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**The nature of semantic memory deficits in Alzheimer's disease:
Evidence from event-related brain potentials and reaction time measures**

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A Thesis

in

The Department

of

Psychology

**Presented in Partial Fulfilment of the Requirements
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Abstract

Sarah Auchterlonie

The nature of semantic memory deficits in Alzheimer's disease:

Evidence from event-related brain potentials and reaction time measures

Semantic memory impairment is commonly observed in patients with dementia of the Alzheimer type (DAT); however the nature of the impairment is unclear. Some researchers argue that the deficit is a loss of information within semantic memory; whereas others argue that semantic memory impairment may result from a failure to access available information. The goal of this study was to investigate the nature of semantic memory deficits in patients with DAT. Reaction time (RT) and the N400 event-related brain potential (ERP) were measured in a word-picture semantic priming paradigm. Age-related changes in semantic priming were assessed by comparing young and elderly adults; differences due to DAT were assessed by comparing elderly adults and DAT patients. For patients, pictures were classified as a function of the individual's naming ability to determine whether naming deficits reflected a failure to access a picture's name or a deterioration of its semantic representation. As expected, the young and elderly showed robust priming effects for both RT and ERP measures. DAT patients showed significant RT priming for named stimuli, yet no RT priming for unnamed stimuli. For ERP priming effects, the patient group was heterogeneous, with some patients showing ERP priming and others not. The results are discussed in terms of the access failure and deterioration hypotheses of semantic memory deficits in dementia of the Alzheimer type.

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Table of Contents

| | |
|---|-----|
| List of Figures | vii |
| List of Tables | x |
| Introduction | 1 |
| Method | 21 |
| Participants | 21 |
| Materials | 24 |
| Procedure | 27 |
| Results | 34 |
| Naming Data | 35 |
| Event-Related Potential Data | 35 |
| Behavioural Data | 50 |
| Neuropsychological Data | 69 |
| Discussion | 79 |
| References | 93 |
| Appendix A: Health Screening Questionnaire | 105 |
| Appendix B: Education Level and Occupational Ranking | 109 |
| Appendix C: Consent Form for Young and Elderly Adults | 112 |
| Appendix D: Consent Form for DAT Patients | 115 |
| Appendix E: Example of Picture Stimuli | 118 |

| | |
|---|-----|
| Appendix F: Example of Word Stimuli | 119 |
| Appendix G: List of Picture Stimuli with Word Primes | 120 |
| Appendix H: Average ERP Waveforms for DAT Primers | 126 |
| Appendix I: Average ERP Waveforms for DAT Non-Primers | 132 |

List of Figures

| | |
|--|----|
| 1. Layout of Electrodes | 30 |
| 2. Time Course of Stimulus Presentation | 32 |
| 3. Performance on Confrontational Naming Task for Young Adults, Elderly Adults, and DAT Patients | 36 |
| 4. ERP Grand Average Waveforms of Word Primes for Named Stimuli at the Parietal Midline Site (Pz) for Young Adults | 37 |
| 5. ERP Grand Average Waveforms of Word Primes for Named Stimuli at the Parietal Midline Site (Pz) for Elderly Adults | 38 |
| 6. ERP Grand Average Waveforms of Word Primes for Named Stimuli at the Parietal Midline Site (Pz) for DAT Patients | 39 |
| 7. ERP Grand Average Waveforms of Word Primes for Unnamed Stimuli at the Parietal Midline Site (Pz) for DAT Patients | 40 |
| 8. ERP Grand Average Waveforms for Named Pictures Preceded by Related and Unrelated Words at the Parietal Midline Site (Pz). a) Young Adults; b) Elderly Adults | 43 |
| 9. ERP Grand Average Waveforms for Named Pictures Preceded by Related and Unrelated Words at the Parietal Midline Site (Pz). a) Elderly Adults; b) DAT Patients | 45 |
| 10. ERP Grand Average Waveforms for Named Pictures Preceded by Related and Unrelated Words at the Parietal Midline Site (Pz). a) DAT Primers; b) DAT Non-Primers | 48 |
| 11. ERP Grand Average Waveforms for Named Pictures Preceded by Related and Unrelated Words at the Parietal Midline Site (Pz). a) DAT Patients (Named Stimuli); b) DAT Patients (Unnamed Stimuli) | 49 |
| 12. ERP Grand Average Waveforms for Named Pictures Preceded by Related and Unrelated Words at the Parietal Midline Site (Pz). a) DAT Primers (Named Stimuli); b) DAT Primers (Unnamed Stimuli) | 51 |

| | |
|---|----|
| 13. ERP Grand Average Waveforms for Named Pictures Preceded by Related and Unrelated Words at the Parietal Midline Site (Pz). a) DAT Non-Primers (Named Stimuli); b) DAT Non-Primers (Unnamed Stimuli) | 52 |
| 14. Number of Omitted Trials for Named Stimuli for Young Adults, Elderly Adults, and DAT Patients | 54 |
| 15. Number of Omitted Trials for Named and Unnamed Stimuli for DAT Patients | 55 |
| 16. Percent Correct for Named Stimuli for Young Adults, Elderly Adults, and DAT Patients | 57 |
| 17. Percent Correct for Named Stimuli for Elderly Adults, DAT Primers, and DAT Non-Primers | 58 |
| 18. Percent Correct for Named and Unnamed Stimuli for DAT Patients | 60 |
| 19. Percent Correct for Named and Unnamed Stimuli. a) DAT Primers; b) DAT Non-Primers | 61 |
| 20. Reaction Time for Named Stimuli for Young Adults, Elderly Adults, and DAT Patients | 63 |
| 21. Reaction Time for Named Stimuli for Elderly Adults, DAT Primers and DAT Non-Primers | 65 |
| 22. Reaction Time for Named and Unnamed Stimuli for DAT Patients | 67 |
| 23. Reaction Time for Named and Unnamed Stimuli. a) DAT Primers; b) DAT Non-Primers | 68 |
| 24. Performance on Mini-Mental Status Examination (MMSE) for Young Adults, Elderly Adults, and DAT Patients | 70 |
| 25. Performance on Mini-Mental Status Examination (MMSE) for DAT Primers and DAT Non-Primers | 71 |
| 26. Performance on Boston Naming Test (BNT) for Young Adults, Elderly Adults, and DAT Patients | 72 |

27. Performance on Boston Naming Test (BNT) for DAT Primers and DAT
Non-Primers74

28. Performance on the Phonemic Fluency Task (Letters F, A, and S) for
Young Adults, Elderly Adults, and DAT Patients75

29. Performance on the Phonemic Fluency Task (Letters F, A, and S) for DAT
Primers and DAT Non-Primers76

30. Performance on the Semantic Fluency Task (Category: Animals) for
Young Adults, Elderly Adults, and DAT Patients77

31. Performance on the Semantic Fluency Task (Category: Animals) for
DAT Primers and DAT Non-Primers78

List of Tables

| | |
|--|----|
| 1. Average Demographic Data for the Young Adults, Elderly Adults, and DAT Patients | 22 |
| 2. Average Values and T-tests for Word Attributes as a Function of Condition | 26 |
| 3. Average Demographic Data for the DAT Primers and DAT Non-Primers | 46 |

Semantic memory is the component of long term memory which concerns our knowledge about the meaning of words, objects, and concepts (Patterson & Hodges, 1995). The semantic memory for the concept of a kangaroo, for example, might include knowledge that it is a brown animal that lives in Australia, carries its young in a pouch, and jumps around. In contrast to episodic memory, information held in semantic memory is no longer defined by particular events (Tulving, 1983). Thus, to remember the above-mentioned facts about the kangaroo, it is not necessary to remember when and how such information was learned.

Examples of semantic memory tasks include: naming line drawings or objects, answering general knowledge questions, defining words, and generating category exemplars. In a recent study assessing how memory changes as a function of age, a variety of episodic and semantic memory tests were administered to participants ranging in age from 35 to 80 years old (Nyberg, Bäckman, Erngrund, Olofsson, & Nilsson, 1996). Results showed that whereas age was a significant predictor of performance for episodic tests, it did not explain any variance in performance for the semantic tests. Hence, Nyberg and his colleagues reported that, when background variables such as years of education and blood pressure were controlled for, there were no age effects in semantic memory.

In examining semantic memory and aging, Kausler (1991) cites evidence that on measures of vocabulary, general knowledge and picture naming, elderly adults

perform similarly to younger adults. Hence, it seems that the ability to perform semantic memory tasks generally remains stable across adulthood.

Advances in understanding the processes involved in semantic memory can be achieved by researching disorders in which semantic memory is affected. Dementia of the Alzheimer type (DAT) is a degenerative brain disorder that eventually affects virtually all aspects of a person's life. One of the hallmark symptoms for patients with DAT is an impairment in semantic memory (Salmon, Butters, & Chan, 1999; Tippett, Grossman, & Farah, 1996).

As part of a longitudinal project, Weingartner and colleagues assessed patients both before and after the presumed onset of Alzheimer's disease (Weingartner, Kawas, Rawlings, & Shapiro, 1993). Results from this study showed that changes in semantic memory were apparent in patients with DAT before other clinically relevant symptoms, and these deficits worsened as the disease progressed. Given that there are changes in semantic memory for patients with DAT which are not apparent in healthy elderly individuals, testing patients with DAT should yield important information about the nature of semantic memory. For example, understanding how semantic memory progressively breaks down in Alzheimer's disease can shed light on how this type of memory is structured, and perhaps how it is resilient in normal aging.

Naming impairment is a common feature of Alzheimer's disease (Hodges,

Patterson, Graham, & Dawson, 1996; Gainotti, Di Betta, & Silveri, 1996). Patients with DAT are markedly impaired at confrontational naming tasks, that is, naming various objects or line drawings (Ralph, Patterson, & Hodges, 1997; Shuttleworth & Huber, 1988; Chertkow, Bub, & Seidenberg, 1989).

It has been suggested that the ability to name an item is dependent upon having semantic knowledge of that item. Hodges and colleagues (1996) investigated the relation between naming ability and semantic information by asking DAT patients to name and generate definitions of line drawings. Results revealed that patients with DAT generated definitions for unnamed items that were significantly less complete and specific than definitions generated for named items. Hodges et al. concluded that the findings from this study support the hypothesis that successful naming requires intact semantic knowledge.

The type of naming errors that patients with DAT make has also been investigated. Hodges, Salmon, and Butters (1991) classified the errors produced by patients with DAT on a confrontational naming task into three categories: non-responses, visually-based errors, and semantically-based errors. A visually-based error occurred when an object was misperceived and consequently misnamed (e.g., naming a pretzel as a snake). Semantically-based errors included naming another item from the same category (e.g., naming an apple as a grapefruit) or naming the superordinate category (e.g., naming animal instead of pig). Patients with DAT had

significantly more semantically-based errors than visually-based errors, suggesting that the naming deficit is one involving semantic memory.

Although there have been many studies on semantic memory impairments in Alzheimer's disease, the nature of the impairment remains unclear. Some researchers believe that the deficit is a loss of information within semantic memory (Hodges, Salmon, & Butters, 1992; Chertkow & Bub, 1990; Grossman, Mickanin, Robinson, & D'Esposito, 1996). Other researchers, however, believe that the semantic memory impairment may result from a failure to access available information (Nebes & Brady, 1989, 1991; Chenery, 1996; Hamberger, Friedman, Ritter, & Rosen, 1995).

Warrington and Shallice (1984) have suggested the following criteria to clearly distinguish loss of semantic knowledge from an inability to retrieve the information. First, there should be consistency of failure to access a particular item across a number of different tests and test sessions. Therefore, if an item cannot be named, nor can a general knowledge question be answered, it is more likely that information about that item is lost. Second, there should be a loss of specific knowledge of an item, but preserved superordinate knowledge. It is assumed that semantic knowledge may be hierarchically organized; thus information should be lost in a bottom up fashion, with specific knowledge deteriorating first. Finally, there should be no benefit from semantic cueing in accessing the item. Hence, if

semantic cues do not aid in accessing information, then this provides further evidence that the information is lost.

Hodges et al. (1992) tested patients with DAT using the criteria proposed by Warrington and Shallice. They administered a battery of tests including the following tasks. The sorting task involved subjects sorting items into global categories (i.e., living item vs. man-made item), superordinate categories (i.e., land animal vs. sea animal), and subordinate categories (i.e., large animal vs. small animal). The confrontational naming task required participants to name line drawings. The verbal definitions test instructed participants to produce accurate descriptions of various objects. For the category fluency test, subjects were given a specific category (i.e., vegetables, animals, etc.) and were asked to generate as many exemplars as possible in a given time period. Results of these tests showed a consistency in item-to-item performance, in that if a DAT patient was unsuccessful in responding to an item on one test, the patient was likely to be unsuccessful with the same item across many tests. Evidence that patients with DAT have lost specific knowledge of items came from the category fluency test. DAT patients were able to sort items into global categories and were only mildly impaired at sorting items at the superordinate level. For subordinate categories, however, patients were markedly impaired; they could not sort items on the basis of specific attributes. Hodges et al. (1992) concluded that the pattern of results obtained from the battery

of tests supported the hypothesis that there is a deterioration of the semantic network in Alzheimer's disease.

Using multidimensional scaling and Pathfinder analyses, Chan and colleagues assessed the semantic networks in patients with DAT (Chan, Butters and Salmon, 1997). In this study, mild, moderate, and severely demented patients were compared with age-matched healthy adults. Participants were asked to complete a triadic comparison task and a word-picture matching task. Each trial for the triadic comparison task involved showing participants a sheet with three animal names positioned in the form of an equilateral triangle. For this task, the participant was to indicate the two animals that were most alike. The word-picture matching task consisted of matching labels with the name of each animal to the correct drawing. As compared to elderly controls, results showed that DAT patients relied less on abstract attributes, such as domesticity, for categorizing concepts. In addition, the number of associative links that the patients' network shared in common with the controls decreased as the severity of dementia increased. Finally, the number of links in the network increased with the severity of dementia. These results suggest that semantic networks in patients change and become less similar to controls as the disease progresses. Chan et al. argue that individuals with intact semantic knowledge have fewer connections because information is clearly and concisely organized. They hypothesized that the increased number of links in the DAT patients' networks were

suggestive of loss of semantic knowledge, in that concepts are organized in a more chaotic way, with many connections. The authors concluded that the results from this study provide evidence that the structure of semantic knowledge deteriorates in a systematic manner throughout the progression of Alzheimer's disease.

In contrast, other investigators propose that the deficit in semantic memory for patients with DAT results from an inability to retrieve available information. Nebes and Brady (1991) argue that although patients can be impaired on a wide variety of tasks, they are not impaired on all tasks. Nebes and Brady postulate that impairment on certain tasks is due to the nature of the task, namely tasks that require a substantial amount of attention and effort. If a task requires less attention and is more automatic, then patients with DAT can demonstrate intact semantic knowledge. Therefore, the access viewpoint argues that it is the type of task that influences whether or not patients with DAT are successful.

Nebes and Brady claim that an automatic task, such as one involving semantic priming, can show intact semantic processes for patients with DAT. Semantic priming experiments are created under the assumption that semantic memory is organized as a complex network of associated concepts (Collins & Loftus, 1975). Concepts that have similar properties are more strongly associated with each other than those that share less in common. Under this assumption, the concepts 'table' and 'chair' should be strongly connected, for they both have four legs, are furniture,

and can be made out of the same materials. In contrast, the concepts 'table' and 'apple' should have a weak connection for they have no semantic features in common. A semantic priming experiment assumes, for example, that the word 'table' should be processed more quickly if it were preceded by the word 'chair' (i.e., because of the strong associations) than if it had been preceded by the word 'apple'. Priming experiments have frequently employed lexical decision tasks (LDT). In a LDT, for example, a subject has to decide whether a string of letters (i.e., the probe) is a word. Studies have shown that if the probe is related to the preceding word or sentence then reaction time is faster than if the probe was unrelated to the previous context (Meyer & Schvaneveldt, 1976). Semantic priming experiments have used various stimuli including word pairs, sentences, and pictures (Neely, 1991).

Nebes and Brady (1991) showed young controls, elderly controls, and DAT patients sentences where the last word was missing. Participants then had to decide whether a presented word was a suitable ending to the sentence. The sentences varied in the level of semantic context constraint. A low context constraint sentence, for example, was "Bill reached in his pocket to get a", whereas an example of a high constraint sentence was "The hunter shot and killed a large....". For low constraint sentences there are many possibilities for the final word (i.e., quarter, handkerchief, gun, etc.). In contrast, high constraint sentences do not have many possible sentence endings (i.e., deer, moose). Results showed that the DAT patients

were significantly slower in responding than both the young and elderly control groups, while, the young and elderly did not differ significantly from each other. The degree of constraint greatly influenced the response time, in that the young and elderly controls responded most quickly to terminal words of high constraint sentences. This was also true for patients with DAT, showing that the level of semantic context present in the sentences influenced their performance. Nebes and Brady concluded that these findings show that patients are capable of using semantic information in an automatic task, such as semantic priming, which does not require great effort.

In a recent review of the priming literature for patients with DAT, Ober and Shenaut (1995) also support the access viewpoint. They believe that when patients with DAT engage in tasks that require less attention, results show that patients do have intact semantic memory processes.

In support of the access viewpoint, some studies have shown that for patients with DAT, priming is comparable to that in elderly controls (Gabrieli, Keane, Stanger, Kjelgaard, Corkin, & Growdon, 1994; Fleischman, Gabrieli, Reminger, Vaidya, & Bennett, 1998; Ober, Shenaut, & Reed, 1995; Hartman, 1991). Others have found that priming occurs with patients with DAT, but to a lesser degree than found in elderly controls (Beatty, English, & Winn, 1998; Silveri, Monteleone, Burani, & Tabossi, 1996).

Semantic priming experiments involving patients with DAT, however, have not yielded consistent results. Some studies showed no priming in patients with DAT (Salmon, Shimamura, Butters, & Smith, 1988; Burke, Knight, & Partridge, 1994). In contrast, hyperpriming has been found in some studies with patients with DAT (Chertkow, Bub, & Seidenberg, 1989; Balota & Duchek, 1991). Hyperpriming occurs when individuals show increased priming effects relative to another group.

In most experiments, priming is measured by response speed such as reaction time (RT) during a lexical decision task or naming task. In such studies, this is the only available indicator as to whether or not priming has occurred, and to what extent. One drawback to these traditional behavioural measures is that they require overt responding. Elderly individuals may have more difficulty with fine motor activity; in addition, there may be an overall slowing in motor control. Hence, differences in overt responding, such as those measured by reaction time, may not be a true measure of mental processing speed.

An alternative to these measures which could yield additional information about semantic priming are event-related potentials (ERPs). ERPs are a valuable, non-invasive tool that measure electrical activity of neural tissue recorded at the scalp. From the recording of ongoing brain activity known as the electroencephalogram (EEG), ERPs are derived by isolating time-locked responses

to a particular event (Coles & Rugg, 1995). ERPs can be positive or negative deflections and are elicited in response to the presentation of a stimulus (Ridderinkhof & Bashore, 1995). An ERP component is measured by the amplitude in microvolts (μV) and latency in milliseconds (ms) relative to stimulus onset. Understanding of the strength and timing of different stages of cognitive processing can be gained by examining various ERP components (Coles & Rugg, 1995). Hence, ERPs can measure internal psychological or cognitive processes which may not be detected through behavioural methods. Unlike behavioural measures such as reaction time or accuracy, ERPs do not necessarily require an overt response by the subject. This is advantageous, for it allows the examination of cognitive processes in real time (i.e., as they occur), without the possible obtrusiveness of tasks required by behavioural measures. Tasks requiring behavioural responses can also be criticized for not being ecologically valid. For example, the LDT is a task that subjects do not experience in everyday life when reading sentences or words. ERPs can circumvent this problem by measuring automatic responses to stimuli, regardless of how natural or artificial the task.

One ERP component that can yield important information about semantic processing is the N400. The N400 occurs at approximately 400 ms after stimulus onset and is negative in amplitude. N400 amplitude varies inversely with semantic priming; that is, it is elicited by non-primed or unexpected stimuli. The N400 was

first described in 1980 by Kutas and Hillyard. In a semantic priming experiment, sentences that varied in word endings were presented to subjects. In some sentences the final word was semantically deviant (e.g., “He spread the warm bread with *socks*”). In other sentences the final word was semantically correct but was presented in a large letter size (e.g., “She put on her high heeled **SHOES**”). To serve as a baseline measure, other sentences were presented that were neither semantically nor physically deviant (e.g., “It was his first day at work”). Results of this study showed a large negative deflection with a latency of about 400 ms after stimulus onset for the semantically deviant sentences. This component was much smaller for the physically deviant sentences and the normal sentences. This study and subsequent work demonstrated that the N400 reflects processes that are semantic in nature (Kutas & Van Petten, 1988). A surprise ending is not sufficient to elicit the N400, as evidenced from the physically deviant condition where the N400 was small in amplitude. The N400 was elicited when the sentence ending was semantically inappropriate, indicating that this ERP component is a sensitive marker for semantic processing.

Since the landmark study by Kutas and Hillyard, many studies have replicated the occurrence of the N400. The N400 has been elicited by the last word of a sentence when it was semantically unrelated to the previous sentence context (auditory: Connolly & Phillips, 1994; visual: Connolly, Phillips, & Forbes, 1995).

It has also been elicited in word pairs for the target words that were preceded by semantically unrelated words (Harbin, Marsh, & Harvey, 1984; Neville, 1985). The N400 has also been elicited in studies using faces (Bobes, Valdes-Sosa, & Olivares, 1994), and pictures (Barrett & Rugg, 1990; Holcomb & McPherson, 1994).

Over the last few years, a limited number of studies have used the N400 to study semantic memory impairments with patients with DAT (Hamberger et al., 1995; Schwartz, Kutas, Butters, Paulsen, & Salmon, 1996; Iragui, Kutas, & Salmon, 1996; Ford et al., 1996; Castaneda, Ostrosky-Solis, Perez, Bobes, & Rangel, 1997; Ostrosky-Solis, Castaneda, Perez, Castillo, & Bobes, 1998; Revonsuo, Portin, Juottonen, & Rinne, 1998; Ford et al., 2001) and have yielded inconsistent results.

Hamberger and colleagues (1995) reported priming as measured by N400 amplitude in patients with DAT. Participants were presented visually with sentences and asked to make a sense/nonsense decision to the terminal words of each sentence. Each sentence was a highly constrained sentence (e.g., “The guard sounded the...”). The terminal words varied in relatedness to the sentence, from a best completion ending (e.g., “The guard sounded the *alarm*”), to an unrelated/nonsense ending (e.g., “The guard sounded the *molars*”). ERPs were recorded to the terminal word of each sentence. Results showed that the N400 amplitude increased as terminal words were decreasingly primed by the sentence context. Results were similar in young controls and patients with DAT, indicating that the patients benefitted from

the semantic constraints present in sentences and the relatedness of the terminal words. The patients' ERPs showed better discrimination between different stimulus types than did their behavioural responses, in that the patients made a significant number of errors in making sense/nonsense judgements. This result led Hamberger et al. to conclude that disruption in semantic processing must occur after the N400 is generated, but before the behavioural response.

Schwartz et al. (1996) also demonstrated electrophysiological priming effects in DAT. Participants heard the name of a category, which was said aloud by the experimenter, then the name of an object appeared on a monitor. The participant's task was to decide whether or not the object was part of the category named. ERPs were recorded to the visual presentation of the related or unrelated words. Results showed that patients with DAT showed priming effects; however, they showed smaller priming effects (i.e., reduced N400 amplitudes) as compared to the elderly controls, who, in turn, showed smaller priming effects than the young controls.

In contrast, no N400 priming was observed by Iragui et al. (1996) who compared young and elderly controls and patients with DAT. All participants listened to a context phrase (e.g., a musical instrument) followed by visual presentation of a target word. The target word was either congruent (e.g., piano) or incongruent (e.g., skull) to the context phrase. Results showed that in the elderly control group the N400 was reduced in amplitude and delayed in latency relative to

the young control group. In the patients with DAT, the N400 effect was delayed and flatter in amplitude as compared to young and elderly controls. Results comparing congruent and incongruent conditions for patients with DAT showed no significant difference in amplitude, indicating that no reliable priming effects occurred.

Ford and her colleagues (1996) also found no N400 priming effects. Participants listened to sentences that ended with a final word that was either congruent or incongruent to the sentence context. ERPs were recorded to the final word of each sentence. As expected, in the young and elderly control groups the N400 effect was large to nonprimed words (i.e., incongruent word endings) and small to primed words (i.e., congruent word endings). Results showed, however, that for patients with DAT, the N400 was large in amplitude for both primed and non-primed words. The absence of a smaller N400 for the primed words showed that patients did not benefit from congruent word endings, thus suggesting an impairment of semantic knowledge.

Other studies have not found priming effects. In two similar picture priming studies (Casteneda et al., 1997; Ostrosky-Solis et al., 1998) participants were presented visually with congruent and incongruent picture pairs. For each picture pair, ERPs were recorded to the onset of the second picture. Results showed that young and elderly controls showed ERP priming effects. Patients with DAT,

however, did not show a priming effect. Upon further analysis, it was determined that in the primed condition (i.e., congruent pairs) there was no difference in N400 amplitude between patients with DAT and young and elderly controls. Differences were only found in the non-primed condition (i.e., incongruent pairs), in that the N400 amplitude was significantly reduced in patients with DAT as compared to both young elderly controls. Hence, the lack of priming effect in the DAT patients could be explained by the reduced N400 amplitude for the incongruent pairs.

In a Finnish study, Revonsuo and colleagues (1998) did not show priming effects. Participants listened to semantically congruous and incongruous sentences and had to decide if the sentence was either “ordinary and sensible” or “unusual and senseless”. Results showed that for patients with DAT, the amplitude of the N400 was similar for both semantically congruous and incongruous sentences. In trying to explain inconsistent results in studies involving the N400 and patients with DAT, Revonsuo and colleagues (1998) postulate that there seems to be a tendency that severely demented DAT patients are more likely to have a reduced N400 amplitude. Evidence for this hypothesis is difficult to find, however, since in most studies specific data on level of dementia is limited. Most studies report an overall clinical dementia rating range for the group; information on dementia rating for individual patients is not usually reported. Other explanations the authors suggested for the differing results included: differences in tasks employed, stimulus presentation, and

modality across the different studies.

Ford and colleagues (2001) conducted the most recent study investigating patients with DAT using ERPs. In a picture-word priming experiment, the participant's task was to indicate with a button press whether or not the word matched the previous picture. The word was either a match (i.e., word was the name of the picture) or a non-match (i.e., word was from the same semantic category as the picture). A week prior to ERP testing, patients' confrontational naming ability was assessed, hence trials for the ERP study were sorted into named and unnamed pictures. Results suggested that patients with DAT showed ERP priming for both named and unnamed pictures. Ford and colleagues stated that these results provided evidence of preserved knowledge in patients with DAT, since patients also showed priming for pictures they could not originally name (i.e., suggesting that information about unnamed items had not deteriorated completely).

