease have both been associated with a general slowing in cognitive tasks such as the lexical decision task. Therefore, it is possible that some of the difference in speed that we observe can be due mostly to aging. However, it seems unlikely that this is the case since the Duñabaetia and colleagues (2009) study had very closely matched AD participants and older adults (both mean age = 72) yet they also found that the AD group was significantly slower than the older adults.

Contrary to previous reports in the literature suggesting an over-acceptance of nonword or pseudoword stimuli in individuals with AD compared to healthy older adults (Glosser, et al., 1997; Madden et al., 1999; Snyder, Holland, & Forbes, 1996), we did not observe any difference in error rate between those with AD and the older adults. Also in contrast to previous results that showed no difference in error rate between young and older adults (Myerson et al., 1997), the young adults in the current study made more errors than either the older adults or the individuals with AD. Surprisingly, this difference was driven by the younger adults' over-acceptance of pseudoword stimuli. When compared to both of the other participant groups, young adults made many more errors to pseudowords (15% versus 7% for older adults and 9% for individuals with AD) while the 3 groups had comparable error rates for nonwords and words. This difference suggests that the young adults may have been using a different strategy, i.e. more strongly relying on the ∑ criterion of global lexical activity ("respond 'word' if many similar word representations are activated") in order to perform the task while the older adults and those with AD relied more heavily on activity from the target word representation thus providing support for Grainger and Jacob's MROM model of lexical processing that proposes the existence of these two separate procedures that can be used when performing lexicality judgements.

N Effects in Lexical Processing

When looking at the neighbourhood density effects, our findings for the young adult group reflect those that have previously been reported in the literature. In the current study, we observe that a large N is facilitatory for words but is inhibitory for nonwords and this effect is seen in reaction times, as well as in error rate for the young adults.

However, it appears that with aging there is a change in how neighbourhood density is processed; the older individuals in the current study are no longer as sensitive to N when compared to young adults and this deficit is more pronounced with the presence of AD. Our results contrast with those of Balota and colleagues (2004) who observed an inhibitory effect of N on words for older adults. They also contrast with those of Stadtlander (1995) who observed that older adults responded faster to words with a low neighbourhood density. However, as with Duñabaetia, Marin and Carreiras (2009) who reported facilitatory N effects for words for older adults, the older adults in the current study follow a similar pattern of performance as the young adults when it comes to reaction times for words, i.e. they respond faster to high N words but slower to high N pseudowords. However, older adults differ from the younger group in the amount of facilitation (RTs) for the high N words and inhibition for the high N pseudowords, which is smaller for the older adults. Furthermore, and in contrast to Duñabaetia, Marin and Carreiras (2009), older adults in the current study differ from young adults in terms of error rate. Specifically, while older adults, like young adults, still show inhibition (i.e., more errors) to high N pseudowords, they no longer show facilitation (i.e., fewer errors) to high N words. Therefore, the changes in N effects that are observed with aging appear to differentially affect the processing of words and pseudowords. This difference becomes even more striking when we look at the individuals with AD: unlike Duñabaetia, Marin and Carreiras (2009) who found a facilitatory N effect for words for both RTs and error rate in individuals with AD, neighbourhood density did not appear to influence the processing of words for individuals with AD as they did not show a difference in error rate or in RT to low versus high N words in the current study. However, individuals with AD are still sensitive to N effects when processing pseudowords; as was shown earlier, they made significantly more errors to pseudowords with a high neighbourhood density than to those with a low density and were significantly slower in responding to pseudowords that had a large N than to those with a small N.

Why Are Older Adults and Individuals with AD Still Sensitive to N for Pseudowords but not for Words?

We observe that as people age they become less sensitive to N, specifically for words, and that this type of performance becomes more prominent in individuals who have Alzheimer's disease. It has been proposed in the aging literature that cognitive changes associated with age are largely caused by a slowing or failure of inhibitory mechanisms (Hasher & Zacks, 1988, Robert & Mathey, 2007). When performing a speeded lexicality judgement task, this slowing of inhibition is believed to affect the process of selecting the correct lexical entry from a pool of its activated neighbours. This suggests that, as the size of a target stimulus' neighbourhood increases, the difficulty of selecting the correct entry should also increase thus leading to the prediction that older adults should have more difficulty with all stimuli (words and pseudowords) that have a large N. Yet, this was not what we observed for either the older adults or for the individuals with AD. Both groups showed no difference in error rate and, in the case of those with AD, also in RT, when making lexicality judgements to words with high or low neighbourhood density. However, they still showed sensitivity to N when processing pseudowords.

While the current findings cannot be explained by slowing or failure of inhibitory mechanisms in older adults, it may be that a slowing of activation mechanisms for neighbours might be contributing to the dissociation of N effects in words versus pseudowords that are observed in the current study. According to the MROM model both the facilitatory effect of neighbourhood density on RTs to words and the inhibitory effects to pseudowords that have been observed in young adults for lexical decision tasks are caused by the same mechanism: enhanced lexical activity when N is large (Grainger & Jacobs, 1996). Words with a large N (that generate more global lexical activity) will be processed faster than words that only have a few or no neighbours due to enhanced activity of partially-activated neighbours. On the other hand, this increase in activation will slow down processing (and lead to more errors) for pseudowords. However, according to the model, this is only possible if individuals are sensitive to N properties early on in the course of the experiment. If so, the presence of many high N stimuli paired with the inclusion of illegal nonwords (as was the case in the current experiment) will lead participants to set a longer response threshold (a higher T criterion) and a lower ∑ global activation criterion.

In the current study we observed that having a large N appears to differentially affect how words and pseudowords are processed as people age. While this alteration seems to begin as people age, the effect becomes more pronounced with the presence of AD. Like young adults, older adults and individuals with AD were slower to respond to and made significantly more errors to high versus low N pseudowords but, unlike young adults, both showed an altered effect of neighbourhood density for the word stimuli, i.e. a decrease or absence of facilitation. However, these results are not incompatible with Grainger and Jacobs' model as long as it allows for the possibility of a change in timing of activation of lexical neighbours with advanced age.

We propose that, with age, the activation of lexical neighbours still occurs, but more slowly than for young individuals. As a consequence, this may be influencing the threshold values that are set for both the T and ∑ criteria and may cause older individuals and those with AD to rely primarily on activity generated by the target's individual lexical representation (M criterion) to perform a lexical decision, in contrast to younger adults who appear to rely more on global lexical activity (∑ criterion). As mentioned above, sensitivity to N early on in the course of the experiment will lead participants to set a higher T criterion and a lower ∑ global activation criterion. However, if neighbours are being activated at a slower rate in older adults and in those with AD then it may cause them to not change their response strategy (i.e. they will not raise their ∑ criterion or lower their T criterion) and rely more on M, and this may have a differential effect on word versus pseudoword processing. For pseudowords, despite a high(er) T criterion, with no local representation that can be activated to stop the processing, slowly activated neighbours appear to still have enough time to interfere. Hence the N effect for pseudowords (i.e. the inhibition effect that was observed for high N pseudowords) will remain. Conversely, when processing words, which have a lexical representation, a lexical decision can be performed once the representation has been activated (M criteria attained) despite a short(er) T criterion. However, since activation of neighbours is slowed, there may be little or no facilatatory N effect generated by neighbourhood global lexical activity in the time taken for the word's representation to be activated. Hence, the facilitatory effect of N for words is not observed. While our results are compatible with the MROM model, they are not easily accounted for by

Chen and Mirman's (2012) model that proposes that weakly activated lexical neighbours will have a facilitatory effect on words. However, this may be due to the fact that the model is not meant to simulate lexical decisions but instead is meant to be applied across various tasks and modalities.

Conclusions

The current study points to an alteration in the processing of neighbourhood density in lexical processing that begins in healthy aging and becomes more pronounced with the presence of AD. The changes in N processing that we have observed as people age seem to be due to a longer amount of time required in order to activate lexical neighbours which interferes with N effects for words but not for pseudowords.

While a slowing in activation of lexical neighbours that begins in healthy aging appears to be responsible for this change it remains unclear how the presence of AD may be further contributing to the change. It is possible that the general cognitive slowing that is associated with AD, rather than any additional lexicon specific slowing in the activation between lexical neighbours, may be responsible for the decline in performance relative to that of the healthy older adults. This would suggest that the observed changes in how N is processed by those with AD may be solely an extension of the normal aging process. Alternatively, it may be that the presence of AD can affect the organization and/or the timing of activation of lexical neighbours within the mental lexicon which would suggest a qualitative difference from the normal aging process. Finally, a combination of these two effects may be at work.

Additional research in these areas is warranted to further investigate whether a slowing of activation or other factors may be contributing to the dissociation of N effects observed for words versus pseudowords and to explore how and to what extent the AD neurodegenerative process may contribute to changes in processing N. Such investigations can increase our understanding of what lexical features may be affected with onset of AD and thus help differentiate healthy from pathological aging long before overt manifestations are evident.

Lastly, results from studies such as this one, conducted with aging individuals and those with neurological conditions, can provide information for models of lexical processing regarding word recognition that may in turn allow these models to better account for lexical processing changes occurring across the adult lifespan.

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Appendix A

List of Stimuli

High neighbourhood density experimental word stimuli, (number of lexical neighbours):

bread (7), bubble (7), bullet (7), butter (13), cage (15), clock (9), copper (12), corn (16), couch (8), crown (8), finger (9), flame (7), gate (17), glass (5), goose (5), grain (5), grass (9), honey (11), horse (10), jungle (5), ladder (8), lily (5), liver (17), milk (10), mouse (10), navel (5), pickle (5), plate (10), pocket (7), puddle (9), roof (8), shark (9), snake (6), spark (6), spider (5), spike (7), tent (17), tiger (6), towel (6), tower (15).

Low neighbourhood density experimental word stimuli, (number of lexical neighbours):

album (0), apple (2), arrow (0), bacon (2), bulb (2), cabin (0), camel (1), canal (2), cheese (1), cigar (0), cliff (1), cloud (2), dragon (0), eagle (0), elbow (1), fence (2), flour (2), fossil (0), ghost (1), guitar (0), helmet (1), kiosk (0), knife (0), lentil (2), maple (1), menu (2), motor (1), needle (0), olive (2), pearl, (2), pencil (0), ranch (1), robot (0), ruby (2), sphere (0), sugar (0), thumb (2), tongue (1), vinyl (1), wheat (2).

High neighbourhood density filler word stimuli, (number of lexical neighbours):

alter (6), bake (18), bend (17), burst (6), bury (10), carry (7), cease (6), chew (11), crawl (5), dive (17), earn (7), fade (15), flex (7), flush, (5), foster (8), gather, (5), glow (8), hang (14), heal (17), hire (13), invest (5), leap (10), lick (15), mock (15), parse (6), ponder (7), refine (5), render (12), repent (5), scare (11), settle (5), shake (12), shine (12), sing (16), smack (5), steer (5), strive (8), vary (6), wash (12), wink (16).

Low neighbourhood density filler word stimuli, (number of lexical neighbours):

accuse, (0), adhere (0), admire (0), admit (2), advise (1), annoy (0), assert (2), assess (1), assign (0), attach (1), cancel (2), comply (1), convey (2), defend (1), ignore (0), delete (0), derive (1), digest (2), divert (2), divide (1), employ (0), equate (0), evolve (0), freeze (2), imply (1), absorb (1), insist (0), insult (0), invade (0), knock (2), perish (1), pursue (0), regret (1), relax (2), rescue (1), resign (1), reveal (2), unite (2), utter (1), yield (2).

High neighbourhood density pseudoword stimuli, (number of lexical neighbours):

acle, (7), ansle (6), beath (6), bettle (8), burdle (5), colb (7), culp (5), dari (5), delp (8), dulp (5), dunt (16), fibe (10), foris (7), fower (12), frab, (10), fump (11), grafe (7), grink (5), hant (13), homper (5), hulf (6), jink (14), keld (6), loap (8), lunk (16), mear (18), montis (5), muned (6), narp (9), noot (11), noster (8), perg (8), pime (12), pisk (7), plom (8), plone (6), serry (8), slun (8), talb (5), tunk (17).

Low neighbourhood density pseudoword stimuli, (number of lexical neighbours):

acril (2), afel (1), brazar (1), casip (0), chond (1), clesh (2), dendu (0), dunry (1), edas (2), eglym (0), egol (2), finab (1), fiple (1), fodum (1), forex (1), geddop (0), goind (2), henel (0), jodar (0), krelt (1), kulm (0), leraf (0), londu (1), mamet (0), mupin (1), ougil (0), muki (1), netu (2), nivar (0), paupis, (0), pedak (1), petust (0), poish (1), reshew (0), sapil (1), serol (2), stru (2), tular (0), vacop (0).

Nonwords stimuli (all 0 lexical neighbours):

afxy, akwih, atmofr, awgsiq, bdui, bnua, cfru, cgaj, cmlih, ctmovk, cuhlw, dlupfb, xjoh, dpagb, ebkfu, ehgd, elokju, fbsua, feglrb, fwnef, gakfp, gdulw, gpelti, gsdu, gwtys, hdob, hlufc, ifmlej, iqldo, iwerpd, jadcr, jdemc, jpulm, kbiw, kftonb, lpekg, kpsia, lbym, lgicb, lwafg, mcif, mjadc, mlopf, nhfusb, ncyz, nfadx, nlpoc, nvudfa, obfjl, olfg, opdku, pbsi, pmisg, pgef, pxunl, qlih, qmig, rfajh, rjau, rmloh, rtingd, rtlu, sdopl, sgacbe, sgydf, sxuf, tcegd, tfdi, tkotm, tmlu, usbixg, uvfmi, vbhke, vcadf, vgak, yjfbu, ymdni, zdikm, zgsa, zmul.

Table 4.1 – Stimuli Types

	Words- experimental*		Pseudowords		Nonwords
Description	**Noun**		**Legal**		**Illegal**
	Low N	**High N**	**Low N**	**High N**	
Example	*"pencil"*	*"honey"*	*"finab"*	*"ansle"*	*"tlkmp"*
n	40	40	40	40	80
Mean N	0.98	8.9	0.80	8.6	0
(range)	(0-2)	(5-17)	(0-2)	(5-18)	
Mean # letters	5.2	5.1	5.0	4.5	4.9
(range)	(4-6)	(4-6)	(4-6)	(4-6)	(4-6)
Mean # syllables	1.7	1.5	1.8	1.3	
(range)	(1-2)	(1-2)	(1-2)	(1-2)	
Mean frequency	11.1	11.6	0	0	0
(range)	(3.2-28.3)	(3.3-32.2)			

*80 filler words (verbs) were also included in the experiment in order to have a 1:1 ratio of word and not "not a word" stimuli. Verbs had a mean length of 5.26 letters (range 4-6) and 1.6 syllables (range 1-2), and a mean frequency of 10.2 occurrences per million.

Table 4.2 – Mean Error Rate and Reaction Time (RT) in ms for Young Adults, Older Adults, and Individuals with AD

	Young Adults				Older Adults				Individuals with AD			
Stimulus Types	**Error Rate**		**RT**		**Error Rate**		**RT**		**Error Rate**		**RT**	
	Mean	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**	**Mean**	**95% CI**
Words High N	2%	1-3%	561	542-851	1%	0-3%	700	668-732	2%	0-3%	996	819-1172
Words Low N	5%	4-6%	598	575-622	3%	1-5%	719	688-749	3%	1-5%	996	821-1171
Pseudowords High N	23%	17-28%	809	761-857	10%	6-14%	987	903-1070	12%	7-17%	1511	1244-1779
Pseudowords Low N	7%	5-9%	735	692-779	5%	0-9%	870	809-931	5%	3-8%	1279	1051-1507
Nonwords	1%	1-1%	566	545-586	1%	0-2%	675	649-700	2%	1-4%	1012	798-1225

Table 4.3 – Fit Statistics for the 3 Covariance Structures that were Considered for the Mixed-Model ANOVAs

3 (Group) x 3 (Stimulus type) mixed-model ANOVA

Covariance structure	-2LogL	Number of parameters	AIC	AICc	BIC
Compound Symmetry (CS)	2535.7	2	2539.7	2539.8	2544.2
Heterogeneous CS	2492.6	4	2500.6	2500.8	2509.5
Unstructured	***2460.2***	***6***	***2472.2***	***2472.2***	***2485.6***

3 (Group) x 2 (Lexicality) x 2 (Density) mixed-model ANOVA

Covariance structure	-2LogL	Number of parameters	AIC	AICc	BIC
Compound Symmetry (CS)	3420.8	2	3424.8	3424.9	3429.3
Heterogeneous CS	3340.5	5	3350.5	3350.7	3361.7
Unstructured	***3230.5***	***10***	***3250.5***	***3251.4***	***3272.8***

Figure 4.1 - Mean RTs (in ms) for the 3 Stimuli Types

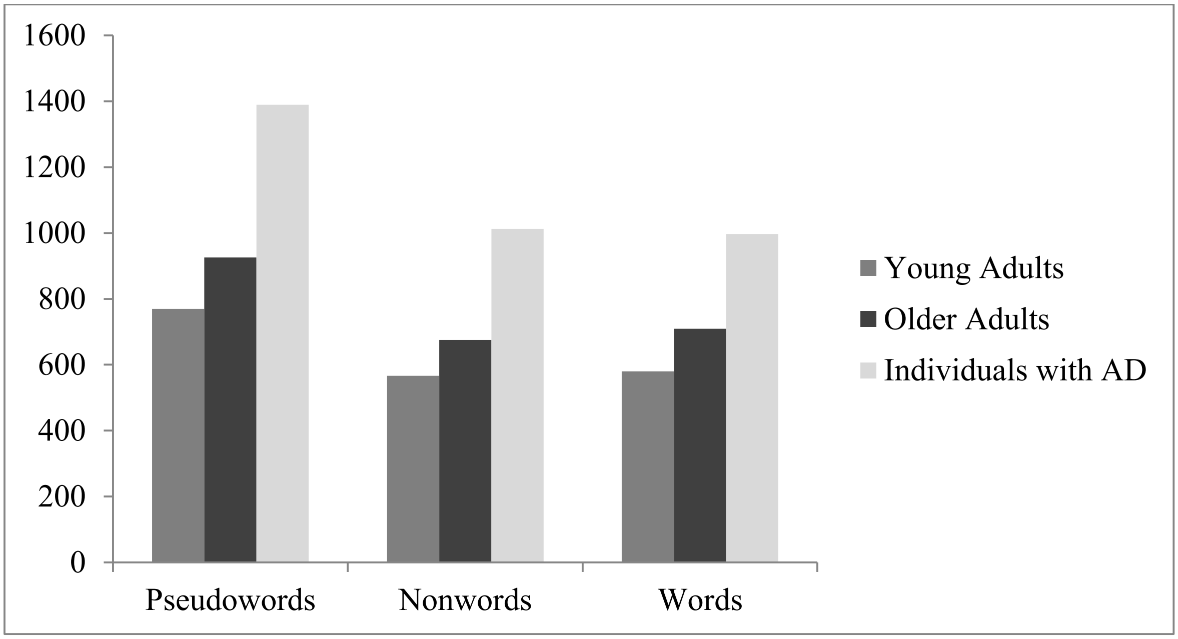
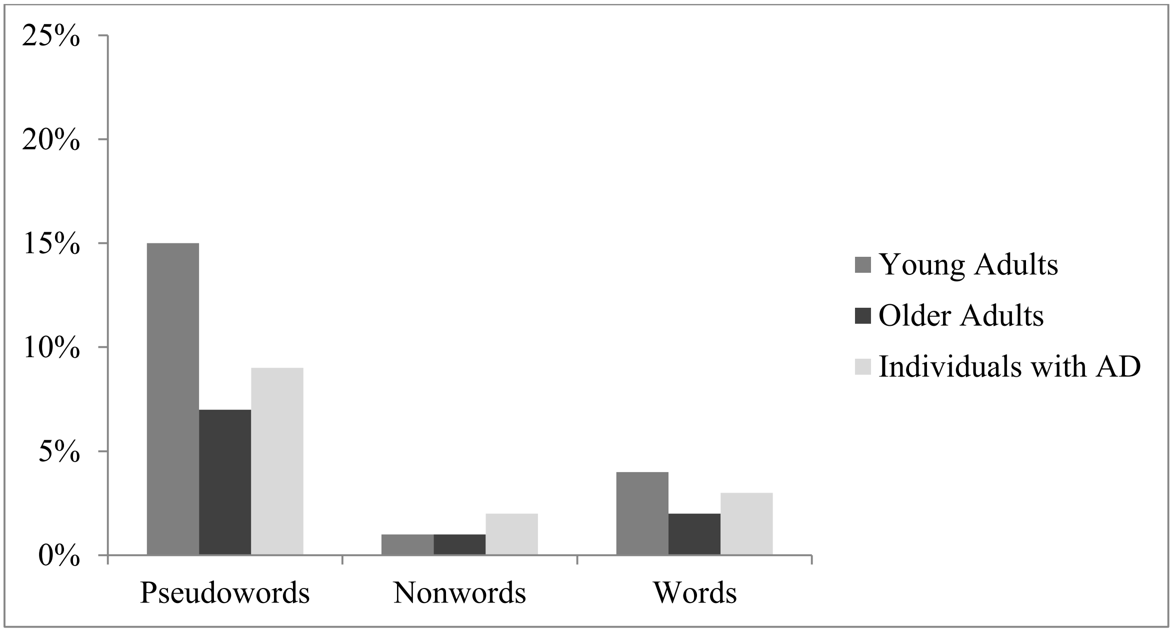


Figure 4.2 - Mean Error Rates for the 3 Stimuli Types



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CHAPTER 5: ***Manuscript 2.*** *Electrifying the Lexical Decision: Examining a P3 ERP Component Reflecting Early Lexical Categorization*

Preface to Manuscript 2

Manuscript 1 provided insight into differences in performance on lexicality judgements between the young and the aging groups. However, while the behavioural results in the lexical decision task from Manuscript 1 reflect the end result of lexical processing, ERP results can provide insight into what is occurring during the various stages of processing. With the anticipation that results obtained from the combination of both methodologies could provide a more comprehensive understanding of how lexicality is processed across the lifespan, we developed a novel ERP testing paradigm (the lexical decision oddball task). Though based on a well-established paradigm from the attention literature, the task has never been performed with linguistic stimuli in the participant groups addressed in this study. Therefore, the overarching aims of the following manuscript were 1) to validate the utility of this novel methodology when studying early stages of lexical processing in young adults and 2) to collect data for the young adult group that will serve as a reference point with which to compare observations from the healthy older adult and AD groups in Manuscript 3.

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Title Page

Electrifying the Lexical Decision:

Examining a P3 ERP Component Reflecting Early Lexical Categorization

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Abstract

The current research utilizes lexical decision within an oddball ERP paradigm to study early lexical processing. Nineteen undergraduate students completed four blocks of the lexical decision oddball task (Nonword targets among Words, Word targets among Nonwords, Word targets among Pseudowords, and Pseudoword targets among Words). We observed a reliable P3 ERP component in conditions where the distinction between rare and frequent trials could be made solely based on lexical status (Words among Nonwords and Nonwords among Words). We saw a reliable P3 to rare words among frequent pseudowords, but no P3 was observed when participants were asked to detect pseudowords in the context of frequent word stimuli. We argue that this observed modulation of the P3 results is consistent with psycholinguistic literature that suggests that two criteria are available during lexical access when performing a lexicality judgement, a non-lexical criterion that relies on global activation at the word level and a lexical criterion that relies on activation of a lexical representation (Coltheart, Rastle, Perry, Langdon, & Ziegler, 2001; Grainger & Jacobs, 1996).

Keywords: lexical processing; lexicality; lexical decision; event-related potentials (ERP); oddball task; P3 component

Visual word recognition is considered to be an automatic process in which a series of printed letters are mapped onto representations of known words stored in memory (Balota, Yap, & Cortese, 2006). The average adult reader can read three to four words per second. However, given that word recognition occurs at such rapid speed, it may be easy to forget that it is the end result of a series of steps or processes each taking time and cognitive effort to perform. The term lexicality refers to the status of a string of letters (or sounds) as being a word in a particular language, for example, the string of letters "cat" has a lexical status in English while "jof" does not. An integral part of knowing a language is having the ability to recognize words in one's language. In languages that use an alphabetical orthography, letter strings that do not correspond to a real word can differ in orthographic and phonological structure: while "jof" is an orthographically legal and pronounceable letter string in English (i.e. a pseudoword), a different string of letters such as "nfu" (i.e. a nonword) is neither legal nor pronounceable.

Visual word recognition relies on mechanisms of attention, on sensory and perceptual analyses, as well as on working memory and long-term memory systems (Barber & Kutas, 2007). Research in this domain to date has provided valuable insight into the notion of different levels of analysis in language processing (Balota, Yap & Cortese, 2006). When processing a string of visually presented letters, the brain initially processes the physical characteristics of the stimulus before progressively accessing orthographic, phonological, and semantic codes of the word, each of which must be stored in memory (Hauk, Davis, Ford, Pulvermuller, & Marslen-Wilson, 2006; Holcomb & Grainger, 2006; Liu & Perfetti, 2003).

The ability to process lexicality, i.e. to reliably differentiate between words and word-like stimuli, is considered to be a core component underlying language comprehension. When asked to perform lexicality judgements, participants show a difference in performance to pseudowords versus nonwords by being both faster and more accurate when rejecting non-pronounceable letter strings than pronounceable letter strings (Ratcliff, Gomez, & McKoon, 2004). This suggests that pseudowords are likely being associated to additional sources of information, such as familiarity of letter combinations, quality of the phonological code, or the capacity to access word representations, that are not available or available to a lesser degree for nonwords and that the investigation into how readers process these two different nonword types can allow for the exploration of the earliest stages of visual word recognition which involve processing of prelexical orthographic and phonological information (Massol, Midgley, Holcomb, & Grainger, 2011).

One central goal in language research has been to describe and measure the time course of the cognitive and brain processes that provide access to a word's lexical properties and meaning after it has been visually presented (Proverbio & Ardoni, 2008). Furthermore, one important variable that will eventually have to become an intrinsic part of any viable computational model of word recognition is the time course within which different types of information become available and are used in the process of allowing a letter string to be recognized (or not) as a word (Barber & Kutas, 2007). The temporal dynamics of visual word recognition have been investigated using both behavioural psycholinguistic methodologies and electrophysiological measures, including event-related potentials (ERPs). A major distinction between these different methodologies involves the nature of the dependent variables that they seek to measure. Whereas behavioural methodologies measure variables associated with an overt response such as the latency or accuracy of a button-press response to a task and thus reflect the conclusion of a complex series of processes (Stemmer & Connolly, 2011), electrophysiological methodologies measure variables associated with electrical brain activity in response to the performance of a task in real time. Furthermore, electrophysiological measures also allow the investigation of automatic processes, in contrast to behavioural responses which can be influenced by more conscious decisions or strategies from participants (Kaan, 2007).

An ERP consists of a sequence of components that each reflects electrical activity associated with temporally discrete cognitive/neural processes (Fabiani, Gratton & Federmeier, 2007). ERP components are described based on their polarity (positive or negative), topography, latency, amplitude, responsiveness to experimental factors, and assumed neural generators (Donchin & Coles, 1991; Fabiani, Gratton & Federmeier, 2007). These ERP components can be used to make inferences about how and when various stages of a cognitive process, such as visual lexical processing, occur from the moment a stimulus is presented until after the behavioural response is executed (Herring, Taylor, White, Crites Jr., 2011). Tasks employing ERPs offer an on-line and time-continuous index of visual lexical processing (Bentin Mouchetant-Rostaing, Giard, Echallier, & Pernier, 1999; Stemmer & Connolly, 2011) as it unfolds following the presentation of a stimulus and are thus ideal for studying the various steps or stages involved in word recognition.

ERPs have been used in numerous language studies and have provided valuable information regarding how written words are processed in isolation (Bentin, et al.,1999; Carreiras,Vergara & Barber, 2005; Grossi & Coch, 2005; Hauk, Davis, Ford, Pulvermuller, & Marslen-Wilson, 2006; Hauk, et al., 2006; Mado Proverbio, Vecchi & Zani, 2004; Ziegler, Besson, Jacobs, Nazir, & Carr, 1997), within sentences (DeLong, Quante, & Kutas, 2014; Molinaro, Barber, & Carreiras, 2011; Thornhill & Van Petten, 2012), or as a part of larger texts (Kuperberg, Paczynski, & Ditman, 2011; Yang, Perfetti, & Schmalhofer, 2007) in healthy young adults. While many language-related ERPs elicited to the processing of sentences or text have been identified, including the N400, the late positivity or P600, and the left anterior negativity (LAN), the current study focuses on how written words are processed when presented in isolation.

Language-Related ERPs in Visual Word Processing

ERP tasks probing different levels of processing have been used to study written word recognition thus leading to the identification of specific and well defined components that have been associated with particular steps or processes performed during visual word processing. In this section, we provide a brief overview of these language-related components as well as the P3 component (sometimes referred to as the P300). Although not strictly a component directly associated with visual word processing, the P3 is of particular interest in this study.

We begin with research combining ERPs with the masked priming technique (i.e. the very short presentation of a prime stimulus followed by a clearly visible target stimulus) (Holcomb & Grainger, 2006; Grainger & Holcomb, 2009). In their review, Holcomb and Grainger (2009) have identified and described a series of ERP components that are sensitive to masked repetition priming of words. The first component, a focal bipolar ERP effect, called the N/P150, is sensitive to the degree of overlap in features between the prime and target (greater effects for targets with total featural overlap with their primes and intermediate effects for targets with some overlap) is believed to reflect the level of processing of visual features. After the N/P150, a subsequent negative-going component, the N250, is sensitive to the degree of prime-target orthographic overlap (larger effects for targets with overlap in all but one letter with the prime compared to targets that have a complete overlap) and is thought to reflect processing of sublexical orthographic and phonological representations used to map letters onto whole-word form representations. Next, a positive-going component, the P325, is sensitive to processing within whole-word representations and is larger for repeated compared to unrelated words but does not differentiate between repeated and unrelated pseudowords. (For a full review, see Grainger & Holcomb, 2009).

Now, we turn to research combining ERPs with tasks presenting lexical stimuli in isolation (i.e. without a prime). Originally identified by Bentin and colleagues (1999) when using a size decision task, the reading-related N170, a left-lateralized temporo-occipital negativity, was found to be greater in amplitude to orthographic (i.e. words, pronounceable nonwords (pseudowords), and consonant strings (nonwords)) than non-orthographic stimuli (i.e. symbol strings and forms). The N170 has been observed in numerous subsequent reading studies (Maurer, Brandeis, & McCandliss, 2005; Maurer, Brem, Bucher, & Brandeis, 2005; Simon, Bernard, Largy, Lalonde, & Rebai, 2004) and is considered to be the earliest occurring ERP component that reflects orthographic processes in skilled readers (Hasko, Groth, Bruder, Bartling, & Schulte-Körne, 2013). This component has been shown to consistently differentiate between letter strings and low-level visual stimuli and is thought to reflect a form of similarity gradient in that the more a stimulus resembles a letter string the larger N170 component it will elicit (Maurer & McCandliss, 2008).

The N200 component was first described by Nobre and colleagues (1994) in a study of ERPs recorded using intracranial implanted electrodes from the inferior temporal lobe. Over a series of tasks, participants were shown visually presented strings of letters (words, pseudowords and nonwords) and pictures (scrambled and normal faces, scrambled and normal cars, butterflies) and the authors found a negative component peaking at approximately 200 ms. after the presentation of the stimulus that differed in spatial distribution according to whether it was elicited by the various types of letter strings or by faces (Nobre, Allison, & McCarthy, 1994). The N200 was subsequently investigated in a later study, also using intracranial implanted electrodes (Allison, Puce, Spenser, & McCarthy, 1999) where the authors observed that the N200 was significantly larger to strings of letters (regardless of their phonological legality) than to any other category of stimuli (faces, number strings, and objects) in the fusiform and other inferior posterior sites. Since both the N200 and the N170 fail to distinguish between pronounceable and unpronounceable letter strings and do not appear to be influenced by the semantic context in which stimuli are presented; components peaking in the latency range around 200 ms are believed to be sensitive to orthography and are likely to be associated with a prelexical mechanism of letter processing thus reflecting a shallow-level process (Coch & Mitra, 2010; Grossi & Coch, 2005).

Higher-level analysis appears to be reflected by negative components that peak past 200 ms of which the N350 and the N400 have been the most extensively investigated. Bentin and colleagues (1999) first identified the N350 component when comparing word, pseudoword, and nonword stimuli in a modified lexical decision task. They observed a negative deflection for both words and pseudowords, but a positive peak for nonwords, starting at about 270 ms and lasting approximately 250 ms following stimulus presentation. This component, named the N350, was proposed to distinguish between pronounceable and non-pronounceable stimuli and was assumed to be specifically elicited only by phonologically legal stimuli. More recently, a number of studies have investigated the N350 component in the processing of real words (Ruz and Nobre, 2008; Spironelli & Angrilli 2007; Spironelli & Angrilli, 2009; Spironelli, Penolazzi & Angrilli, 2010) and have supported the claim that the N350 reflects phonological processing, although it is still unclear that the component is only elicited by phonologically legal stimuli since these studies included only word (and not pseudoword or nonword) stimuli.

The N400 component was originally proposed to reflect the processing of a semantically inconsistent word in sentence final position in the written modality (Kutas & Hillyard, 1980) or in the auditory modality (McCallum, Farmer & Pocock, 1984) peaking at about 400 ms after the offending word. However, more recent studies conducted with lists of visually presented words, nonwords and pseudowords (not sentences) have shown that the N400 is sensitive to lexical properties of letter strings; while both words and pseudowords elicit a N400 component, words elicit smaller N400s than pseudowords. In contrast, nonwords do not elicit the component (Swaab, Leroux, Camblin, & Boudewyn, 2012). These findings have contributed to the notion that the N400 component (when elicited by a visually presented letter string) may be associated with an attempt to extract meaning from a potential word (Coch & Mitra, 2010; Deacon, Dynawska, Ritter, & Grose-Fifer, 2004) and may therefore reflect a lexical and/or semantic search.

The P3 Component

While the P3 component is not strictly a component associated with word processing, it has been extensively used in studies of language processing. The P3 represents the brain's electrophysiological response to a stimulus that is unexpected or "surprising" and thus can be elicited by "low-probability task-relevant stimuli during stimulus classification tasks in auditory, visual, and somatosensory modalities" (Olichney, Yang, Taylor, & Kutas, 2011). In young individuals, the P3 component is characterized by a positive voltage wave that occurs approximately 300 ms after the onset of the target stimulus and is maximal over midline centro-parietal electrode sites (Olichney et al., 2011).

The P3 has been documented as an index of attentional resources associated with context updating, updating of the neural representation of a stimulus in memory, stimulus-categorization, and processing capacity (Ashford, Coburn, Rose, & Bayley, 2011; Juckel, Karch, Kawohl, Kirsch, Jäger, et al., 2012; Polich, 2007). In the canonical P3-eliciting experiment, the oddball task, two stimulus types are presented in random order, with one type occurring more frequently (usually 80% of the trials) than the other. Participants are asked to discriminate between infrequently-occurring stimuli targets and frequently-occurring stimuli by responding, either covertly (by counting) or overtly (by making a button-press response) to the rare targets. The rare stimulus is known to elicit the P3 component while the frequent stimulus solely reflects components of sensory processing (Polich & Corey-Bloom, 2005). The amplitude of the P3 component is sensitive to the allocation of attentional resources during task processing and has been extensively documented as an indicator of the degree to which a given stimulus has sufficient informational salience to warrant a shift in allocation of attention (Osterhout & Holcomb, 1995).

The oddball task has been used to investigate and describe the time course and topography of some ERP components, including the N170 and N350 components described above, that are elicited during the reading of words, pseudowords and nonwords (Bentin et al., 1999). The authors applied this common technique to study visual word processing by asking participants to identify rarely occurring stimuli (for example, words) when they were presented among a different, and frequently-occurring, type of frequent stimuli (such as consonant strings). In four different tasks, they manipulated the distinction between rare and frequent stimuli in order to try to isolate a different level of processing for each task (i.e. visual; phonological/ phonetic; phonological/lexical; and semantic). In the oddball task, it is typical to focus on the rare (oddball) stimuli in the critical analyses because they reliably elicit a robust P3 ERP component. While a P3 component was indeed observed for the rare trials in the three lexical decision conditions that made up the phonological/lexical task, Bentin and colleagues chose to use P3 amplitude and latency as a general measure of processing difficulty or effort between the four tasks. Having observed P3 components whose amplitude and latency were mediated, in their opinion, by the processing demands of the different tasks they elected to analyse the ERPs elicited to the frequent trials as these were believed to be "unmasked" by the P3 and would therefore better reflect the neural activity associated with processing each task. Although the study remains one of the most comprehensive in the literature, despite using a traditional oddball paradigm the authors did not attempt to draw any language-focused theoretical conclusions that may have been related to reliable differences in P3 amplitude that were observed in the lexical decision tasks. As a result, they did not explore whether this component could be used as an indicator of an individual's ability to make use of lexicality as a salient feature when making lexicality judgements within an oddball task.

The Current Study

Our study addresses this gap in the literature by focusing on the P3 component. Since P3 amplitude is significantly larger when an individual encounters a stimulus that differs in a salient fashion from its antecedent context, we propose that P3 amplitude can be used as a metric of an individuals' ability to use lexicality as a salient feature early in the course of lexical processing, when performing the lexical decision oddball tasks. In this way, the current study can provide a novel contribution to the lexical processing and word recognition literature by employing a well-established paradigm, the P3-oddball task, in combination with the traditional lexical decision task to investigate lexicality judgements. While behavioural results in a traditional lexical decision task reflect the end result of lexical processing, ERP results can provide insight in to what is occurring during the stages of processing.

In order to capitalize on the strengths of the oddball task and in keeping with the traditional P3 literature, the present study focused on an analysis between the rare/frequent conditions. The presence of a P3, if elicited, can be interpreted as indicative of an allocation of attentional resources to a stimulus (Brandeis, Banaschewski, Baving, Georgiewa, Blanz, et al., 2002), normally as a precursor to more complex processing (Ilardi, Atchley, Enloe, Kwasny, & Garratt, 2007) while a reduction in P3 amplitude can be interpreted as indicative of a significant change in the individual's ability to selectively attend to the task-critical stimulus type or effectively create categories that can be used to distinguish between different stimuli types. Since the P3 component has been shown to be an indicator of the degree to which a stimulus has sufficient informational salience to warrant a shift in allocation of attention we would expect to observe a reliable and robust P3 when comparing words and nonwords because these stimuli types are quite distinct (i.e. they are dissimilar from each another in both orthographic/phonological legality and lexical status). In contrast, it is possible that no robust P3 would be observed when comparing words and pseudowords since they are less distinct (i.e. they are only dissimilar from each other in terms of lexical status but both are orthographically/phonologicalally legal).

Methods

Participants

Nineteen undergraduate students (14 female) taking an Introductory Psychology course at the University of Kansas participated in the study. The participants were right-handed, native English speakers and had normal or corrected-to-normal vision.

Materials and Procedures

Each participant completed four (4) blocks of the lexical decision oddball task via E-Prime 2.0 experiment software (Psychological Software Tools, Pittsburgh, PA). Each block had 200 trials: 40 (20%) rare and 160 (80%) frequent trials. The order in which participants received the blocks was counterbalanced and testing was performed in a single session. Crucially, three (3) stimuli types were chosen based on their orthographic/phonological structure, as well as on their lexical status: words are both pronounceable and have a real lexical status; nonwords are not pronounceable nor do they have a lexical status; and pseudowords are pronounceable but do not have a lexical status. Since a difference in performance to pseudoword versus nonword stimuli has consistently been observed in traditional lexical decision tasks we elected to investigate both of these stimuli types in relation to words thus allowing for the exploration of orthographic and phonological processing in the early stages of visual word recognition. Block 1 was made up of rare nonwords among frequent words (Nw-W); block 2 had rare pseudowords among frequent words (Ps-W); block 3 had rare word among frequent nonwords (W-Nw); and block 4 comprised rare word among frequent pseudowords (W-Ps). In this way, and in contrast to Bentin and colleagues (1999), we can contrast performance on both types of “not a word” stimulus types (i.e. pseudowords and nonwords) in relation to words when words are used as both rare and the target (frequent) trials. Examples of stimuli types presented in each block are presented in Table 5.1.

--Insert Table 5.1 here—

Eight hundred unique stimuli were used, 200 nonwords, 200 pseudowords, and 400 real words. All stimuli were controlled for number of letters (3 to 7 letters) and number of syllables (1 or 2 syllables). Nonwords had a mean length of 5.2 letters and pseudowords had a mean length of 5.0 letters. Word stimuli were monomorphemic concrete nouns with a mean length of 5.1 letters and a low frequency of occurrence in English (mean of 7.9 per million) according to the USENET database (Shaoul & Westbury, 2006). See Appendix A for a full list of stimuli.

In every block, each trial began with the presentation of a centrally-presented stimulus for 750 ms, followed by a blank screen for 250 ms. Next, a response prompt, indicating that they could make their behavioural response, was presented for 1500 ms. Participants made a button press response. To maintain response mapping across blocks participants were always asked to respond "YES" if the stimulus they saw in the trial was a word and "NO" if it was not. Behavioural data (accuracy) was collected for each block of the oddball task using E-Prime experiment software. Response time (RT) was not collected since participants were asked to delay making a behavioural response and, as a result, their time taken to respond was not thought to reflect true on-line processing of the stimuli.

EEG Recording and Processing

Electroencephalogram (EEG) data were collected for each trial using Neuroscan data collection software and a 40-channel NuAmps amplifier, using silver-silver chloride electrodes. A QuickCap electrode cap with 34 monopolar electrodes was placed according to the 10/20 reference system and each scalp site was referenced to linked mastoids. Electrodes were placed above and below the left eye and at the outer canthi to monitor blinks and eye movements (electro-oculogram; EOG). Electrode impedances were measured using a criterion of 5 kΩ, per manufacturer guidelines. The EEG and EOG data were digitized online at a sampling rate of 250 Hz and were filtered with bandpass cuttoffs of 0.1 - 30 Hz. EEG waveforms were time-locked to each stimulus onset and were segmented from 200 ms prior to stimulus onset to 1000 ms after stimulus onset. Eye-movement artifacts due to blinks were corrected off-line (Gratton, Coles, & Donchin, 1983). A trial was identified as bad if it had movement artifacts of greater than ±50 μV and was rejected prior to averaging. All participants had at least 30 of 40 useable rare and frequent trials per block in order to be included in the analyses (Cohen & Polich, 1997). In order to isolate the P3 component associated with the successful early categorization of the lexical status of the stimulus (i.e. "word" or "not a word"), a traditional windowed analysis was conducted on individual average files. The a priori time window of 500-650 ms was chosen and the Pz electrode was selected for analysis. This window was selected based on previous P3 work done utilizing linguistic stimuli (for example see, Ilardi et al., 2007).

Analytic Design

For the ERP analyses, the 40 rare trials and 40 frequent trials (chosen at random during the programming of the experimental block) were used. To investigate whether the lexical decision oddball tasks employed in this study evoked a reliable P3, we compared the mean amplitude of the rare trials to frequent trials in the critical time window of 500-650 ms at the Pz electrode using a 2 (Trial type: rare, frequent) X 4 (Block: Nw-W, Ps-W, W-Nw, W-Ps) mixed-model ANOVA. To examine whether lexical decision oddball tasks evoked a P3 component to the rare trials the mean amplitude of the target trials was compared to the frequent trials using simple planned comparisons (1 (Group) X 2 (Trial type: target, frequent) ANOVA.

Results

Behavioural Data

Error rates for each block of lexical decision oddball tasks for the 80 experimental trials are presented in Table 5.2.

--Insert Table 5.2 here—

Behavioural accuracy was high across the 4 blocks (average error rate = 7 %). Results from the within-participant ANOVA for error rate showed a significant main effect of Trial type ($F(1,18) = 11.50$; $p < 0.003$). As might be expected because of the simple impact of expectancy from trial to trial (i.e. a local context effect), we found that frequent trials in each block were more accurate than rare trials. The main effect of Block was also significant ($F(3,54) = 3.34$; $p < 0.001$). Doing planned comparisons between the four blocks indicated that the W-NW and NW-W trials cluster together and these two trial types are significantly more accurate than the Ps-W and W-Ps conditions. Thus, one could conclude from these data that there is a clear distinction in the difficulty of lexical decision task depending on the kind of “not a word” trial being considered. When the participants were asked to differentiate words from pseudowords the task simply becomes harder.