It has been suggested that there is considerable overlap in the processing of pictures and words (Margolin, Pate, & Friedrich, 1996; Pratarelli, 1994). There seems to be controversy as to whether pictures can prime words (Margolin et al., 1996; Bajo, 1988); however, the latest study conducted by Ford and colleagues (2001) seems to provide evidence that pictures can prime words. Nevertheless, previous research has shown that words can prime pictures (Phillips, Auchterlonie, & Chertkow, 2000; Bajo, 1988; Irwin & Lupker, 1983).

One of the advantages of the Ford et al. (2001) study is that trials were separated as a function of naming ability. This is important, as there is still debate as to whether a naming deficit reflects an impairment in object recognition due to semantic memory loss, or an impairment in word retrieval (Thompson-Schill, Gabrieli, & Fleischman, 1999).

The present study also evaluated the semantic degradation versus access failure hypothesis in Alzheimer's disease using the N400. The following predictions were made. If patients with DAT failed to name a picture due to an impairment in word retrieval from an otherwise intact semantic representation, then such pictures should be primed when preceded by a related concept. If, on the other hand, the naming failures are due to an impairment in the semantic representation of the concept, then incomplete or no priming should result. In this study, confrontational naming ability was first assessed in patients with DAT. As in previous research, it was expected that patients with DAT would be able to name some items and not others (Salmon et al., 1999; Bayles, Tomoeda, & Trosset, 1990; Shuttleworth & Huber, 1988). Pictures from the naming task were then used in a word-picture semantic priming task.

Pictures were preceded either by a related word or an unrelated word. A promising approach to studying and understanding cognitive processes involved in memory is to combine electrophysiological measures of brain activity with traditional

behavioural measures (Dunn, Dunn, Languis, & Andrews, 1998). Hence, in this study ERP and behavioural measures such as reaction time were recorded. For each participant, electrophysiological responses to pictures were sorted and examined on the basis of whether or not each picture had been successfully named during the confrontational naming task. Priming was expected to occur in the related condition as demonstrated by a smaller N400 amplitude relative to the unrelated condition. For each trial, participants were also asked to make a decision as to whether the word and picture were related or unrelated to each other.

Differences due to semantic memory deficits were investigated in this study by comparing healthy elderly adults to patients with DAT. This study also compared young and elderly adults to assess changes in priming as seen in normal aging. From previous research, it was expected that both young and elderly adults would both show priming effects (Ostrosky-Solis et al., 1998; Phillips et al., 2000).

For all participants, it was expected that for the named items the N400 would be largest in amplitude for the unrelated (non-primed) condition. The differing patterns of results were expected for the unnamed items for the patients with DAT. The uniqueness of this study is that any results obtained would yield interesting information.

If the patients with DAT showed priming effects for pictures that were both named and unnamed (smaller N400 amplitude in the related condition than in the

unrelated condition), then it could be concluded that semantic priming took place for the unnamed items. This would provide evidence for the access failure viewpoint because the patients were able to access semantic representations of pictures that could not be named.

On the other hand, if patients did not show priming for the unnamed pictures, this would provide evidence for loss of semantic knowledge. If this were the case, then for unnamed items, the N400 amplitude would be similar for both the related and unrelated conditions. In other words, the patients with DAT would not benefit from the semantic relatedness of the word to the picture, showing that the underlying semantic structure of the unnamed items is impaired. If this pattern were found, then it would support the deterioration viewpoint.

Method

Participants

Three groups of subjects were tested: 15 young adults, 15 elderly adults, and 9 patients with DAT. Three of the elderly adults were replaced: one individual was replaced due to their performance on the picture naming task being similar to the patient group, the other two participants did not understand the behavioural task during the word-picture priming experiment. The young adults were recruited mainly from undergraduate classrooms at Concordia University and through word of mouth. The elderly adults were recruited both from an advertisement placed in a local newspaper and a subject pool from the laboratory of Dr. Phillips. The young and elderly adults were given a health and language screening questionnaire that was administered over the telephone (see Appendix A). Inclusion criteria for the young and elderly groups included proficiency in English, self-reported good health and no prior history of heart disease, alcoholism, head injury, or other major medical illness which might influence cognitive functioning. The young and elderly groups each consisted of 7 males and 8 females. Mean years of education and age are shown in Table 1. For years of education, there was no significant difference between the young and elderly groups, $t(27) = .08$, $p = .93$.

The patients with DAT were recruited from the Memory Clinic at the Jewish General Hospital (a tertiary-care facility). Patients met criteria for possible or

Table 1

Average Demographic Data for the Young Adults, Elderly Adults, and DAT Patients

| | Age | Education |
|----------------|---------------|---------------|
| Group | (<u>SD</u>) | (<u>SD</u>) |
| Young Adults | 24.4 | 15.1 |
| | (4.60) | (1.82) |
| Elderly Adults | 70.7 | 15.0 |
| | (5.68) | (2.70) |
| DAT Patients | 79.3 | 10.8 |
| | (4.24) | (3.70) |

probable diagnosis as defined by the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's Disease and Related Disorders Association (ADRDA) Work Group (McKhann et al., 1984). The DAT patients had a dementia of mild to moderate rating (i.e., a Clinical Dementia Rating [CDR] score of 0.5 to 1.0). The group of DAT patients consisted of 4 males and 5 females. Table 1 shows the mean years of education and age of the patient group. A statistically significant difference of age was found between the elderly adults and patients with DAT, $t(22) = -3.95$, $p < .001$; on average, the DAT patients were older than the elderly adults. In addition, a significant difference in years of education was also found between the two groups, $t(22) = 3.23$, $p = .004$; the elderly group, on average had more years of education than the DAT patient group.

Appendix B shows the years of education and, where available, the occupation for each elderly adult (see Table B1) and DAT patient (see Table B2). In addition, a Hollingshead numeric value was assigned; the Hollingshead index (Hollingshead, 1975) is an ordinal scale for ranking occupations. For each occupation a numeric value ranging from 1 to 7 can be assigned. The scale is hierarchical, with lower numbers representing higher level occupations. For example, a value of 1 is given to occupations such as high executives, major professionals; whereas a value of 7 is given for unskilled occupations such as janitors,

and attendants. The elderly group obtained an average ranking of 3.13 (SD = 1.46), and the DAT patient group received an average ranking of 3.14 (SD = 0.90). T-tests revealed no significant differences in ranking for occupational level between the two groups, $t(20) = -0.02$, $p = .99$.

Materials

Two separate consent forms were used: one for the young and elderly groups, the other for the DAT patient group. The forms differed only in the explanation of the purpose of participation (see Appendices, C and D).

The picture stimuli consisted of 161 line drawings of objects (Snodgrass & Vanderwart, 1980). High resolution pictures were selected and edited. Each picture was cropped and resized so that the longest dimension (whether height or width) for each picture was 4 inches. To avoid eye strain for the participants, the colour for each image was inverted to become a white line drawing on a black background. Each image was saved as a cut file at a lower resolution of 72 dots per inch. For an example of an image see Appendix E. The pictures used were from various categories, including fruits and vegetables, animals, tools, and household items. These pictures were selected on the basis of previous research showing that 60-95 % of normal elderly adults could name the items correctly (Chertkow, 1998, unpublished data).

The word stimuli were presented in white 48 point Arial font on a black

background (see Appendix F). The words for the related condition were normed on 10 young and elderly pilot subjects using a 5-point scale, where 1 indicated not at all related, and 5 indicated very related; only words receiving a score of 3.5 or higher were used. The words for the unrelated condition were selected in order to match the related words on frequency (Kucera & Francis, 1967), word length, and imagery (Pavio, Yuille, & Madigan, 1968). Characteristics for each word were taken from the MRC Psycholinguistic Database on the University of Western Australia's website (http://www.psy.uwa.edu.au/MRCDataBase/uwa_mrc.htm) T-tests revealed no significant differences between conditions on these characteristics (see Table 2).

Neuropsychological Tests

The following neuropsychological tests were used.

The Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) contains 30 questions that briefly test cognitive functioning, attention, short-term, and working memory. It is most effective in distinguishing the degree of deficit in patients with dementia (Small, Viitanen, & Backman, 1997).

The Boston Naming Test (BNT; Kaplan, Goodglass, & Weintraub, 1983) consists of 60 black and white line drawings to be named. It is used in dementia assessment as an indicator of both presence and degree of semantic deterioration (Ross & Lichtenberg, 1998).

Table 2

Average Values and T-tests for Word Attributes as a Function of Condition

| | Related | Unrelated | | |
|---------------|---------|-----------|---------|-------------|
| Attributes | Words | Words | T-value | Probability |
| Letter Length | 5.6 | 5.5 | 0.5 | 0.60 |
| Frequency | 43.5 | 28.5 | 1.2 | 0.24 |
| Concreteness | 566.4 | 580.2 | -1.47 | 0.14 |
| Imagery | 563.7 | 577.1 | -1.86 | 0.06 |

Measures of verbal fluency can be separated into two tasks: phonemic fluency and semantic fluency. The phonemic fluency task requires subjects to generate words that begin with a given letter (Thurstone & Thurstone, 1938), whereas, the semantic fluency task requires subjects to generate words that belong to a certain category (Newcombe, 1969). The phonemic fluency task was conducted for the letters F, A, and S, and the semantic fluency task was conducted for the category of animals; for each task, an individual had a minute to respond. The verbal fluency tasks assess the ability to access and make use of semantic knowledge; thus, they are believed to be an indirect measure of semantic memory impairment (Chertkow & Bub, 1990).

Procedure

Informed consent was obtained for all participants, and when desired, patients signed the consent forms in the presence of a relative or spouse. The whole testing session lasted approximately 1½ to 2 hours. At the end of the experiment, all participants were reimbursed for parking or travel expenses and received compensation for their participation.

Neuropsychological Testing

Young and elderly adults were administered the following neuropsychological tests: the Mini-Mental State Examination, the Boston Naming Test, and the Verbal Fluency Test (both phonemic and semantic tasks). Patients with DAT were not given

these tests, as they had been administered at an earlier occasion as part of an assessment battery at the Memory Clinic.

Picture-Naming Task

Prior to ERP testing, the confrontational naming task was administered to each participant. The naming task consisted of the 161 picture stimuli. Each image was presented separately on a SVGA monitor and participants were given 20 seconds to name aloud the object shown. If the participant named the picture in less than 20 seconds, the experimenter advanced the trial to the next picture; if the participant did not respond within 20 seconds, the following picture automatically appeared. All responses were recorded manually by the experimenter. A correct response was achieved when the picture was named appropriately. An incorrect response was noted when the participant failed to generate a name for the picture or named it inaccurately. For each participant, the naming data were then coded for the electrophysiological testing to identify which stimuli fell into the named or unnamed category. Therefore, each participant had an individualized set of pictures for the named and unnamed conditions in the semantic priming experiment.

Electrophysiological Recording

Electrophysiological data collection and analysis was carried out on an IBM compatible computer system with commercially available software to control stimulus presentation and data collection (Neuroscan, Inc.). Scalp electrical activity was recorded

using a nylon electrode cap containing tin electrodes (Electrocap, Inc.). Using the International 10-20 System for electrode placement (Jasper, 1958), electroencephalogram (EEG) activity was recorded from three midline sites (Fz, Cz, Pz), and 7 lateral sites over each hemisphere (left: F3, F7, C3, T3, T5, P3, O1; right: F4, F8, C4, T4, T6, P4, O2). A cephalic (forehead) location was used as ground. Figure 1 shows the layout of the sites that were recorded. Electrodes were placed on the earlobes to serve as a linked reference. Electro-oculogram activity (EOG) was recorded from electrodes placed at the outer canthi of both eyes (horizontal EOG) and above and below the left eye (vertical EOG). EOG artifacts were corrected off-line for all participants using a regression algorithm (Gratton, Coles, & Donchin, 1983). For two of the patients with DAT, EOG activity was not satisfactorily corrected. In their case, corrected trials in which EOG activity exceeded a peak amplitude of -75 to $+75 \mu\text{V}$ were excluded from the averages. All data were baseline corrected. Electrical impedance was kept at, or below 5 kilo-ohms. EEG data were amplified in a DC to 100Hz bandwidth, digitized at a rate of 200Hz, and recorded and stored on a computer hard drive for subsequent analysis. The electrophysiological time epoch was 1100 ms per trial, 100 ms prior to picture onset and the entire duration of the picture (1000 ms). ERPs for named pictures were averaged for each participant across both priming conditions; patients with DAT had additional ERP averages computed for unnamed pictures.

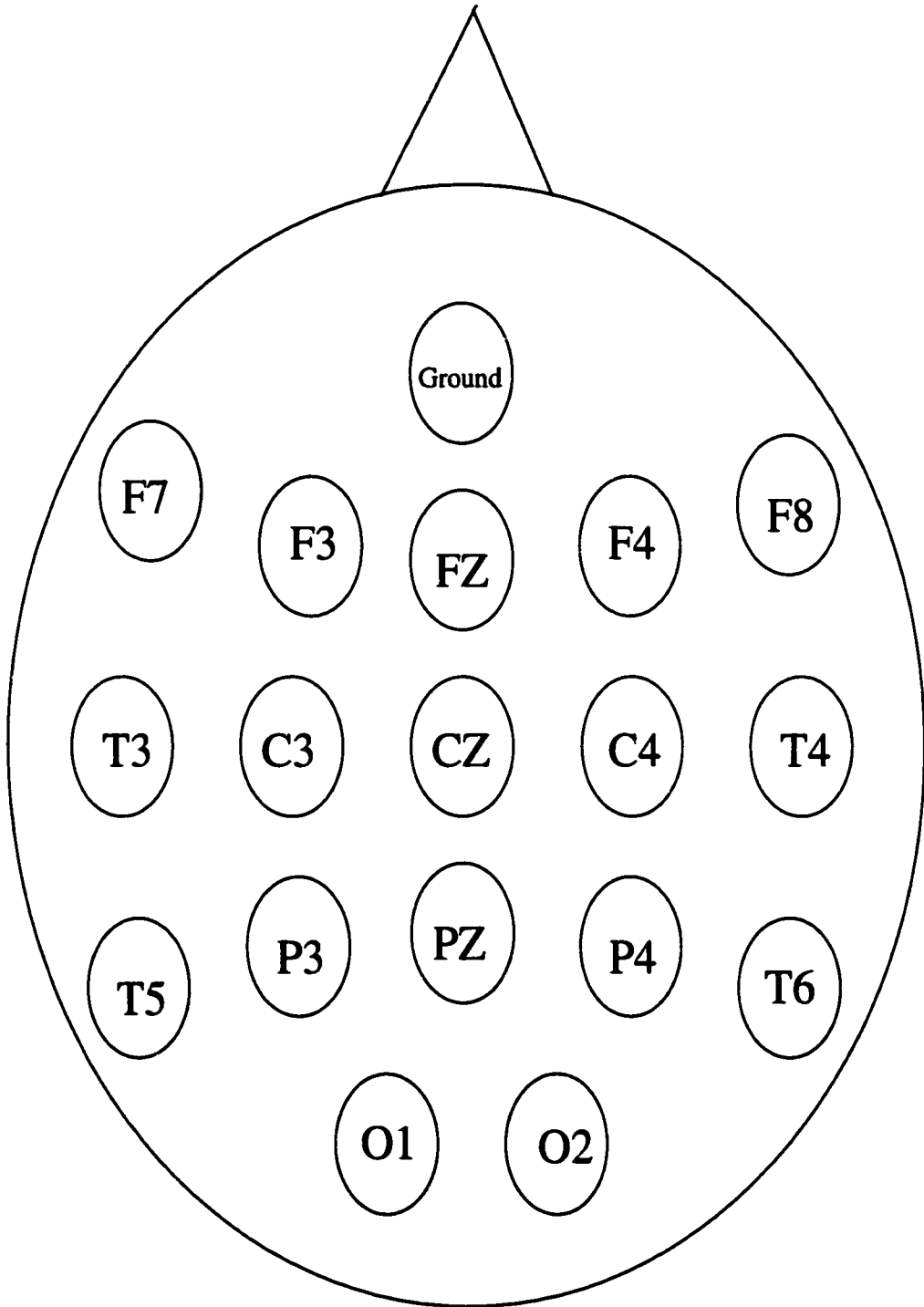


Figure 1. Layout of electrodes.

Word-Picture Priming Task

Two priming conditions were tested: related and unrelated word prime. For the related condition, the word was either semantically related to the picture it preceded (e.g., [word] wool - [picture] sheep), or of the same semantic category (e.g., [word] cheetah - [picture] leopard). The unrelated condition consisted of a word that was from a different category than the image it preceded (e.g., [word] envelope - [picture] sheep). For a full list of the word primes used, see Appendix G.

As stated previously, based on the performance on the naming task, the pictures that each participant failed to name were coded differently so they could be averaged separately. Each picture from the named and unnamed categories was presented in each of the priming conditions (related, unrelated) yielding a total of 322 word-picture pair trials.

During the word-picture experiment, participants sat in a comfortable chair that was placed approximately 1 metre away from the stimulus monitor. Word-picture pairs were presented on an IBM compatible computer in an order determined by a balanced Latin square. Each item of each pair was presented sequentially on the centre of the screen, at a visual angle that extended between 2.70 to 12.95 degrees. Each trial consisted of the presentation of a word prime followed by a picture target. Figure 2 shows the time course of stimulus presentation. Word duration was 300 ms followed by a blank screen for 270 ms. The picture was then presented for up to 2000 ms.

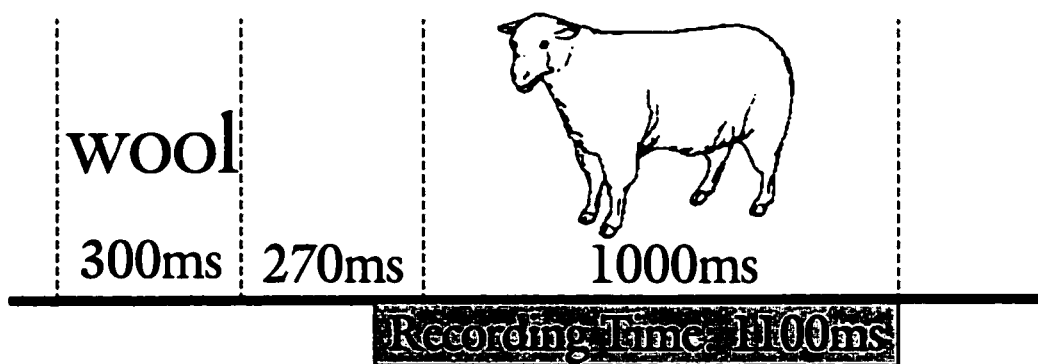


Figure 2. Time course of stimulus presentation.

Participants were instructed to respond as quickly as possible by pressing a “yes” button if the word and picture pair were related, and a “no” button if the pair were not related. As soon as a button was pressed the picture disappeared and was replaced by a blank screen for 1000 ms. Following the blank screen a new trial commenced. Practice trials were given to ensure that participants understood the task. The assignment of “yes” or “no” for the buttons was counterbalanced, so that half of the participants pressed the left button for a “yes” response and the other half pressed the left button for a “no” response. Reaction time data and response accuracy were recorded for each participant.

Prior to stimulus presentation, participants were instructed to pay attention to the word-picture pairs in order to judge their relatedness. Participants were also asked to refrain from talking and moving during presentation of the word and picture. In addition, participants were given short breaks, and were frequently asked if they were comfortable. Throughout the testing session, task instructions were repeated for the patients with DAT to ensure that they remembered task demands and remained as alert as possible.

Results

T-tests or repeated measures analyses of variance (ANOVAs) were conducted on the naming, neuropsychological, event-related potential, and behavioural data using SPSS v.10.1 statistical software for Windows. The Greenhouse-Geisser (1959) non-sphericity correction was employed when appropriate. Main effects of variables are described only if they did not interact with other variables. In the case of significant interactions, the highest order interaction is reported. Tukey A post-hoc tests were conducted on findings that were statistically significant at $\alpha = .05$ level.

When necessary, up to five main analyses were conducted for each dependent measure. (1) Age-related differences were assessed by comparing young and elderly groups. (2) Elderly adults and patients with DAT were compared to assess differences due to Alzheimer's disease, while controlling for age effects. (3) As described in greater detail below, patterns of priming in the patient group was heterogeneous. Hence, the group was divided into a DAT primer and DAT non-primer group according to whether or not they appeared to show ERP priming. Thus, analyses comparing elderly adults, DAT primers, and DAT non-primers were also conducted. (4) Since the DAT patients were the only group that had sufficient unnamed stimuli, behavioural and ERP differences as a function of naming were assessed within this group only. (5) Similarly, an analysis with DAT primers and DAT non-primers for the named and unnamed stimuli was conducted to assess if there were statistically reliable differences between the

two patient sub-groups. The results of these latter analyses are reported only when they provide information that was not yielded by the analyses conducted on the DAT patient group as a whole.

Naming Data

Figure 3 shows the correct naming performance from the confrontational naming task for each group. As expected, from the 161 line drawings presented, the young and elderly were able to name most of the pictures. T-tests showed that there was no difference between the young and elderly adults on naming ability, $t(28) = .64$, $p = .53$. As predicted, the patients with DAT were able to name significantly fewer pictures than the elderly adults, $t(22) = 10.23$, $p < .001$.

Event-Related Potential Data

Word Primes

Event-related potentials should be equivalent for the related and unrelated prime words, as these were matched on characteristics such as concreteness, length, imagery, and frequency. For the named stimuli, ERP grand averages at Pz for the words across prime conditions are shown in Figure 4 for the young adults, Figure 5 for the elderly adults, and Figure 6 for the patients with DAT. Figure 7 shows the ERP grand average at Pz for the words for the unnamed stimuli for the DAT patients. Upon visual inspection of these figures, there is no notable difference in amplitude across prime conditions. For the named stimuli, separate 2×5 (Prime x Time) ANOVAs were

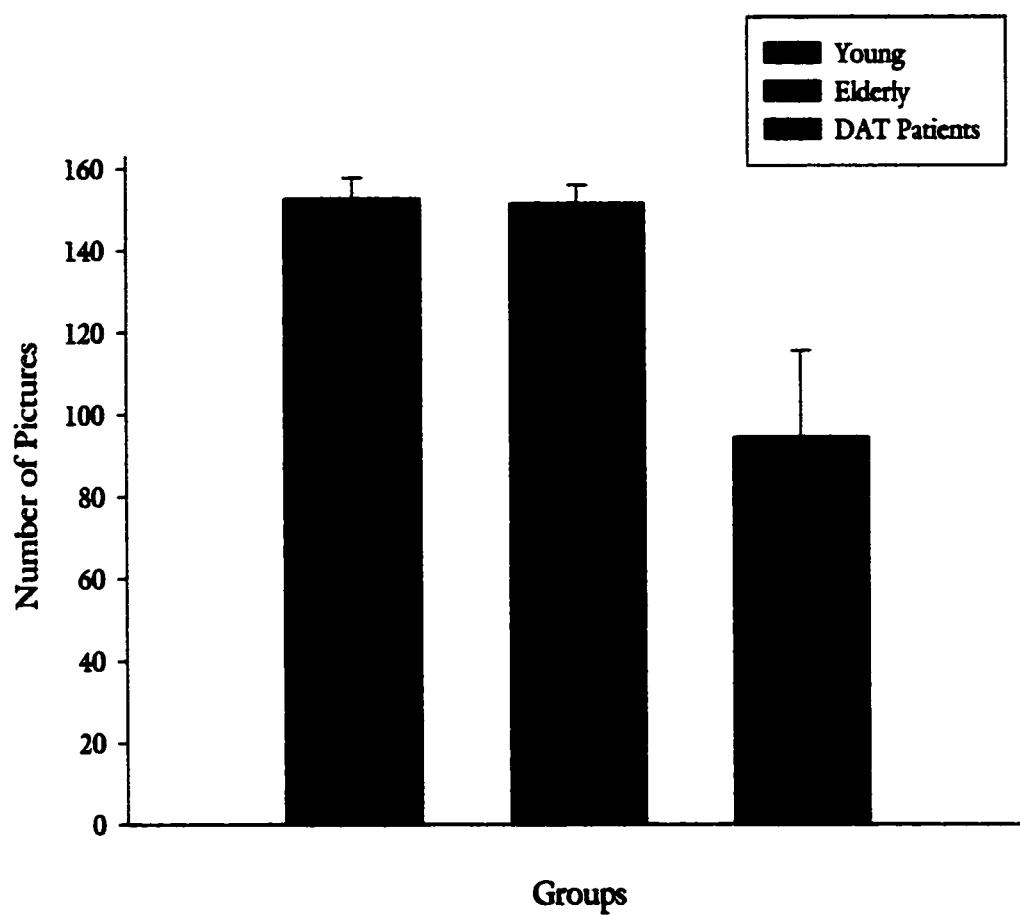


Figure 3. Performance on confrontational naming task for young adults, elderly adults, and DAT patients.

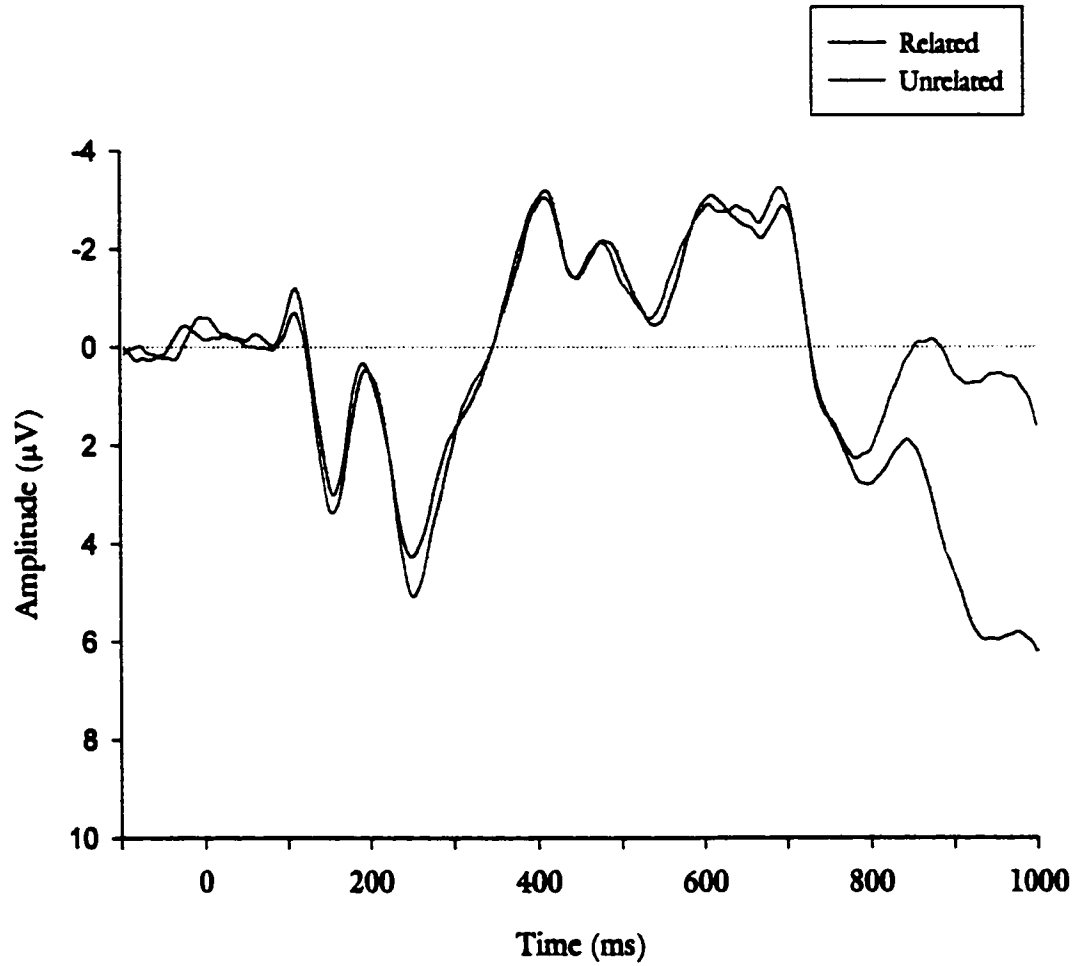


Figure 4. ERP grand average waveforms of word primes for named stimuli at the parietal midline site (Pz) for young adults.

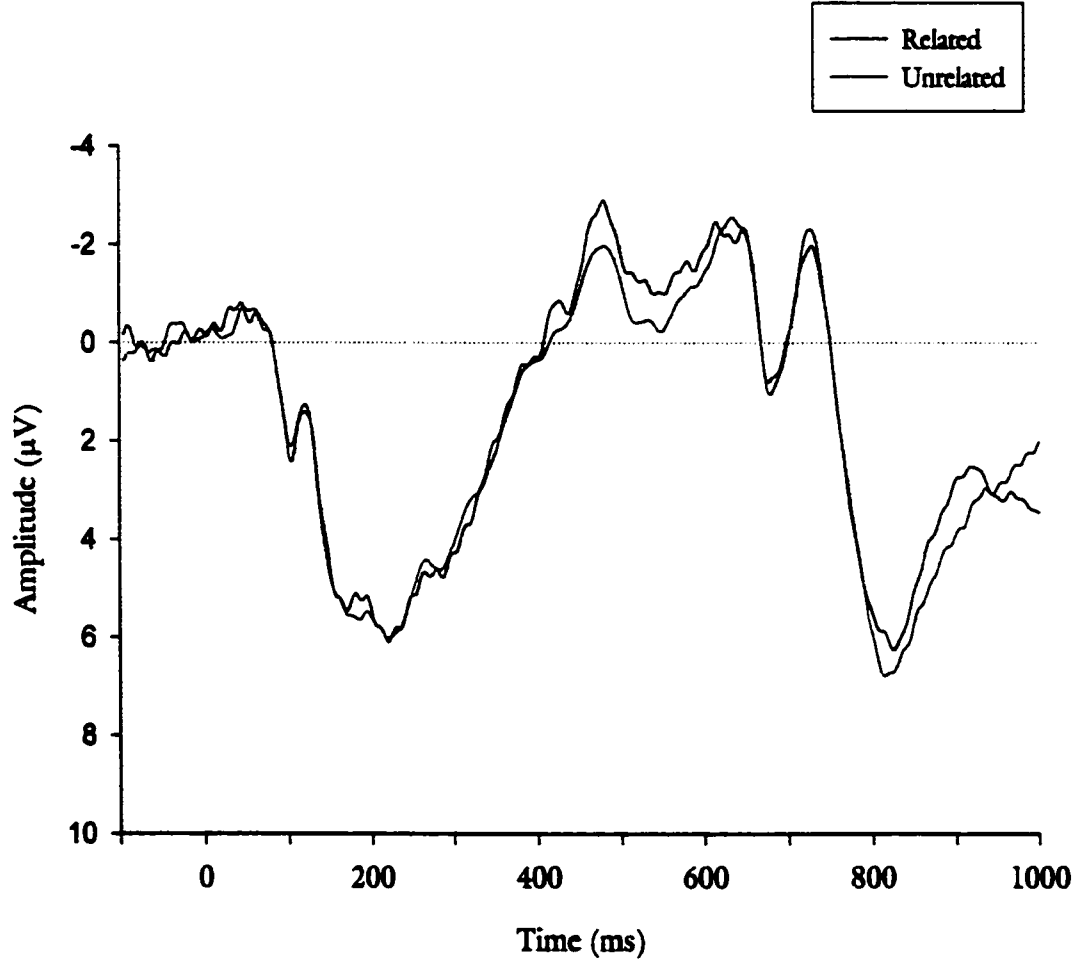


Figure 5. ERP grand average waveforms of word primes for named stimuli at the parietal midline site (Pz) for elderly adults.

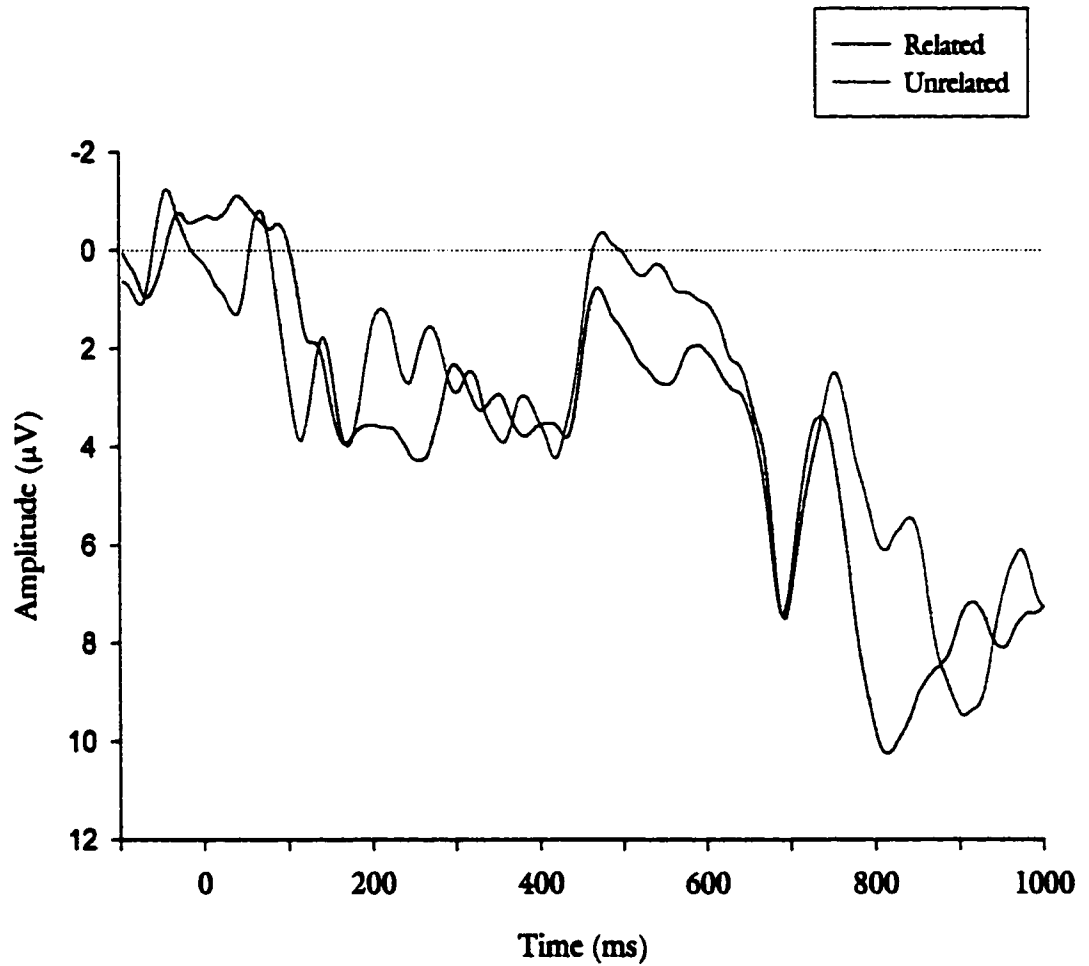


Figure 6. ERP grand average waveforms of word primes for named stimuli at the parietal midline site (Pz) for DAT patients.

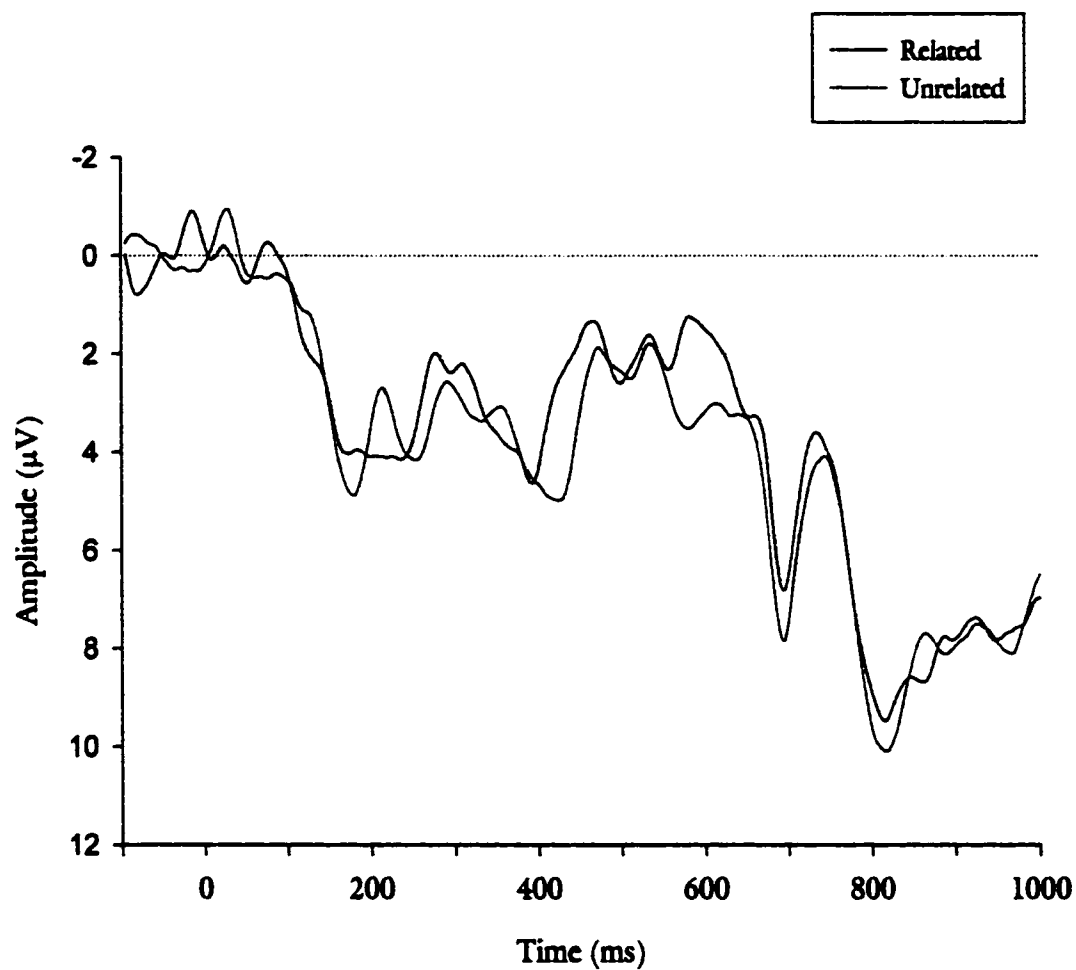


Figure 7. ERP grand average waveforms of word primes for unnamed stimuli at the parietal midline site (Pz) for DAT patients.

conducted for the young adults, elderly adults, and patients with DAT. There was no significant main effect of prime for any of the groups (young adults: $F(1,14) = 1.3$, $p = .274$; elderly adults: $F(1,14) = 0.03$, $p = .862$; DAT patients: $F(1,8) = 0.05$, $p = .822$). Similarly for the unnamed stimuli for the DAT patients, there was no main effect of prime, $F(1,8) = 0.15$, $p = .71$. Thus, there was no effect of condition prior to the presentation of the target picture.

Picture Targets

The N400 priming effect should be prominent approximately 400 ms post-stimulus onset of the picture targets. Hence, ERP priming will be observed if the N400 amplitude for unrelated pictures is more negative than for related pictures. All further ERP priming analyses were conducted on the picture targets.

A $2 \times 2 \times 3$ (Group \times Prime \times Region) ANOVA was conducted to assess topographical differences in N400 amplitude for the young and elderly groups. Electrode sites were grouped into 3 different regions (Anterior: Fz, F3, F4, F7, F8; Central: Cz, C3, C4; Posterior: T5, T6, Pz, P3, P4, O1, O2). There was a significant Prime \times Region \times Group interaction, $F(2,56) = 6.3$, $p = 0.007$. Post-hoc analysis revealed that the young group showed a significant priming effect over all 3 regions; however, the elderly group showed a priming effect at the posterior region only.

A similar analysis was conducted to assess topographical differences in N400 amplitude for the elderly adults and patients with DAT. There was a significant Prime

X Region X Group interaction, $F(2,44) = 4.2$, $p = 0.026$, which revealed priming at the posterior region for the elderly group, and no priming at any of the three regions for the patients with DAT.

Due to the distribution of the N400, all further analyses were conducted on data from the posterior region which was further divided into 3 locations (Left: T5, P3, O1; Central: Pz; Right: T6, P4, O2). In addition, all further analyses contrasted the mean potential amplitudes in 100 ms time windows from 200 to 700 ms post-stimulus onset, yielding five time intervals.

Young and Elderly Adults. ERP grand average waveforms at the Pz electrode site for the named stimuli are shown in Figure 8, panel a, for the young group and Figure 8, panel b, for the elderly group. As can be observed from both panels, the N400 peaks around 400 ms, and is more negative in amplitude for the unrelated condition.

A $2 \times 2 \times 3 \times 5$ (Group x Prime x Site x Time) ANOVA was conducted to assess N400 amplitude for young and elderly adults. A significant Prime x Site x Group interaction was found, $F(2,56) = 5.4$, $p = 0.008$. Post-hoc analysis revealed that the young showed a priming effect at all 3 posterior regions, whereas the elderly showed the priming effect at the central and right regions, but not at the left. There was a significant Prime x Time x Group interaction, $F(4,112) = 5.1$, $p = 0.013$, which revealed that the young showed significant priming between 300 to 500 ms post-

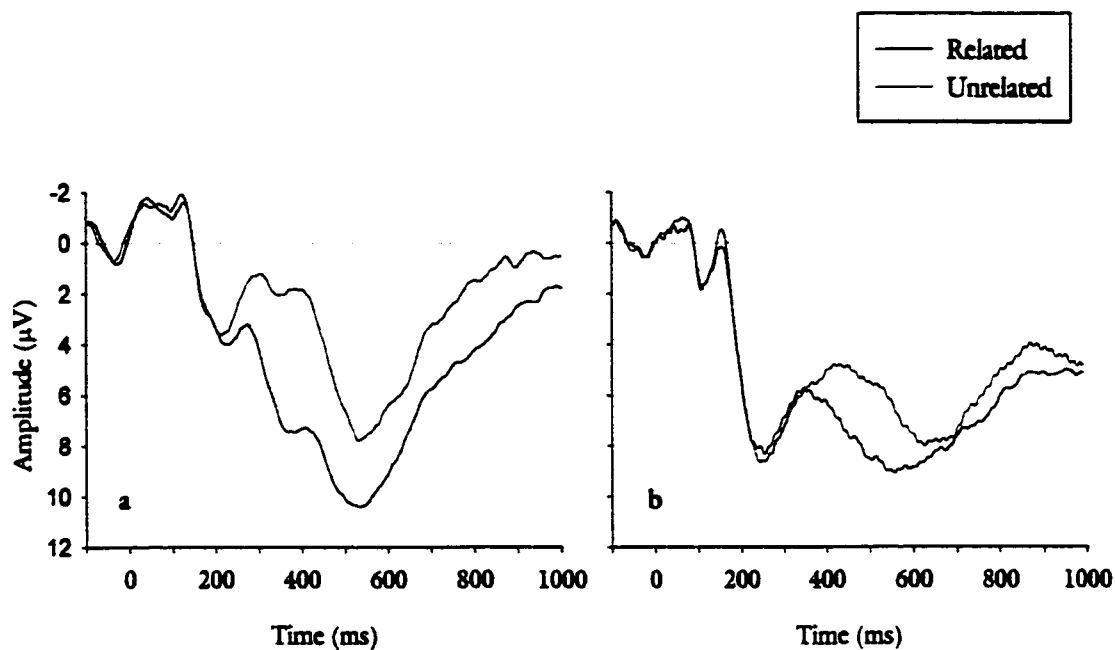


Figure 8. ERP grand average waveforms for named pictures preceded by related and unrelated words at the parietal midline site (Pz). a) Young adults; b) elderly adults.

stimulus onset; whereas the elderly showed reliable priming between 400 to 600 ms. There was a significant Prime x Site x Time interaction, $F(8,224) = 3.3$, $p = 0.017$, which showed that when collapsed over young and old, significant priming was found between 300 to 600 ms for the left location, between 200 to 700 ms for the central location, and between 300 to 700 ms for the right location.

Elderly Adults and Patients with DAT. Comparisons between elderly adults and patients with DAT for the ERP grand average waveforms at the Pz electrode site for the named stimuli are shown in Figure 9, panel a, for the elderly group and Figure 9, panel b for the DAT patient group. As can be observed, for the patients with DAT there is no obvious difference in N400 amplitude between prime conditions. N400 amplitude was assessed with a $2 \times 2 \times 3 \times 5$ (Group x Prime x Site x Time) ANOVA for elderly adults and patients with DAT. There was a significant Prime x Time x Group interaction, $F(4,88) = 6.6$, $p = 0.002$, which revealed that a priming effect was observed in the elderly between 400 to 600 ms post-stimulus onset; however, there were no significant priming effects at any time interval for the DAT patient group.

Upon visual inspection of each DAT patient's waveforms for named stimuli, it was observed that some patients appeared to show an ERP priming effect, whereas others did not. For further analyses, the patient group was separated (based on visual inspection of the degree to which they showed an N400 priming effect) into two sub-groups: DAT primers ($n = 5$) and DAT non-primers ($n = 4$). Table 3 shows the

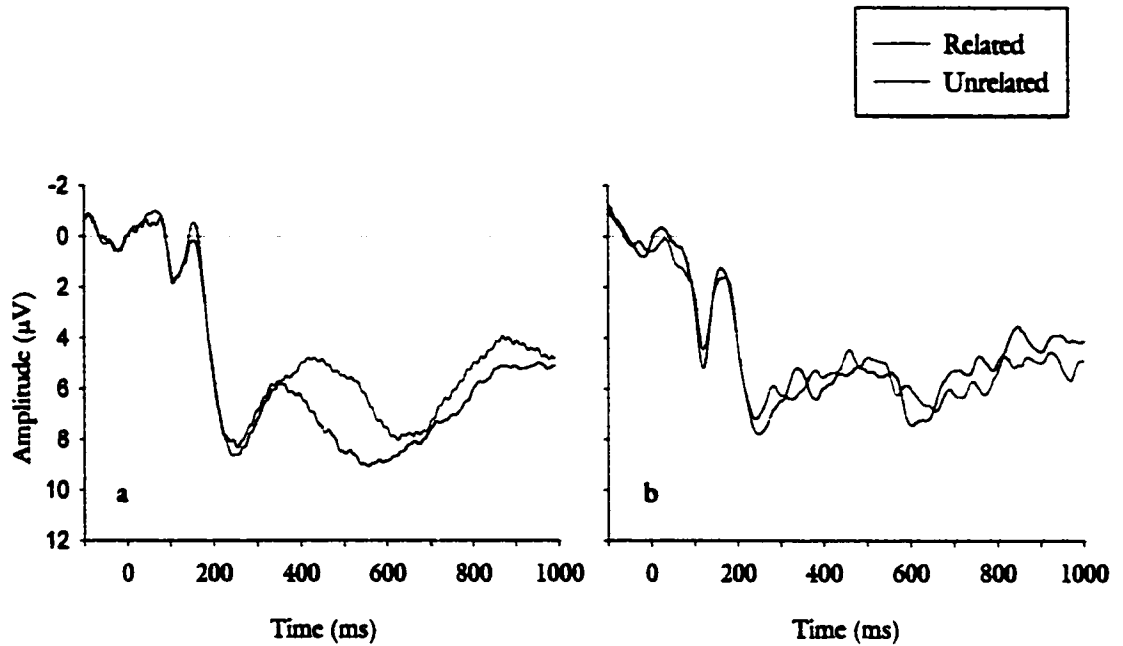


Figure 9. ERP grand average waveforms for named pictures preceded by related and unrelated words at the parietal midline site (Pz). a) Elderly adults; b) DAT patients.

Table 3

Average Demographic Data for the DAT Primers and DAT Non-Primers

| | Age | Education |
|-----------------|--------|-----------|
| Group | (SD) | (SD) |
| DAT Primers | 78.6 | 11.6 |
| | (4.28) | (4.10) |
| DAT Non-Primers | 80.3 | 9.8 |
| | (4.65) | (3.4) |

demographic information for these two groups. The two sub-groups do not differ from each other on age, $t(7) = -0.55$, $p = .59$, or years of education, $t(7) = .72$, $p = .49$. For individual waveforms of the patients that compose each of these groups, see Appendix H, panels a, for the DAT primers, and Appendix I, panels a, for the DAT non-primers.

Elderly Adults, DAT Primers, and DAT Non-Primers. ERP grand average waveforms at the Pz electrode site for the named stimuli are shown in Figure 10, panel a, for the DAT primers and Figure 10, panel b, for the DAT non-primers. As can be observed, the grand average shows the N400 to be more negative in amplitude in the unrelated condition for the DAT primers, whereas there is no observable difference in N400 amplitude for the DAT non-primers. A $3 \times 2 \times 3 \times 5$ (Group x Prime x Site x Time) ANOVA was conducted for elderly adults, DAT primers and DAT non-primers. Analysis showed a significant Prime x Time x Group interaction, $F(8,84) = 3.9$, $p = 0.006$, which revealed that the elderly showed priming; however, perhaps due to lack of power, the DAT primers and the DAT non-primers did not.

Named versus Unnamed Stimuli for Patients with DAT. Figure 11 shows the grand average waveforms at Pz electrode site for the patients with DAT for the named stimuli (panel a), and for the unnamed stimuli (panel b). Upon visual inspection, there does not seem to be a difference in N400 amplitude between prime conditions. A $2 \times 2 \times 3 \times 5$ (Naming x Prime x Site x Time) ANOVA was conducted. There were no

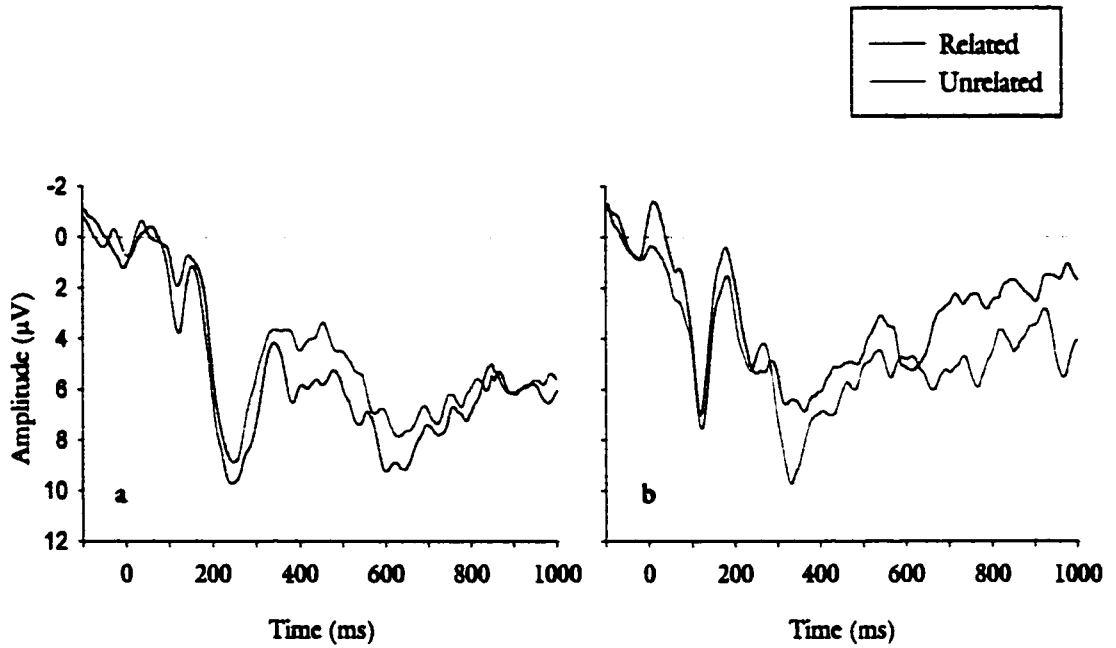


Figure 10. ERP grand average waveforms for named pictures preceded by related and unrelated words at the parietal midline site (Pz). a) DAT primers; b) DAT non-primers.

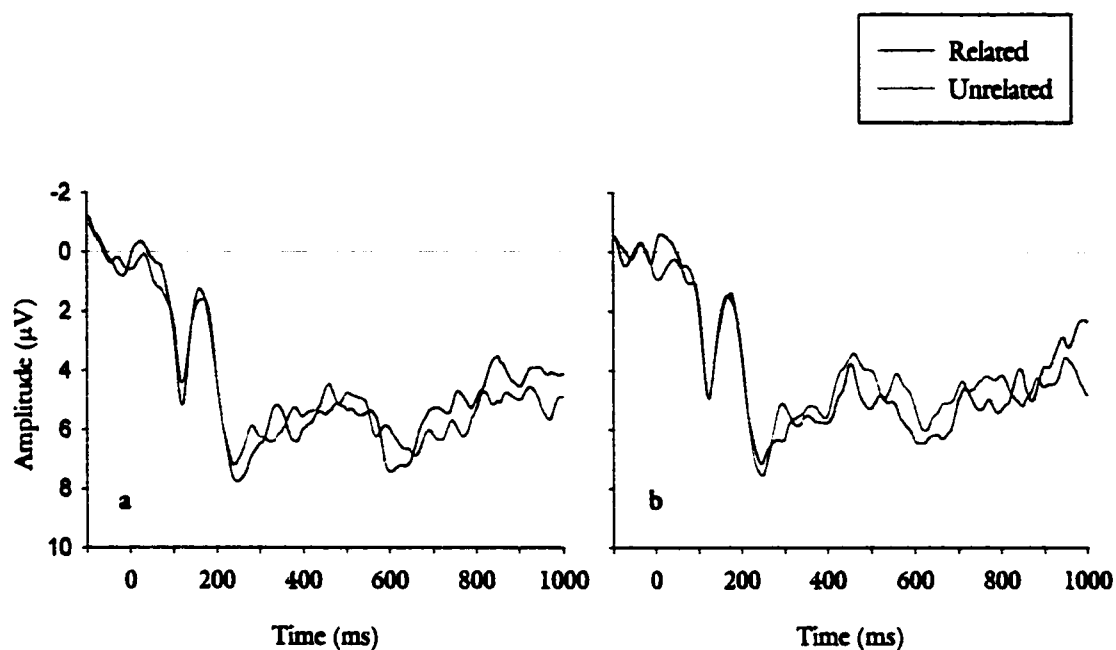


Figure 11. ERP grand average waveforms for pictures preceded by related and unrelated words at the parietal midline site (Pz). a) DAT patients (named stimuli); b) DAT patients (unnamed stimuli).

significant results in this analysis.