The interaction between Trial type and Block did not reach the level of statistical significance ($F(3,54) = 2.32$; $p = 0.09$). Because the p value for this interaction was less than 0.10 we did post-hoc comparisons for the rare and frequent trials independently; however, we did not find that the differences seen in the block main effect were altered in any way when examining rare and frequent trials separately.

P3 ERP Data

P3 amplitude observed in each of the four experimental blocks is displayed in Figure 5.1.

--Insert Figure 5.1 here—

Results from the within-participant ANOVA showed a significant main effect of Trial type ($F(1,18) = 45.84$; $p < 0.0001$). As predicted in any P3 Oddball task, the main effect of Trial type reflects that the P3 for rare trials in each block was greater in amplitude than the P3 shown by the frequent trials in that block (the overall mean amplitude for rare trials was 4.31 μV and overall mean amplitude for frequent trials was 1.63 μV). Thus, we observed the critical “P3 effect” in our study which required lexical categorization. The main effect of Block was not significant ($F(3,54) = 0.42$; $p = 0.74$). Finally, there was a significant interaction between Trial type and Block ($F(3,54) = 3.05$; $p = 0.04$) which will be discussed next.

ERP waveforms for each experimental block are presented in Figures 5.2-5.5. Results of the planned comparisons showed that, for the two blocks contrasting words with nonwords (W-Nw and Nw-W) participants displayed a significantly larger P3 response for the rare trials than to the frequent trials (see Figures 5.2-5.3). The P3 amplitude was significantly larger for rare words (Mean μV = 4.93) compared to the frequent nonwords (Mean μV = 1.65) in the W-Nw block ($F(1, 18) = 21.09$; $p = 0.0002$) and for rare nonwords (Mean μV = 5.02) compared to the frequent words (Mean μV = 1.08) in the Nw-W block ($F(1, 18) = 41.18$; $p = <0.0001$). However, for blocks contrasting words with pseudowords (W-Ps and Ps-W), participants only displayed a significant difference in P3 response in the W-Ps block (see Figure 5.4). The P3 component for the rare words (Mean μV = 4.22) was significantly larger compared to the frequent pseudowords (Mean μV = 1.44), ($F(1, 18) = 23.54$; $p = 0.0001$) in the W-Ps block, but the difference in the P3 component for the rare pseudowords (Mean μV = 3.08) was not significant when compared to the frequent words (Mean μV = 2.34), ($F(1, 18) = 1.05$; $p = 0.32$) in the Ps-W block (see Figure 5.5).

--Insert Figures 5.2-5.5 here—

Discussion

The present study on word recognition aimed to explore early lexical processing by employing a well-established paradigm, the P3-oddball task, while making a lexicality judgement. Our main goal was to investigate whether the P3 component could be used as an indicator of an individual's ability to make use of lexicality as a salient feature early in the course of lexical processing. Based on our results, it seems clear that there is a definite utility in combining the P3 oddball paradigm from the ERP attention and memory literatures with the classic lexical decision task. The lexical decision oddball tasks employed in this study evoked a reliable P3, with rare stimuli having a more positive going P3 component in comparison to the frequent trials. Thus, overall the lexicality distinction is reflected in the readers' ability to create clear classes or categories of stimuli (word vs. "not a word"). We know this because we see the salient rare stimuli evoking a stronger P3 when these two categories of stimuli are presented, much as is seen in any other P3 oddball task (see Olichney, Yang, Taylor, & Kutas, 2011 for review). If there had been no P3 then we would assume that the features needed to form two distinct stimulus categories ("word" vs. "not a word") were not available or salient enough to allow for clear classification.

As importantly, although our main effect analyses indicate that young adults made use of lexicality as a salient stimulus feature in the current study, not every condition we tested elicited a P3 component (as reflected in our interaction term). The inclusion of three stimulus types (words, pseudowords--possible but non-existent words and nonwords--not possible words) across the four combinations allowed us to observe that this modulation in P3 response appears to be mediated by individuals' sensitivity to the phonological legality of the stimuli when making a lexical categorization early in the course of lexical processing. In the blocks with rare and frequent trials that were most distinct (W-Nw and Nw-W blocks, with the stimuli types being dissimilar from each another in both orthographic/phonological legality and lexical status), we saw a reliable, robust P3 ERP component suggesting that individuals were able to use existing rules prescribing lexicality in one's language to quickly create effective early "word" and "not a word" categories for these two blocks. We also see a reliable P3 generated by rare trials in the blocks where the majority of the stimuli presented are pseudowords and rare items are words (W-Ps block). The size of the P3 seems to be somewhat numerically attenuated, but nonetheless, we do see a P3 in this block. Finally in the block of trials where the majority of stimuli are words and the rare stimulus is a pseudoword (Ps-W block), no P3 was found for the rare (pseudoword) trials. This suggests that sensitivity to the presence of orthographic/ phonological legality may be impeding their ability to create effective “word” and/or “not a word” categories that can distinguish between the two legal stimuli types quickly enough to be used by selective attention, but this is only the case when the expectancy has been set up that the stimuli to be read are real words.

Based on the behavioural error data which showed that participants made more errors in the blocks that contrasted word and pseudoword stimuli (W-Ps: 10%; Ps-W: 8%) than in those contrasting words with-nonwords (W-Nw: 6%; Nw-W: 4%), one might assume that tasks requiring the differentiation of words from pseudowords are simply harder than tasks that require differentiating words from nonwords. However, these behavioural results reflect the end stage of lexical processing. The ERP results, which reflect what is occurring during an earlier stage of lexical processing (prior to the participant making a behavioural response), provided key information that allowed us to observe a difference in how individuals were processing words and pseudowords in the W-Ps versus the Ps-W experimental blocks.

We propose that the P3 component, when evoked in the current study, is a reflection of a successful early stage of lexical discrimination, i.e. the successful early categorization of a stimulus as being either a “word” or “not a word”, which can be used by selective attention to quickly differentiate the lexical categories early in the course of lexical processing. The modulation of the P3 component in contrasting contexts that we observe is consistent with IAC models of word recognition such as the multiple read-out model (MROM; Grainger & Jacobs, 1996) and the dual-route cascaded model (DRC; Coltheart, Rastle, Perry, Langdon, & Ziegler, 2001). These models posit that there are two criteria that can be used when making a lexicality judgement; a lexical activation criterion (an individual word level unit reaches an activation threshold) or a "fast guess" criterion that is based on the level of global activation generated at the word level (i.e. a high overall level of activation at the word level). While the first criterion can only be reached by real words, the second can be reached by both words and pseudowords. If either criterion is reached then a "YES" response will be made. On the other hand, a "NO" response is made if neither criterion is reached prior to the lapse of a pre-determined time criterion. The lexical activation criterion is assumed to be fixed and not under strategic control, i.e. a participant cannot voluntarily speed or slow this process by shifting a response criterion. However, both the global activation and time criteria are adjustable with both stimulus-driven and/or task related factors influencing these criteria. Therefore, in the current study, when words are the frequent stimuli we would expect that the criterion of global activation would be set lower and possibly that the time criterion would be set lower as well. On the other hand, when the pseudowords are the frequent trials, we would expect that the criterion of global activation would be raised or that individuals switch to the lexical activation criterion.

It has been suggested in the literature that, although individuals make use of both criteria, young adults may tend to prefer the criterion of global activation when making lexicality judgements in a lexical decision task (Stadtlander. 1995). We also seem to observe that young adults indeed favour the global activation criterion when performing lexicality judgements as part of an oddball task. More specifically, in the current task, participants' early sensitivity to global activation associated with the orthographic and phonological legality of stimuli seems to be guiding their performance. This is advantageous in the two blocks containing nonwords (Nw-W and W-Nw blocks), where there is no ambiguity in orthographic/phonological legality between the rare and frequent stimuli types. Since there is little or no global activation being generated by the nonwords that can impede the creation of early effective "word" and "not a word" categories we observe robust P3 components for these blocks.

In stark contrast, in the Ps-W block, where responding "YES" when there is a high level of global activation will almost always be the correct response given the abundance of words (80%) in the block, we see that the strategy of reliance on global activation becomes problematic. Because the pseudowords also generate global activation, this reliance on the criteria of global activation appears to have interfered with the readers' ability to create an effective "not a word" category. Therefore, even though we are looking at the brain responses of literate young adult college students, both the stimulus features and the context or expectancies generated by the list makeup in this block result in our participants showing no P3. This is quite a noteworthy outcome.

Finally, in the block where there was no difference in orthographic/ phonological legality between stimuli types present (W-Ps blocks) and where frequent stimuli look like words, but are not, this reading context made it less advantageous to rely of the global activation criterion. In this block the participants were able to create effective "word" and "not a word" categories again. The IAC models would argue that, in this block, young adults are shifting to rely more on a lexical activation criterion when making this judgement. This shift from the preferred to a less preferred strategy might explain why the P3 response in the W-Ps block the component was somewhat numerically attenuated when compared to what was seen for either block contrasting words with nonwords. There may also have been some interference in creating a "not a word" category in this block, but nonetheless the categories were effectively utilized as reflected in a reliable P3.

While a traditional P3 component elicited to non-linguistic stimuli typically has a mean latency of approximately 300 ms following stimulus presentation, in the current study we observed that task conditions requiring the processing of linguistic stimuli led to a delay in latency of the component. This was consistent with previous ERP studies indicating that a considerable amount of initial processing is shared by all orthographic stimuli regardless of their legality with a divergence in waveforms associated with phonologically legal versus illegal stimulus types occurring relatively late, i.e. in the 300-350 ms timeframe (Bentin et al., 1999; Spironelli, Penolazzi & Angrilli, 2010). It is also in line with ERP research pointing to an even later divergence between waveforms associated with an attempt to access a lexical representation for legal stimuli, i.e. in the 400 ms timeframe (Coch & Mitra, 2010; Deacon et al., 2004). Given that our tasks required stimuli to be processed at least until phonological legality could be determined (for the blocks contrasting words and nonwords) and until an attempt to determine lexical status could be performed (for the blocks contrasting words and pseudowords) in order to elicit a P3, it is not surprising that the component was delayed.

Future Direction

The lexical decision oddball tasks in the current study were successful in showing differences in performance based on sensitivity to the orthography/phonology of the stimuli in the early stages of lexical processing in literate young adults. One very interesting application of this interesting methodological tool would be to utilize this paradigm not to study factors related to stimulus characteristics, but instead to look at the influence of individual differences. For example, previous research by Atchley, Haldermam and Buchanan (2003) suggests that individuals with dyslexia show a significant reduction in sensitivity to orthography/phonology in lexical processing. This population would be very interesting to investigate utilizing the P3 lexical decision oddball tasks discussed here. We would predict that individuals with dyslexia would show a robust P3 component in all four of our experimental blocks since they are not influenced by the orthographical/phonological legality of stimuli and can therefore more effectively attend to differences in lexical status between the stimuli. Furthermore, this methodology could prove to be quite revealing when used with individuals with aphasia and apraxia following stroke. Particularly in cases of apraxia, this methodology can provide insight into residual language abilities since the P3 component can be elicited even when no behavioral response is asked for (often referred to as the passive P3 paradigm), thus allowing the study of lexicality even in participants who cannot make an overt reliable response.

In addition, in order to continue to explore sensitivity to orthography/phonology in healthy adult readers, the lexical decision oddball task could be modified to contrast nonwords and pseudowords and thus use P3 amplitude to investigate orthography/phonology without the confounding effect of lexical status. Furthermore, the current study was specifically designed to elicit the P3 component and accordingly we employed a 20/80 ratio of rare to frequent stimuli within each block. While the oddball task is the ideal experimental task to elicit the P3 component, future studies using the traditional lexical decision task ratio of 50/50 word and "not a word" stimuli could be valuable in investigating the degree to which participants rely on the global activation criterion in relation to new task demands. This traditional ratio could also be used to further explore sensitivity to orthography/phonology in the early stages of lexical processing by investigating the N350 component when it is elicited to words versus pseudowords or nonwords. This component has been linked to phonological/orthographical processing for real words (Ruz and Nobre, 2008; Spironelli & Angrilli 2007; Spironelli & Angrilli, 2009; Spironelli, Penolazzi & Angrilli, 2010) and has been proposed to be elicited only by orthographically/ phonologically legal stimuli thus potentially distinguishing between pronounceable and non-pronounceable stimuli (Bentin et al., 1999).

While additional research is warranted to further probe sensitivity to orthography/phonology in the early stages of lexical processing, our results show a definite utility in combining the ERP P3 oddball task with the classic lexical decision task. The combination allowed us to obtain crucial information that would not have been possible by using the lexical decision task alone.

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Appendix A

Stimuli for Nw-W block

Rare: afxy, atbfej, bgifsar, bkafdp, byxteg, cbolprt, ctmovk, dlifupl, dvka, ejsd, fctob, gbdu, hkaj, iqldo, kdinpsm, lnig, mkhul, ncyz, nduy, nvudfa, odcgek, pfu, pjnu, pmcuhm, qlih, rfajh, rjau, sdym, sfvud, sgydtf, sxuf, tgix, tkotm, tvatdw, uqg, wkuf, xpkag, ydbsw, ygfm, ztwoljn.

Frequent: agenda, amulet, ankle ,ant ,ark, atlas, balloon, banjo, beach, beagle, bean, beaver, biscuit, blade, blanket, branch, bread ,broom, bullet, button, cabin, cabinet, cage, calcium, cartoon, castle, cave, chalk, chariot, cheese, cigar, clock, coal, coin, costume, cottage, crane, crown, crust, curtain, dagger, daisy, diary, doll, donkey, dove, dungeon, eagle, elf, fiddle, finger, flea, flower, fog, funnel, fur, garlic, ghost, gnome, grape, grass, gravel, guitar, hamster, hoe, horn, hose, island, ivy, jaguar, jam, jelly, jewel, ketchup, kidney, kiosk, kitchen, knife, lard, lemon, lentil, lily, lion, luggage, maple, moose, motel, mud, muffin, mug, muscle neck, nose, oak, paddle, panther, parrot, pawn, penny, phantom, photo, picnic pie, pillar, pillow, pine, pocket, podium, potato potty, powder ,pulpit, quilt, racket, raven, ribbon, robe, robot, ruby, rum, rust, sesame, shirt, shrimp, skin, slate, sleeve, snail, spark, spout, stadium, statue, swan, syrup, tank, tent, thigh, thumb, tire, tissue, tobacco, tomato, tomb, tower, train, tray, trout, tub, turtle, veil, venom, vest, violin, voucher, wheat, wood, worm, yam, yarn, zinc.

Stimuli for Ps-W block

Rare: adlym, aif, beath, bluke, breon, casip, chond, clesh, denfol, dunt, durse, egol, flate, fodum, gallis, ganny, gonder, gupin, hant, keld, krelt, kulm, leraf, lomb, lunky, mamet, montis, muned, mursk, pand, paupis, pung, queld, sedin, serry, sleer, sowel, stru, surine vold.

Frequent: anchor, arcade, arrow, asphalt, bacon, baggage, ballot, banana, banner, bell, belt, bikini, blouse, boat, bra, bubble, bulb, bunker, butter, cactus, camel, camera, canal, canoe, casino, cereal, chin, chrome, clam, cliff, cloud, cocoa, coffee, copper, cord, cotton, couch, coupon, coyote, crab, cradle, cube, cyprus, dill, dock, dolphin, dome, domino, donut, dough, dragon, elbow, elk, falcon, ferret, ferry, flame, flour, foil, forest, fork, frost, garage, garden, gate, gel, gem, ginger, glass, goat, goose, grain, gravy, hawk, helmet, herb, honey, horse, jade, jaw, jungle, kiwi, ladder, lark, latch, laurel, leather, lime, liver, lizard, lobster, lynx, magnet, malt, mantle, maze, menu, mint, moon, motor, mummy, navel, nest, nickel, nylon, ocean, palace, parcel, pasta, patio, peach, pearl, penguin, plate, pool, porch, pretzel, ranch, rink, saliva, salmon, salt, sausage, screen, seed, shack, shark, shrub, silk, sled, snake, soap, sock, soup, spice, spider, spike, spindle, spoon, squid, stereo, sugar, taxi, tile, toad, toilet, torso, towel, trophy, tuna, turbine, turkey, vase, vinegar, vinyl, wagon, wand, weasel, wool, yoke.

Stimuli for W-Nw block

Rare: apple, axle, cedar, chain, comet, corn, dessert, dish, fence, fossil, furnace, gorilla, grenade, harbour, harp, hood, hoop, iris, lettuce, mop, mouse, mustard, olive, piano, pony, puddle, pumpkin, purse, roof, shell, shoe, silver, sphere, stove, tiger, tongue, tort, vine, wax, zebra.

Frequent: abjosdl, akwih, amvp, atmofr, awgsiq, bcluh, bdui, bnua, bopltr, bwtav, cfru, cgaj, cjusep, cksialr, cmlih, cuhlw, dbeljy, dcbi, dfurfpl, dhomg, dlupfb, dokjerw, dpagb, ebkfu, ehgd, ejdkib, ejsu, elokju, ewmji, fbsua, feglrb, fnubdw, fspu, fwnef, gakfp, gduldw, gjewgmi, gpelti, gsdu, gwtys, hcu, hdob, hlufc, hnoplg, htduz, htewab, ifmlej, igbuhdm, ikdp, itpsv, ivgsfu, ivqo iwerphd, ixdfasf, jadcr, jbawefd, jdemca, jksu, jmopsk, jpni, jpulm, kbiw, kdu, kebmy, kftonb, kpohsl, kpsia, kvba, kyfdenh, lbym, lcokjuo, lgicb, lpekga, lwafg, lxufdp, mcif, mdiwox, mgu, mjadc, mlopf, mrufrsy, mstuhji, msupkt, mtsu, nfadx, nfu, nhfusbc, njsiwp, nlpoc, nsrihjk, obfjl, odfmnr, olfg, opbz, opdku, osngulb, pbsi, pfmu, pgedf, pjdwug, pmsgvi, pxunl, qbakjd, qglyna, qmig, qsfum, qsheb, rbmolpy, rmloh, rshbisa, rtingd, rtlu, rvikjt, sdopl, sdusfod, sfhi, sgacbe, tcegd, tcsidgb, tdsamg, tgmufka, tmlu, ubdfe, ucvm, udgm, ukvofgd, uplkjs, usbixg, uvdalbd, uvfmi, vbhke, vcadf, vgak, vimgslu, vsfo, vsukfv, vwjosf, wadfv, wdifv, wgposmt, wkajfu, wnga, wsetja, xbmi, xdapg, xfe, xfidhw, xjoh, xlhduy, yhbr, yhjnsa, yjfbu, yjl, ymdni, yufnlup, zdikm, zgsa, zmaslg, zmul, zojtf.

Stimuli for W-Ps block

Rare: ace, album, angel, bamboo, beer, birch, bridge, cabbage, cameo, cobra, cork, crayon, dart, diploma, dune, gravel, gum, hutch, lamp, leaf, lotus, maggot, milk, needle, oar, panda, parsley, pear, pencil, pickle, pig, poison, poppy, rattle, sauce, spade, sponge, ticket, topaz, wasp.

Frequent: acle, acril, afel, afrud, ansle, arl, balpet, bargow, belk, bennel, betle, betso, bettle, bith, botter, brabe, brazar, bund, burdle, butine, cairil, choibe, cinler, ciress, clido, colb, crale, cruff, culp, cuton, darg, daridather, delp, dendu, dest, dith, dovil, dunry, durim, edas, eglym, fambol, farus, fathan, fergle, fibe, finab, fing, fiple, folex, foris, fower, frab, frain, fump, fungar, fush, geddop, gedim, gellon, glem, glycan, goind, gorna, gort, grach, grafe, grink, grum, grupet, guddle, hadur, hartel, henel, hepent, herit, homper, honder, hulf, imop, indest, inlest, janner, jeckin, jick, jink, jodar, kender, kest, klead, kravis, lerd, loap, lober, londu, lunk, markel, marrot, meap, mear, mittle, muki, nake, narp, nattle, nedoc, nerin, netu, nivar, noot, noster, nustol, onged, ougil, pangle, paril, pathat, pedak, pender, perg, pime, pisk, plive, ploke, plom, plone, poish, ponfer, pordan, povol, racern, reshew, roany, rother, sapil, sedin, sepol, serol, siddle, slun, sterma, talb, talt, teklin, tosk, trib, tular, tummer, tunk, turmey, twint, vacop, vatil, vlower, wint, woon, wush, yarel, yock.

Table 5.1 - Description of Stimuli for the Four (4) Blocks of the Lexical Decision Oddball Task

Block	Rare Stimuli (n= 40)	Frequent Stimuli (n= 160)
Nw-W	Nonwords *'ncyz'*	Words *'bread'*
Pw-W	Pseudowords *'clesh'*	Words *'patio'*
W-Nw	Words *'harp'*	Nonwords *'jadcr'*
W-Ps	Words *'lamp'*	Pseudowords *'dovil'*

Table 5.2 - Error Rate for the Four (4) Blocks of the Lexical Decision Oddball Task

Block	Rare Trials (n = 40)		Frequent Trials (n = 40)		Total (n = 80)	
	mean	SD	mean	SD	mean	SD
Nw-W	4%	7%	4%	5%	4%	6%
Ps-W	9%	7%	8%	8%	8%	7%
W-Nw	6%	5%	5%	6%	6%	6%
W-Ps	13%	12%	7%	8%	10%	10%

Figure 5.1 - P3 Component Amplitude (in µV) for each Experimental Block of the Lexical Decision Oddball Task.