Named versus Unnamed Stimuli for DAT Primers and DAT Non-Primers. For the named and unnamed stimuli, ERP grand average waveforms at the Pz electrode site are shown in Figure 12, panels a and b respectively, for the DAT primers, and Figure 13, panels a and b, for the DAT non-primers. Visual inspection of these waveforms suggest a difference in N400 amplitude for the DAT primers, with the N400 more negative for the unrelated condition; there does not seem to be observable differences for the DAT non-primers. Differences as a function of naming for the two patient groups were assessed using a $2 \times 2 \times 2 \times 3 \times 5$ (Group x Naming x Prime x Site x Time) ANOVA. There was a significant Prime X Site X Group interaction, $F(2,14) = 6.9$, $p = 0.010$, which showed that the DAT primers showed priming at the midline posterior region, whereas the DAT non-primers do not show priming at any region. Statistical analysis did not show a difference in priming as a function of naming. Heterogeneity also existed for the unnamed stimuli, however, with some patients showing an apparent priming effect, while others did not. Individual waveforms for the unnamed stimuli for each of these groups are shown in Appendix H, panels b, for the DAT primers and Appendix I, panels b, for the DAT non-primers.

Behavioural Data

Behavioural data was obtained simultaneously with ERP data. Participants' reaction times (RT) were measured, as relatedness judgements for each word-picture

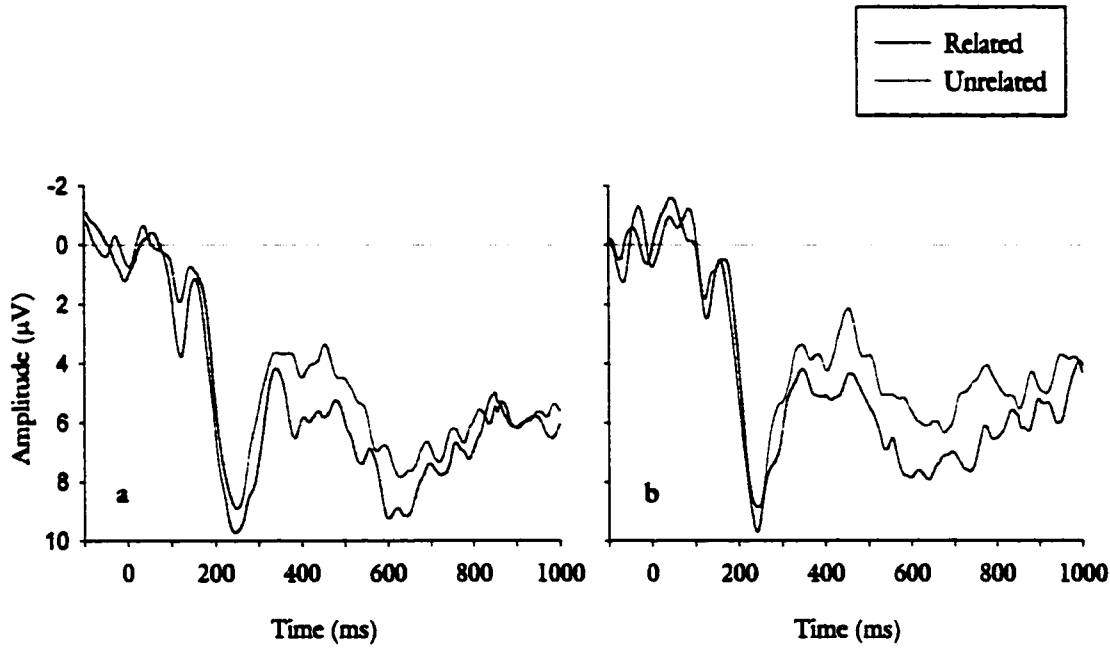


Figure 12. ERP grand average waveforms for pictures preceded by related and unrelated words at the parietal midline site (Pz). a) DAT primers (named stimuli); b) DAT primers (unnamed stimuli).

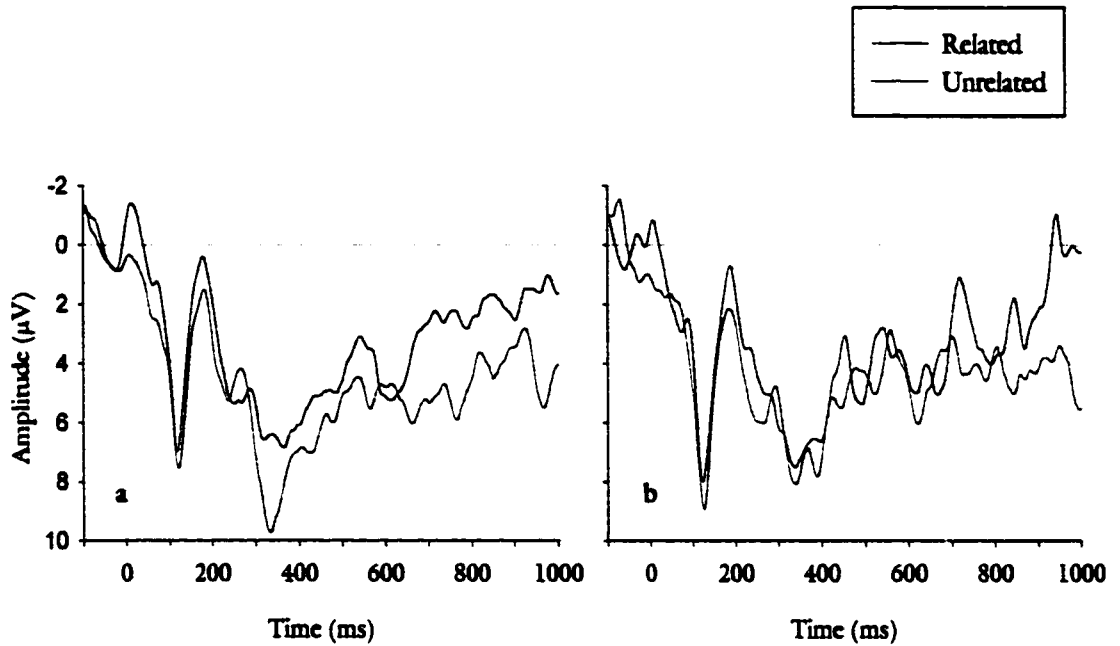


Figure 13. ERP grand average waveforms for pictures preceded by related and unrelated words at the parietal midline site (Pz). a) DAT non-primers (named stimuli); b) DAT non-primers (unnamed stimuli).

pair were made. One DAT patient was omitted from the behavioural data analyses due to a very low frequency of responding.

Response Rate

The number of trials in which each participant failed to generate a response was measured. Figure 14 shows the average number of omitted trials for the named stimuli for the young and elderly groups, and the DAT patient group in each priming condition.

Elderly Adults and Patients with DAT. A 2 x 2 (Group x Prime) ANOVA was conducted for elderly adults and DAT patients. There was a significant Prime x Group interaction, $F(1,21) = 15.3$, $p = 0.001$, which revealed that DAT patients failed to generate a response for more trials than did elderly adults. In addition, for the named stimuli, patients with DAT, on average, failed to respond to more trials in the unrelated as compared to the related condition.

Named versus Unnamed Stimuli for Patients with DAT. Figure 15 shows the number of omitted trials for the DAT patients for the named and unnamed stimuli, across the prime conditions. A 2 x 2 (Naming x Prime) ANOVA was conducted to investigate differences in number of omitted trials as a function of naming. There was a significant Naming x Prime interaction, $F(1,7) = 6.9$, $p = 0.034$, which showed that there were more omitted trials for the named stimuli as compared to the unnamed stimuli. More specifically, for the named stimuli in the unrelated condition there were

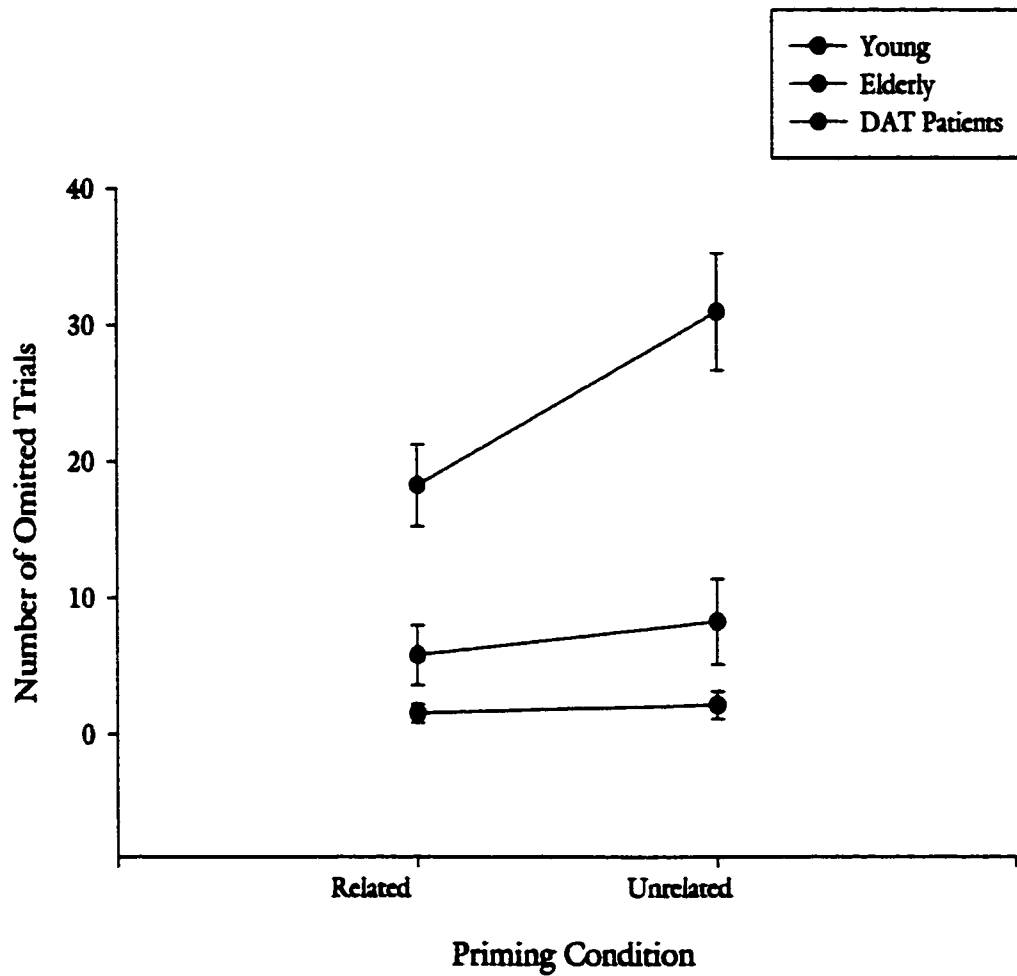


Figure 14. Number of omitted trials for named stimuli for young adults, elderly adults, and DAT patients.

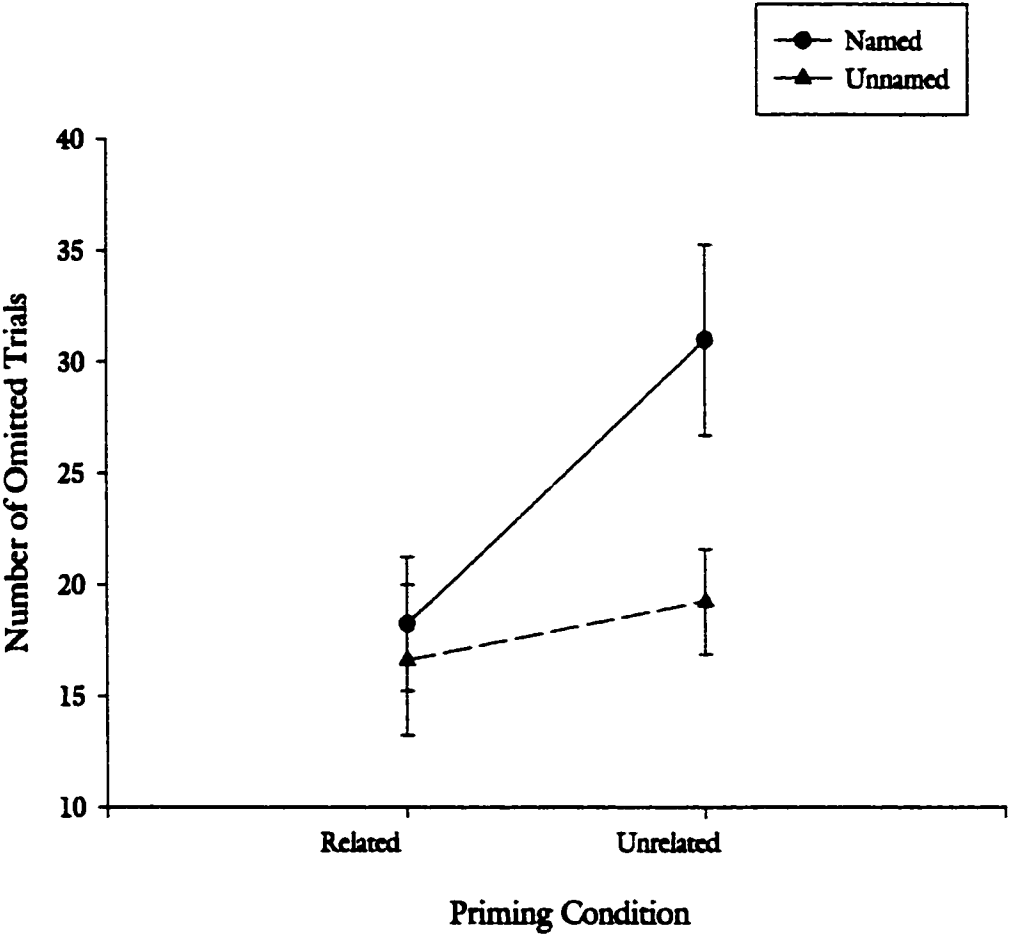


Figure 15. Number of omitted trials for named and unnamed stimuli for DAT patients.

significantly more omitted trials as compared to the other three conditions (named stimuli - related; unnamed stimuli - related; unnamed stimuli - unrelated).

Percent Correct

Percent correct was calculated by taking the number of correct responses and dividing it by the number of trials to which each participant responded. Figure 16 shows the percent correct for the named stimuli for the young and elderly adults, and patients with DAT for each priming condition.

Young and Elderly Adults. A 2 x 2 (Group x Prime) ANOVA revealed a significant main effect of prime, $F(1,28) = 17.0, p < 0.001$. Young and elderly adults were more accurate when responding in the unrelated condition as compared to the related condition. There were no difference in accuracy between the young and elderly groups, $F(1,28) = 0.2, p = 0.681$.

Elderly Adults and Patients with DAT. A 2 x 2 (Group x Prime) ANOVA revealed a between group main effect, $F(1,21) = 9.5, p = 0.006$, indicating that the elderly adults were more accurate than the DAT patients.

Elderly Adults, DAT Primers, and DAT Non-Primers. Figure 17 shows the percent correct for named stimuli for the elderly adults, DAT primers and DAT non-primers. A 3 x 2 (Group x Prime) ANOVA was conducted to assess differences in percent correct for these 3 groups. There was a significant Prime x Group interaction, $F(2,20) = 6.3, p = 0.008$, which revealed that the elderly and DAT primer groups

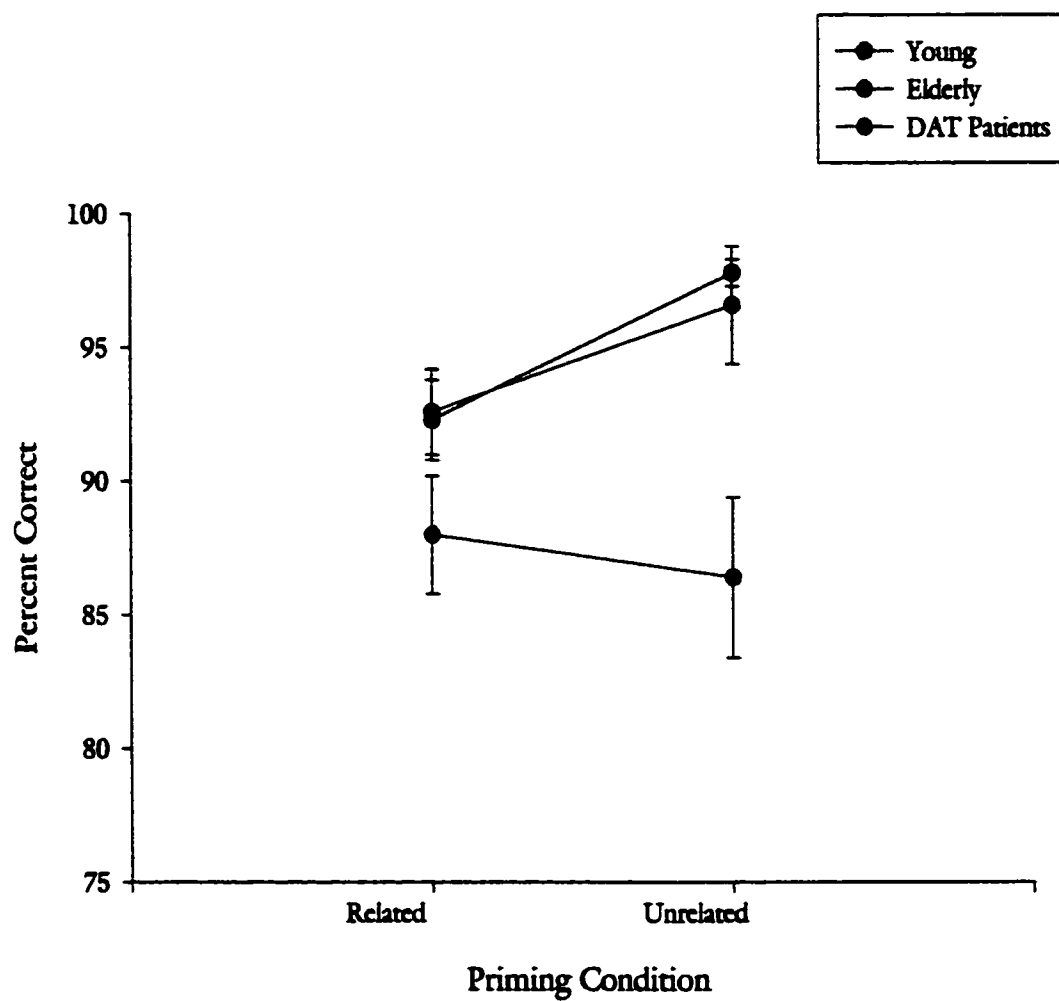


Figure 16. Percent correct for named stimuli for young adults, elderly adults, and DAT patients.

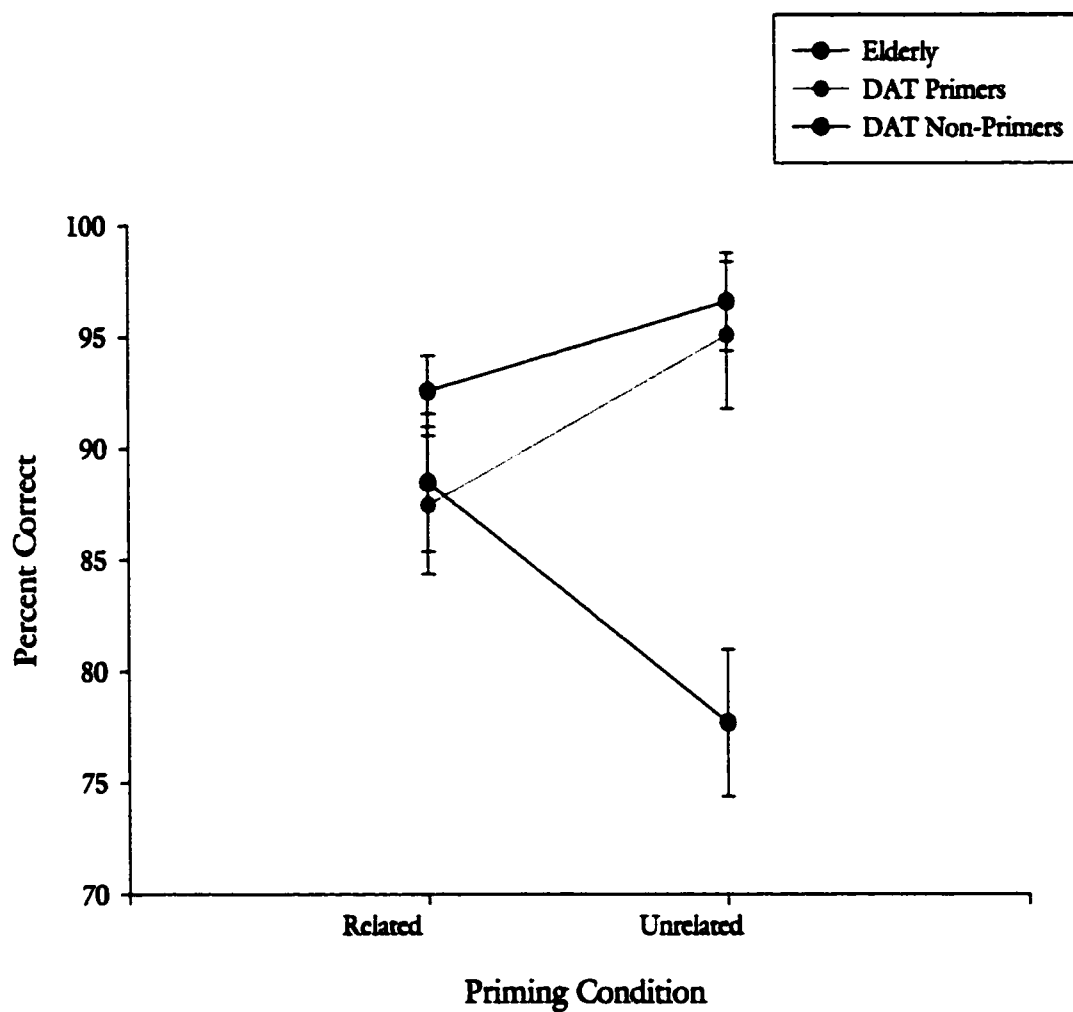


Figure 17. Percent correct for named stimuli for elderly adults, DAT primers, and DAT non-primers.

did not differ from each other; however the DAT non-primers differed significantly from the other two groups. As seen in Figure 17, the elderly and DAT primers were more accurate in the unrelated condition, whereas the DAT non-primers showed the opposite pattern and were less accurate in the unrelated condition.

Named versus Unnamed Stimuli for Patients with DAT. Percent correct for patients with DAT is shown in Figure 18 for the named and unnamed stimuli across prime conditions. A 2 x 2 (Naming x Prime) ANOVA revealed a significant Naming x Prime interaction, $F(1,7) = 6.7, p = 0.036$, which showed that for the named stimuli there was no significant difference in accuracy as a function of prime. For the unnamed stimuli, however, the patients responded less accurately in the related as compared to the unrelated condition.

Named versus Unnamed Stimuli for DAT Primers and DAT Non-Primers. Percent correct for the named and unnamed stimuli across prime conditions is shown in Figure 19, panel a, for the DAT primers, and Figure 19, panel b, for the DAT non-primers. A 2 x 2 x 2 (Group x Naming x Prime) ANOVA was conducted for the DAT primers and DAT non-primers. There was a significant Prime x Group interaction, $F(1,6) = 6.5, p = 0.044$, and a strong trend for a Naming x Group interaction, $F(1,6) = 5.9, p = 0.051$. Unfortunately, when analyzing the Prime x Group interaction it is collapsed over naming, and when analyzing the Naming x Group interaction it also is collapsed over the priming condition.

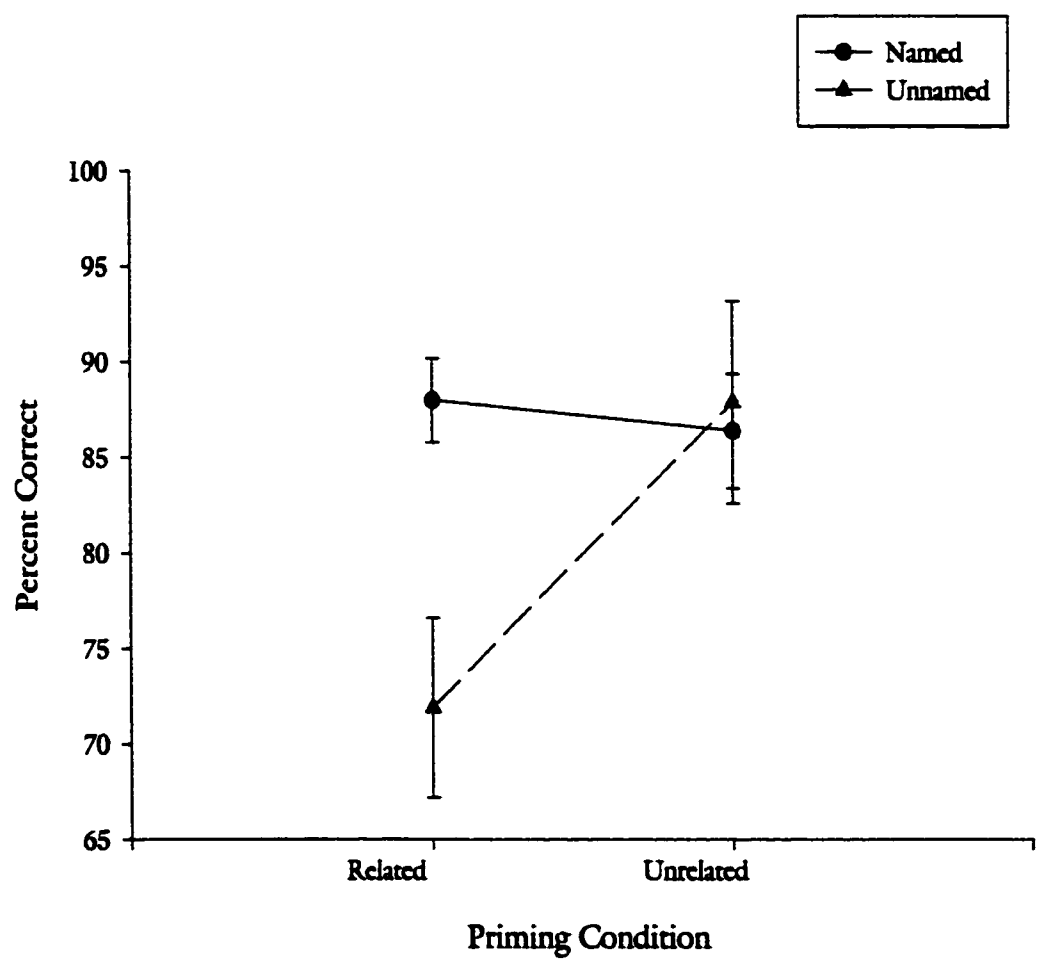


Figure 18. Percent correct for named and unnamed stimuli for DAT patients.

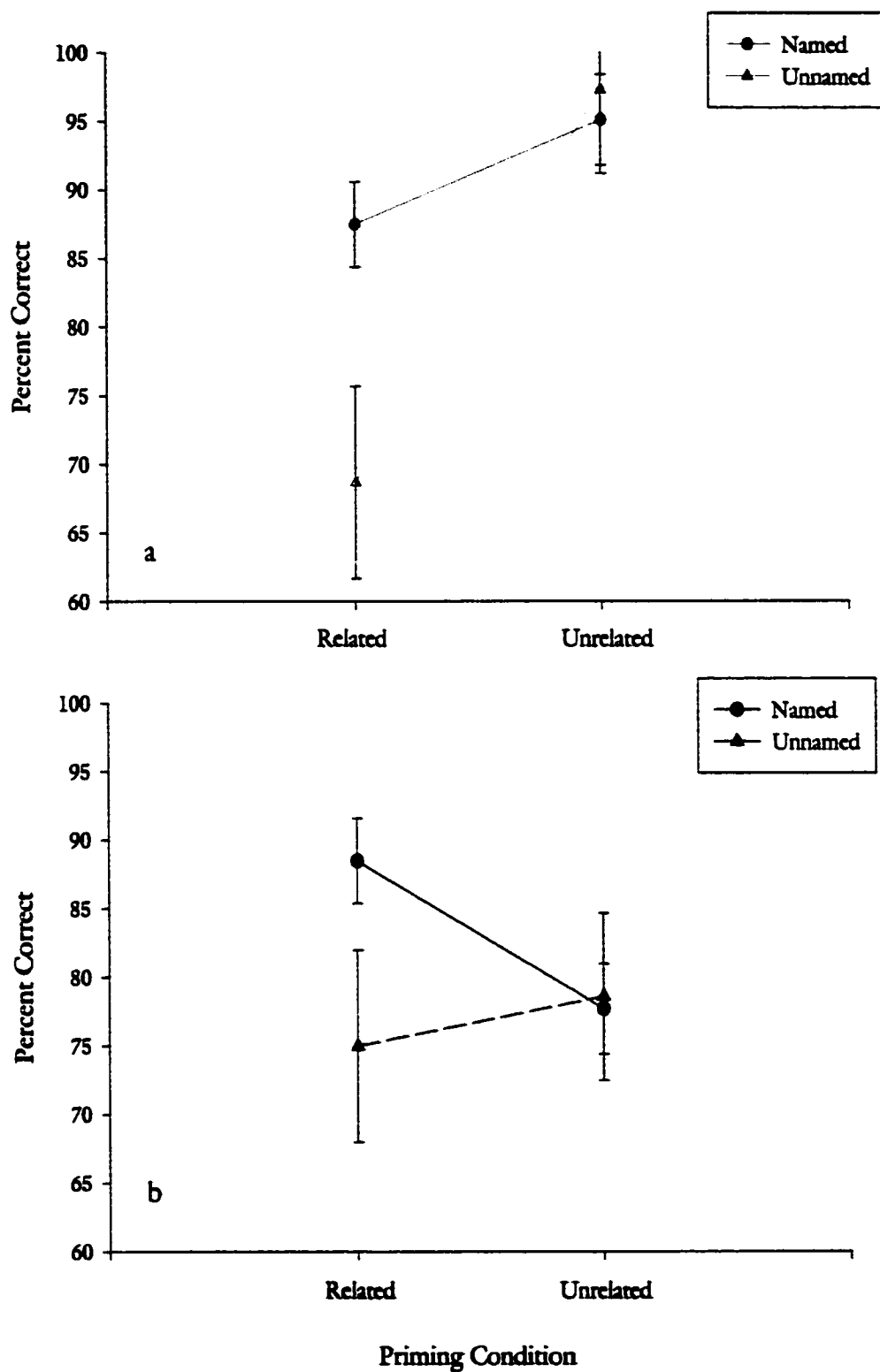


Figure 19. Percent correct for named and unnamed stimuli. a) DAT primers; b) DAT non-primers.

Visual inspection of Figure 19 suggests that in the related condition, both the DAT primers and DAT non-primers were more accurate for the named stimuli than for the unnamed stimuli. In the unrelated condition there was no apparent difference as a function of naming for the two groups. There seems to be a difference in pattern of accuracy for the two groups; in comparison to each group's related condition, the DAT primers were more accurate in the unrelated condition for named and unnamed stimuli, whereas the DAT non-primers were less accurate for named stimuli and more accurate for unnamed stimuli.

Reaction Time (RT)

Reaction time was recorded to each participant's judgement on each trial. Response latencies exceeding 3 standard deviations above each participant's mean and response latencies less than 100 ms were treated as outliers and were excluded from individual averages. Statistical analyses were conducted on reaction times for correct responses only. Figure 20 shows the average reaction times for the named stimuli for the young and elderly adults, and patients with DAT for each prime condition.

Young and Elderly Adults. A 2 x 2 (Group x Prime) ANOVA was conducted to assess RT priming for the young and elderly groups. There was a significant main effect of prime, $F(1,28) = 22.6, p < 0.001$, indicating that both the young and elderly adults were faster at responding to pictures following a related prime as compared to an unrelated prime. There was a group main effect, $F(1,28) = 42.0, p < 0.001$,

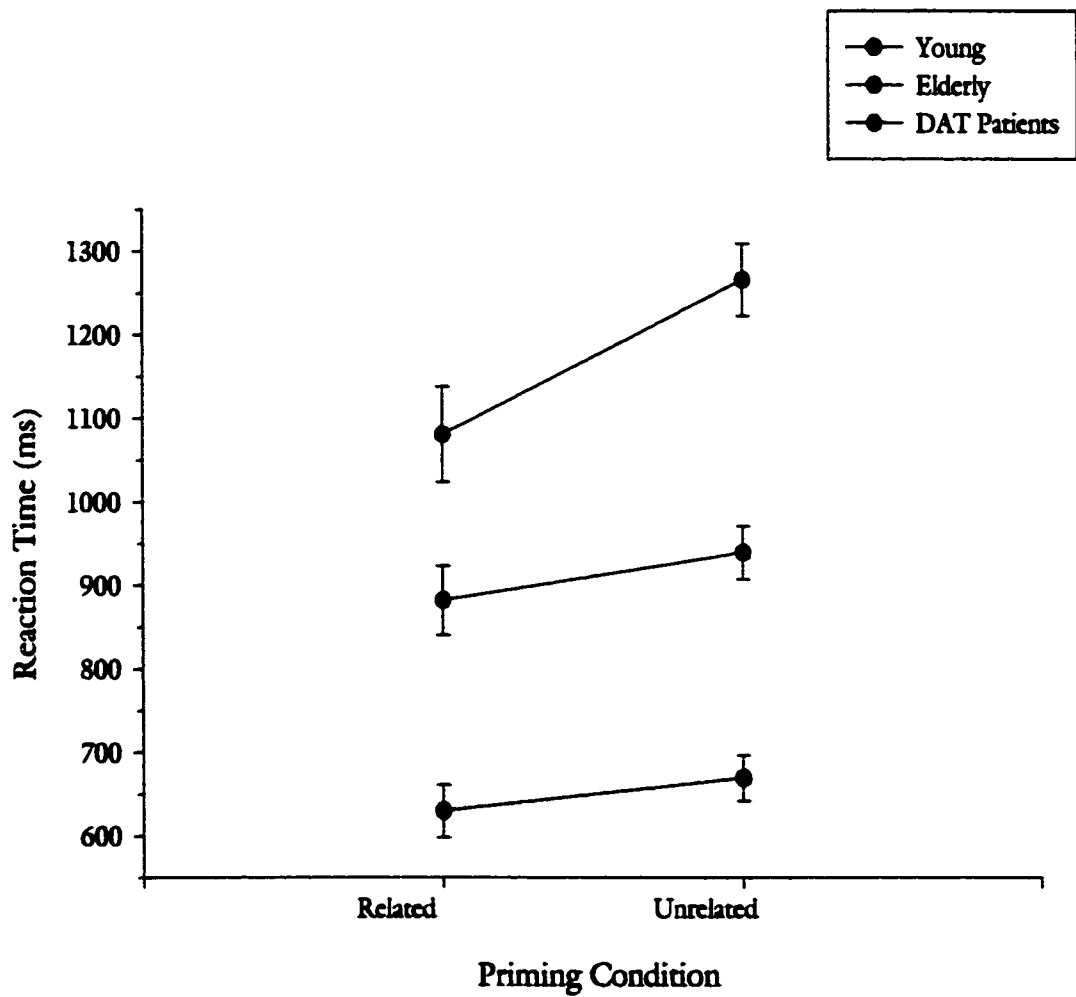


Figure 20. Reaction time for named stimuli for young adults, elderly adults, and DAT patients.

which indicated that, overall, the young responded significantly faster than the elderly.

Elderly Adults and Patients with DAT. Group differences in RT priming were assessed in a 2 x 2 (Group x Prime) ANOVA. There was a Prime x Group interaction, $F(1,21) = 11.9, p < 0.001$. As can be observed in Figure 20, the patients with DAT were significantly slower in responding than the elderly adults, but showed proportionately more priming than the elderly. To obtain the proportional difference, the reaction time for the unrelated condition was divided by the reaction time for the related condition. The elderly group obtained a value of 1.06, and the DAT patient group obtained a value of 1.17, showing that patients with DAT were 17% faster when responding to related targets than unrelated targets, whereas elderly adults were only 6% faster.

Elderly Adults, DAT Primers, and DAT Non-Primers. Figure 21 shows the average reaction times for the named stimuli for the elderly adults, DAT primers, and DAT non-primers. A 3 x 2 (Group x Prime) ANOVA was conducted to assess group differences in RT priming. There was a significant Prime x Group interaction, $F(2,20) = 8.2, p = 0.003$, which indicated that the DAT primers and DAT non-primers had slower overall reaction times, but showed significantly more priming than the elderly group. The proportional difference of related and unrelated prime conditions for the three groups are as follows: elderly: 1.06; DAT primers: 1.12; DAT non-primers: 1.22. The proportional differences between groups are not statistically significant, however,

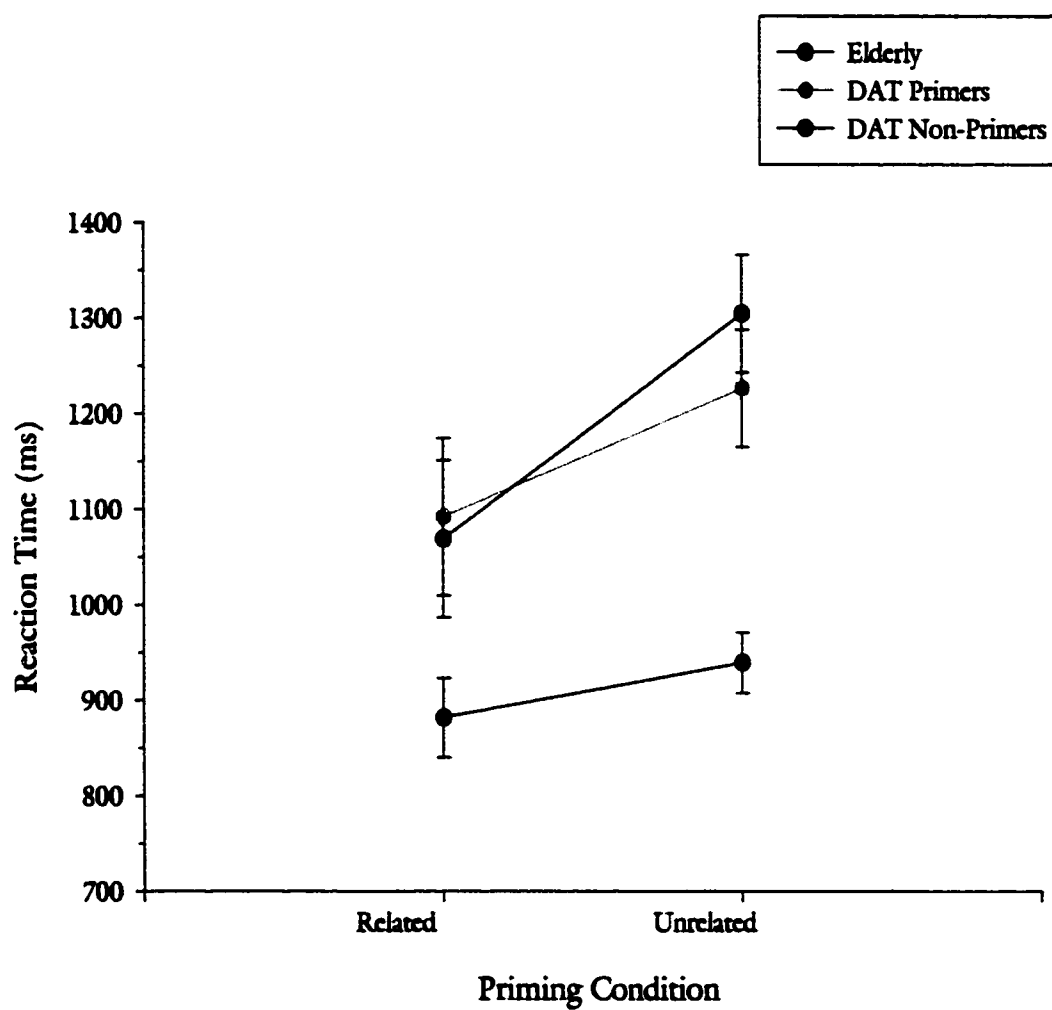


Figure 21. Reaction time for the named stimuli for elderly adults, DAT primers, and DAT non-primers.

a trend can be observed in which the DAT non-primer group appeared to show more priming than the DAT primer and elderly groups, and the DAT primer group appeared to show more priming than the elderly.

Named versus Unnamed Stimuli for Patients with DAT. Figure 22 shows the average reaction times for the named and unnamed stimuli across prime conditions for the patients with DAT. A 2 x 2 (Naming x Prime) ANOVA was conducted to assess RT priming as a function of naming. There was a significant Naming X Prime interaction, $F(1,7) = 19.5, p = 0.003$. As can be observed in Figure 22, DAT patients showed RT priming for the named stimuli; however no RT priming for the unnamed stimuli. The proportional difference for the named stimuli was 1.17, whereas for the unnamed stimuli the value was only 1.01.

Named versus Unnamed Stimuli for DAT Primers and DAT Non-Primers. The average reaction times for the named and unnamed stimuli across prime condition are shown in Figure 23, panel a for the DAT primers, and Figure 23, panel b for the DAT non-primers. A 2 x 2 x 2 (Group x Naming x Prime) ANOVA was conducted to assess RT priming as a function of naming for the two patient groups. There was only a significant Naming x Prime interaction, $F(1,6) = 28.0, p = 0.002$. However, there was a trend for a Group x Naming x Prime interaction, $F(1,6) = 4.09, p = 0.090$. As can be observed in Figure 23, panel a, it appears that the DAT primers show RT priming for the named stimuli, yet no RT priming for the unnamed stimuli. In

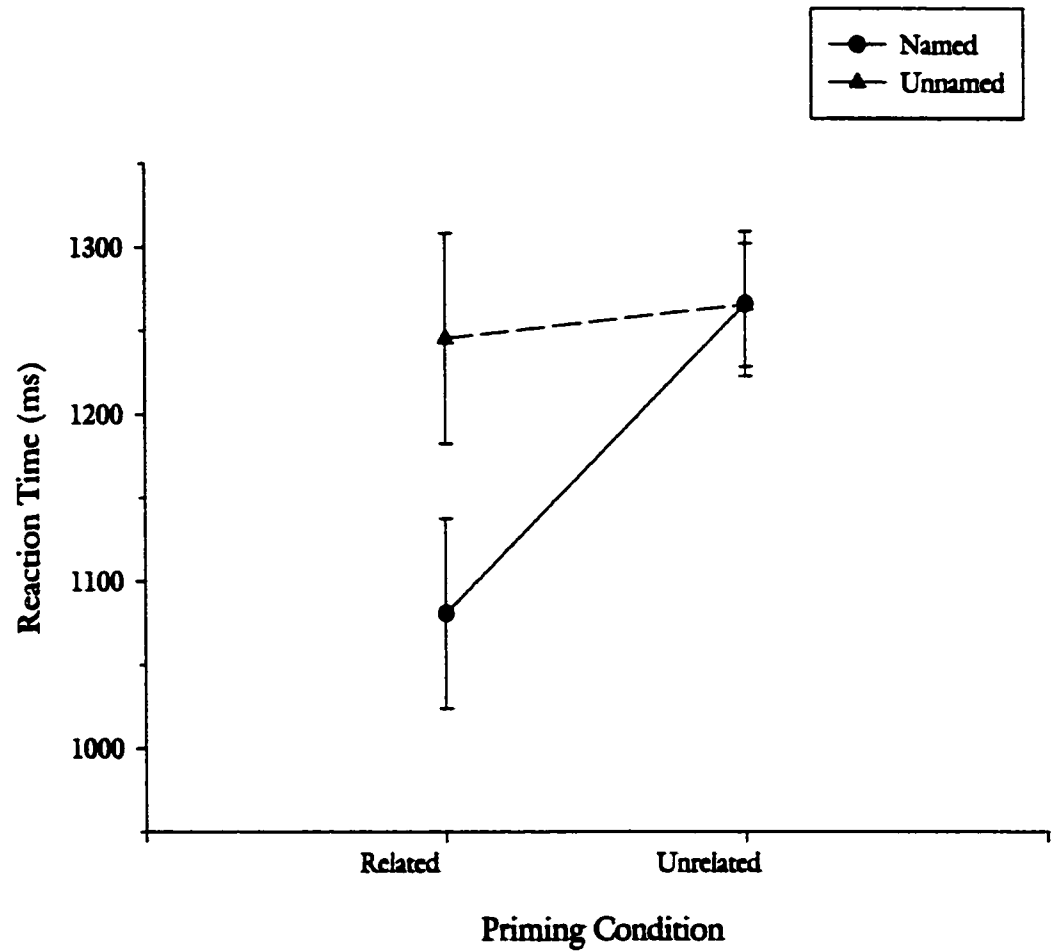


Figure 22. Reaction time for named and unnamed stimuli for DAT patients.

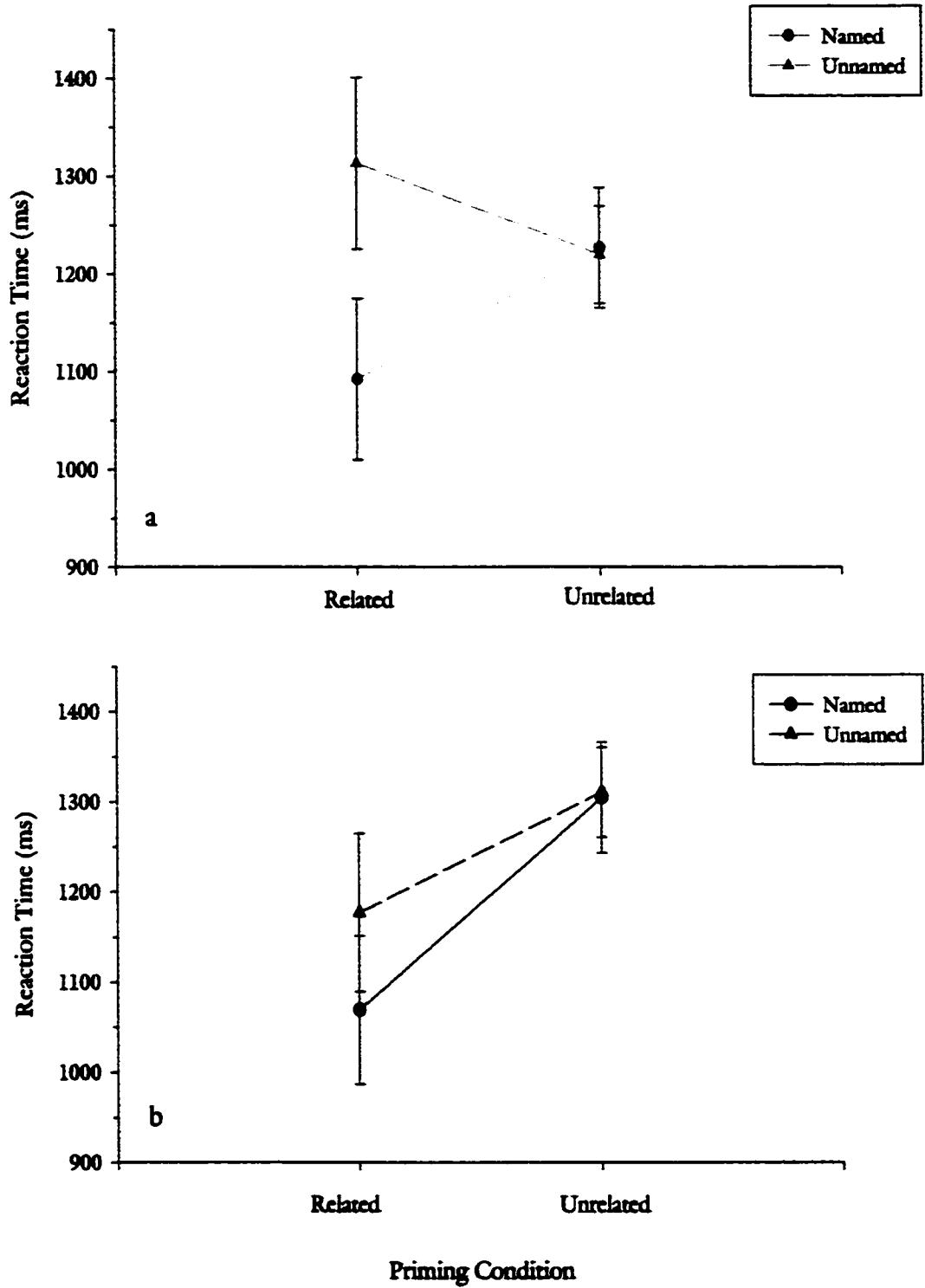


Figure 23. Reaction time for named and unnamed stimuli. a) DAT primers; b) DAT non-primers.

contrast, as seen in Figure 23, panel b, it appears that the DAT non-primers show RT priming for both named and unnamed stimuli.

Neuropsychological Data

For each neuropsychological measure, most participants were assessed. Occasionally data were unavailable on some tests for patients with DAT and elderly adults.

Mini-Mental Status Examination (MMSE)

Figure 24 shows the scores obtained on the MMSE for each group. The young and elderly groups had a near-perfect performance on this measure; t-tests showed that there were no differences between the two groups, $t(28) = .96$, $p = .35$. As expected, DAT patients performed significantly poorer on this measure as compared to elderly adults, $t(21) = 6.25$, $p < .001$. As can be observed in Figure 25, there was no difference between DAT primers and DAT non-primers on this measure, $t(6) = .00$, $p = 1.00$.

Boston Naming Test (BNT)

Naming performance for each group on the BNT is shown in Figure 26. As expected, the young and elderly groups were able to name most of the pictures, and there were no significant differences between the groups, $t(28) = -1.76$, $p = .08$. However, DAT patients were able to name significantly fewer items on this test than elderly adults, $t(22) = 8.58$, $p < .001$. An analysis of DAT primers and DAT non-

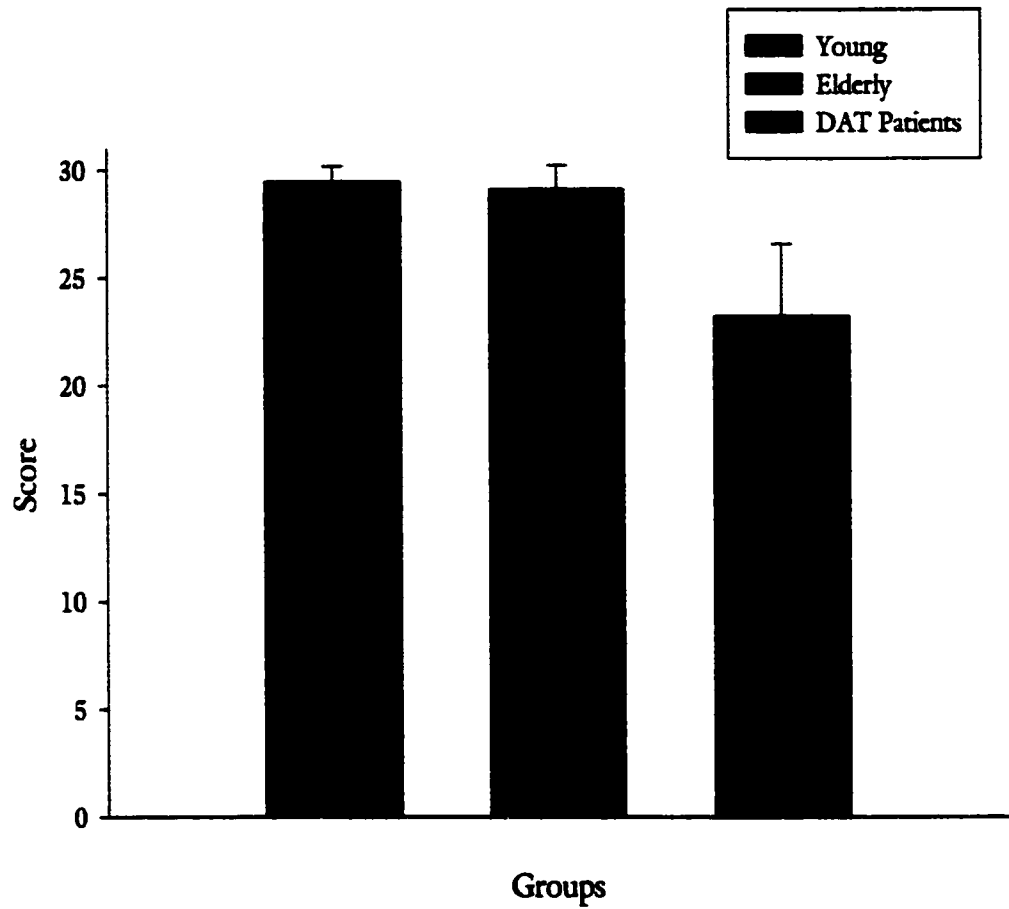


Figure 24. Performance on Mini-Mental Status Examination (MMSE) for young adults, elderly adults, and DAT patients.