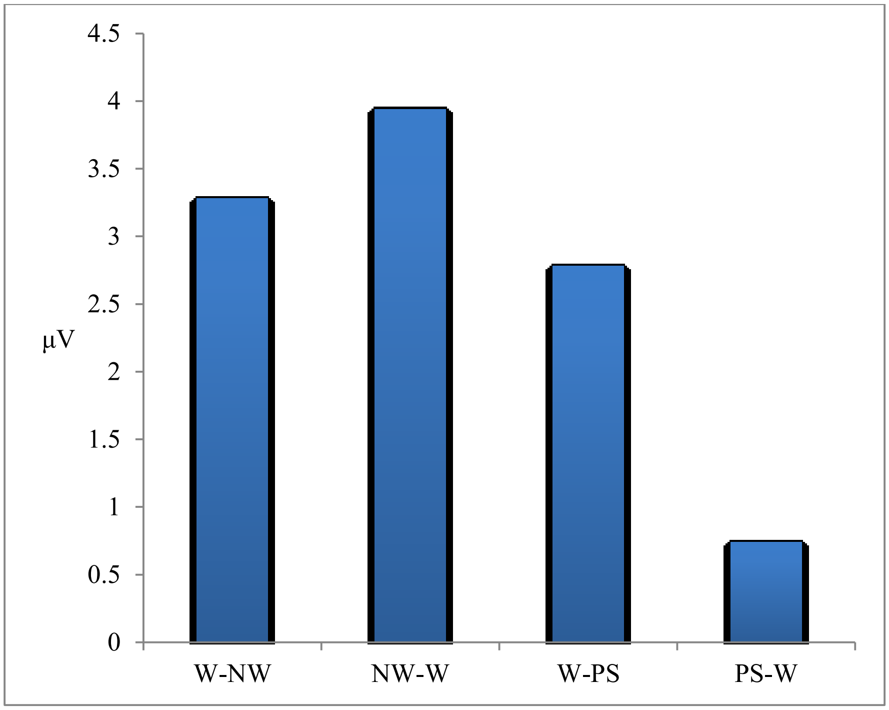


Figure 5.2 - Grand-Average ERPs Time-Locked to Stimulus Onset at the PZ Electrode in the W-Nw Block: Rare Condition (red line), Frequent Condition (blue line)

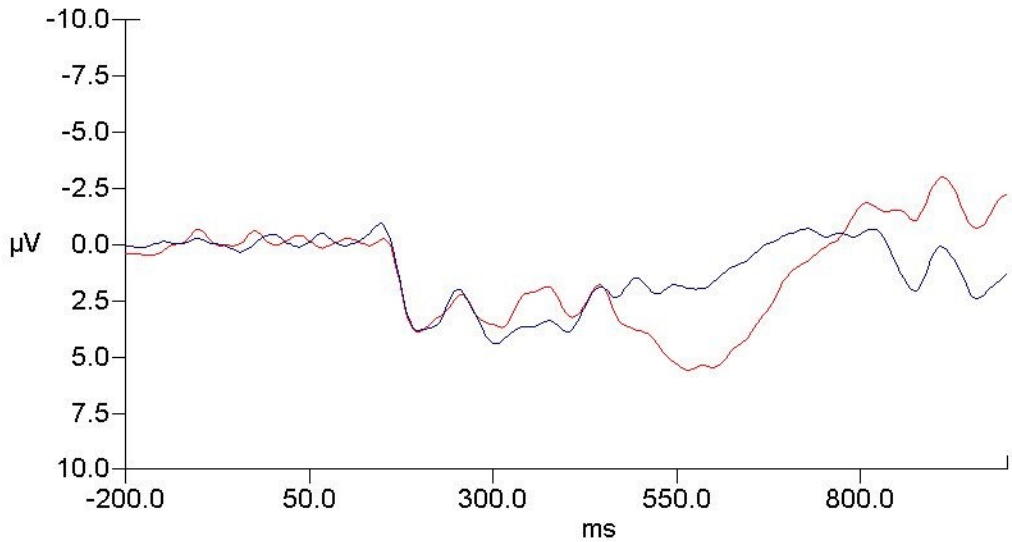


Figure 5.3 - Grand-Average ERPs Time-Locked to Stimulus Onset at the PZ Electrode in the Nw-W Block: Rare Condition (red line), Frequent Condition (blue line)

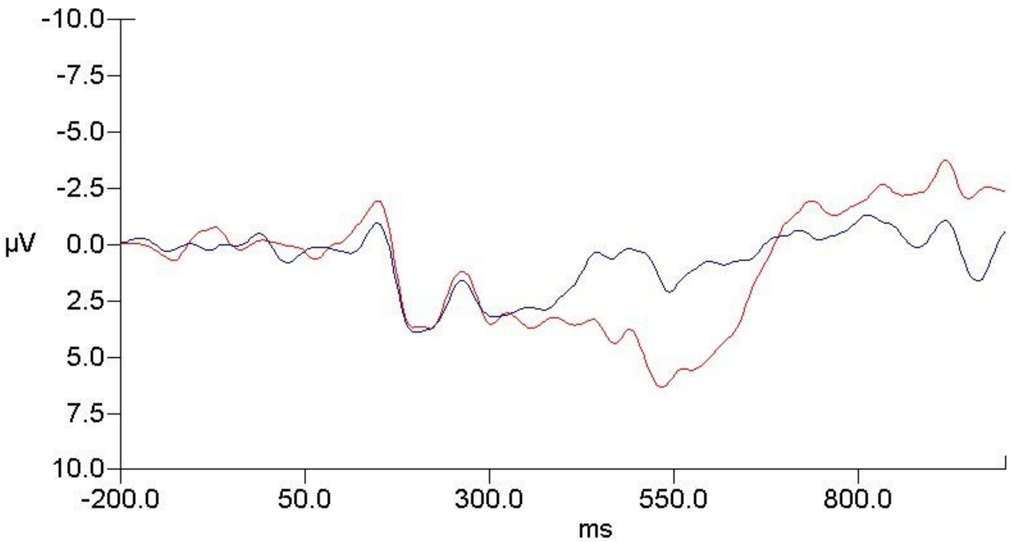


Figure 5.4 - Grand-Average ERPs Time-Locked to Stimulus Onset at the PZ Electrode in the W-Ps Block: Rare Condition (red line), Frequent Condition (blue line)

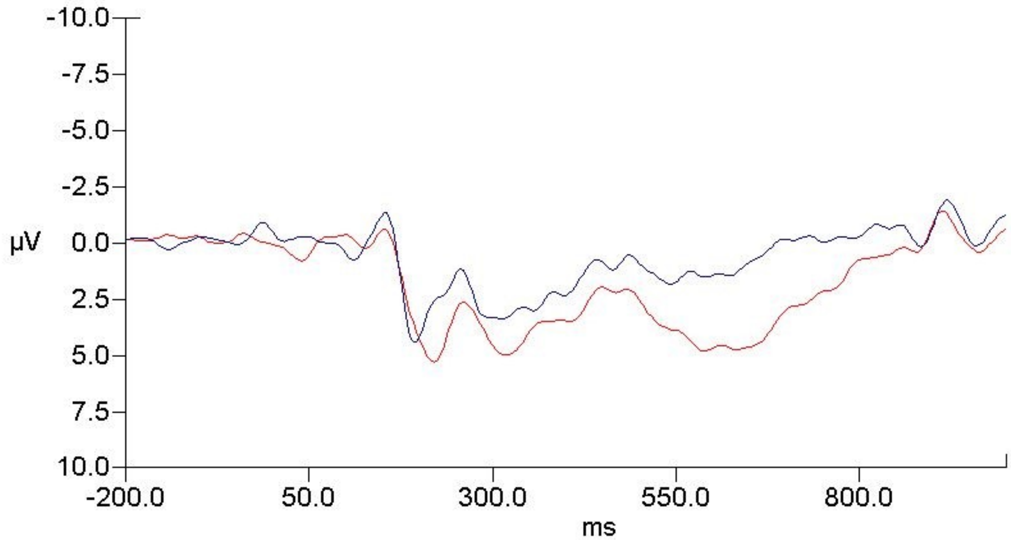
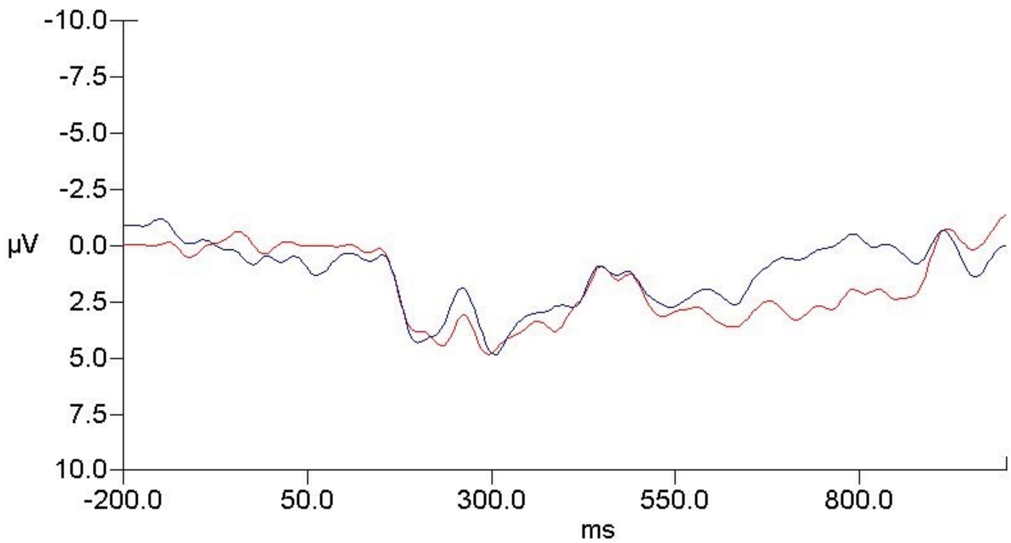


Figure 5.5 - Grand-Average ERPs Time-Locked to Stimulus Onset at the PZ Electrode in the Ps-W Block: Rare Condition (red line), Frequent Condition (blue line)



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CHAPTER 6: ***Manuscript 3.*** *Processing Lexicality in Healthy Aging and Alzheimer's Disease: P3 ERP Amplitude as an Index of Early Lexical Categorization*

Preface to Manuscript 3

Findings from Manuscript 1 indicate that individuals with AD are slower in processing lexicality (i.e. they were slower at making lexicality judgements) than both healthy groups. However, to our surprise, those with AD did not show the overt deficit in over-accepting pseudowords relative to healthy older adults that had previously been reported in the literature. Furthermore, both older groups showed an alteration in the processing of neighbourhood density (N) when making lexicality judgements. Given these findings, one could be led to assume the individuals with AD can perform lexicality judgments with a level of accuracy comparable to that of the older adults, albeit at a much slower pace and hence they are only qualitatively different from the older adults. However, our intent from the onset has been to explore processing lexicality using a combination of on-line behavioural psycholinguistic methodology and electrophysiological / event-related potential (ERP) methods in order to obtain a more complete understanding of potential changes that may be occurring with age and with AD.

Results from Manuscript 2 established that there is a definite utility in combining the P3 oddball paradigm from the ERP attention and memory literature with the classic lexical decision task. The lexical decision oddball tasks that were used evoked a reliable P3, with rare stimuli having a more positive-going P3 component in comparison to the frequent trials in the young adults. Findings from Manuscript 2 were also significant since they have provided us with a baseline with which to compare the older groups' performance on these novel tasks.

The overarching aim of the following manuscript was to investigate lexicality judgements in these two populations using both behavioural psycholinguistic methodology (the lexical decision task) and electrophysiological / ERP methodology (lexical decision oddball tasks) to enhance our understanding of processing lexicality in individuals with AD and to provide insight into how these individuals may differ from healthy older adults. Furthermore, in order to rule out any overt deficits in selective attention that may be affecting performance on the lexical decision oddball tasks, we also evaluated these cognitive abilities using non-verbal tasks.

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Title Page

Processing lexicality in healthy aging and Alzheimer's disease: P3 ERP amplitude as an index of early lexical categorization

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Abstract

Determining whether a letter string has lexical status, i.e. processing lexicality, is a core component of reading during visual word recognition. With age, the time taken to distinguish words from word-like stimuli increases. Moreover, individuals with Alzheimer's disease (AD) are not only slower, but may also exhibit limitations in processing pseudoword stimuli. To explore how processing lexicality may change with aging and the presence of AD, we conducted two experiments investigating lexicality judgements using on-line behavioural psycholinguistic methodology (lexical decision task) and electrophysiological / event-related potential (ERP) methods; lexical decision oddball tasks probing four comparisons : words among nonwords (W-Nw); words among pseudowords (W-Ps); nonwords among words (Nw-W); pseudowords among words (Ps-W).

Results from the behavioural lexical decision task showed that while those with AD were slower in making lexicality judgements than older adults they performed at a rate of accuracy that was comparable to that of older adults. However, results from the ERP tasks showed that the two groups behaved differently with regard to elicitation of P3 ERP component response. Older adults showed a P3 in the two blocks contrasting words and nonwords but those with AD showed a P3 only in two blocks where words were the frequent trials.

The pattern of ERP responses observed suggests that older adults are sensitive to the orthography/phonology of the stimuli early in the course of lexical processing. In blocks where rare and frequent stimuli were most distinct (W-Nw; Nw-W), a P3 was elicited for older adults. However, they no longer showed a P3 in the more difficult blocks with overlap in stimulus orthographic/ phonological legality (W-Ps; Ps-W), suggesting that they were not creating

effective “word” and “not a word” categories early in the course of lexical processing. In contrast, those with AD showed a P3 only to blocks where words were the frequent stimuli suggesting that they were no longer sensitive to the orthography/phonology of the stimuli.

The ERP P3 amplitude results were instrumental in showing a quantitative difference between the healthy older adults and those with AD and highlight the importance and usefulness of combining behavioural psycholinguistic and ERP methodologies. Moreover, we propose that the observed alteration in P3 performance that was found in those with AD, in combination with other linguistic/cognitive markers, shows promise in highlighting differences between healthy aging and early dementia.

Highlights

- We investigated changes in processing lexicality in aging and Alzheimer's disease (AD).
- We combined psycholinguistic and ERP methods to obtain complementary information.
- ERP P3 results were instrumental in showing a difference between the groups.
- P3 results suggest that those with AD are less sensitive to orthography/phonology.
- Alteration in P3 performance shows promise as a possible marker of AD.

Keywords

Alzheimer's disease (AD); aging; event-related potential (ERP); lexicality judgements; lexical decision; visual word recognition

1 Introduction

Visual word recognition, the ability to accurately and quickly determine whether a string of letters has a lexical status, is a core component for the reading and comprehension of written language (Gold, Andersen, Jicha, & Smith, 2009). The recognition of one of the many thousands of written words that adults know is a complex, multi-step process (Hauk, Davis, Ford, Pulvermuller, & Marslen-Wilson, 2006). However, despite this complexity, this process is accomplished rapidly in young adults with word-specific information beginning to be accessed in the first 200 milliseconds (ms) after presentation (Sereno & Rayner, 2003). As we age many types of cognitive processes begin to slow down. While tasks in some non-lexical cognitive domains tend to show more age-related slowing than lexical tasks (Lima, Hale, & Myerson, 1991), even with many years of exposure to words over a lifetime, the time taken to make lexicality judgements also increases with age.

As early as 1981, Bowles & Poon found that older adults had longer response times (RTs) when performing a lexical decision task requiring the discrimination between high and low frequency nouns and orthographically and phonologically legal pseudowords. More recently, additional studies have also reported findings showing that older adults are consistently slower to perform lexicality judgements when compared to young adults across several languages and across a variety of word types controlled for different lexical properties such as frequency, neighbourhood density and/or frequency, and syntactic class (Balota, Cortese, Sergent-Marshall, Spieler, & Yap, 2004; Kavé and Levy, 2005; Moberg, Ferraro, & Petros 2000; Ratcliff, Thapar, Gomez, & McKoon, 2004; Roberts & Mathey, 2007; Stadtlander, 1995; Taler & Jarema, 2007).

When seeking to estimate the rate of slowing of performance on lexical decision tasks caused by aging, Madden (1992) found that that RTs increased with age at a rate of 4 ms per year for perceptually intact targets and 10 ms per year for degraded targets. Similarly, a meta-analysis of 22 lexical decision experiments found that older adults' RTs were 250 to 300 ms longer than those of young adults (Myerson, Hale, Chen, & Lawrence, 1997). However, while older adults are consistently slower when making lexicality judgements, this increase in response latency is not necessarily accompanied by a decline in accuracy rates. Some lexical decision studies report no difference in error rates between older and younger adult groups (Balota et al., 2004; Lima et al., 1991; Myerson et al., 1997; Robert & Mathey, 2007). However, Taler and Jarema (2007) reported a higher overall error rate for older adults (2007) while Stadtlander (1995), Ratcliff and colleagues (2004), and Azevedo, Kehayia, Atchley, and Nair (2015) found that the older adults were more accurate when compared to young adults.

1.1 Visual Word Recognition in Alzheimer's Disease (AD)

Language impairments, particularly impairments in the ability to process lexical and semantic knowledge, are often observed in those with AD, even early in the course of the disease (Taler & Phillips, 2008). The majority of individuals with AD exhibit word-finding difficulties from the onset of the disease (Appell, Kertesz & Fisman, 1982; Bayles & Kaszniak, 1987; Duong, Whitehead, Hanratty, & Chertcow, 2006; Joubert et al, 2006) and word recognition becomes impaired with the progression of the disease (Cuetos, Herrera, & Ellis, 2010).When looking at tasks in which individuals with AD and healthy older adults are required to make lexicality judgements, numerous studies have shown that those with AD are consistently slower when compared to older adults across different languages and across a range of words with different lexical properties such as frequency, regularity, neighbourhood density, and number of semantic associates (Caza & Moscovitch, 2005; .Duñabeitia, Marín, & Carreiras, 2009; Duong et al., 2006; Madden, Welsh-Bohmer, & Tupler, 1999).

In addition to having longer RTs, individuals with AD also appear to show a decrease in accuracy when compared to older adults when making lexicality judgements. A decline in the ability to accurately process lexicality (the ability to reliably differentiate between words and word-like stimuli) has been reported in some studies and suggests the presence of a selective deficit in ability of individuals with AD to process pseudowords (legal and pronounceable strings of letter, such as "*poble"*) (Cuetos, Herrera, & Ellis, 2010; Glosser, Kohn, Friedman, Sands, & Grugan, 1997; Madden, Welsh-Bohmer, & Tupler, 1999).

In an off-line auditory lexical decision task probing words and pseudowords, Glosser and colleagues (1997) found that individuals with AD and healthy older adults performed at comparable rates of accuracy for the word stimuli, i.e. they correctly responded "YES" to words. However, individuals with AD performed significantly worse than older adults on pseudoword stimuli, i.e. they incorrectly responded "YES" to many pseudowords. Furthermore, in a modified version of the lexical decision task requiring participants to indicate the real word presented on a page with three legal pseudoword foils, older adults made few errors while those with AD made significantly more errors, choosing a pseudoword foil, especially when the word presented had a late age of acquisition (AoA)(Cuetos, Herrera, & Ellis, 2010). This over-acceptance of pseudowords has also been observed in an on-line lexical decision task (Madden, Welsh-Bohmer, & Tupler, 1999) where the authors noted that the most prominent finding regarding the error data was the difficulty that individuals with AD displayed for legal pseudoword trials. While young and older adults both performed at similar rates of accuracy for words and pseudowords, those with AD made significantly more errors to pseudowords. However, they showed similar accuracy for words when compared to young and to older adults.

Taken together, these studies suggest that processing lexicality may be vulnerable to disruption by the AD disease process in a manner that may only become apparent when pseudoword stimuli are used. However, since many language screening tests use words (and not pseudowords) to evaluate linguistic abilities, there is a possibility that deficits in processing lexicality are being missed and that the language abilities of individuals with AD may actually be over-estimated.

1.2 Event-Related Potentials (ERPs) Investigating Visual Word Recognition

More recently, the addition of electrophysiological measurements of event-related brain potentials (ERPs) has contributed supplementary information regarding the cognitive processes that underlie visual lexical processing and word recognition that would not be available using traditional psycholinguistic methodologies alone. While the spatial resolution of electroencephalography (EEG) is poor, its temporal resolution is exceptional and permits the study of brain activation associated with ongoing cognitive processes in real time. Thus, whereas traditional psycholinguistic studies can provide an estimate of the total time taken to visually process a word (including the time taken to make a response), the use of ERPs offers the possibility of describing the process as it unfolds over time. When investigating lexical processing, several psycholinguistic tasks, such as letter search, passive reading, semantic categorization, and lexical decision, have been used to elicit language-related or language-sensitive ERPs (Bentin, McCarthy, & Wood, 1985; Bentin, Mouchetant-Rostain, Giard, Echallier, & Pernier, 1999; Sereno, Rayner, & Posner, 1998; Simon, Bernard, Largy, Lalonde, & Rebai, 2004; Ziegler, Besson, Jacobs, Nazir, & Carr, 1997).

When studying visual word recognition, ERP tasks allow for more flexibility in investigating the timecourse of lexical access and activation than traditional lexical decision tasks (where only RTs and error rate can be measured) because they have the potential to identify some component(s) which may prove to be sensitive to one or more of the processes involved in word recognition. Therefore, the combination of ERPs and a lexical decision task can allow for a more in-depth investigation into processing steps that underlie visual word recognition. One way to do this is to ask participants to perform lexicality judgements on strings of letters presented within an oddball task. In a traditional oddball task participants are asked to attend to a rarely occurring stimulus when it is presented among a different, and frequently-occurring, type of stimulus (circles presented among squares, for example). However, in a lexical decision oddball task the rare stimuli are words presented among frequently occurring nonwords or pseudowords (or vice-versa). While this methodology has been used with young adults (Bentin et al., 1999), we are not aware of any studies that have employed this methodology with healthy older adults or individuals with AD.

The traditional oddball paradigm described above is known to elicit the P3 component (also referred to as the P300) for the rare event trials in healthy adults. The P3 component, in young adults, represents the brain's electrophysiological response to a stimulus that is unexpected and can be elicited by "low-probability task-relevant stimuli during stimulus classification tasks in auditory, visual, and somatosensory modalities" (Olichney, Yang, Taylor, & Kutas, 2011). The presence of a P3 can be interpreted as indicative of an allocation of attentional resources to a stimulus (Brandeis, Banaschewski, Baving, Georgiewa, Blanz, et al., 2002), normally as a precursor to more complex processing (Ilardi, Atchley, Enloe, Kwasny, & Garratt, 2007). Furthermore, a reduction in P3 amplitude can be interpreted as indicative of a significant change in the individual's ability to selectively attend to the task-critical stimulus type or effectively create categories that can be used to distinguish between different stimuli types. Therefore, because P3 amplitude is significantly larger when the individual encounters a stimulus that differs in a salient fashion from its antecedent context, we intend to show that the P3 amplitude can be employed to determine the degree to which healthy aging adults and individuals with AD can make use of lexicality as a salient stimulus feature in a lexical decision oddball task. In a review of P3 research with individuals with AD (Polich & Corey-Bloom, 2005), two important observations about their P3 components were made. First, it is clear that despite the generalized neurocognitive decline, which is the hallmark of AD, a reliable P3 can be observed in individuals with AD. This is a critical observation, given that some other patient populations do not readily show a reliable P3 (for example, research by Bruder, Tenke, Stewart, Towey, Leite, et al.,1995; and Röeschke, Wagner, Mann, Fell, Grözinger, et al., 1996 has demonstrated a significant attenuation of the P3 in patients with depression). Secondly, the Polich and Corey-Bloom review suggests that AD patients' ERP data can differ from the data of age-matched controls in two distinct ways: in both P3 amplitude and P3 latency.