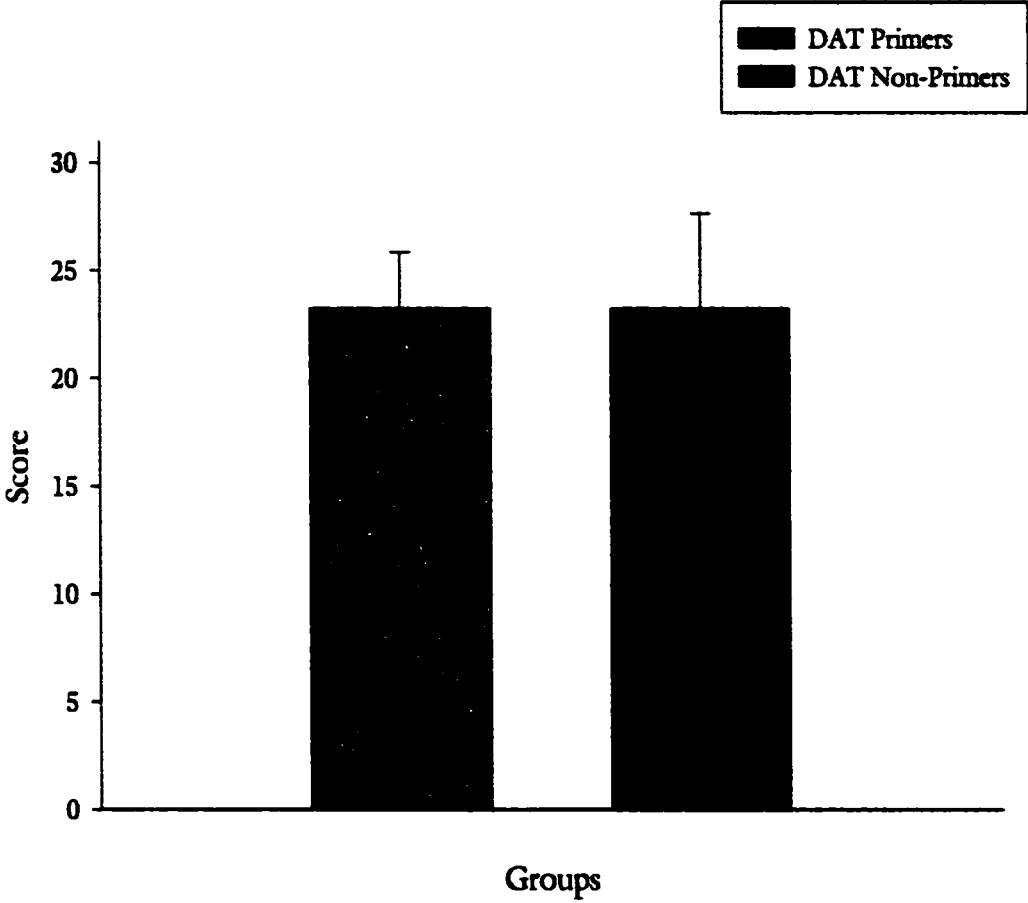


Figure 25. Performance on Mini-Mental Status Examination (MMSE) for DAT primers and DAT non-primers.

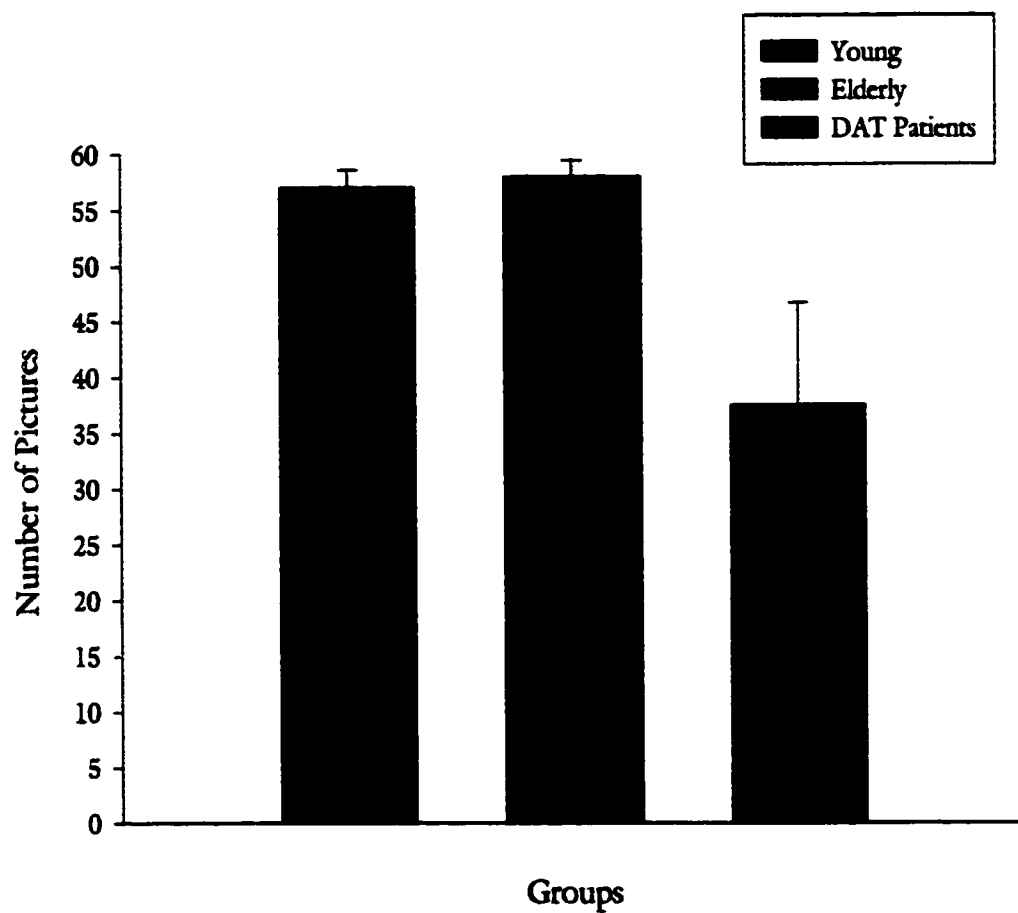


Figure 26. Performance on Boston Naming Test (BNT) for young adults, elderly adults, and DAT patients.

primers resulted in no differences between the two patient groups on this measure, $t(7) = .28$, $p = .78$, (see Figure 27).

Verbal Fluency

Phonemic Fluency. Figure 28 shows each group's average number of words generated on the phonemic fluency task for the letters F, A, and S. The young and elderly groups did not differ significantly on total number of words generated, $t(26) = 0.17$, $p = .86$. In comparison to the elderly adults, the DAT patients generated significantly fewer words, $t(18) = 5.67$, $p < .001$. Figure 29 shows the DAT primers and DAT non-primers performance on the phonemic fluency task; there was no significant difference in the amount of words generated by the two groups, $t(5) = 0.47$, $p = .65$.

Semantic Fluency. The average number of words generated on the semantic fluency task for the category of animals is shown in Figure 30 for the young, elderly, and DAT patient groups. The young group were able to generate more animals than the elderly group, $t(26) = 3.30$, $p = .003$. In addition, the elderly group were able to generate significantly more names of animals than the DAT patient group, $t(20) = 4.70$, $p < .001$. The performance of the DAT primers and DAT non-primers on this measure is shown in Figure 31; there were no differences between patient groups, $t(7) = 0.25$, $p = .81$.

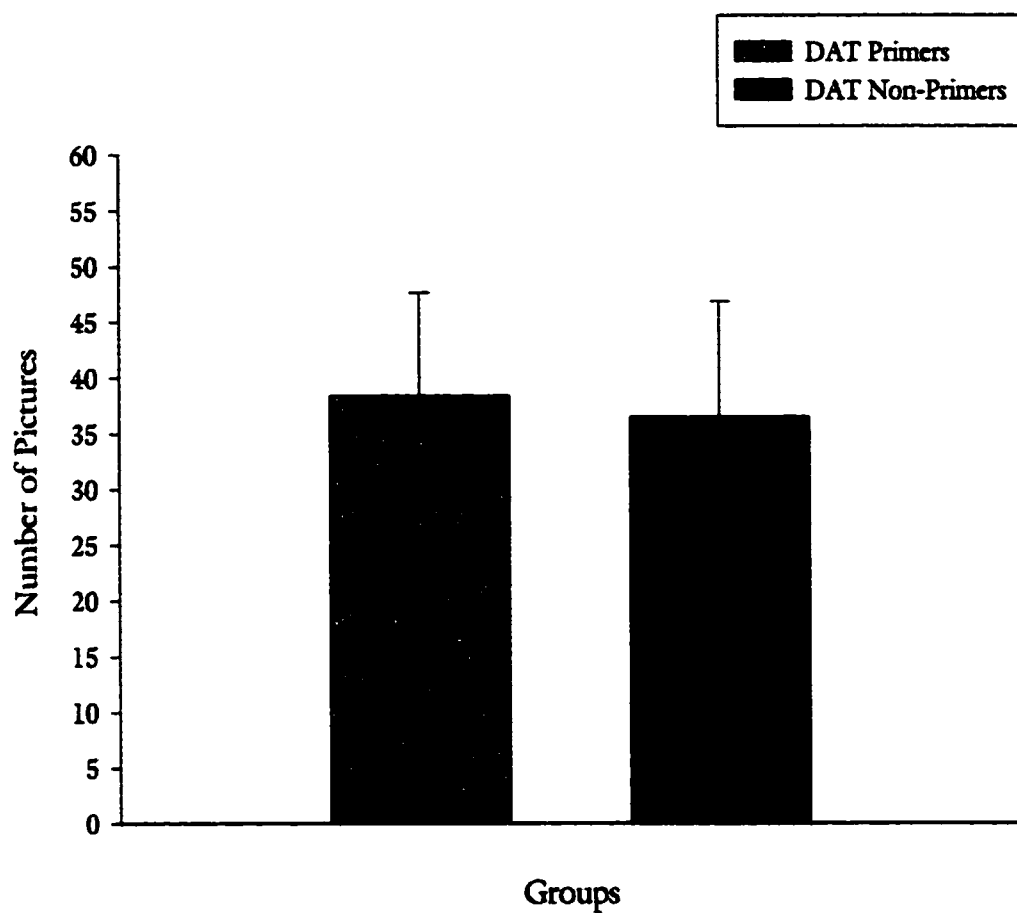


Figure 27. Performance on Boston Naming Test (BNT) for DAT primers and DAT non-primers.

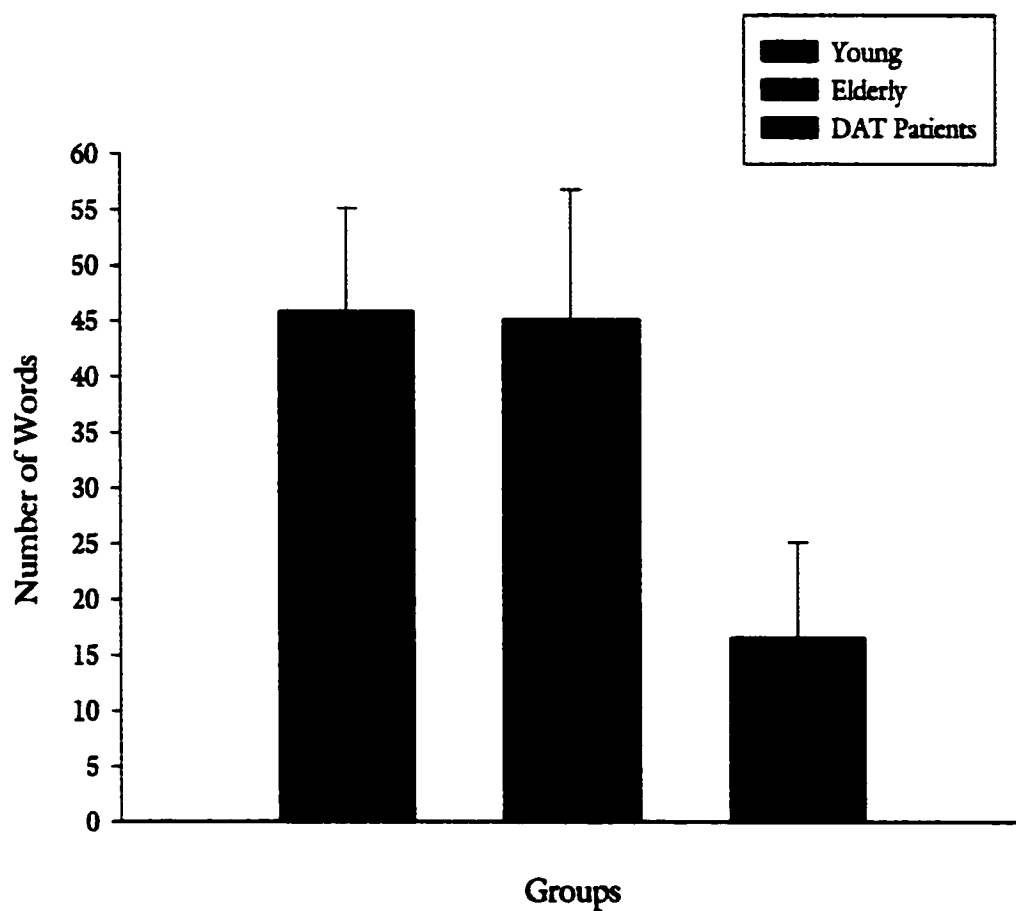


Figure 28. Performance on the Phonemic Fluency Task (letters F, A, and S) for young adults, elderly adults, and DAT patients.

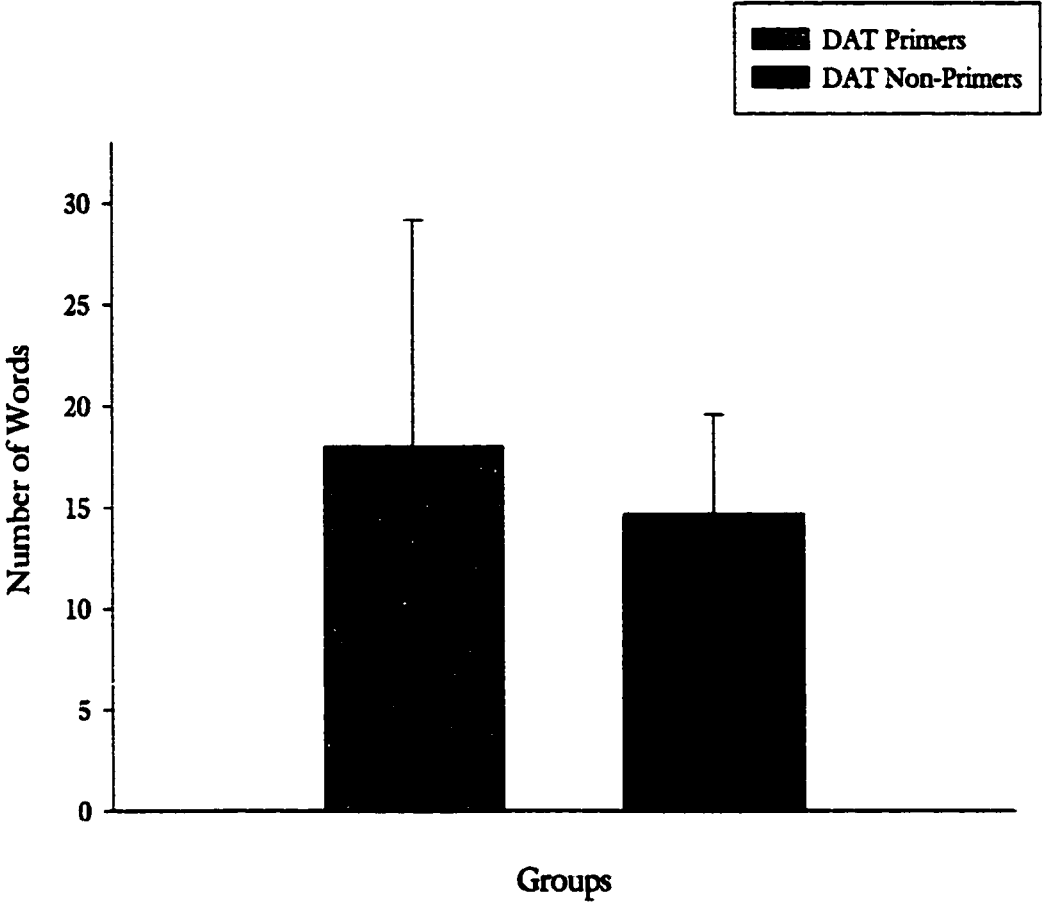


Figure 29. Performance on the Phonemic Fluency Task (letters F, A, and S) for DAT primers and DAT non-primers.

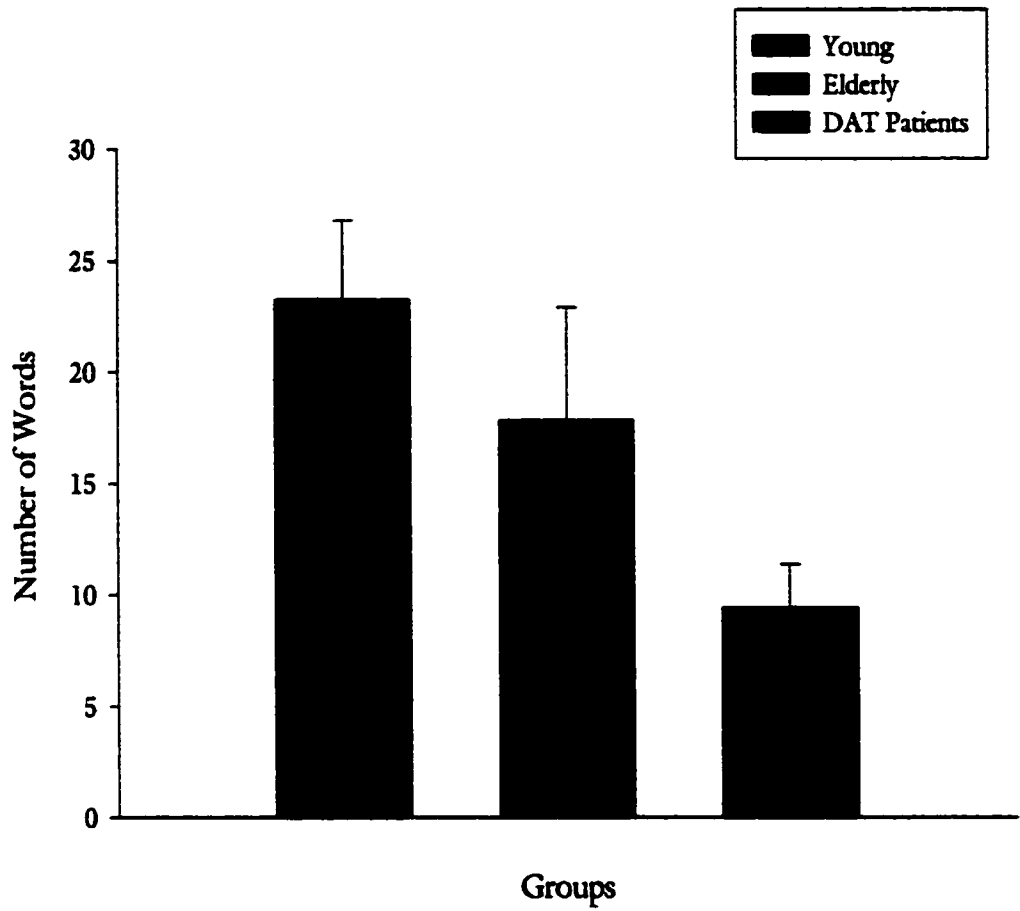


Figure 30. Performance on the Semantic Fluency Task (category: animals) for young adults, elderly adults, and DAT patients.

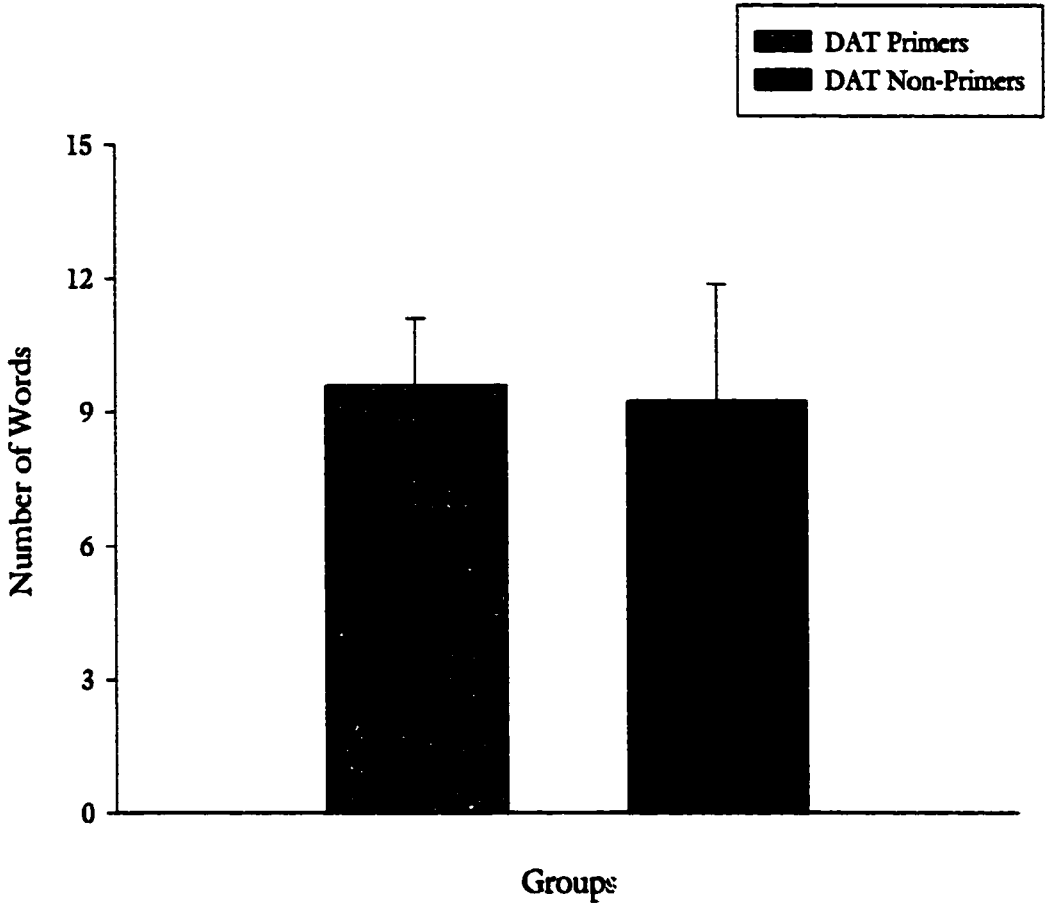


Figure 31. Performance on the Semantic Fluency Task (category: animals) for DAT primers and DAT non-primers.

Discussion

In this study, the two measures of priming were the N400 ERP component and reaction time (RT). For ERP priming to occur, the N400 amplitude should be more negative in the unrelated as compared to the related prime condition. For RT priming to occur, reaction time should be faster for the related condition than for the unrelated condition.

Young and Elderly Adults. From the present study, it is evident that the young group showed both ERP and RT priming effects. For the young adults, anterior, central, and posterior regions showed ERP priming effects, as evidenced by a difference in N400 amplitude for unrelated versus related targets in all regions. However, consistent with other studies (Brown, Hagoort, & Chwilla, 2000; Connolly, Phillips, & Forbes, 1995), the N400 effect was strongest in the posterior regions. As expected, the N400 effect was strongest between 300 to 500 ms post-stimulus onset. Overall, the ERP priming effects for the young adults were particularly robust; as seen in Figure 8, panel a, there is more than a $6\mu V$ difference between the two priming conditions.

Reaction time measures showed that the young adults were fast to respond. The young group also showed faster reaction times for related than for unrelated targets; these RT priming effects are comparable to results from other priming studies, (Hamberger, Friedman, Ritter, & Rosen, 1995).

The elderly group also showed both ERP and RT priming effects. For the ERP

measure, there was a restriction in topographical region; statistically, the N400 effect was observed in posterior regions only. As expected, there was also a delay in latency of the N400 for the elderly. The N400 priming effect was significant between 400 to 600 ms post-stimulus onset, which is a 100 ms time interval later than was observed in young adults. This is consistent with previous studies that show, in comparison to the young, the N400 for the elderly is most prominent at a later time interval (Iragui et al., 1996; Schwartz et al., 1996). Also consistent with the literature, the elderly group showed slower overall reaction times as compared to the young (Laver & Burke, 1993). The degree of RT priming seems equivalent for young and elderly, as calculated proportions were similar for the two groups.

As predicted, the young and elderly groups were able to name most pictures; hence, there was an insufficient number of unnamed stimuli to be analyzed for the young and elderly groups. There were also no differences in level of accuracy between the young and elderly. Although accuracy was high in both conditions, the young and elderly were more accurate at responding in the unrelated condition as compared to the related condition. This finding could be due to the selection of words for both conditions. In the unrelated condition, the words were selected from a completely different semantic category (e.g., word-envelope, picture-sheep); hence, it should not have been too difficult to decide that the word and picture were unrelated. In the related condition, however, the judgement was perhaps more difficult because the

individual had to understand the relation between the word and the picture. For most items this was presumably not difficult (e.g. word-wool, picture sheep), yet there were a few items (i.e., those that received lower ratings in the pilot study) where the choice may have been more difficult (e.g. word-graceful, picture-swan).

As expected, the young and elderly groups performed well within the expected norms for the neuropsychological measures. The young and elderly also did not differ from each other on the Mini-Mental Status Examination and the Boston Naming Test. However, there were age-related differences on the fluency measures. More specifically, the young and elderly were statistically equivalent for the phonemic fluency task, yet the young were able to generate more words on the semantic fluency task. It should be noted that there was overlap in performance on the semantic fluency task, with the number of animals generated ranging from 18 to 29 for the young, and 12 to 25 for the elderly. The results of the neuropsychological data generally support the finding that there were negligible age-related differences in performance on measures of naming, fluency, and general cognitive functioning.