Most studies investigating the P3 component in healthy older adults and in individuals with AD have employed simple discrimination tasks, with the majority using auditory stimuli (Verleger, Kömpf, & Neukäter, 1992; Polich & Corey-Bloom, 2005). An increase in P3 latency and decrease in P3 amplitude have been consistently shown to be associated with healthy aging (Anderer, Saletu, Semlitsch, & Pascual-Marqui, 2003; Ashford, Coburn, Rose, & Bayley, 2011; Juckel, Karch, Kawohl, Kirsch, Jäger, et al., 2012; van der Lubbe & Verleger, 2002) and it has been estimated that P3 latency increases with healthy aging at a rate of 1.0 to 2.0 ms every year (Anderer et al., 2003; Ashford et al., 2011; Olichney et al., 2011). Moreover, alterations in P3 appear to become more pronounced in individuals with AD. A greater increase in latency (approximately 2 standard deviations above the mean for healthy older adults) has been reported (Olichney & Hillert, 2004; Olichney et al., 2011) and this delay in P3 latency is believed to be in proportion to dementia severity (Ashford et al., 2003; Lai, Lin, Liou, & Liu, 2010; Saito, Yamakazi, Matsuoka, Matsumoto, Numachi, et al., 2001).

While fewer P3 tasks have been conducted in the visual modality, those undertaken have also shown changes in the P3 component in healthy aging and in those with AD. In a task examining three types of line drawings (a repetitive background stimulus, an infrequent target stimulus, and an infrequent novel stimulus) in which participants were asked to make a response to the target stimulus, Daffner and colleagues (2001) reported that P3 amplitude to novel stimuli was significantly smaller in individuals with AD when compared to healthy older adults at midline and lateral electrode sites. However, P3 amplitude to the target stimuli did not vary between the two groups at the midline sites but was somewhat smaller for those with AD at lateral sites. In addition, the latency of the P3 did not differ between the two groups in response to the novel or to the target stimuli at midline electrode sites. In a simple discrimination task with horizontal and vertical lines (50-50 proportion of each stimulus type) in which participants were asked to respond only when they saw a vertical line, Saito and colleagues (2001) reported a decrease in P3 amplitude for individuals with AD compared to healthy older adults but no difference in P3 latency between the two groups.

It is important to note that neither of these studies used the oddball task, which is the most common experimental task utilized to elicit the P3 ERP component. In contrast, when using a visual (and an auditory) oddball task, Polich and Pitzer (1999) found that P3 latency was delayed and its amplitude was reduced for both the auditory and visual tasks in individuals with

AD and that the group differences were larger in the visual modality than in the auditory one. More recently, Polich and Corey-Bloom (2005) also used visual and auditory oddball tasks to study the P3 component in AD. For each modality, three tasks were used and task difficulty was manipulated by varying how easily the target and frequent stimuli could be discriminated. The authors found that P3 amplitude was smaller for individuals with AD compared to healthy older adults. Also, amplitude decreased with the increase in task difficulty and was smaller in the auditory modality than in the visual. P3 latency was found to be marginally longer for those with AD and peak latency increased with task difficulty and was shorter in the auditory modality when compared to visual modality.

Although there have been a number of P3 studies conducted with individuals with AD (Ally, Jones, Cole, & Budson, 2006; Chapman, Nowlis, McCrary, Chapman, Sandoval et al., 2007; Katada, Sato, Ojika, & Ueda, 2004; Lee, Lee, Moon, Moon, Kim, et al., 2013; Pokryszko-Dragan, Słotwiński, & Podemski, 2003; Polich & Corey-Bloom, 2005), we are not aware of any research that has employed the P3 oddball task to specifically examine changes in the ability to process lexicality. In this way, though the P3 task has been established as a viable task to use with individuals with AD, the current research is innovative in that it uses this established task to study deficits in the processing of lexicality in this patient population.

1.3 The Current Study

In order to further explore how processing lexicality may change with aging and the presence of AD, we conducted two experiments that investigate lexicality judgements in these two populations using on-line behavioural psycholinguistic methodology (Experiment 1) and electrophysiological / event-related potential (ERP) methods (Experiment 2). Furthermore, in order to rule out any overt deficits in selective attention that may be affecting performance on the lexical decision oddball tasks, we also evaluated these cognitive abilities (Experiment 2). We anticipate that this combination of methodologies can enhance our understanding of processing lexicality in individuals with AD and provide insight on how these individuals may differ from healthy older adults.

2 Experiment 1 (Lexical Decision Task)

2.1 Methods

Participants were 18 individuals with probable AD (11F, 7M) and 24 healthy older adults (17 F, 7 M). All were dominant English speakers and had normal or corrected-to-normal vision and were primarily recruited via the Memory Clinic of the Douglas Mental Health University Institute in Montréal, Québec. The older adult (OA) group had a mean age of 68 years (range: 50-88) and, on average, had 14.5 years of education (range: 10-20). All scored 26/30 or above on the Montreal Cognitive Assessment (MoCA, Nasreddine, Phillips, Bédirian, Charbonneau & Whitehead, 2005) thus ruling out the presence of cognitive impairments in this group (Luis, Keegan & Mullan, 2009; Nasreddine et al., 2005).

The probable AD group had a mean age of 75 years (range: 57-83) and averaged 15 years of education (range: 7-21 years). The criteria specified by the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA; McKhann, Drachman, Folstein, Katzman, Price et al., 1984; McKhann, Knopman, Chertkow, Hyman, Jack Jr. et al., 2011) were used for the diagnosis of probable AD that was performed by a psychiatrist with extensive experience with this population. The Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975; Folstein, Robins, & Helzer, 1983) was used to evaluate AD severity. Only individuals with AD whose score on the MMSE ranged from 20 to 29 (mild severity, Feldman & Woodward, 2005; Feldman, Van Baelen, Kavanagh, & Torfs, 2005) were included in this study. All participants were carefully assessed by study staff to ensure that they were capable of complying with the requirements of cognitive testing. The study was approved by the Douglas Institute Research Ethics Board and written informed consent was obtained from all participants.

The on-line visual lexical decision task was performed in a single session using E-Prime experiment software (Psychological Software Tools, Pittsburgh, PA). The task comprised 320 trials in total: 80 experimental words (concrete monomorphemic nouns); 80 filler words (verbs); 80 pseudowords; and 80 nonwords. All stimuli were controlled for length (4-6 letters and 1-2 syllables) and the words had a low frequency of use (between 2 and 50 occurrences per million) according to the USENET database (Shaoul & Westbury, 2006). Pseudowords were strings of letters that are permissible in English spelling and are pronounceable (e.g. *fodum*) and nonwords were non-permissible and unpronounceable letter strings (e.g. *mlopf*). Both pseudowords and nonwords were included within the study in order to investigate the potential over-acceptance of these two stimuli types that has previously been reported in the literature and also to allow a better comparison with the stimuli in Experiment 2. Each trial began with the presentation of a fixation cross for 500 ms and then a stimulus was presented in lowercase letters. The stimulus remained on the screen until the participant made a response by pressing one of two buttons on a keyboard. Once a response was made 500 ms was allowed to pass before the next stimulus was presented. Stimuli were randomized for each participant and participants were given a break midway through the experiment. Participants were instructed to decide as quickly and as accurately as possible whether the stimulus was a word or not. We conducted 10 practice trials before beginning the experiment to ensure that participants were comfortable with the task.

Response time (RT, in ms, measured from stimulus onset until a response was made) and error rate were collected for all trials.

2.2 Statistical Analysis

Participants who made 50% or more errors for any of the stimuli types were excluded from all analyses. This cut-off led to the exclusion of one (1) individual with AD and resulted in a final total of 41 participants. For the older adults, trials with an incorrect response or with a lexicality judgement response time over 2 standard deviations from the group mean (for each stimulus type) were removed from the RT analysis and led to an average of 3% of trials being excluded. For the AD participants, trials with an incorrect response or a response time over 2 standard deviations from their individual mean (for each stimulus type) were not included in the RT analysis and led to the exclusion of an average of 4% of trials. Data for the filler trials (the verbs) were not included in the analyses for either of the two participant groups. Mean correct lexical decision response times and percent error for each stimulus type are presented in Table 6.1.

Stimulus Types	Older Adults				Individuals with AD			
	Error Rate		RT		Error Rate		RT	
	mean	SD	mean	SD	mean	SD	mean	SD
Words	2%	3%	710	69	2%	3%	963	336
Pseudowords	7%	7%	917	150	9%	8%	1381	483
Nonwords	1%	2%	669	57	2%	3%	998	414

Table 6.1 - Error Rates and Response Times (RTs) in ms for Lexicality Judgements for Older Adults and Individuals with AD (Exp. 1)

Given that the error rates did not follow a normal pattern of distribution we chose to proceed with analysis of this variable using the Wilcoxon-Mann-Whitney nonparametric test. In addition, we used signal detection sensitivity (d') to further probe potential differences in how the two groups made errors. Sensitivity to stimuli characteristics (d') was calculated using the adjusted formula: d' = z(hit rate) – z(false alarms), with the hit rate being correct detections of the words and false alarms being incorrect responses to either nonwords or pseudowords. Differences in response latencies between the participant groups on the lexical status of the stimuli were investigated using a 2 (Group: older adults (OA) and individuals with AD (AD)) x 3 (Stimulus type: words, pseudowords and nonwords) mixed-model analysis of variance (ANOVA).

2.3 Results

2.3.1 Error Rates

When looking at overall error rates, older adults and individuals with AD both had a low error rate (3%, range: 0-11% and 4%, range: 0-12% respectively). Results from the Wilcoxon-Mann-Whitney test show that the two groups displayed a similar pattern of performance across the 3 stimulus types. There was no difference in error rates between groups for words: Z= -0.01, p = 0.98; pseudowords: Z= 1.05, p = 0.29; or nonwords: Z= 1.41, p = 0.16 (see Figure 6.1).

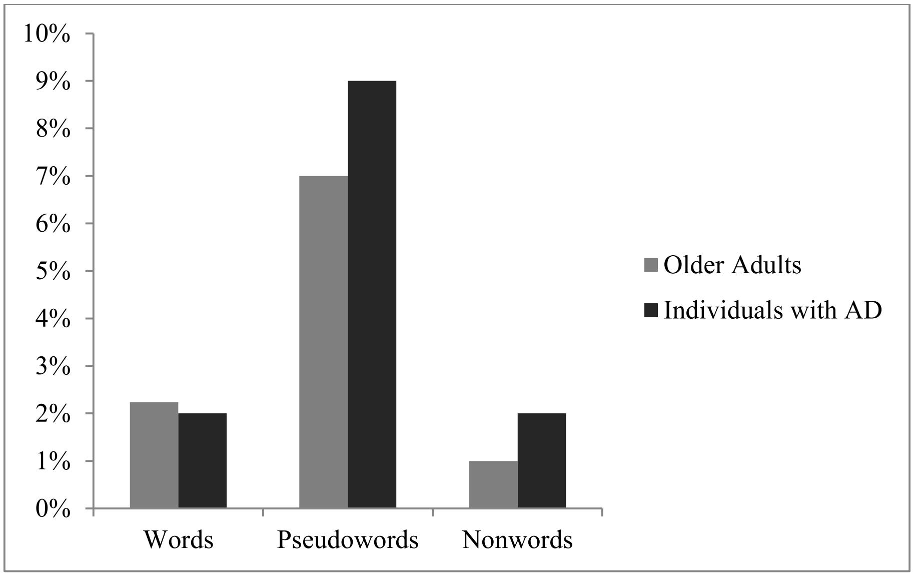

Figure 6.1 - Mean Error Rates for Lexicality Judgements for Older Adults and Individuals with AD (Exp. 1)

However, when comparing within groups, each group made significantly more errors to pseudowords than to words (both groups: $p > 0.0001$) and to pseudowords than to nonwords (both groups: $p > 0.0001$). While those with AD did not show a significant difference in errors between nonwords and words ($p = 0.98$), the older adults made fewer errors to nonwords than to words ($p = 0.03$). We also compared the error rates using signal detection sensitivity (d'). The d' analysis showed that while both groups were good at discriminating pseudowords from words (OA: d' = 3.48; AD: d' = 3.36) each group was better at discriminating between nonwords and words (OA: d' = 4.34; AD: d' = 4.05).

2.3.2 Response Time (RT)

While we observe no difference in error rates between the two participant groups, individuals with AD were significantly slower (significant main effect of Group ($F(2, 78) = 8.95$; $p > 0.0001$) than the healthy older adults. Post-hoc tests showed that those with AD were significantly slower compared to older adults for each of the stimuli types (words: $p = 0.006$;

pseudowords: $p > 0.0001$; and nonwords: $p > 0.0001$) (see Figure 6.2). Furthermore, when comparing within groups, both groups were slower to respond to pseudowords than to words (both groups: $p > 0.0001$), but faster to respond to nonwords versus pseudowords (both groups: $p > 0.0001$).

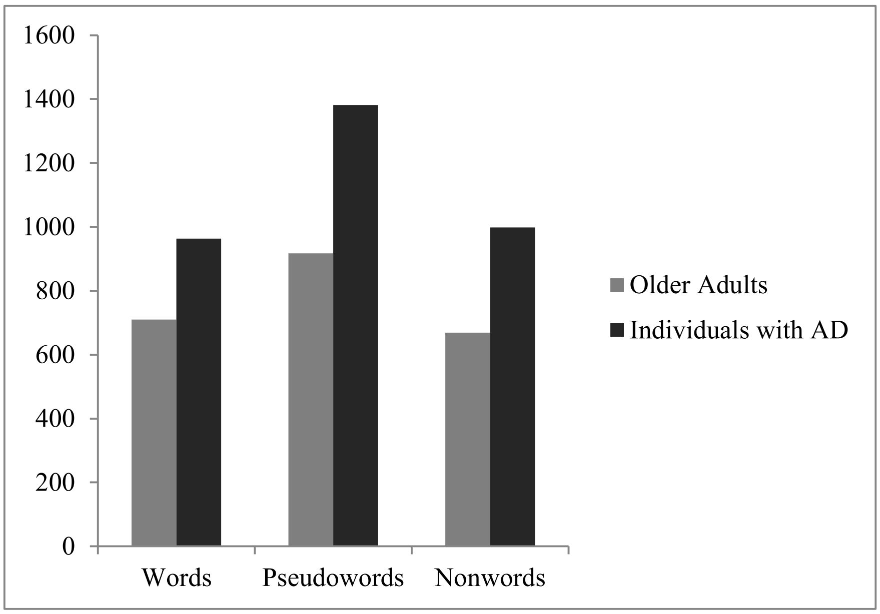

Figure 6.2 - Mean Response Times (RTs, in ms) for Lexicality Judgements for Older Adults and Individuals with AD (Exp. 1)

Based on the behavioural data, it would appear that while those with AD are much slower in processing lexicality than healthy older adults, they do not show the overt deficit in over-accepting pseudowords or nonwords relative to healthy older adults that has previously been reported in the literature. However, these behavioural results reflect the end result of lexical processing. To complement these data and obtain a better understanding of the processes underlying lexicality judgements, we turn to ERP tasks in order to explore what is occurring during an earlier stage of lexical processing that occurs prior to the participant making a behavioural response.

3 Experiment 2 (Event-Related Potentials (ERPs) - Lexical Decision Oddball Tasks)

The ERP tasks in Experiment 2 require the coordination of different cognitive abilities. These include linguistic abilities (to make the lexicality judgements) as well as abilities in other areas of cognition such as selective attention. In order to address this, we had participants perform a brief attention screening that comprised two short tasks measuring selective attention (number Stroop and Useful Field of View) prior to performing the ERP tasks in order to provide a general evaluation of these non-language related abilities and rule out an overt impairment at this level that may interact with individuals' performance on the lexical decision oddball tasks.

3.1 Methods

Participants were 10 individuals with probable AD (6F, 4M) and 17 healthy older adults (11 F, 6 M). The older adult group had a mean age of 69.0 years (range: 55- 85) and, on average, had 14.1 years of education (range: 10- 18). The probable AD group had a mean age of 76.6 years (range: 70- 83) and averaged 17.6 years of education (range: 12- 21 years). Recruitment location, inclusion criteria, diagnosis criteria, and severity determination were identical to those described for Experiment 1. All individuals who participated in the second experiment also first participated in Experiment 1. Testing for each experiment occurred in separate sessions, with approximately two weeks between sessions. Experiment 1 was always performed before Experiment 2.

3.2 Attention Screening

As indicated earlier, two standardized neuropsychological tasks measuring attention processes were administered: the number Stroop task (Flowers et al., 1979; Stroop, 1935; MacCleod, 1991) and the Useful Field of View Task (UFOV 6- Visual Awareness, Inc., Chicago). The number Stoop is a variant of the classic Stroop task that involves numbers rather than colors. Participants were presented with number words (either "one", "two" or "three") on a computer screen and were asked to either name the number or to count how many words were on the screen. Four sets of 20 trials were presented in random order; in two of the trial sets the participants were asked to name the number written on the screen while in the other two trials they were asked to count the number of words on the screen. Each set of trials could be either congruent (the name and the count match (e.g. "two two") or incongruent (e.g. "two two two"). Instructions were provided before the beginning of each set of trials and participants responded by pressing the appropriate number key on a keyboard. We conducted 4 practice trials before beginning each trial to ensure that participants were comfortable with the task. Response time and error rate were collected for each trial. While the classic Stroop task is more commonly used, it can be difficult to administer with older and/or cognitively impaired individuals as the response (a key press that corresponds to a colour) requires them to learn the mapping between the colour on the screen-key on the keyboard. Furthermore, there is a greater variability in colour perception with older adults that might impact the results of the task. By using the number Stroop we hoped to overcome these potential limitations. The Useful Field of View Task (UFOV) comprises three subtests that each measure age-related changes in information processing speed, proficiency in dividing attention, and the ability to ignore irrelevant information (Edwards, Vance, Wadley, Cissell, Roenker, et al., 2005). In the first subtest, participants were asked to identify a visual target (a car or a truck) presented at fixation. In the second, participants had to identify a central target and localize a peripheral target while in the third subtask participants were asked to make the same two responses, but with the added difficulty of the peripheral target being embedded among distractors.

3.3 ERP Tasks

Four blocks of the 20/80 lexical decision oddball task were administered in one single session using E-Prime experiment software (Psychological Software Tools, Pittsburgh, PA). Presentation was counterbalanced for each participant in order to control for possible order effects. Each block had 200 trials: 40 (20%) rare trials and 160 (80%) frequent trials and participants were asked to respond "YES" if the stimulus they saw in the trial was a word and "NO" if it was not. Eight hundred unique stimuli were used, 200 nonwords, 200 pseudowords, and 400 real words (see Appendix A for a full list of stimuli). All stimuli were controlled for number of letters (3 to 7 letters and 1 or 2 syllables) and the words were concrete nouns with a low frequency of occurrence in English (mean of 11 per million) according to the USENET database (Shaoul & Westbury, 2006). The stimuli types were manipulated based on their phonological structure and their lexical status: words were both orthographically/phonologically legal and had a real lexical status (e.g. cigar); pseudowords were orthographically/phonologically legal but did not have a lexical status (e.g. acle); and nonwords were orthographically/ phonologically illegal and did not have a lexical status (e.g. nduy). Block 1 comprised rare nonwords among frequent words (Nw-W), Block 2 comprised rare pseudowords with frequent words (Ps-W), Block 3 comprised rare words among frequent nonword (W-Nw), and Block 4 comprised rare words with frequent pseudowords (W-Ps). A Latin-square design was used to balance block presentation. Each trial began with the presentation of a stimulus for 750 ms, followed by a blank screen for 250 ms. Next, a response prompt, indicating that they could make their behavioural response, was presented for 1800 ms. We conducted 20 practice trials before beginning each experimental block to ensure that participants were comfortable with the task. Behavioural data (accuracy) were collected in each block of the oddball task using E-Prime experiment software. Response time was not collected since the task required that individuals delay making a behavioural response until they saw a response prompt. For the ERP analyses, the 40 rare trials and 40 frequent trials (chosen at random during the programming of the experimental block) were used for analysis.

Electroencephalogram (EEG) data were collected for each trial using Neuroscan data collection software and a 40-channel NuAmps amplifier, using silver-silver chloride electrodes. A QuickCap electrode cap with 34 monopolar electrodes was placed according to the 10/20 reference system. Each scalp site was referred to linked mastoids. Electrodes were placed above and below the left eye and at the outer canthi to monitor blinks and eye movements (electro-oculogram; EOG). Electrode impedances were measured using a criterion of 5 kΩ, per manufacturer guidelines. The EEG and EOG data were digitized on-line at a sampling rate of 250 Hz, and were filtered with bandpass cuttoffs of 0.1 - 30 Hz. EEG waveforms were time-locked to each stimulus onset and were segmented from 200 ms prior to stimulus onset to 1000 ms after stimulus onset. Eye-movement artifacts due to blinks were corrected off-line (Gratton, Coles & Donchin, 1983). A trial was identified as bad if it had movement artifacts of greater than ±70 μV and was rejected prior to averaging. In order to isolate the P3 component associated with the successful early categorization of a stimulus as being either a “word” or “not a word”, a traditional windowed analysis was conducted on individual average files. The a priori time window of 500-650 ms was chosen and the Pz electrode was selected for analysis. The selection of this window was both data driven as well as based on previous P3 work done utilizing linguistic stimuli (Azevedo, Atchley, & Kehayia, in press). Furthermore, exploratory analyses conducted on our data in the 500-650, 500-700, and 550-700 ms time windows confirmed that the greatest deflection in P3 occurred in the 500-650 ms time window. The Pz electrode was selected based on altready existing P3 literature that suggests that the component is maximal at this site for young adults (Bentin et al., 1999) as well as for older adults and individuals with AD (Parra, Ascencio, Urquina, Manes, & Ibáñez, 2012).

3.4 Statistical Analysis

3.4.1 Attention Screening

In the number Stroop, some individuals with AD had difficulty in response mapping, i.e. they were not consistently able to make a button-press response in the time allotted by the task. They were, however, able to verbally make their response. Given this unforeseen difficulty, individuals with AD who showed this difficulty were given the option to respond verbally and their response was imputed by the experimenter. Consequently, only response accuracy was included for analysis. Trials from the two congruent sets and those from the two incongruent sets were collapsed to form two overall sets (congruent and incongruent). Due to the presence of many perfect scores we elected to use A' instead of d' to evaluate stimulus sensitivity.

For the UFOV, a report providing an overall threshold value for each of the three subtests of the test is automatically generated following completion of the task. The three-test total for each participant was compared to normative scores (Edwards, Ross, Wadley, Clay, Crowe, et al., 2006) to determine if participants were within the performance norms expected for their age and level of education.

3.4.2 ERP, P3 Component

To examine whether lexical decision oddball tasks evoked a P3 component to the rare trials for each participant group in any of the blocks, we compared the mean amplitude of the rare trials to frequent trials in the critical time window of 500-650 ms at the Pz electrode using simple planned comparisons. Furthermore, to investigate whether there was a difference in P3 amplitude between the two participant groups we used a 2 (Group: OA, AD) X 2 (Trial type: rare, frequent) X 4 (Block: Nw-W, Ps-W, W-Nw, W-Ps) mixed-model ANOVA.

3.5 Results

3.5.1 Attention Screening

Results for both tasks used in the attention screening are presented in Appendix B. Results from the A' analysis for the accuracy data show that both groups are performing well above threshold in this task. The mean A' score for the OA group was 0.98 (range: 0.94 - 1) and 0.95 (range: 0.88 - 1) for individuals with AD. Two sample t-tests showed no significant difference in mean A' scores between the two groups ($t = -1.69$, $p = 0.12$) indicating that, although the older adults performed slightly better than those with AD, neither group appears to show an attention deficit when performing the number Stroop task. Furthermore, while individuals with AD had difficulty in making an overt button press response in this task and this differentiated them from the older adults, it is likely that a higher-order deficit, and not an attention deficit, is responsible for this difficulty given that both groups showed a high sensitivity to the stimuli (A') in this task. For the UFOV, when compared to norms for their age and level of education (Edwards et al., 2006), only one healthy older adult and three individuals with AD had a three-test total score that was below their expected norms. All other participants' performance indicated normal attention as measured by this task. Overall, the combined results from these two tasks suggest that both participant groups' attention processes are within normal levels and that any potential disruptions in the P3 component, if found, are not be likely to be primarily attributable to marked deficits in these cognitive domains.

3.5.2 ERP, Response Accuracy

Error rates for each block of lexical decision oddball tasks for the 80 experimental trials are presented in Tables 6.2 and 6.3. Overall older adults were highly accurate for each of the four blocks while individuals while AD had a higher error rate for each block. It is important to note that the non-speeded nature of the ERP tasks seems to have worked against those with AD; the bulk of the behavioural errors made by these individuals were actually non-responses (69% of errors overall). We believe that this effect was related to the fact that individuals were asked to delay making their behavioural response. This proved to be difficult for many of those with AD and in many trials they responded before the prompt (thus their response was not registered and was counted as an error). We observed a high rate of non-response errors for all four experimental blocks (93% of errors in the Nw-W block; 46% of errors in the Ps-W block, 74% of errors in the W-Nw block, and 67% of errors in the W-Ps block). Although it is not possible to know how many of these non -responses represent actual errors, given their low error rate in Experiment 1, it seems likely that the high error rate observed for those with AD in Experiment 2 is an artifact caused by different task demands and does not reflect their true ability to perform lexicality judgements.

Block	**Rare Trials (n = 40)**		**Frequent Trials (n = 40)**		**Total (n = 80)**	
	mean	**SD**	**mean**	**SD**	**mean**	**SD**
Nw-W	2%	6%	3%	6%	2%	6%
Ps-W	3%	5%	5%	4%	4%	4%
W-Nw	2%	3%	3%	9%	3%	7%
W-Ps	4%	3%	7%	9%	6%	7%

Table 6.2 - Mean Error Rates for ERP Lexical Decision Oddball Tasks for Older Adults (Exp. 2)

Block	Rare Trials (n = 40)		Frequent Trials (n = 40)		Total (n = 80)	
	mean	SD	mean	SD	mean	SD
Nw-W	11%	10%	25%	17%	18%	16%
Ps-W	13%	11%	22%	16%	17%	14%
W-Nw	20%	21%	26%	22%	23%	21%
W-Ps	13%	13%	15%	14%	14%	13%

Table 6.3 - Mean Error Rates for ERP Lexical Decision Oddball Tasks for Individuals with AD (Exp. 2)

3.5.3 ERP, P3 Component

ERP waveforms for both participant groups for each block are presented in Figures 6.3-6.10. Results from the mixed model ANOVA showed a significant main effect of Block and of Trial Type ($F(1,75) = 3.29$; $p = 0.03$ and $F(1.25) = 24.69$; $p < 0.0001$ respectively) and a marginally significant interaction between Group and Block ($F(1,75) = 2.61$; $p = .06$) in the 500-650 ms window. No other effects were significant. Given that our a priori goal was to examine whether any block of the lexical decision oddball task evoked a P3 component for either participant group we compared the rare trials to the frequent trials in the critical 500-650 ms time window at the Pz electrode for each group using simple planned comparisons. For the older adults, results of the planned comparisons showed that, for the two blocks that contrast words with nonwords (W-Nw and Nw-W), older adults displayed a significantly larger P3 response for the rare trials than for the frequent trials. The P3 amplitude was significantly larger for rare words (Mean µV = 2.45) compared to the frequent nonwords (Mean µV = -0.05) in the W-Nw block ($F(1, 16) = 8.08$; $p = 0.01$) and for rare nonwords (Mean µV = 3.7) compared to the frequent words (Mean µV = 1.22) in the Nw-W block ($F(1, 16) = 10.48$; $p = 0.005$) (see Figures 6.3 and 6.4).

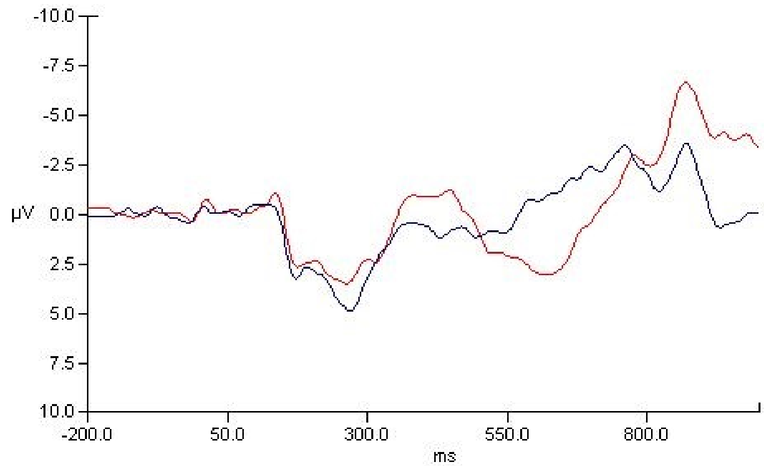

Figure 6.3 - Grand-Average ERPs Time-Locked to Stimulus Onset at the PZ Electrode for the OA Group in the W-Nw Block (Exp. 2): Rare Condition (red line), Frequent Condition (blue line)

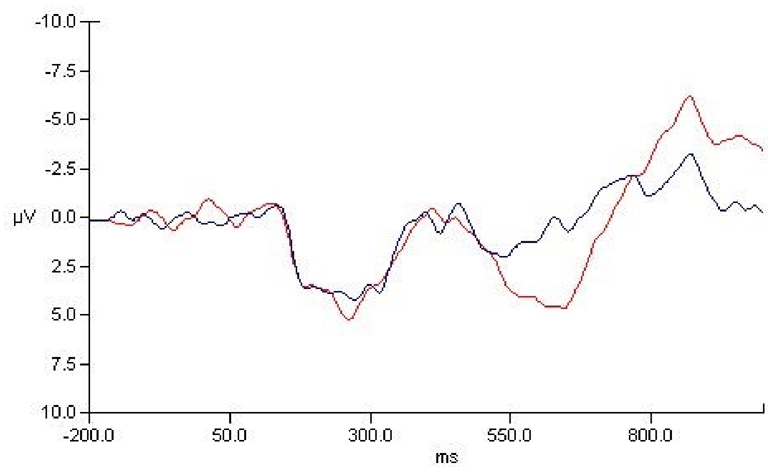

Figure 6.4 - Grand-Average ERPs Time-Locked to Stimulus Onset at the PZ Electrode for the OA Group in the Nw-W Block (Exp. 2): Rare Condition (red line), Frequent Condition (blue line)

However, for blocks contrasting words with pseudowords (W-Ps and Ps-W) older adults did not display a significant difference in P3 response for the rare trials compared to the frequent trials. In the W-Ps block there was a non-significant difference in P3 component for the rare words (Mean µV = 1.48) compared to the frequent pseudowords (Mean µV = 0.89), $F(1, 16) = 0.64$; $p = 0.43$) and for the Ps-W block there was also a non-significant difference in P3 component for the rare pseudowords (Mean µV = 1.5) compared to the frequent words (Mean µV = 0.93), $F(1, 16) = 0.45$; $p = 0.51$) (see Figures 6.5 and 6.6).

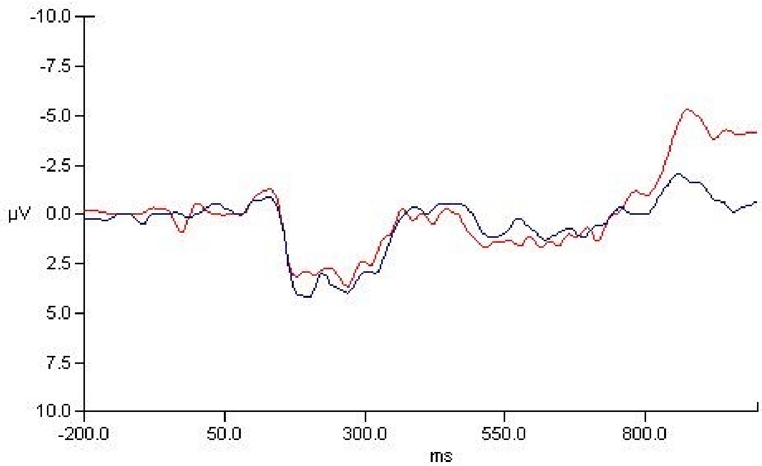

Figure 6.5 - Grand-Average ERPs Time-Locked to Stimulus Onset at the PZ Electrode for the OA Group in the W-Ps Block (Exp. 2): Rare Condition (red line), Frequent Condition (blue line)

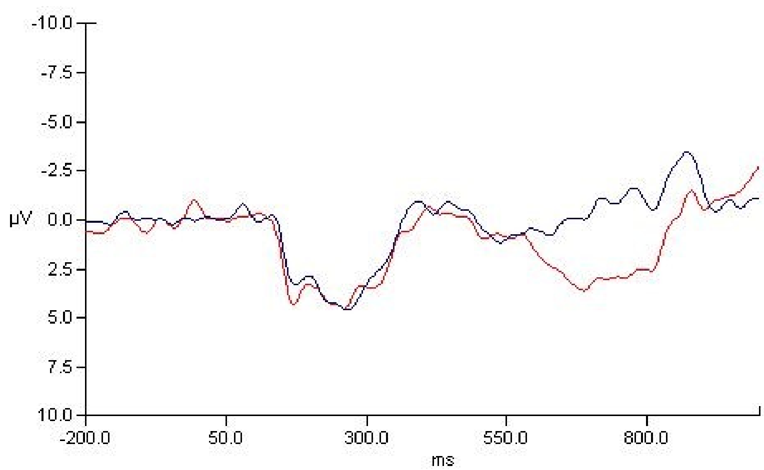

Figure 6.6 - Grand-Average ERPs Time-Locked to Stimulus Onset at the PZ Electrode for the OA Group in the Ps-W Block (Exp. 2): Rare Condition (red line), Frequent Condition (blue line)

In contrast, individuals with AD showed a different pattern in their ERP responses. Results of the planned comparisons showed that, for the two blocks in which words make up the frequent trials (Ps-W and Nw-W), those with AD displayed a larger P3 response for the rare trials than for frequent trials. The P3 amplitude was significantly larger for rare pseudowords (Mean µV = 1.9) compared to the frequent words (Mean µV = 0.32) in the Ps-W block ($F(1, 9) = 9.04$; $p = 0.02$) and there was a trend towards significance for rare nonwords (Mean µV = 3.02) compared to the frequent words (Mean µV = 0.65) in the Nw-W block ($F(1, 9) = 3.92$; $p = 0.08$) (see Figures 6.7-6.8).

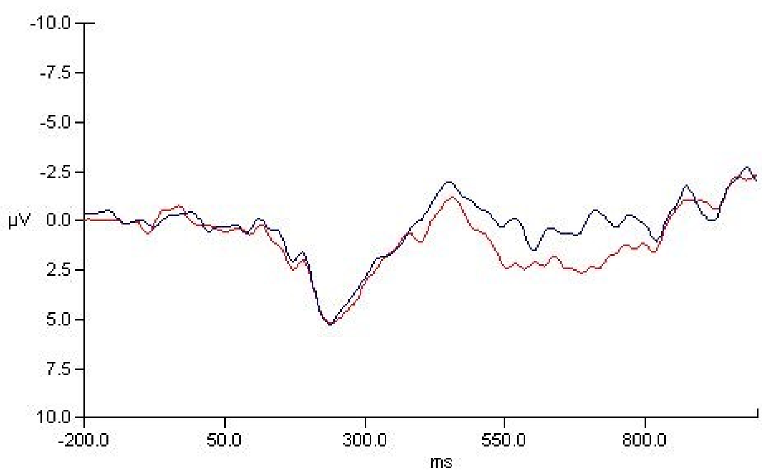

Figure 6.7 - Grand-Average ERPs Time-Locked to Stimulus Onset at the PZ Electrode for the AD Group in the Ps-W Block (Exp. 2): Rare Condition (red line), Frequent Condition (blue line)

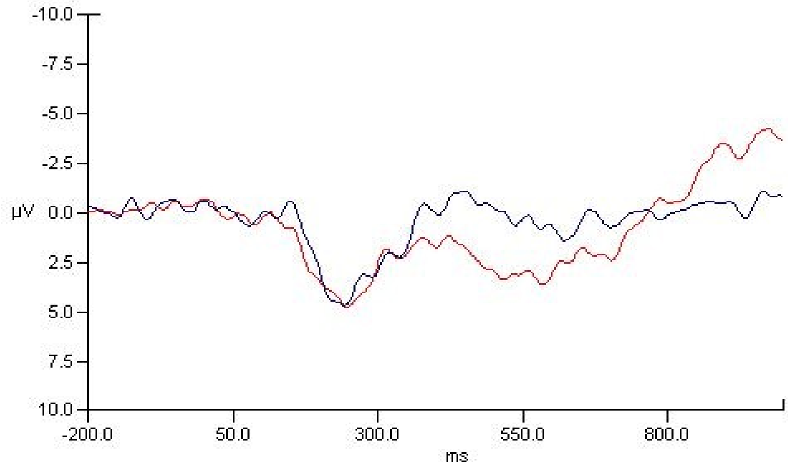

Figure 6.8 - Grand-Average ERPs Time-Locked to Stimulus Onset at the PZ Electrode for the AD Group in the Nw-W Block (Exp. 2): Rare Condition (red line), Frequent Condition (blue line)

Conversely, when nonwords or pseudowords comprised the frequent trials (W-Ps and W-Nw) individuals with AD did not display a significant difference in P3 response for the rare trials than to the frequent trials. In the W-Ps block there was a non-significant difference in P3 component amplitude for the rare words (Mean µV = 3.22) compared to the frequent pseudowords (Mean µV = 2.33), $F(1, 9) = 1.04$; $p = 0.33$) and for the W-Nw block there was also a non-significant difference in P3 component for the rare words (Mean µV = 1.49) compared to the frequent nonwords (Mean µV = 0.63), $F(1, 9) = 1.15$; $p = 0.31$) (see Figures 6.9-6.10).

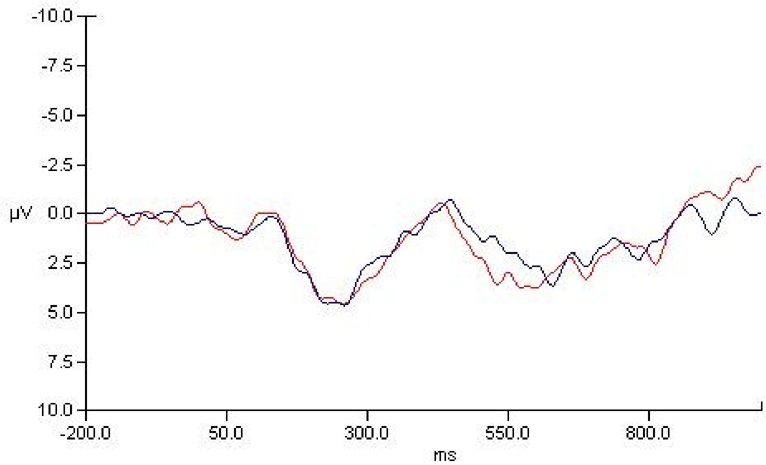

Figure 6.9 - Grand-Average ERPs Time-Locked to Stimulus Onset at the PZ Electrode for the AD Group in the W-Ps Block (Exp. 2): Rare Condition (red line), Frequent Condition (blue line)

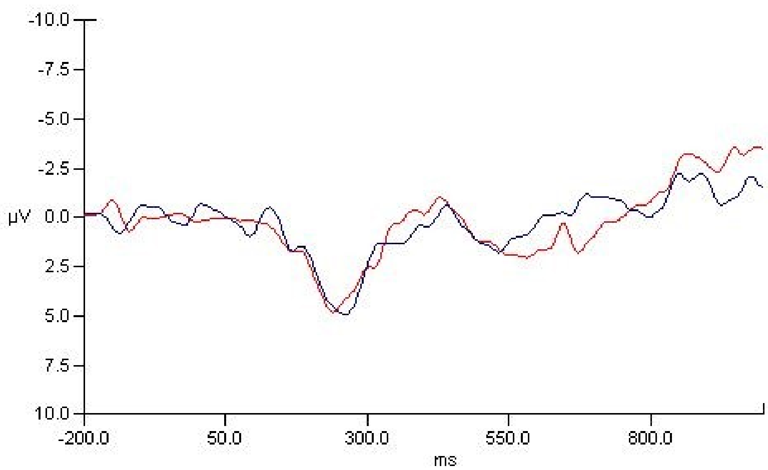

Figure 6.10 - Grand-Average ERPs Time-Locked to Stimulus Onset at the PZ Electrode for the AD Group in the W-Nw Block (Exp. 2): Rare Condition (red line), Frequent Condition (blue line)

4 Discussion

With the onset of AD, changes occur in the way people process lexicality that are mainly manifested by a slowdown when performing lexicality judgements. In order to further probe these changes, we conducted two experiments investigating lexicality judgements in healthy older adults and in individuals with AD. Consistent with results in the current literature, we found that individuals with AD were slower in making lexicality judgements than older adults in the lexical decision task in Experiment 1. However, in contrast to some previous reports in the lexical decision task (Cuetos, Herrera, & Ellis, 2010; Glosser, Kohn, Friedman, Sands, & Grugan, 1997; Madden, Welsh-Bohmer, & Tupler, 1999), those with AD in the current study performed at a rate of accuracy that was comparable to that of older adults. Our lexical decision task included both pseudoword and nonword stimuli within the same task, which could have made pseudoword stimuli appear even more word-like in contrast to the nonwords. While this stimulus manipulation could have potentially contributed to an over-acceptance of pseudowords, this response pattern was not observed. Furthermore, while we did observe that those with AD appeared to have made a significant number of errors in Experiment 2, upon closer inspection we observed that these errors mostly consist of responses made before the response prompt was presented. As a result, these responses were not recorded and were counted as errors. Although it is impossible to know how many of these non-responses were true errors we would argue that, given the high rate of accuracy for Experiment 1, it is likely that the high error rate across all trial types (words, pseudowords, and nonwords) observed for those with AD in experiment 2 is an artifact caused by task demands and does not reflect their true ability to perform lexicality judgements. It is our belief that an inhibitory dysfunction associated with AD is likely to be responsible for this pattern of responses. While this difficulty in inhibiting their behavioural response in the ERP tasks was unforseen it was not entirely surprising given that individuals with AD frequently show inhibitory dysfunction even early in the course of the disease (Amieva, Lafont, Auriacombe, Carret, Dartigues, et al. 2002; Collette, Amieva, Adam, Hogge, Van der Linden, Fabrigoule, & Salmon, 2007).Thus, it seems that unlikely the presence of mild AD is associated with a selective over-acceptance of pseudowords when performing the behavioural lexical decision task.

In fact, looking only at the behavioural results from Experiment 1, one could be lead to assume that individuals with AD perform lexicality judgements with a high level of accuracy, albeit at a much slower pace than the healthy older adults, and hence they appear to be showing the general slowing in processing speed that has been associated with AD but not necessarily an overt linguistic deficit. However, the ERP P3 amplitude results from Experiment 2 were instrumental in showing a linguistically-related deficit which differentiated between the healthy older adults and those with AD and highlight the importance and usefulness of combining behavioural psycholinguistic and ERP methodologies. As previously mentioned, the behavioural results in the lexical decision task reflect the end result of lexical processing, while the ERP results provide insight in to what is occurring during the stages of processing. The presence of a robust P3 component in the current study is believed to reflect an initial stage of lexical categorization, i.e. the successful early categorization of a stimulus as being either a “word” or “not a word” which can be used by selective attention to quickly differentiate the lexical status (word versus “not a word”) during processing. While the ERP results should be interpreted with caution given the small sample size in the AD group, we found that although both groups successfully made use of lexicality as a salient stimulus feature (as reflected by a robust P3 component in certain experimental blocks) the conditions that elicited this component were different between the two groups thus suggesting that a change in how lexicality is processed is occurring in those with AD.