The young and elderly were well matched on demographic variables. The ratio of males to females was identical for each group. Similarly, years of formal education were virtually equivalent. Matching on education was an important design issue, however, it should be noted that there is perhaps a cohort effect in that it is more unusual for the elderly population to have numerous years of education. Therefore, it

may be possible that given the higher level of education in the elderly group, the elderly adults tested in this study may have performed better than would be expected from most elderly adults in the general population.

Elderly Adults and Patients with DAT. The patients with DAT were recruited after testing of the young and elderly was completed. As is often the case when recruiting from a clinical population, there was a limited number of willing participants. This led to a smaller sample than was originally anticipated. In addition, given the small patient pool, matching patients to elderly adults on age and level of education was not possible. Further testing will take these demographic differences into account. DAT patients with higher levels of education and lower age, and more aged elderly adults with lower education levels will be tested to better match the two groups.

It should be noted that although the elderly and DAT patient groups were not equivalent on years of education, they had similar occupations. Using the Hollingshead index (Hollingshead, 1975) to rank each elderly adult and DAT patient, statistical analysis revealed no differences in ranking of occupational level between the two groups. Hence, although the elderly and DAT patient groups differ on years of formal education, they do not differ on occupational level attained.

As expected, the patients with DAT differed from the elderly adults on all neuropsychological measures. This provides evidence that the patient group differs from the healthy elderly group on measures of cognitive impairment, naming ability,

and fluency.

Within this study, the two dependent variables of priming provided a somewhat different insight into the nature of the semantic deficits in patients with DAT. For the ERP measures, there were unfortunately no reliable ERP priming effects for the DAT patient group. Regardless of whether the stimuli could be named or not, ERP priming was not consistently observed in the DAT patients. As mentioned, and can be observed in each patient's individual waveforms (see Appendices H and I), there was large variability within the patient group.

In contrast, reaction time measures for the DAT patients did show priming for the named stimuli, as evidenced by faster reaction times in the related condition. More specifically, DAT patients showed hyperpriming in that they benefitted substantially more than the elderly adults in the related condition.

Some researchers have argued that increased priming effects may be an artifact of general cognitive slowing, as evidenced by overall slower reaction times (Amrhein, 1995; Chertkow, Bub, & Seidenberg, 1989). Reaction time results from the present study show a pattern which reflects slowing for the elderly, and even greater slowing for the DAT patients. The patient group, however, showed more priming as measured by reaction time for the named items in the related condition than could be accounted for by slowing alone.

Ober and Shenaut (1995) reviewed 21 semantic priming studies involving

elderly controls and patients with DAT. All of the studies tested patients with a mild to moderate dementia rating, and all used reaction time as a measure of priming. In the review, Ober and Shenaut differentiated between controlled and automatic processes in priming. Controlled processes are involved in priming experiments that use a long stimulus onset asynchrony (SOA) of 400-500 ms or more. Participants show strategy-driven effects in experiments with longer SOAs; it is believed that when presented with a prime, participants generate a set of potential targets that are related to the prime, and that these targets are processed more quickly than targets that are not in the set (i.e., unrelated targets). Automatic priming occurs with a shorter SOA since these experiments do not allow sufficient time to generate an expectancy set. Ober and Shenaut reported that 9 of the 21 experiments showed hyperpriming results. Of these nine experiments, all employed long SOAs, and thus involved controlled processes. Interestingly, there was only one other study that was classified as a “controlled” experiment that did not demonstrate hyperpriming for the DAT patients.

Given this information, when creating the word-picture semantic priming paradigm for this study, a short SOA was going to be used. Unfortunately, due to limitations of the available software, the program only allowed for a minimum SOA of 570 ms. Therefore, it is a possibility that the RT hyperpriming effects found in this study were the result of a priming task in which controlled, not automatic, processes were used.

In comparison to other semantic priming studies investigating patients with DAT using ERP measures, this study employed the shortest SOA. Most studies used sentence stimuli, where SOA is harder to calculate. In a study that used picture pairs (Ostrosky-Solis et al., 1998), the SOA was 1300 ms; however, even with a longer SOA, priming effects were not observed in patients with DAT. In contrast, the recent Ford study (2001) had an equally long SOA of 1500 ms, and showed priming in DAT patients with ERP measures. It is possible that length of SOA may not result in hyperpriming when using ERP measures, yet may explain results obtained when using reaction time measures.

Another possible explanation of hyperpriming may lie within the findings of Chan and colleagues, who concluded that semantic networks of DAT patients were cluttered and had more links than those of age-matched controls (Chan, Butters, & Salmon, 1997). If this is indeed the case, then following the semantic association theory, those extra links may benefit the DAT patient, and consequently manifest in the form of excessive priming. Of course, this is just a possible explanation; further research needs to be conducted on semantic networks to discover whether the number of links in a patient's network positively correlate with the degree of priming.

Named versus Unnamed Stimuli for Patients with DAT. As expected, each patient with DAT had a sufficient number of unnamed pictures to be able to analyze priming effects as a function of naming.

As can be observed in Appendices H and I, there was notable heterogeneity in ERP priming effects both for named and unnamed stimuli. For example, DAT patient D2 (see Figure H1, panels a and b) appeared to show ERP priming effects for both named and unnamed stimuli. In contrast, DAT patient D3 (see Figure H2, panels a and b) showed a difference in N400 amplitude for named stimuli (i.e., an ERP priming effect), yet no observable difference for unnamed stimuli. Given the heterogeneity across patients in ERP priming, it is not surprising that no significant priming effects were observed. It is thus impossible at this point to draw any conclusions about ERP priming effects for the named and unnamed stimuli.

Reaction time measures as a function of naming revealed that patients with DAT showed priming for named stimuli, yet no priming for unnamed stimuli. If this study used reaction time as its sole measure, then these results would provide supporting evidence for the deterioration hypothesis. In other words, patients with DAT benefitted from the relatedness, as evidenced by faster reaction times for the named items, yet did not show the same pattern for unnamed items. The inability to benefit from the semantic context for the unnamed pictures may suggest a deterioration of semantic memory for these items. It is important to remember, however, that this was not merely a RT study as electrophysiological activity was also measured.

DAT Primers and DAT Non-Primers. It is quite puzzling why some patients showed apparent ERP priming and others did not. For this reason, patients were split

into DAT primers and DAT non-primers to determine whether the two sub-groups differed on neuropsychological or demographic variables. The DAT primer group was selected on the basis of visual inspection of individual waveforms that showed priming for named pictures. Hence, it is not surprising that the grand average for the DAT primers for named stimuli, as seen in Figure 13, panel a, shows the N400 appearing more negative for the unrelated as compared to the related condition. ERP priming effects were found in the DAT primers, however, only when an analysis of named and unnamed stimuli was conducted. This significant finding could be due to the analysis having more degrees of freedom. Therefore, it is quite possible that ERP priming effects were not obtained in the elderly versus DAT group analysis due to a lack of power. Hence, testing a larger number of DAT patients may yield more reliable ERP priming results.

Similar to the entire patient group, when split into DAT primers and DAT non-primers based on observable ERP priming, both patient sub-groups showed RT priming for named stimuli. Interestingly, when calculating proportion of priming, it appeared that the DAT non-primers showed more priming than the DAT primers, who showed more priming than the elderly.

For unnamed stimuli, there was a strong trend for the DAT primers and DAT non-primers to show opposite results for reaction time measures. Figure 23, panel a reveals that DAT primers showed RT priming effects for named stimuli, yet no RT

priming for unnamed stimuli. In contrast, as seen in Figure 23, panel b, it appears that non-primers show RT priming for both named and unnamed stimuli. This result may at first appear to be counterintuitive, however, the RT priming trend observed in the DAT non-primers for the unnamed stimuli could be another case of hyperpriming.

In a RT priming experiment conducted by Chertkow, Bub, and Seidenberg (1989), items were categorized as intact (i.e., DAT patients responded correctly to probe questions assessing knowledge) or degraded (i.e., DAT patients responded incorrectly to probe questions). Results from that study revealed that DAT patients showed an increased priming effect for degraded items as compared to intact items. Chertkow and colleagues argued that excessive priming occurs when semantic memory has deteriorated. Given that priming facilitates the processing of information, Chertkow et al. suggest that DAT patients who are at a disadvantage (i.e., because information is lost or deteriorated) actually benefit from the facilitation effects of priming proportionately more than individuals with intact information. In the present study, it could be possible that ERPs are sensitive to subtleties of semantic memory impairments, and thus, DAT non-primers have less semantic knowledge, which, in turn, manifests itself as RT hyperpriming.

It is unclear why the two sub-groups may be different. It is of interest, however, that these two patient groups that appeared to differ on ERP priming measures, also differed on other measures. For example, for percent correct, as seen in Figure 17, the

DAT primer and elderly groups were more accurate in responding to the unrelated condition; yet the DAT non-primer group showed the opposite pattern (i.e., less accurate in the unrelated condition). No significant differences between the DAT primers and DAT non-primers were found on demographic or neuropsychological variables. The absence of differences could be interpreted in several ways. First, it is possible that the groups do not differ on these measures, thus, no differences were observed. In contrast, it could be possible that the groups do differ on these measures, but given the small sample size of each sub-group, these real differences were not detected. Finally, the groups may not differ on the variables measured, but may differ in some way that has not been measured. The correct interpretation of the lack of apparent differences between the two groups will only be obtained with a larger patient group.

Does having two priming measures add to our understanding of the nature of semantic memory deficits or confuse the findings? Although the results obtained in this study are not clearcut, having both behavioural and electrophysiological measures can lead to a greater understanding of underlying semantic processes. ERPs are still a beneficial measure; in fact, one patient who was unable to complete the behavioural task nevertheless showed ERP priming. If reaction time had been the sole measure of priming then no conclusions could have been drawn for this individual. Given the additional ERP measure, however, it is possible to conclude that this patient appeared

to show some degree of priming.

ERPs provide an opportunity to observe activity related to semantic processing, which occurs between onset of stimuli and the time a behavioural response is made. It is fascinating that contradictory results were found for the ERP and RT measures. These divergent results are consistent with other studies. Ford and colleagues (2001) for example, also showed differing results between RT and ERP measures. In their study, they found ERP priming for both named and unnamed stimuli; yet only RT priming for named stimuli. Consistent with Ford and colleagues, this study found a similar pattern of results for RT measures. For ERP measures, results from the present study differs from those obtained by Ford et al., 2001. These differences can perhaps be explained by the prime conditions that were used. Ford and colleagues used an identity prime (picture-camel, word-camel) and unrelated prime (picture-camel, word-fox). In the N400 literature, it is frequently observed that with the correct manipulation, an N400 gradient can be observed: unrelated prime condition appearing most negative in amplitude; followed by related prime condition; and finally identity prime condition (Hamberger et al., 1995; Auchterlone, 1999). It is possible that the ERP priming effects observed in the Ford et al. study may exist because two extremes of the gradient were being compared.

It should be noted, however, that the unrelated prime condition used by Ford et al. employed word targets from the same category as the picture primes. Hence, the

words were not completely unrelated to the picture primes. The participant's task was to determine if the picture and word were a match or not. In some cases it is perhaps easier to make a match/no match decision, than a related/unrelated decision as the latter involves a deeper level of semantic processing. In comparing the accuracy rates of the present study to Ford et al., it seems that accuracy was comparable for named stimuli. For unnamed stimuli, our study had a lower level of accuracy for related decisions, but a higher accuracy for unrelated decisions. Intuitively this makes sense: if a picture is not able to be named, it would be easier to judge that the word and picture were a match (i.e., the same), than it would be to determine that it is related, as the latter requires a deeper level of semantic processing. On the other hand, for an unnamed picture it would be easier to judge that a word and picture were unrelated, as the word and picture pair are from different semantic categories, than it would be to determine if they are a non-match, as the pair were from the same semantic category in the Ford et al. study.

It is also necessary to point out that ERP measures are perhaps not as stable as reaction time measures. Thus, more individuals may need to be tested to form a clearer picture into the nature of semantic memory deficits. Future research will include the testing of additional patients within this paradigm. In addition, a semantic battery is currently being developed. This battery contains sixty of the most commonly named and unnamed pictures. For each picture, four semantic questions have been created.

The questions refer to size, speed, colour, location, and other general knowledge pertaining to each picture. This semantic battery will be administered to all of the patients that have been tested, and to all future patients. It is believed that the information from the semantic battery, along with the ERP and RT measures, will shed light on the true nature of semantic memory deficits in patients with DAT.

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Appendix A
Health Screening Questionnaire

- Trouble hearing: NO / YES
Hearing Aid: Left / Right

- Have you ever been unconscious, had a head injury or had blackouts? NO / YES

Cause:

Duration:

Treatment:

Outcome:

- Have you been seriously ill or hospitalized in the past 6 months? NO / YES

Duration:

Cause:

If Yes - Treatment: With what? Since when? Current status?

Do you have now, or have you had in the past -

- | | | | |
|--|----------|---|----------------------------|
| • Stroke | NO / YES | When? | Transient ischemic attack? |
| • Heart disease | NO / YES | Nature (MI, angina, narrowing of arteries): | |
| • High blood pressure | NO / YES | Controlled? | |
| • High Cholesterol | NO / YES | | |
| • Bypass surgery | NO / YES | | |
| • Surgery | NO / YES | Nature: | |
| • Seizures | NO / YES | Age Onset: | Freq: |
| | | Cause: | Treatment: |
| • Epilepsy | NO / YES | | |
| • Diabetes | NO / YES | Type I / Type II | Age Onset: |
| Insulin dependent? | NO / YES | Treatment: | |
| • Thyroid disease | NO / YES | | |
| • Frequent headaches | NO / YES | Tension / migraine | |
| • Dizziness | NO / YES | | |
| • Trouble walking/unsteadiness | NO / YES | | |
| • Serious illness (e.g. liver disease) | NO / YES | | |
| • Neurological disorders | NO / YES | | |
| • Exposure to toxic chemicals (that you know of)? | NO / YES | | |
| • Depression | NO / YES | | |
| • Anxiety | NO / YES | | |
| • (Other) psychological difficulties? | NO / YES | | |

Medication

| | | |
|------|------------------------|----------------------------------|
| Type | Reason for consumption | Age/Duration of consumption/Dose |
|------|------------------------|----------------------------------|

Hormone replacement? / Steroids?

Alcohol, Tobacco, Drug Consumption (1 drink = 1 beer, 1 glass of wine, 1 oz of liquor)

- Current/Past

| | | | |
|--|----------------------------------|------|--------------------|
| | Amount (per day/week/month/year) | | |
| | Present | Past | Age of Consumption |

Alcohol

Tobacco

if Yes: packs/day
(exclude if 20 pack-years)

Drug use

Present Problems - Are you currently troubled by any of the following?

- Concentration / Attention problems NO / YES Nature:
- Memory problems NO / YES Nature:
- Difficulties finding words NO / YES Nature:

What is your **general state of health** (1-5, where 1 is poor and 5 is excellent)? 1 2
3 4 5

Address for correspondence:

Appendix B

Education Level and Occupational Ranking

Table B1

Years of Education, Occupational Information, and Hollingshead Category for Each Elderly Adult

| Elderly Adults | Education | Occupation | Hollingshead |
|----------------|-----------|------------------------|--------------|
| | | | Category |
| E1 | 16 | salesman | 4 |
| E2 | 9 | athletic trainer | 5 |
| E3 | 14 | personal shopper | 4 |
| E5 | 13 | cashier at dept. store | 6 |
| E6 | 19 | quality controller | 2 |
| E7 | 13 | secretary | 4 |
| E10 | 15 | economist | 1 |
| E11 | 17 | CEGEP teacher | 2 |
| E12 | 12 | technician for airline | 4 |
| E13 | 15 | executive secretary | 4 |
| E14 | 18 | public relations | 3 |
| E15 | 16 | assessor for New York | 3 |
| E16 | 17 | teacher | 2 |
| E17 | 18 | engineer | 1 |
| E18 | 13 | elementary teacher | 2 |

Table B2

Years of Education, Occupational Information, and Hollingshead Category for EachDAT Patient

| DAT Patients | Education | Occupation | Hollingshead |
|--------------|-----------|--|-------------------|
| | | | Category |
| D1 | 10 | N.A. ¹ | N.A. ¹ |
| D2 | 8 | interior designer | 3 |
| D3 | 7 | salesperson | 4 |
| D4 | 17 | accountant | 2 |
| D5 | 13 | bookkeeper | 4 |
| D6 | 13 | N.A. ¹ | N.A. ¹ |
| D7 | 13 | director for research of chemicals related to wood | 2 |
| D8 | 5 | owned construction company | 3 |
| D9 | 11 | retailer | 4 |

¹Information not available

Appendix C

Consent Form for Young and Elderly Adults

Jewish General Hospital
Department of Clinical Neurosciences
Electrophysiological Investigation of Semantic Memory

**Consent Form for the Jewish General Hospital Study of
Electrophysiological Investigation of Semantic Memory**

Purpose of the Study:

The purpose is to determine whether a certain waveform in electrical brain activity (like EEG) reflects how we process certain kinds of information and knowledge about everyday concepts.

Details of the Study:

The study will take place in the EEG laboratory of the Department of Neurology, Jewish General hospital. To record the EEG, a nylon cap containing small sensors (electrodes) will be placed on my head. In order to prepare the skin to obtain proper readings, the scalp area underneath each sensor will be lightly rubbed. While the recordings are being made, I will be watching a computer screen on which there will be some words and/or pictures presented. I will be asked to pay attention to the information in order to be able to answer questions about it (for example, whether two items are related to one another or not). I understand that while I may not be able to answer every question perfectly, the most important thing will be that I will try to do my best.

This study will require one (1) visit to the EEG laboratory, which should last approximately 1½ to 2 hours. Transportation can be arranged for me or I will be reimbursed for my travel. Since this test is not diagnostic in any manner and is for research purposes only, I understand that the study results will not be made available to me. However, any other relevant clinical findings will be communicated to my doctor.

Disadvantages and Risks of Participating in the Study:

EEG testing is a painless and non-invasive (using no foreign substances like medications, tubes, or needle injections) procedure. Nevertheless, while the scalp is being prepared for recording, some people may experience a mild and temporary discomfort where the skin is being rubbed. It is also possible that I will find it boring or frustrating to look at the information on the computer screen. However, I will be given frequent breaks whenever required to avoid this. I understand that, in the *unlikely* event that any finding of possible clinical significance is made and communicated to my physician, it may be recommended that I have additional testing which would not have taken place if I had not participated in this study.

Advantages to Participating in the Study:

The researchers hope to learn more about what brain processes are involved when one sees a meaningful word or picture. Although this will not benefit me directly, this research could add to our scientific understanding of how everyday knowledge about the world is represented in the brain.

Jewish General Hospital
 Department of Clinical Neurosciences
Electrophysiological Investigation of Semantic Memory

Confidentiality:

I understand that my participation in this study is *confidential*, that is, the researcher will know but will not disclose my identity in any published report or scientific communication. My records will not be identified by name; instead a subject code will be used. If the present study is published, only group results will be mentioned, insuring my confidentiality as a participant in this experiment.

Withdrawal from the Study:

I understand that my participation in this study is voluntary and, if I agree to participate, I may withdraw my consent and discontinue participation *at any time* without negative effects.

Participant's/Patient's Rights:

I have fully discussed and understood the purpose and procedure of this study and have had the opportunity to ask any questions.

The following is the name, address, and telephone number of the Hospital's Patient representative, who is not associated with this study and to whom I may address my concerns about this study:

**Mrs. Lianne Brown, 3755 Côte Ste. Catherine Road, Montreal, Quebec, H3T 1E2;
 tel: 340-8222 ext. 5833.**

The following is the name, address, and telephone number of the researcher whom I may contact for answers to questions about the research or any injuries or adverse reactions which might occur:

Dr. Natalie Phillips, Dept. of Psychology, Concordia University, 7141 Sherbrooke Street West, Montreal, Quebec, H4B 1R6; tel: 848-2218

Signature:

I have understood the contents of this consent form and have had the opportunity to ask questions. I agree to participate in this study.

| | | |
|-------|--|------------|
| _____ | _____ | _____ |
| Date | Signature of Subject | Print Name |
| | _____ | _____ |
| | Signature of Investigator | Print Name |
| | _____ | _____ |
| | Signature of person explaining informed consent | Print Name |

August 2000

All participants will receive a copy of this consent form

Appendix D

Consent Form for DAT Patients

Jewish General Hospital
Department of Clinical Neurosciences
Electrophysiological Investigation of Semantic Memory

**Consent Form for the Jewish General Hospital Study of
Electrophysiological Investigation of Semantic Memory**

Purpose of the Study:

The purpose is to determine whether a certain waveform in electrical brain activity (like EEG) reflects how we process certain kinds of information and knowledge about everyday concepts. Since I may have mild difficulty in using such information (e.g., having a word "on the tip of my tongue"), I have been asked to participate.

Details of the Study:

The study will take place in the EEG laboratory of the Department of Neurology, Jewish General hospital. To record the EEG, a nylon cap containing small sensors (electrodes) will be placed on my head. In order to prepare the skin to obtain proper readings, the scalp area underneath each sensor will be lightly rubbed. While the recordings are being made, I will be watching a computer screen on which there will be some words and/or pictures presented. I will be asked to pay attention to the information in order to be able to answer questions about it (for example, whether two items are related to one another or not). I understand that while I may not be able to answer every question perfectly, the most important thing will be that I will try to do my best.

This study will require one (1) visit to the EEG laboratory, which should last approximately 1½ to 2 hours. Transportation can be arranged for me or I will be reimbursed for my travel. Since this test is not diagnostic in any manner and is for research purposes only, I understand that the study results will not be made available to me. However, any other relevant clinical findings will be communicated to my doctor.

Disadvantages and Risks of Participating in the Study:

EEG testing is a painless and non-invasive (using no foreign substances like medications, tubes, or needle injections) procedure. Nevertheless, while the scalp is being prepared for recording, some people may experience a mild and temporary discomfort where the skin is being rubbed. It is also possible that I will find it boring or frustrating to look at the information on the computer screen. However, I will be given frequent breaks whenever required to avoid this. I understand that, in the *unlikely* event that any finding of possible clinical significance is made and communicated to my physician, it may be recommended that I have additional testing which would not have taken place if I had not participated in this study.

Advantages to Participating in the Study:

The researchers hope to learn more about what brain processes are involved when one sees a meaningful word or picture. Although this will not benefit me directly, this research could add to our scientific understanding of how everyday knowledge about the world is represented in the brain.

Jewish General Hospital
 Department of Clinical Neurosciences
Electrophysiological Investigation of Semantic Memory

Confidentiality:

I understand that my participation in this study is *confidential*, that is, the researcher will know but will not disclose my identity in any published report or scientific communication. My records will not be identified by name; instead a subject code will be used. If the present study is published, only group results will be mentioned, insuring my confidentiality as a participant in this experiment.

Withdrawal from the Study:

My participation in this study is voluntary and, if I agree to participate, I may withdraw my consent and discontinue participation *at any time without affecting my medical care*.

Participant's/Patient's Rights:

I have fully discussed and understood the purpose and procedure of this study and have had the opportunity to ask any questions.

The following is the name, address, and telephone number of the Hospital's Patient representative, who is not associated with this study and to whom I may address my concerns about this study:

**Mrs. Lianne Brown, 3755 Côte Ste. Catherine Road, Montreal, Quebec, H3T 1E2;
 tel: 340-8222 ext. 5833.**

The following is the name, address, and telephone number of the researcher whom I may contact for answers to questions about the research or any injuries or adverse reactions which might occur:

Dr. Natalie Phillips, Dept. of Psychology, Concordia University, 7141 Sherbrooke Street West, Montreal, Quebec, H4B 1R6; tel: 848-2218

Signature:

I have understood the contents of this consent form and have had the opportunity to ask questions. I agree to participate in this study.