The pattern of ERP responses observed suggests that older adults are sensitive to the orthography/phonology of the stimuli early in the course of processing while performing ERP lexical decision oddball tasks. In the context where the rare and frequent stimuli are most distinct (W-Nw and Nw-W blocks), with stimuli types that are dissimilar from one another in both orthographic/phonological legality and lexical status, older adults were able to quickly create effective "word" and "not a word" categories (as reflected by a robust P3 component to the rare stimuli trials in these blocks). However, older adults no longer showed a P3 in the 500-650 ms time window in the more difficult blocks that had an overlap in orthographic/phonological legality between the rare and frequent stimuli types (W-Ps and Ps-W blocks). This suggests that sensitivity to orthographic and phonological legality interfered with the older adults' ability to create effective "word" and/or "not a word" categories that can distinguish between the two orthographically/phonologically legal stimuli types quickly enough to be used by selective attention in these blocks.

While the modulation in P3 response seen for older adults in the current study is very similar to what has previously been observed in younger adults (Azevedo, Atchely, & Kehayia, in press), it contrasts with the ERP results where individuals with AD do not show a reliable P3 in both blocks where the rare and frequent stimuli are most distinct. Conversely, those with AD showed a P3 component only in the context where words were the frequently presented stimuli (Ps-W and Nw-W blocks). It is important to note that a P3 component was elicited to both the pseudoword and nonword rare trials in these blocks despite the two stimuli types differing in orthographic/phonological legality. The presence of a P3 to both of these stimuli types suggests that those with AD are no longer sensitive to the orthographic or phonological legality of the rare stimuli when they are presented among an abundance of frequent words; both the orthographically/phonologically legal pseudowords and the orthographically/phonologically illegal nonwords are effectively characterized as being the same (i.e. "not a word") and hence both stimuli types elicited a P3 component.

While a traditional P3 component typically has a latency of approximately 300-600 ms when elicited to non-linguistic stimuli, in the current study we observed that task conditions requiring the processing of linguistic stimuli have led to a delay in latency of the component. This delay was also observed in our previous lexical decision oddball task conducted with young adults (Azevedo, Atchley, & Kehayia, in press). It is also in line with previous ERP studies that investigate the timeline of lexical processing steps that must be performed before a "word" or "not a word" categorization can be made (and thus must occur before a P3 component can be elicited in any of our ERP tasks). Before a P3 could be elicited in the two blocks contrasting words and nonwords, each stimulus first had to be processed at least until orthographic/phonological legality could be determined. ERP research has shown that a divergence in waveforms associated with phonologically legal versus illegal stimulus types occurs relatively late, i.e. in the 300-350 ms timeframe (Bentin et al., 1999; Massol et al., 2011; Massol, Grainger, Midgley & Holcomb, 2012; Spironelli, Penolazzi & Angrilli, 2010). Furthermore, before a P3 could be elicited in the two blocks contrasting words and pseudowords, an attempt to determine the lexical status of the stimulus needed to be performed since both stimuli types were legal. ERP research points to an even later divergence in waveforms associated with an attempt to access a lexical representation for legal stimuli, i.e. in the 400 ms timeframe (Coch & Mitra, 2010; Deacon , Dynowska, Ritter, & Grose-Fifer, 2004). Therefore, since elicitation of the P3 was dependent on initial processing steps involved in processing lexical stimuli we were not surprised that this component was delayed in our tasks.

The modulation of the P3 component in contrasting contexts is consistent with IAC models of word recognition, such as the multiple read-out model (MROM; Grainger & Jacobs, 1996) and the dual-route cascaded model (DRC; Coltheart, Rastle, Perry, Langdon, & Ziegler, 2001), that posit the existence of two criteria that can be used to make a lexicality judgement. A "YES" response can be made when a specific word level unit reaches an activation threshold (i.e. a lexical activation) or based on a "fast guess" criterion that is sensitive to the level of global activation at the word level (i.e. if there is a high overall level of activation at the word level). Alternatively, a "No" response is given if, after a pre-specified time, no word representation is sufficiently activated to meet a threshold. We propose that the degree of dependence on each of these two criteria differs between the two groups based on their sensitivity to phonology early in the course of lexical processing. Older adults appear to favour the criterion of global activation while those with AD seem to be insensitive to the global activation caused by orthographic and phonological legality of stimuli in the initial stages of lexical processing and instead rely on the lexical activation criterion. For older adults, in the blocks where there is overlap in orthographic/phonological legality between the two stimuli types being contrasted (Ps-W and W-Ps blocks), the legality of both the words and pseudowords leads to an increase in global lexical activation for both stimuli types which appears to make the creation of effective "word" and "not a word" categories difficult in the time required to be available for use by selective attention; hence we do not observe a P3 in these conditions. However, since there is little or no global activation being generated by the nonwords that can impede the creation of effective "word" and "not a word" categories, a robust P3 is elicited for the blocks where there is no orthographic/phonological overlap between the stimuli types (Nw-W and W-Nw blocks). In contrast, since those with AD appear to be insensitive to orthography/phonology early in the course of processing, they will use the criterion of lexical activation. If individuals with AD were sensitive to any global activation generated by the orthography/phonology of the pseudowords then we would expect to observe a P3 in both the Nw-W and W-Nw blocks but not in the Ps-W or W-Ps blocks. However, what we observe is that a P3 is only elicited in the blocks where the frequent stimuli are words (Ps-W and Nw-W blocks) and this reliance on the lexical activation criterion leads them to treat both nonwords and pseudowords as being the same ("not a word") since neither can activate a lexical representation.

In addition, their insensitivity to orthography/phonology, and the consequent reliance on the criterion of lexical activation, may also be contributing, above and beyond any effects of general slowing in processing speed that is known to be present in individuals with AD, to the slowing of behavioural response times that are observed when making lexicality judgements. This would suggest that a linguistically-related deficit is also contributing to the slowing of response times when individuals with AD make a lexicality judgement.

A reduction in P3 component amplitude can occur due to an alteration in attentional processes, yet the absence of a P3 component observed in the AD group for any ERP block of Experiment 2 is not likely to be attributable to a deficit in this cognitive domain. While the attention screening we performed was not comprehensive, the results suggest that neither participant group displayed a marked alteration in attentional processes that would interfere with their ability to selectively attend to task critical stimuli in the ERP tasks. However, the pattern of P3 response observed for those with AD contrasts with what we observed in this study for the older adults (and what we have previously observed for young adults). Furthermore this pattern appears to be mediated by a decrease in sensitivity to the orthography/phonology of the stimuli in those with AD; thus we strongly believe that these findings suggest that their alteration in performance is more likely to be language-related than related only to attention.

The ERP results point to a change in how lexicality is processed early in the course of lexical access in individuals with AD. However, their lower accuracy rate to pseudoword stimuli in the behavioural lexical decision task in Experiment 1 suggests that some additional stage(s) of processing is being performed allowing those with AD to process the orthographic/phonological legality of stimuli and leading them to perform lexicality judgements in a manner that is comparable to that of the healthy older adults. If individuals with AD were truly insensitive to orthography/phonology throughout the whole course of lexical processing we would expect them to have similarly low error rates to all three stimuli types. However, both participant groups made significantly more errors to pseudowords than to words or to nonwords in the lexical decision task.

The current study was designed specifically to elicit the P3 component and consequently we employed a 20/80 ratio of rare to frequent stimuli. While the oddball task used here is the ideal experimental task to elicit the P3 component it does not easily permit us to investigate subsequent ERP components that may reflect orthographic/phonological processing. One possible way to further investigate the extent to which individuals with AD are sensitive to orthography/phonology could be to investigate the N350 component. This component has been linked to phonological processing (Ruz and Nobre, 2008; Spironelli & Angrilli 2007; Spironelli & Angrilli, 2009; Spironelli, Penolazzi & Angrilli, 2010) and is thought to distinguish between pronounceable and non-pronounceable stimuli since it is elicited only by orthographically/ phonologically legal stimuli (Bentin et al., 1999) in healthy young adults.

While additional research is needed to further probe this apparent deficit in processing lexicality in those with AD, further research is also warranted to investigate if (and how) this linguistic deficit may also be contributing to the behavioural slowing of RTs that was observed in the lexical decision task, over and above general slowing in processing speed. Moreover, we propose that this observed alteration in P3 performance that was found in those with AD shows promise as a linguistic marker that, in combination with other linguistic/cognitive markers, can potentially differentiate between healthy aging and early dementia.

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Appendix A

Stimuli for Nw-W block

Rare: afxy, atbfej, bgifsar, bkafdp, byxteg, cbolprt, ctmovk, dlifupl, dvka, ejsd, fctob, gbdu, hkaj, iqldo, kdinpsm, lnig, mkhul, ncyz, nduy, nvudfa, odcgek, pfu, pjnu, pmcuhm, qlih, rfajh, rjau, sdym, sfvud, sgydtf, sxuf, tgix, tkotm, tvatdw, uqg, wkuf, xpkag, ydbsw, ygfm, ztwoljn.

Frequent: agenda, amulet, ankle ,ant ,ark, atlas, balloon, banjo, beach, beagle, bean, beaver, biscuit, blade, blanket, branch, bread ,broom, bullet, button, cabin, cabinet, cage, calcium, cartoon, castle, cave, chalk, chariot, cheese, cigar, clock, coal, coin, costume, cottage, crane, crown, crust, curtain, dagger, daisy, diary, doll, donkey, dove, dungeon, eagle, elf, fiddle, finger, flea, flower, fog, funnel, fur, garlic, ghost, gnome, grape, grass, gravel, guitar, hamster, hoe, horn, hose, island, ivy, jaguar, jam, jelly, jewel, ketchup, kidney, kiosk, kitchen, knife, lard, lemon, lentil, lily, lion, luggage, maple, moose, motel, mud, muffin, mug, muscle neck, nose, oak, paddle, panther, parrot, pawn, penny, phantom, photo, picnic pie, pillar, pillow, pine, pocket, podium, potato potty, powder ,pulpit, quilt, racket, raven, ribbon, robe, robot, ruby, rum, rust, sesame, shirt, shrimp, skin, slate, sleeve, snail, spark, spout, stadium, statue, swan, syrup, tank, tent, thigh, thumb, tire, tissue, tobacco, tomato, tomb, tower, train, tray, trout, tub, turtle, veil, venom, vest, violin, voucher, wheat, wood, worm, yam, yarn, zinc.

Stimuli for Ps-W block

Rare: adlym, aif, beath, bluke, breon, casip, chond, clesh, denfol, dunt, durse, egol, flate, fodum, gallis, ganny, gonder, gupin, hant, keld, krelt, kulm, leraf, lomb, lunky, mamet, montis, muned, mursk, pand, paupis, pung, queld, sedin, serry, sleer, sowel, stru, surine vold.

Frequent: anchor, arcade, arrow, asphalt, bacon, baggage, ballot, banana, banner, bell, belt, bikini, blouse, boat, bra, bubble, bulb, bunker, butter, cactus, camel, camera, canal, canoe, casino, cereal, chin, chrome, clam, cliff, cloud, cocoa, coffee, copper, cord, cotton, couch, coupon, coyote, crab, cradle, cube, cyprus, dill, dock, dolphin, dome, domino, donut, dough, dragon, elbow, elk, falcon, ferret, ferry, flame, flour, foil, forest, fork, frost, garage, garden, gate, gel, gem, ginger, glass, goat, goose, grain, gravy, hawk, helmet, herb, honey, horse, jade, jaw, jungle, kiwi, ladder, lark, latch, laurel, leather, lime, liver, lizard, lobster, lynx, magnet, malt, mantle, maze, menu, mint, moon, motor, mummy, navel, nest, nickel, nylon, ocean, palace, parcel, pasta, patio, peach, pearl, penguin, plate, pool, porch, pretzel, ranch, rink, saliva, salmon, salt, sausage, screen, seed, shack, shark, shrub, silk, sled, snake, soap, sock, soup, spice, spider, spike, spindle, spoon, squid, stereo, sugar, taxi, tile, toad, toilet, torso, towel, trophy, tuna, turbine, turkey, vase, vinegar, vinyl, wagon, wand, weasel, wool, yoke.

Stimuli for W-Nw block

Rare: apple, axle, cedar, chain, comet, corn, dessert, dish, fence, fossil, furnace, gorilla, grenade, harbour, harp, hood, hoop, iris, lettuce, mop, mouse, mustard, olive, piano, pony, puddle, pumpkin, purse, roof, shell, shoe, silver, sphere, stove, tiger, tongue, tort, vine, wax, zebra.

Frequent: abjosdl, akwih, amvp, atmofr, awgsiq, bcluh, bdui, bnua, bopltr, bwtav, cfru, cgaj, cjusep, cksialr, cmlih, cuhlw, dbeljy, dcbi, dfurfpl, dhomg, dlupfb, dokjerw, dpagb, ebkfu, ehgd, ejdkib, ejsu, elokju, ewmji, fbsua, feglrb, fnubdw, fspu, fwnef, gakfp, gduldw, gjewgmi, gpelti, gsdu, gwtys, hcu, hdob, hlufc, hnoplg, htduz, htewab, ifmlej, igbuhdm, ikdp, itpsv, ivgsfu, ivqo iwerphd, ixdfasf, jadcr, jbawefd, jdemca, jksu, jmopsk, jpni, jpulm, kbiw, kdu, kebmy, kftonb, kpohsl, kpsia, kvba, kyfdenh, lbym, lcokjuo, lgicb, lpekga, lwafg, lxufdp, mcif, mdiwox, mgu, mjadc, mlopf, mrufrsy, mstuhji, msupkt, mtsu, nfadx, nfu, nhfusbc, njsiwp, nlpoc, nsrihjk, obfjl, odfmnr, olfg, opbz, opdku, osngulb, pbsi, pfmu, pgedf, pjdwug, pmsgvi, pxunl, qbakjd, qglyna, qmig, qsfum, qsheb, rbmolpy, rmloh, rshbisa, rtingd, rtlu, rvikjt, sdopl, sdusfod, sfhi, sgacbe, tcegd, tcsidgb, tdsamg, tgmufka, tmlu, ubdfe, ucvm, udgm, ukvofgd, uplkjs, usbixg, uvdalbd, uvfmi, vbhke, vcadf, vgak, vimgslu, vsfo, vsukfv, vwjosf, wadfv, wdifv, wgposmt, wkajfu, wnga, wsetja, xbmi, xdapg, xfe, xfidhw, xjoh, xlhduy, yhbr, yhjnsa, yjfbu, yjl, ymdni, yufnlup, zdikm, zgsa, zmaslg, zmul, zojtf.

Stimuli for W-Ps block

Rare: ace, album, angel, bamboo, beer, birch, bridge, cabbage, cameo, cobra, cork, crayon, dart, diploma, dune, gravel, gum, hutch, lamp, leaf, lotus, maggot, milk, needle, oar, panda, parsley, pear, pencil, pickle, pig, poison, poppy, rattle, sauce, spade, sponge, ticket, topaz, wasp.

Frequent: acle, acril, afel, afrud, ansle, arl, balpet, bargow, belk, bennel, betle, betso, bettle, bith, botter, brabe, brazar, bund, burdle, butine, cairil, choibe, cinler, ciress, clido, colb, crale, cruff, culp, cuton, darg, daridather, delp, dendu, dest, dith, dovil, dunry, durim, edas, eglym, fambol, farus, fathan, fergle, fibe, finab, fing, fiple, folex, foris, fower, frab, frain, fump, fungar, fush, geddop, gedim, gellon, glem, glycan, goind, gorna, gort, grach, grafe, grink, grum, grupet, guddle, hadur, hartel, henel, hepent, herit, homper, honder, hulf, imop, indest, inlest, janner, jeckin, jick, jink, jodar, kender, kest, klead, kravis, lerd, loap, lober, londu, lunk, markel, marrot, meap, mear, mittle, muki, nake, narp, nattle, nedoc, nerin, netu, nivar, noot, noster, nustol, onged, ougil, pangle, paril, pathat, pedak, pender, perg, pime, pisk, plive, ploke, plom, plone, poish, ponfer, pordan, povol, racern, reshew, roany, rother, sapil, sedin, sepol, serol, siddle, slun, sterma, talb, talt, teklin, tosk, trib, tular, tummer, tunk, turmey, twint, vacop, vatil, vlower, wint, woon, wush, yarel, yock.

Appendix B

Number Stroop task

	Errors Congruent Trial Set (n = 40)	Errors Incongruent Trial Set (n = 40)	A' (Stimulus Sensitivity)
OA 1	3%	5%	0.98
OA 2	0%	0%	1.00
OA 3	0%	3%	0.99
OA 4	0%	0%	1.00
OA 5	0%	0%	1.00
OA 6	0%	18%	0.96
OA 7	0%	3%	0.99
OA 8	0%	0%	1.00
OA 9	0%	0%	1.00
OA 10	0%	5%	0.99
OA 11	10%	13%	0.94
OA 12	0%	3%	0.99
OA 13	0%	23%	0.94
OA 14	0%	0%	1.00
OA 15	3%	0%	0.94
OA 16	3%	0%	0.94
OA 17	0%	0%	1.00
Mean	1%	4%	0.98
St-Dev	3%	7%	

Performance on the Number Stroop task for older adults

Number Stroop task

	Errors Congruent Trial Set (n = 40)	Errors Incongruent Trial Set (n = 40)	A' (Stimulus Sensitivity)
AD 1	8%	33%	0.88
AD 2	0%	0%	1.00
AD 3	30%	8%	0.89
AD 4	0%	0%	1.00
AD 5	15%	25%	0.88
AD 6	0%	0%	1.00
AD 7	8%	20%	0.92
AD 8	0%	0%	1.00
AD 9	5%	15%	0.95
AD 10	0%	10%	0.98
Mean	7%	11%	0.95
St-Dev	10%	12%	

Performance on the Number Stroop task for individuals with AD

Useful Field of View (UFOV)

	Subtest 1 (Processing Speed-Stimulus Identification)	Subtest 2 (Divided Attention)	Subtest 3 (Selective Attention)	3-Subtest Total	Within Norms for age/ed*
OA 1	17	23	86	126	yes
OA 2	17	60	127	204	yes
OA 3	17	17	87	121	yes
OA 4	17	178	178	373	yes
OA 5	23	37	287	347	yes
OA 6	17	20	203	240	yes
OA 7	17	17	150	184	yes
OA 8	53	500	not administered	n/a	no
OA 9	17	40	97	154	yes
OA 10	37	87	243	367	yes
OA 11	37	157	433	627	yes
OA 12	23	23	130	176	yes
OA 13	17	63	83	163	yes
OA 14	17	20	83	120	yes
OA 15	17	53	77	147	yes
OA 16	17	40	180	237	yes
OA 17	17	70	253	340	yes

Performance on the Useful Field of View (UFOV) task for older adults

** For the UFOV, the three-test total for each participant was compared to normative scores (Edwards et al., 2006) to determine if participants were within the performance norms expected for their age and level of education.*

Useful Field of View (UFOV)

	Subtest 1 (Processing Speed-Stimulus Identification)	Subtest 2 (Divided Attention)	Subtest 3 (Selective Attention)	3-Subtest Total	Within Norms for age/ed*
AD 1	140	500	not administered	n/a	no
AD 2	17	60	263	340	yes
AD 3	40	500	not administered	n/a	no
AD 4	113	113	330	556	yes
AD 5	30	157	316	503	yes
AD 6	17	50	257	324	yes
AD 7	17	103	270	390	yes
AD 8	153	220	340	713	yes
AD 9	133	500	not administered	n/a	no
AD 10	120	223	300	643	yes

Performance on the Useful Field of View (UFOV) task for individuals with AD

CHAPTER 7: *Summary of Results, Discussion, and Conclusion*

This thesis represents an initial step into the examination of processing lexicality (i.e. the ability to quickly recognize words and reject word-like letter strings like "*filow*" or "*knojd*") along the adult lifespan and in individuals with mild AD with the overall goal of investigating and describing potential changes in processing lexicality across these populations.

Over the previous chapters we used distinct methodologies (on-line behavioural psycholinguistic tasks and electrophysiological/event-related potential (ERP) methods) and considered three separate populations to investigate changes in processing lexicality. In this chapter we will aggregate the major findings of the three studies and highlight the importance and significance of the novel information we have acquired. A discussion of the relevant findings has been provided in each manuscript and thus will not be repeated here. However, to place this general discussion in context, a reiteration of the most important findings will be briefly presented.

7.1 Summary of Behavioural Results (Lexical Decision Tasks) from Manuscripts 1 and 3

One important and somewhat surprising finding from this thesis was that when asked to make lexicality judgements to words, nonwords, and pseudowords in a classic behavioural on-line lexical decision task, healthy older adults and individuals with AD showed a similar pattern of response; individuals with AD were slower in processing lexicality (i.e. they were slower at making lexicality judgements) than both healthy younger and older adults but the two older groups had comparable error rates to all three stimuli types (Manuscript 1 and 3). In contrast, young adults made significantly more errors to pseudowords when compared to both older groups (Manuscript 1).

Given that our lexical decision tasks included both pseudoword and nonword stimuli within the same task, which could have made pseudoword stimuli appear even more word-like in contrast to the nonwords, this stimulus manipulation could have potentially contributed to an over-acceptance of pseudowords in all participants. However, in contrast to what we had expected, those with AD did not make more errors to pseudowords when compared to older adults (though both older groups did made more errors to pseudowords than to words or nonwords) (Manuscripts 1 and 3). Thus, it seems unlikely that the presence of mild AD is associated with a selective over-acceptance of pseudowords in the behavioural lexical decision task as had previously been suggested in the literature. Furthermore, since young adults in Manuscript 1 made more errors than either the older adults or the individuals with AD (with this difference being driven by the younger adults' over-acceptance of pseudoword stimuli), this suggests that the young adults may have been using a different strategy from that of the two older groups when performing lexicality judgements in this task.

When looking at neighbourhood density (N) effects (Manuscript 1), our findings for the young adult group reflect those that have previously been reported in the literature: we observed that a large N was facilitatory for words but inhibitory for nonwords and this effect was seen in reaction times, as well as in error rate. However, it appears that with aging there is a change in how neighbourhood density is processed; older individuals were no longer as sensitive to N when compared to young adults and this change was more pronounced with the presence of AD. Specifically, older adults did show inhibition (i.e., more errors and longer RTs) to high N pseudowords. However, when looking at error rates, they no longer show facilitation (i.e., fewer errors) to high N words. This difference became even more striking when looking at the individuals with AD. N did not appear to influence the processing of words for those with AD (i.e. they did not show a difference in error rate or in RT to low versus high N words). However, those with AD were still sensitive to N effects when processing pseudowords; inhibitory effects of N on pseudowords were observed for both error rates and RTs. Therefore, the changes in N effects that are observed with aging appear to differentially affect the processing of words and pseudowords.

Looking only at the behavioural results from Manuscripts 1 and 3, one could be lead to assume that individuals with AD perform lexicality judgements with a similar level of accuracy, albeit at a much slower pace, than the healthy older adults, and hence they appear to be showing the general slowing in processing speed that has been associated with AD but not necessarily an overt linguistic deficit. However, the ERP P3 amplitude results from Manuscript 3 were instrumental in showing a linguistically-related deficit which differentiated between the healthy older adults and those with AD and highlighted the importance and usefulness of combining behavioural psycholinguistic and ERP methodologies.

7.2 Summary of ERP Results (Lexical Decision Oddball) from Manuscripts 2 and 3

The behavioural results in the lexical decision task reflect the end result of lexical processing, while the ERP results provide insight into what is occurring during the stages of processing. The presence of a robust P3 component in the lexical decision oddball tasks is believed to reflect the initial stage of lexical categorization, i.e. the successful early categorization of a stimulus as being either a “word” or “not a word”. We found that although each of the three groups (Manuscript 2 and 3) successfully made use of lexicality as a salient stimulus feature (as reflected by a robust P3 component in certain experimental blocks), the conditions that elicited this component were different between the healthy groups (i.e. young and older adults) and those with AD. This suggests that a change in how lexicality is processed is occurring in those with AD that in turn leads these groups to rely on a different underlying strategy than older adults when performing the tasks.

Young adults (Manuscript 2) and older adults (Manuscript 3) showed a similar pattern of performance in the ERP tasks: in the context where the rare and frequent stimuli were most distinct (W-Nw and Nw-W blocks, with stimuli types that are dissimilar from one another in both orthographic/phonological legality and lexical status), both groups were able to quickly create effective "word" and "not a word" categories (as reflected by a robust P3 component to the rare stimuli trials in these blocks). However, when both stimuli types were orthographically/phonologically legal and a lexical categorization could only be made based on lexical status (rare words among pseudowords (W-Ps) and rare pseudowords among words (Ps-W) blocks) a reliable P3 was no longer observed in either block for older adults and was only observed in the Ps-W block for young adults. In contrast, individuals with AD showed a different pattern of P3 responses. While those with AD did not show a reliable P3 response in either block that had words as targets (rare words among pseudowords (W-Ps) and rare words among nonwords (W-Nw) blocks) they did show a robust P3 component to both blocks where words were the fillers (rare pseudowords among words (Ps-W) and rare nonwords among words (Nw-W)). This suggests that, contrary to the young and older adults, individuals with AD were no longer sensitive to the phonology/orthography of the stimuli, but rather were solely sensitive to a difference in lexical status between the stimuli.

Although a reduction or absence of P3 component amplitude can occur due to an alteration in attentional processes, the absence of a reliable P3 component in any ERP block of our studies is not likely to be attributable to a deficit in this cognitive domain. While the attention screening we performed was not comprehensive, the results suggest that neither of the older participant groups displayed a marked alteration in attentional processes that would interfere with their ability to selectively attend to task critical stimuli in the ERP tasks. Consequently, it appears that the observed alteration in P3 performance in individuals with AD is attributable mainly, if not solely, to a linguistic deficit.

7.3 Discussion

What can we infer about processing lexicality across the adult lifespan and in AD?

When taken together, the results from the three manuscripts suggest that processing lexicality changes across the adult lifespan and in early AD. The behavioural results from Manuscript 1 point to a change in sensitivity to neighbourhood density (N) when making lexicality judgements that begins in healthy aging and appears to become more pronounced with AD. In addition, behavioural results from Manuscript 3 also appear to suggest a similarity between the two older groups that differentiates them from the young adults. However, when probing more deeply, the P3 ERP results uncover a clear difference between the older adults and those with AD during an early stage of lexical processing that had not been evident when looking only at the end result of processing. One might consider the difference in performance between the young and the two older groups on the behavioural tasks might be simply due to a speed-accuracy tradeoff (the young adults were faster but less accurate than the aging groups). However, the difference in ERP results again suggests that the young and older adult groups were processing lexicality in a different manner than those with AD.

Although we observed that young adults showed a difference in behavioural responses compared to the two older groups (Manuscript 1) and that the two healthy groups performed differently with regard to elicitation of P3 ERP component when compared to those with AD

(Manuscripts 2 and 3), we propose that these modulations in responses can be accounted for and modelled by current AIC models of visual word recognition/processing (dual-route cascaded model (DRC) model, Coltheart, Rastle, Perry, Langdon, & Ziegler, 2001; multiple read-out model (MROM), Grainger & Jacobs, 1996). These models propose the availability of two criteria when performing lexicality judgements: a lexical criterion that relies on activation of an individual lexical representation and a non-lexical criterion that relies on global activation at the word level (i.e. respond "YES" if there is a high overall level of activation at the word level). Global activation is believed to be caused by the partial activation of lexical entries that are related to the target in various ways (such as being a lexical neighbour or having an overlap in orthography or phonology, for example). However, an individuals' lexical processing system must be sensitive to these factors in order for them to be able to cause a rise in lexical activation that will then lead to an overall rise in global activation. Furthermore, these factors can only be useful when performing lexicality judgements (or any task) if the mechanisms that support lexical activation work quickly enough for levels of global activation to be useful during the performance of this task.

When looking across the studies that comprise the three manuscripts in this thesis, results suggest that, although both healthy groups can access and use both criteria when making lexicality judgements, young adults tend to favour the criterion of global activation irrespective of the stimuli types and task demands while older adults show more variability by either relying on one criterion or the other depending on task demands and stimuli types. In contrast to older adults, individuals with AD, like young adults, also appear to be rigid in adhering to one criterion when making lexicality judgements. However, unlike young adults, those with AD favoured the criterion of lexical activation regardless of the stimuli types and task demands.

In the classic lexical decision task probing neighbourhood density (N) effects in lexical processing, three stimuli types (words, pseudowords, and nonwords) were included within the same experiment (Manuscript 1). In this situation, the models propose that global activation will primarily be caused by the partial activation of lexical neighbours when N is large (i.e. stimuli with a large N will generate more global activation than stimuli with a small N). The young adults' propensity to favour the criterion of global activation in this task may have been counter-productive as it was associated with an over-acceptance of the pseudoword stimuli. However, it allowed young adults to quickly accept words and reject nonwords and also led to them showing the classic N effect (i.e. facilitation for high-N words and inhibition for high-N pseudowords). In contrast, older adults and those with AD appeared to favour the criterion of lexical activation in this task and this allowed both groups to make fewer errors to the word-like pseudowords when compared to the young adults. However, it is important to note that results from this task suggest that older adults and those with AD were favouring the lexical activation criterion because activation of lexical neighbours was occurring more slowly than for the young adults. Consequently global activation was not available to them early enough to be used when making a lexicality judgement. Therefore, while favouring the lexical activation criterion when processing high-N versus low-N stimuli resulted in fewer errors to the pseudowords, both of the older groups' performance on this task were significantly slower and reflected a deviation from what was observed for the young adults and suggests the presence of an alteration in the processing of neighbourhood density in the two older groups.

On the other hand, the ERP lexical decision oddball tasks only contrasted two stimuli types per experiment (Manuscripts 2 and 3). In this situation where N is not a variable under consideration, the models propose that global activation can be caused by the partial activation of lexical entries that share an overlap in orthography/phonology with the target. In these ERP tasks, young adults (Manuscript 2) appeared to favour the criterion of global activation, as was the case in the classic lexical decision task. Though, in this case, reliance on this criterion seems to have been more advantageous since a robust P3 (signifying that participants successfully made an early categorization of stimuli into “word” and “not a word” categories) was observed in all but one of the four experimental blocks. However, when faced with two stimuli types per experiment (Manuscript 3), older adults switched to favouring the criterion of global activation, thus performing more like young adults in this task. In contrast to both the healthy groups, the individuals with AD again seemed to favour the criterion of lexical activation when performing the ERP tasks and this was manifested as a different pattern of P3 response from that of both the young and older adults. As mentioned above, we propose that dependence on each of these two criteria differed between the groups based on their sensitivity to orthography/phonology early in the course of lexical processing. The pattern of ERP responses observed suggests that young and older adults are sensitive to the orthographic/phonological legality of the stimuli early in the course of processing. This sensitivity appears to hinder early processing of lexicality in the older adults when both the rare and frequent stimuli types are orthographically/phonologically legal (Ps-W and W-Ps) because legality leads to an increase in global lexical activation for both stimuli types which then appears to make the creation of effective “word” and “not a word” categories difficult early on the course of processing; hence we do not observe a P3 in these blocks. However, in the context where the stimuli were most distinct (W-Nw and Nw-W blocks, stimuli types were dissimilar from one another in both orthographic/phonological legality and lexical status), older adults were able to quickly create effective “word” and “not a word” categories, as reflected by a robust P3 component to the rare stimuli trials in these blocks.

This pattern of ERP response contrasts with what we observed for those with AD. Individuals with AD seem to be insensitive to global activation caused by orthographic/ phonological legality of stimuli in the initial stages of lexical processing and therefore instead favoured the lexical activation criterion. If individuals with AD were sensitive to any global activation generated by the orthography/phonology of the pseudowords early in the course of lexical processing then we would expect to observe a P3 in both the Nw-W and W-Nw blocks but not in the Ps-W or W-Ps blocks. However, what we observe is that a P3 is only elicited in the blocks where the frequent stimuli are words (Ps-W and Nw-W blocks) and this reliance on the lexical activation criterion leads them to treat both nonwords and pseudowords as being the same ("not a word") since neither can activate a lexical representation. Overall, it is unclear whether those with AD can still access both criteria when performing lexicality judgements. Their performance on the tasks that comprise this thesis suggests that they strongly favour the lexical activation criterion despite the different constraints that are present within each task. While it is possible that those with AD may still access or use the criterion of global activation when making lexicality judgements we do not see evidence for this in our studies.

It is also worth noting that, although those with AD showed a pattern of P3 response in the ERP tasks that differed from that of the older adults and points to a change in how lexicality is processed early in the course of lexical access, their lower behavioural accuracy rate to pseudoword stimuli in the classic lexical decision tasks (Manuscripts 1 and 3) suggests that some additional stage(s) of processing is being performed that allows those with AD to ultimately perform behavioural lexicality judgements in a manner that is comparable to that of the healthy older adults, albeit at a slower pace. If individuals with AD were truly completely insensitive to orthography/phonology throughout the whole course of lexical processing we would expect them to have similarly low error rates to all three stimuli types. However, both older groups made more errors to pseudowords than to words or to nonwords in the lexical decision task. While additional research is needed to further probe this apparent early deficit in processing lexicality in those with AD, further research is also warranted to investigate if (and how) this deficit may be manifested behaviourally, as a slowing of RTs as was observed in lexical decision tasks.

7.4 The P3 Lexical Decision Oddball Task

One of the most important outcomes from this thesis has been to establish the viability of the lexical decision oddball task across different populations. Based on the ERP results from Manuscripts 2 and 3, it seems clear that there is a definite utility in combining the P3 oddball paradigm from the ERP attention and memory literatures with the classic lexical decision task. The lexical decision oddball tasks employed evoked a reliable P3, with rare stimuli having a more positive-going P3 component in comparison to the frequent trials. We propose that the P3, when evoked in any of our lexical decision oddball tasks, is a reflection of a successful early stage of lexical discrimination, i.e. the successful early categorization of a stimulus as being either a "word" or "not a word", which can be used by selective attention to quickly differentiate the lexical categories early in the course of lexical processing. Thus, this methodology allowed us to observe a lexicality distinction that reflected the readers' ability to create clear classes or categories of stimuli (word vs. "not a word"). This is clear because the salient rare stimuli evoked a robust P3 when these two categories of stimuli were presented much as is seen in any other P3 oddball task.

While both the classic behavioural lexical decision task and the ERP P3 oddball paradigm have been used successfully for many years and have contributed significantly to our current understanding of word recognition and attention respectively, the research from this thesis was novel and exciting because, by combining the two tasks to create the lexical decision oddball task and focusing on the traditional P3 analysis (i.e. the analysis between the rare/frequent conditions), we were able to identify an alteration in the word processing system in the AD group that had not been apparent when using the behavioural methodology alone.

7.5 Limitations

One potentially important limitation of this thesis involves the difference in the language background of our participant groups. The young adults in our studies were all recruited from the Univeristy of Kansas and were monolingual English speakers. In contrast, the older adults and individuals with AD were recruited in Montreal and, while they were dominant English speakers, most were bilingual or even multilingual. It is possible that the dfference in performance across the young and older groups (i.e. the high acceptance of pseudowords observed for the young adults but not for the agings groups) in the lexical decision task in Manuscript 1 may have been influenced by the difference in language background between the groups. Ideally, the variable, language backgrounds of the participants, should have been held constant. This disparity between the groups is now being rectified in a new study inverstigating lexicality in bilingual/multilingual young adults. However, it is worth noting that when looking at our ERP results, we observe a similar pattern in P3 response between the young and older adults, despite the difference in language ackground between these two groups. On the other hand, we observe a different pattern of P3 responses between the older adults and the individuals with AD, despite the similarity in language background between these two groups. These results suggest that language background may not be contributing to the group differences observed in the elicitation of the P3 component in our lexical decision oddball tasks.

Another potential limitation of this thesis concerns a modification we made when creating our novel oddball task. In a traditional P3 oddball task, participants are asked to attend to the rare stimulus type, and to answer either by responding "YES" when the rare stimulus is present or by counting how many rare stimuli they see in a given set of trials. However, had we followed this procedure, this would have meant that in half of the blocks (i.e. the blocks where words were the rare stimulus type: W-Nw and W-Ps) the correct answer to seeing a word would be "YES" but in the other half of the blocks (i.e. the blocks where nonwords or pseudowords were the rare stimulus type: Nw-W and Ps-W) the correct answer when seeing a word would be "NO". While the two healthy groups likely would not have had any difficulty in understanding and following this difference in response mapping between the blocks, it was less clear whether the individuals with AD would also be able to switch their response mapping between the blocks. Therefore, in order to simplify the task and to keep response mapping consistent between all of the lexical tasks in this thesis (behavioural and oddball lexical decision tasks) we decided to alter the procedure by asking our participants to always respond "YES" when they saw a word and "NO" when they saw a letter string that was not a word. However, it is possible that by making this change we may have affected the amplitude of our P3 results. Since we did not specifically ask participants to attend to the rare stimulus type in any of the blocks, it may be possible that the amplitude of our P3 components may have be attenuated compared to if we had asked participants to actively attend to the rare stimuli. However, since the oddball task is known to successfully elicit a P3 component even when participants are not asked to make any behavioural response (often referred to as the passive P3 paradigm) and given that we did observe significant P3 components in each of the three participant groups, we feel confident that this change in procedure was beneficial to our studies as it allowed us to use the task with individuals with AD.

7.6 Future Directions

7.6.1 Extending Recruitment

Given the potential confounding effects of bilingualism/multilingualism mentioned above, in the future we plan to recruit a new group of young adults from the Montreal area so that their language profiles will be more comparable to that of the older adults and individuals with AD from this thesis. Furthermore, we hope to also recruit groups of monolingual healthy older adults and individuals with AD from the Lawrence Kansas area (where the young adults were recruited) in collaboration with Dr. Ruth Ann Atchley, who was coauthor on the manuscripts for this thesis. The addition of these new groups will allow us to more closely examine if (and how) bilingualism/multilingualism versus monolingualism may be contributing to differences in processing lexicality across the adult lifespan and in AD.

7.6.2 Investigating New Populations with the P3 Lexical Decision Oddball Task

The P3 lexical decision oddball task has proven to be simple enough to administer with individuals with early AD and has yielded vital information regarding an alteration in processing lexicality in this vulnerable population. Given its relative simplicity to perform and its usefulness in both young and older healthy populations as well as in those with a cognitive impairment, this methodology can be of significant importance in the future since it allows us to track how people process lexicality across the adult lifespan. One very interesting application of this novel methodology would be to utilize this paradigm not to study factors related to stimulus characteristics, but instead to investigate the influence of individual differences. For example, previous research by Atchley, Haldermam and Buchanan (2003) suggests that individuals with dyslexia show a significant reduction in sensitivity to orthography/phonology in lexical processing and it would be very interesting to investigate this deficit with the P3 lexical decision oddball tasks discussed here. We would predict that individuals with dyslexia would show a robust P3 component in all four of our experimental blocks since they are not influenced by the orthographical/phonological legality of stimuli and can therefore more effectively attend to differences in lexical status between the stimuli.

Furthermore, this methodology could prove to be particularly revealing when used with individuals with aphasia and apraxia following acquired (stroke or traumatic brain injury) or neurodegenerative (primary progressive aphasia) conditions. Particularly in cases of apraxia or cognitive impairment, this methodology can provide insight into residual language abilities since the P3 component can be elicited even when no behavioral response is asked for, thus allowing the study of lexicality even in participants who cannot make a reliable overt response.

In addition, P3 lexical decision oddball tasks could be used to investigate potential changes in processing lexicality in individuals with mild cognitive impairment (MCI) who are in the transitional stage between the cognitive changes associated with normal aging and those associated with AD. Having MCI has been associated with a progression to AD at a significantly faster rate when compared to healthy aging adults. However, not all individuals who have MCI will convert to AD and little is known regarding which individuals with MCI will develop AD and which will remain in the benign MCI group (Kidd, 2008). Since many individuals with MCI have been reported to have language deficits that are comparable to those observed in individuals with AD (Taler & Phillips, 2008), it is possible that a deficit in processing lexicality may also be present in these individuals. Investigating potential changes in P3 response when processing lexicality in this vulnerable population can potentially contribute to a differentiation between healthy aging and early dementia which would allow for the better identification of the most at-risk MCI individuals and contribute to the early diagnosis of Alzheimer's disease and permit earlier treatment options.

7.6.3 Investigating New Stimuli Comparisons with the P3 Lexical Decision Oddball Task

The P3 lexical decision oddball task can also be used to investigate new linguistic stimuli comparisons. In order to complement our behavioural findings from Manuscript 1, our ERP task could be used to compare low N and high N pseudowords and words. Furthermore, in order to help disentangle the effects of orthography versus phonology we could compare pseudohomophones (such as "brane" which do not have an orthographic representation but do have a phonological representation) and pseudowords (which have neither an orthographic nor a phonological representation) and words (that have both an orthographic and a phonological representation).

7.6.4 Investigating Lexicality Effects and Sensitivity to Orthographic/Phonology

While the lexical decision oddball tasks were instrumental in showing a difference in sensitivity to phonological/orthographic legality between the older adults and those with AD early in the course of lexical processing, our tasks were designed specifically to elicit the P3 component and consequently we employed a 20/80 ratio of rare to frequent stimuli. While the oddball task is the ideal experimental task to elicit the P3 component, it does not easily permit us to investigate other ERP components that may reflect orthographic/phonological processing or the attempt to access meaning from a string of letters. One possible way to further investigate the extent to which older adults and individuals with AD are sensitive to orthography/phonology could be to investigate the N350 component using a traditional 50/50 ratio of word and word-like stimuli. This component has been linked to phonological processing (Ruz and Nobre, 2008;

Spironelli & Angrilli 2007; Spironelli & Angrilli, 2009; Spironelli, Penolazzi & Angrilli, 2010) and has been proposed to distinguish between pronounceable and non-pronounceable stimuli since it is elicited only by orthographically/phonologically legal stimuli (Bentin et al., 1999) in healthy young adults. Furthermore, in order to continue to probe differences in processing words, pseudowords, and nonwords in the aging groups we could investigate the N400 component. Studies conducted with young adults using lists of words, nonwords and pseudowords presented in isolation (i.e. in a lexical decision task) have shown that the N400 is sensitive to lexical properties of letter strings. While words and pseudowords both elicit a N400 component, words elicit smaller N400s than pseudowords. In contrast, nonwords do not elicit the component (Swaab, Leroux, Camblin, & Boudewyn, 2012).

7.7 Conclusion

This novel area of research has contributed to a clearer understanding of one specific aspect of visual lexical processing, namely processing lexicality, that appears be sensitive to disruption by neurodegeneration caused by the AD disease process. The ERP results from our study point to a linguistic alteration, at the level of processing lexicality, which is beginning to become apparent in the early stage of AD. While AD is often considered to be a disease affecting memory, a better understanding of the underlying linguistic abilities and disabilities of individuals with AD can help to provide a more comprehensive and well-rounded understanding of AD that can complement what is already much better understood in the domain of memory and other areas of cognition.

The results of this study have both theoretical and clinical implications. We propose that the observed alteration in P3 performance that was found in those with AD, in combination with other linguistic/cognitive markers, shows promise in highlighting differences between healthy aging and early dementia that may potentially contribute to the early diagnosis of Alzheimer's disease. According to the 2009 World Alzheimer's report (Prince and Jackson, 2009), one of the principal goals of dementia management and care is an early diagnosis. The early and accurate detection of AD is essential in order to provide a proper plan of treatment. It allows for prognostic information and counselling to be provided to individuals with AD and their family members (Camicioli, 2006) and permits the involvement of patients in decision making and planning for their future care (Forster, 2006). Furthermore, an early diagnosis can also allow a person with the disease to benefit from available treatment options, including the possibility of a pharmacological intervention. This is particularly important given that early interventions, pharmacological interventions in particular, can improve memory impairments and other cognitive symptoms (Borson, Frank, Bayley, Boustani, Dean, et al., 2013) and could thus delay hospitalization thereby improving the quality of life of individuals with AD.

Furthermore, knowledge obtained regarding how the ability to process lexicality is altered in this population may be used in the future to inform models of word recognition. Given that current models of word recognition are mostly based on the performance of healthy young adults, information regarding how older individuals and those with AD process lexicality is also necessary to ensure that these models accurately represent the process as people age. These insights can also then be used by clinicians to help guide language therapy options that can capitalize on abilities that are preserved and target those that are known to be more susceptible to become impaired in those with AD. Although it is understood that language intervention will not stop the progression of the neurological degeneration that is caused by AD, any delay in the deterioration of linguistic abilities or improvement brought about by language therapy that has been designed to address the specific deficits observed in individuals with AD has the potential to greatly affect the person's quality of life.

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