 Date

 Signature of Subject

 Print Name

 Signature of Investigator

 Print Name

 Signature of person explaining
 informed consent

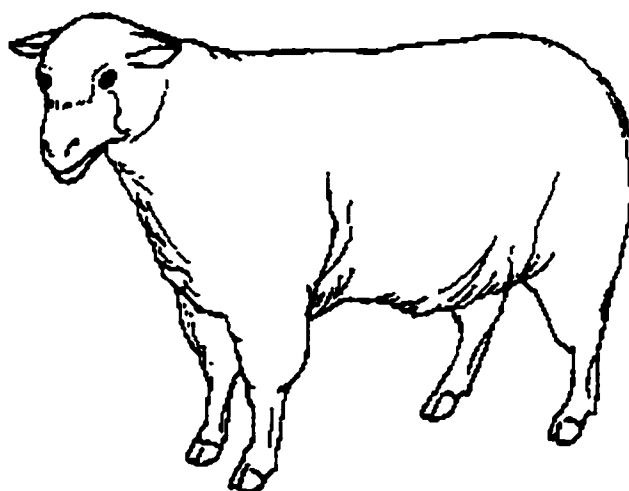
 Print Name

October 2000

All participants will receive a copy of this consent form

Appendix E

Example of Picture Stimuli



Appendix F

Example of Word Stimuli

wool

Appendix G

List of Picture Stimuli with Word Primes

| RELATED WORDS | PICTURES | UNRELATED WORDS |
|---------------|--------------|-----------------|
| polka | Accordion | mansion |
| swamp | Alligator | peas |
| hammer | Anvil | ivy |
| orchard | Apple | map |
| sign | Arrow | glue |
| cigarette | Ashtray | fast |
| broccoli | Asparagus | candy |
| stroller | Babycarriage | field |
| bounce | Ball | cauliflower |
| party | Balloon | tractor |
| farm | Barn | shawl |
| baseball | Baseballbat | bomb |
| sting | Bee | frame |
| buckle | Belt | axe |
| nest | Bird | lamp |
| return | Boomerang | scarf |
| ribbon | Bow | cave |
| soup | Bowl | marker |
| blouse | Button | frog |
| candle | Candelabrum | bus |
| fortress | Cannon | turtle |
| hat | Cap | book |
| rabbit | Carrot | butcher |
| worm | Caterpillar | vest |
| stalk | Celery | razor |
| carriage | Chariot | scallop |
| pie | Cherry | couch |
| checkmate | Chessboard | string |
| wood | Chisel | sundae |
| worship | Church | basin |
| oyster | Clam | leaf |
| laundry | Clothespin | desk |
| sky | Clouds | lock |
| jacket | Coat | apricot |
| brush | Comb | armour |
| shrimp | Crab | skirt |
| king | Crown | piano |
| moose | Deer | turnip |

| RELATED WORDS | PICTURES | UNRELATED WORDS |
|---------------|---------------|-----------------|
| puppet | Doll | grill |
| mule | Donkey | fog |
| handle | Doorknob | grass |
| drawer | Dresser | finger |
| quack | Duck | elbow |
| hawk | Eagle | drum |
| picket | Fence | antelope |
| nail | File | whale |
| pink | Flamingo | fan |
| petal | Flower | anchor |
| clarinet | Flute | cooking |
| touchdown | Football | witch |
| sly | Fox | cookie |
| brass | French-horn | ant |
| pot | Frying-pan | castle |
| neck | Giraffe | nurse |
| billy | Goat | parachute |
| canal | Gondola | blender |
| ape | Gorilla | stem |
| cricket | Grasshopper | moon |
| banjo | Guitar | nature |
| police | Handcuffs | bell |
| angel | Harp | moth |
| propellor | Helicopter | eel |
| crash | Helmet | robin |
| elephant | Hippopotomus | airplane |
| time | Hourglass | bridge |
| iron | Ironing-board | cow |
| canoe | Kayak | goose |
| fork | Knife | beaver |
| eucalyptus | Koala | jelly |
| beetle | Ladybug | sock |
| spots | Leopard | octopus |
| salad | Lettuce | happy |
| iguana | Lizard | pear |
| camel | Llama | mirror |
| crawfish | Lobster | circles |
| glove | Mitten | queen |

| RELATED WORDS | PICTURES | UNRELATED WORDS |
|---------------|---------------|-----------------|
| banana | Monkey | corn |
| summit | Mountain | barrel |
| cheese | Mouse | pipe |
| toadstool | Mushroom | hamster |
| screw | Nail | arctic |
| thread | Needle | chicken |
| leek | Onion | chain |
| citrus | Orange | scissors |
| emu | Ostrich | saucer |
| wise | Owl | bubble |
| paint | Paintbrush | cactus |
| artist | Palette | juice |
| bear | Panda | clip |
| proud | Peacock | collide |
| cashew | Peanut | wolf |
| ink | Pen | parrot |
| eraser | Pencil | sword |
| puffin | Penguin | fern |
| hot | Pepper | astronaut |
| pork | Pig | lemon |
| forceps | Pliers | basket |
| electric | Plug | squid |
| mashed | Potato | radio |
| squash | Pumpkin | goal |
| wallet | Purse | egg |
| music | Record-player | mole |
| horn | Rhino | wax |
| diamond | Ring | stream |
| wicker | Rockingchair | speaker |
| rink | Roller-skate | peach |
| pastry | Rollingpin | butterfly |
| hen | Rooster | brick |
| horse | Saddle | ship |
| yacht | Sailboat | turkey |
| screwdriver | Screw | whisker |
| list | Scroll | cucumber |
| coral | Seahorse | gate |
| otter | Seal | towel |

| RELATED WORDS | PICTURES | UNRELATED WORDS |
|---------------|----------------|-----------------|
| dolphin | Shark | dice |
| wool | Sheep | envelope |
| collar | Shirt | fin |
| badminton | Shuttlecock | melon |
| odour | Skunk | ladder |
| snow | Sled | eggplant |
| slow | Snail | hockey |
| python | Snake | cotton |
| poncho | Sombrero | bracelet |
| pyramid | Sphinx | table |
| web | Spider | bucket |
| weave | Spinning-wheel | cold |
| galaxy | Star | calculator |
| bench | Stool | beret |
| jam | Strawberry | whistle |
| luggage | Suitcase | dragon |
| graceful | Swan | chalk |
| cardigan | Sweater | iceberg |
| light | Switch | heart |
| cymbals | Tambourine | saw |
| army | Tank | knit |
| tent | Teepee | bean |
| tennis | Tennisracket | stupid |
| sew | Thimble | compass |
| cheetah | Tiger | windmill |
| ketchup | Tomato | peaceful |
| tweezers | Tongs | wasp |
| toothpaste | Toothbrush | wire |
| spin | Top | raft |
| stop | Traffic-light | cabbage |
| railway | Train | soap |
| vine | Trellis | missile |
| camera | Tripod | rake |
| car | Truck | television |
| trombone | Trumpet | globe |
| myth | Unicorn | shovel |
| crystal | Vase | hinge |
| cello | Violin | sandwich |

| RELATED WORDS | PICTURES | UNRELATED WORDS |
|---------------|--------------|-----------------|
| squeeze | Vise | olive |
| cart | Wagon | ruler |
| tusk | Walrus | organ |
| hose | Watering-can | stove |
| wishing | Well | thermometer |
| pane | Window | saxophone |
| wine | Wineglass | magnet |
| bolt | Wrench | dress |
| stripes | Zebra | yellow |

Appendix H

Average ERP Waveforms for DAT Primers

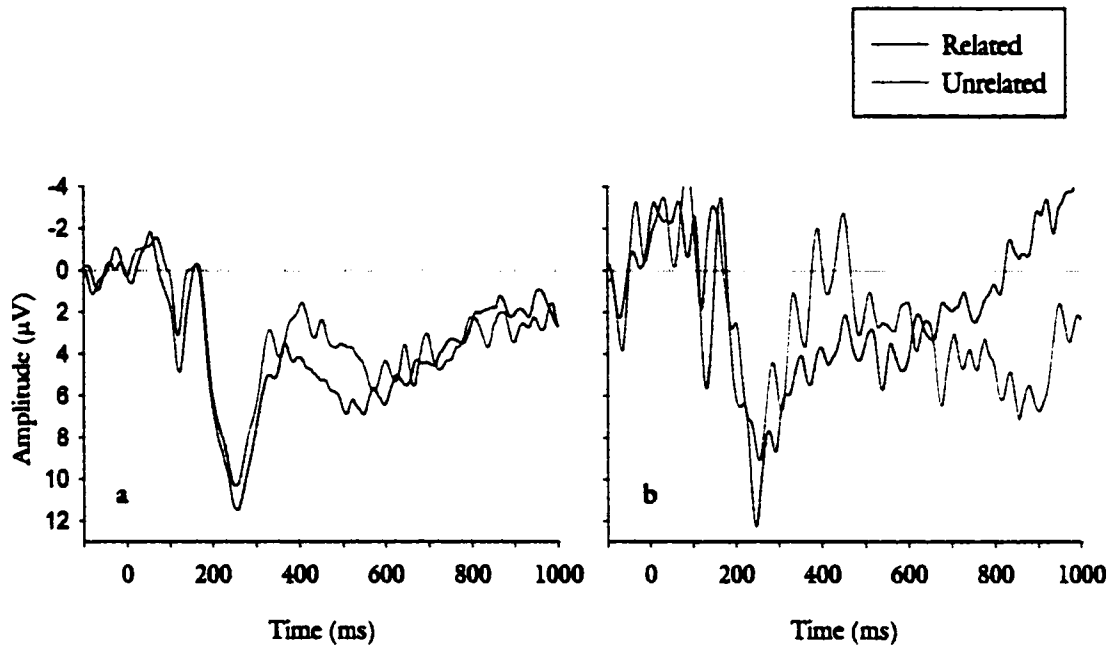


Figure H1. ERP average waveforms for patient D2 for pictures preceded by related and unrelated words at the parietal midline site (Pz). a) Named stimuli; b) unnamed stimuli.

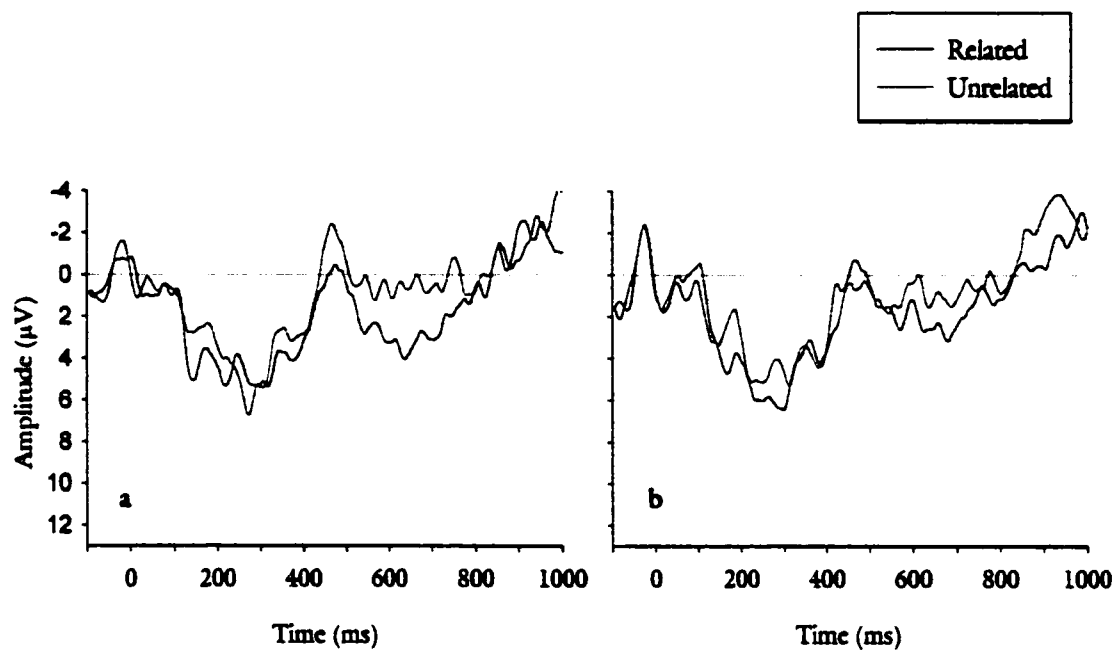


Figure H2. ERP average waveforms for patient D3 for pictures preceded by related and unrelated words at the parietal midline site (Pz). a) Named stimuli; b) unnamed stimuli.

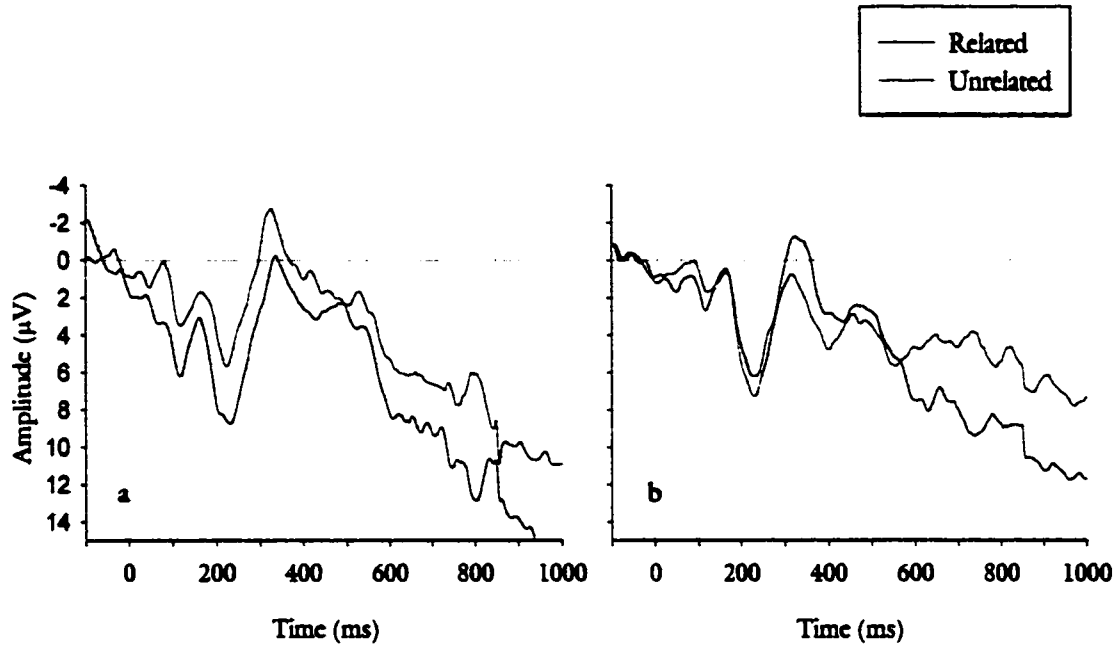


Figure H3. ERP average waveforms for patient D4 for pictures preceded by related and unrelated words at the parietal midline site (Pz). a) Named stimuli; b) unnamed stimuli.

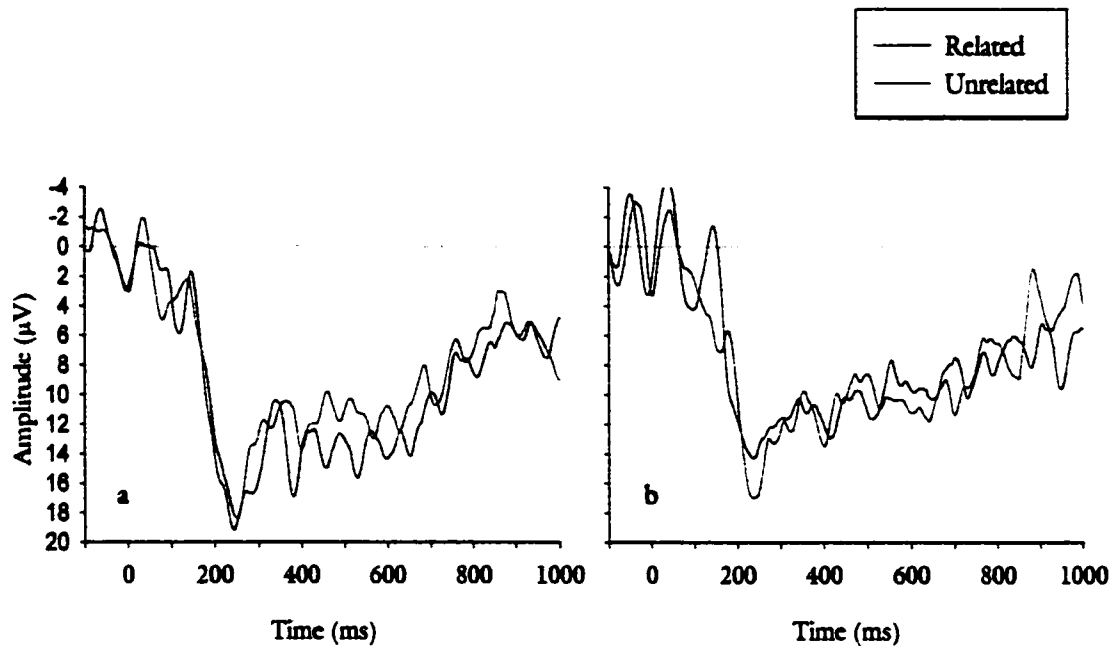


Figure H4. ERP average waveforms for patient D5 for pictures preceded by related and unrelated words at the parietal midline site (Pz). a) Named stimuli; b) unnamed stimuli.

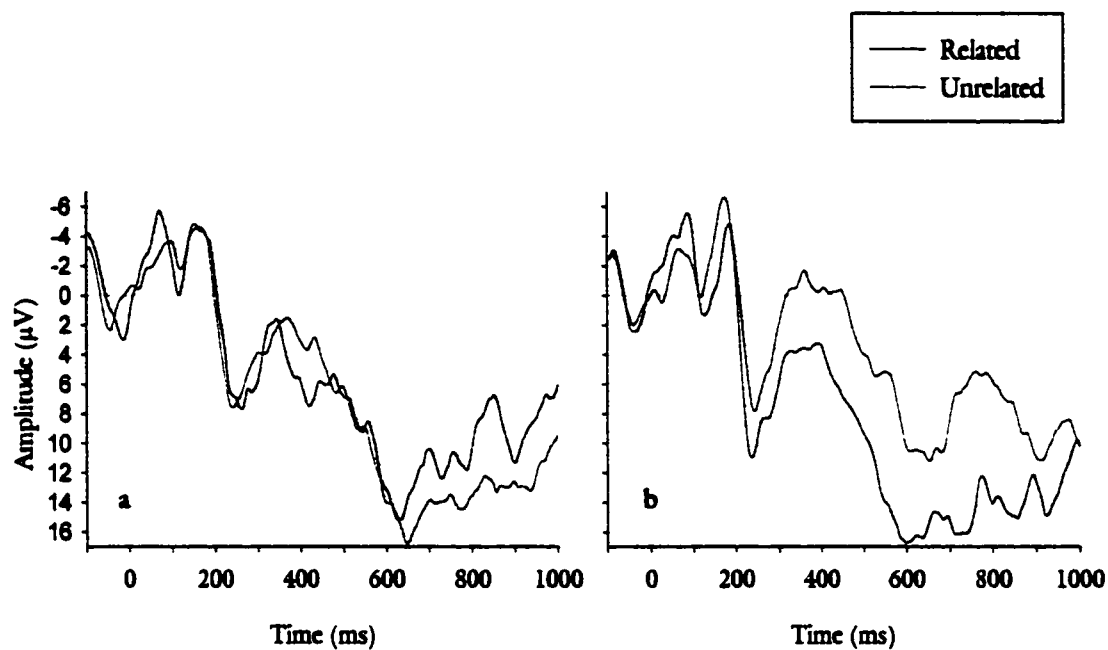


Figure H5. ERP average waveforms for patient D6 for pictures preceded by related and unrelated words at the parietal midline site (Pz). a) Named stimuli; b) unnamed stimuli.

Appendix I

Average ERP Waveforms for DAT Non-Primers

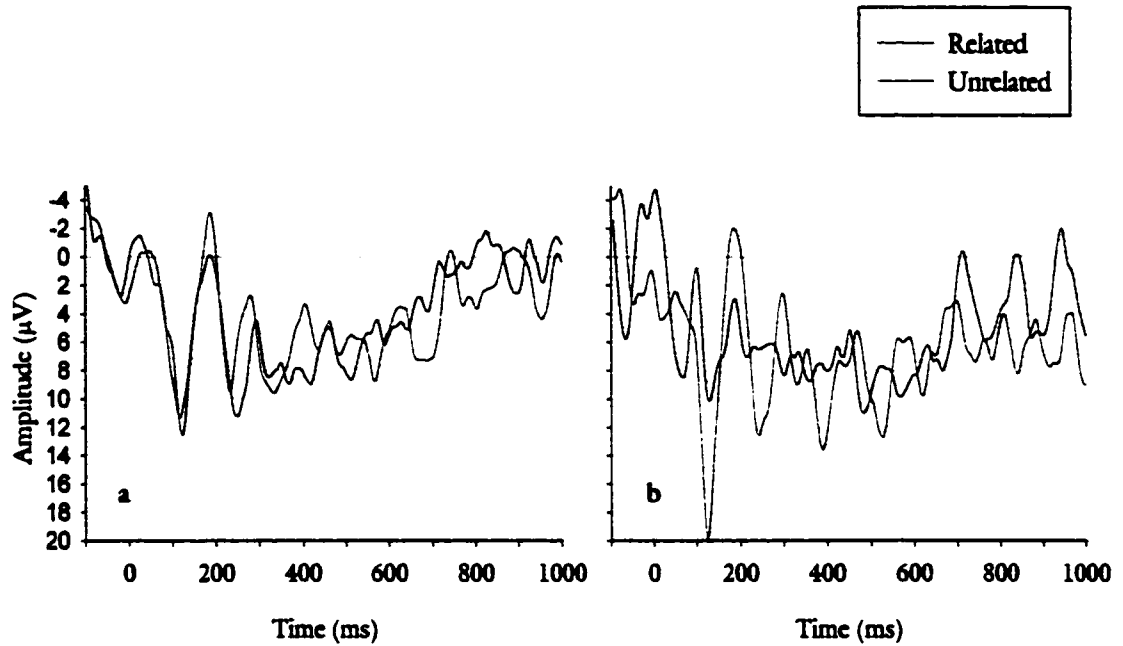


Figure 11. ERP average waveforms for patient D1 for pictures preceded by related and unrelated words at the parietal midline site (Pz). a) Named stimuli; b) unnamed stimuli.

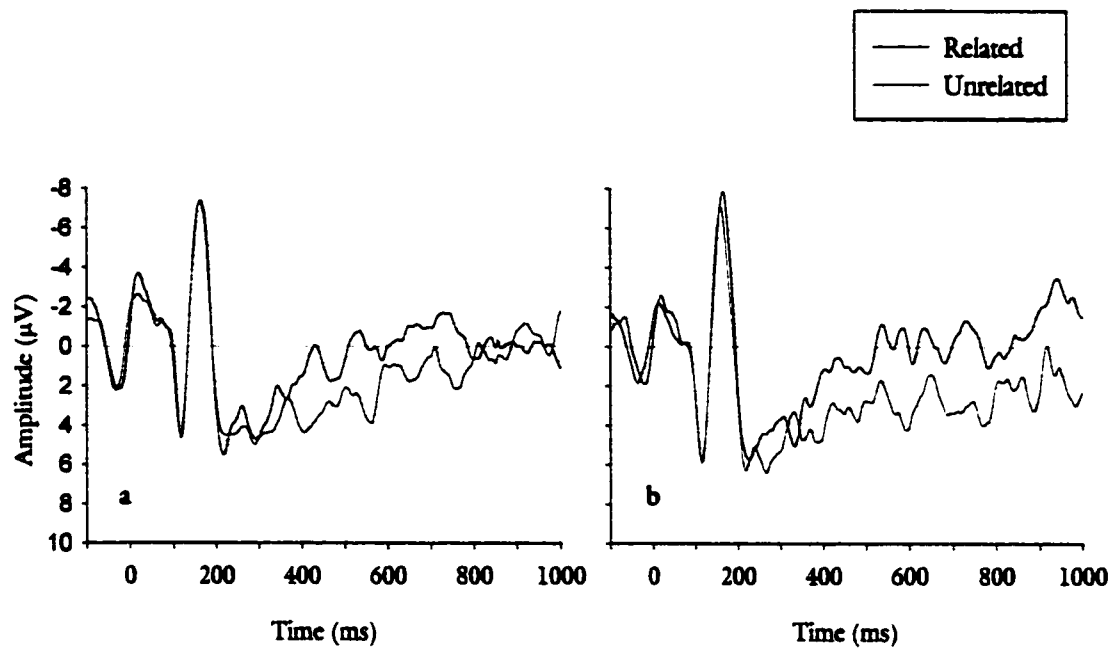


Figure I2. ERP average waveforms for patient D7 for pictures preceded by related and unrelated words at the parietal midline site (Pz). a) Named stimuli; b) unnamed stimuli.

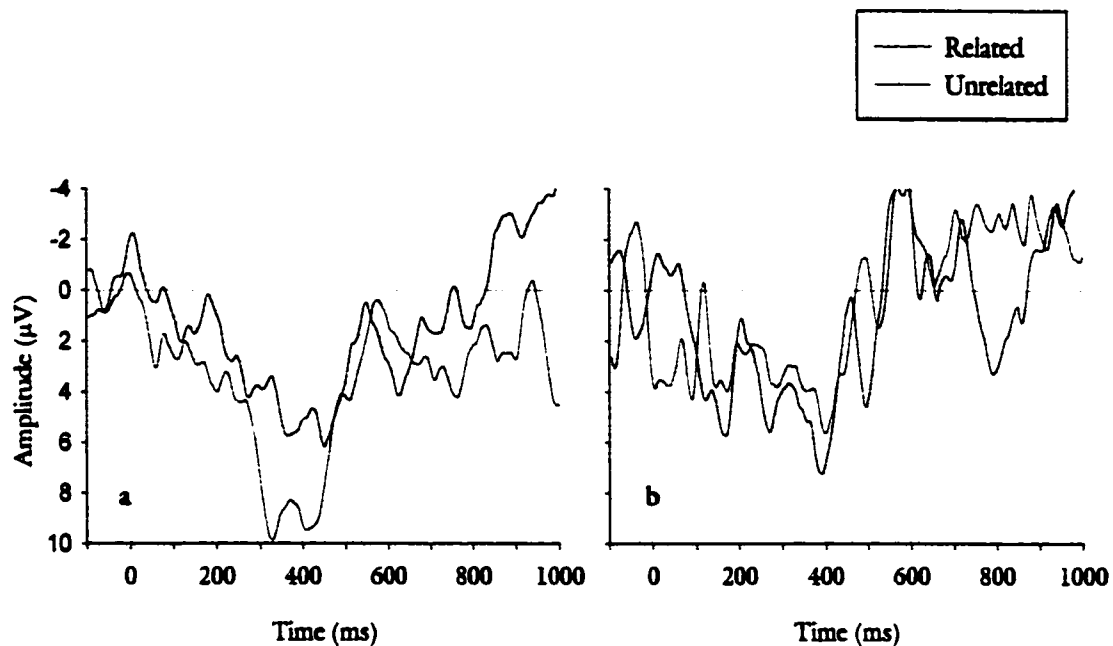


Figure I3. ERP average waveforms for patient D8 for pictures preceded by related and unrelated words at the parietal midline site (Pz). a) Named stimuli; b) unnamed stimuli.

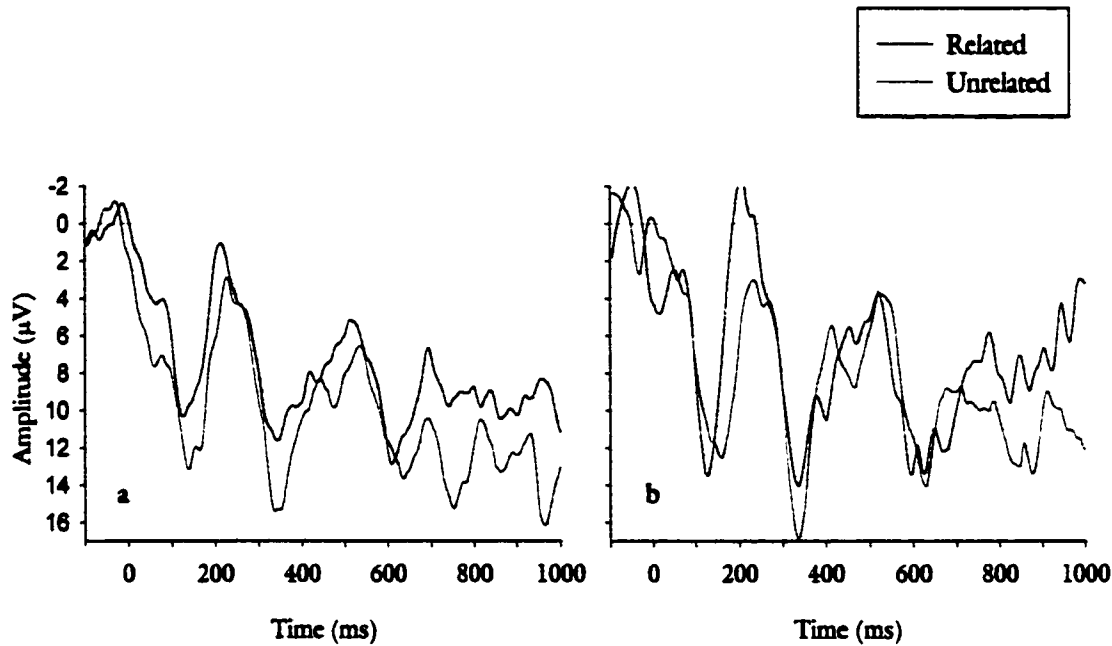


Figure I4. ERP average waveforms for patient D9 for pictures preceded by related and unrelated words at the parietal midline site (Pz). a) Named stimuli; b) unnamed stimuli.