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Effect of Manipulation and Irrelevant noise on Working Memory Capacity

of Patients with Alzheimer's Dementia

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Abstract

The effect of manipulation and distracting noise on immediate serial recall was measured in patients with dementia of the Alzheimer type (DAT), normal elderly individuals and young subjects. Experiment 1 compared serial word recall to word recall in alphabetical order. Alphabetical recall requires the active manipulation of the contents of working memory. Findings indicated that patients were severely impaired in the alphabetical recall task whereas performance of normal elderly subjects was comparable to young subjects. Experiment 2 investigated the effect of different irrelevant auditory backgrounds on immediate digit recall. In this task, both normal elderly subjects and DAT patients performed similarly to the group of young subjects, indicating comparable efficacy to resist auditory distraction. Heterogeneity of performance was assessed in the DAT patients, revealing that the alphabetical tasks yielded particularly heterogeneous performance levels. Finally, the absence of any systematic relationship between the two tasks suggests that they reflect different aspects of working memory.

Key words: working memory, dementia of the Alzheimer type, manipulation, distraction, ageing

Alzheimer's disease is the major cause of dementia. As no biological marker of Alzheimer's disease currently exists, the diagnosis of dementia of the Alzheimer type (DAT) relies on extensive neurological and neuropsychological assessment. In this context, the task of the clinical neuropsychologist is to find evidence for the presence of a cognitive impairment which goes beyond that observed in the normal course of ageing.

There are empirical data suggesting that working memory (WM) is impaired in DAT. WM is a short-term retention system involved in on-line processing and maintenance of information. This memory system plays a major role in numerous cognitive tasks including language comprehension, mental calculation, and the control of actions. A decrease in the span capacities of DAT patients has been reported for numerous types of material (Belleville, Peretz &, Malenfant, 1996; Corkin, 1982; Dannenbaum, Parkinson, & Inman, 1988; Hulme, Lee, & Brown, 1993; Kaszniack, Garon, & Fox, 1979; Kopelman, 1985; Morris, 1984; 1987; Orsini, Trojano, Chiacchio, & Grossi, 1988; Spinnler, Della Sala, Bandera, & Baddeley, 1988). However, span is typically not very helpful in early diagnosis as it is unimpaired in early DAT patients (Corkin, 1982; Martin, Brouwers, Cox & Fedio, 1985; and Orsini et al., 1988).

Other researchers have found that DAT patients are particularly impaired in WM tasks that implicate dual task coordination. DAT patients are impaired in adapted versions of the Brown-Peterson procedure (Belleville et al., 1996; Morris, 1986) whereby subjects are required to memorize letters while performing tasks of increasing difficulty (e.g.: finger tapping, articulation, digit addition). Baddeley and collaborators (Baddeley, Bressi, Della Sala, Logie & Spinnler, 1991; Baddeley, Logie, Bressi, Della Sala, & Spinnler, 1986) have used a divided attention task in which subjects were required to track a visual target with a stylus while at the same time performing a concurrent task of increasing complexity (articulation, tone detection, or recall of sequences of digits). The performance of DAT patients was greatly affected by the dual task condition, particularly when tracking was performed with digit recall.

These studies provide fairly convincing evidence for a WM impairment in DAT, particularly with tasks that implicate executive processes. Executive processes are involved when automatic activation of typical action schemas is inappropriate or insufficient. This occurs in tasks that rely on decision-making, those that are new or those which are demanding (Norman & Shallice, 1986). Recent formulations suggest that there are many distinct components involved in executive tasks (e.g.: Baddeley, 1996; Stuss, Shallice, Alexander, & Picton, 1995; West, 1996). Baddeley (1996) suggested that it is necessary to distinguish different executive abilities pertinent to WM, especially the ability to coordinate two or more concurrent activities, the ability to manipulate information in long-term memory, the ability to act as an attentional controller that selects certain pieces of information and rejects others and the ability to switch retrieval strategies. Whereas previous results have already indicated that dual task coordination was implicated in DAT patients (Baddeley, 1986; Baddeley, Bressi, et al., 1991) nothing is known about the functions of the other components. Thus, the extent of the impairment in DAT patients needs to be tested with tasks that rely on other executive components.

In the present study, WM was assessed with two different tasks. One task requires manipulation, or the act of consciously and actively modifying the format of the information retained in WM (Belleville et al., 1998). Experiment 1 measured WM capacities in a task that required subjects to report a list of words in alphabetical order and in the same order as they were presented (Belleville et al., 1998; Craik, 1986). Alphabetical recall requires subjects to break down the ordered representation, extract alphabetical order from long-term memory, and switch from this order to the series held in the phonological loop. In this condition, subjects have to continuously monitor and control their output, which is likely to involve the central executive component. Behavioral and functional imaging studies provide fairly convincing evidence that the alphabetical procedure involves a frontally located executive system. Impairment in divided attention has been used as a criterion for CE involvement and we have shown that performing a concurrent visuo-spatial task impairs alphabetical recall significantly more than direct recall (Belleville et al., 1998). Furthermore, we have recently shown in a PET study that frontal areas, which are considered to be involved in central executive operations, mediated the alphabetical recall. Activation in the alphabetical relative to direct condition of report was found in the right (BA 10/46) and left (BA 9/6) middle frontal gyrus and in the left parietal area (BA 7) (Collette et al., 1999).

Experiment 2 assessed WM in a task that measured the effect of irrelevant speech effect on immediate serial recall (Colle & Welsh, 1976; Rouleau & Belleville, 1996; Salamé & Baddeley, 1982). In this paradigm, subjects must recall short sequences of visually presented digits while trying to ignore irrelevant background noise. Results typically show decreased memory performance associated with the interfering presence of irrelevant speech, whether familiar or unfamiliar (Colle & Welsh, 1976; Salamé & Baddeley, 1982). Because familiarity is not a relevant factor in the extent of the interfering effect, it has been suggested that this interference effect is phonologically based (Jones & Morris, 1992). According to Hasher and Zacks (1988), cognitive performance is impaired when irrelevant information occupies space in WM that would have otherwise been devoted to more targeted cognitive activities. In this paradigm, subjects are instructed to ignore distracting noise and to focus solely on memorizing digits. To achieve optimal performance in this selective attention task, they have to employ active processes particularly when background interfering speech is used.

The decision to use these particular tasks was motivated by theoretical and clinical concerns. First, Baddeley (1996)'s fractionation of the central executive included dual task coordination, selective attention and the manipulation of information from long term memory. Furthermore, the two tasks include an immediate memory component and were thus directly relevant to WM. Finally, we had evidence that normal aged subjects were not impaired on these selective attention and manipulation tasks (Belleville et al., 1998; Rouleau & Belleville, 1996). This is an important point because we sought tasks that would yield qualitative differences between normal and pathological aging. Specifically, tasks that produce impaired performance only in demented patients may represent more powerful diagnosis tools in the clinical practice.

It is important to determine whether this impairment provides a qualitative marker of the disease, that is, whether normal aging affects performance on these tests. Many studies have provided evidence for a WM impairment in normal aging (Dobbs & Rule, 1989; Foos, 1989; Tun, Wingfield & Stine, 1991; Wright, 1981), which would suggest that DAT and aging lie on a severity continuum. Recent studies suggest that normal aged people are unimpaired on some WM tasks (Baddeley et al., 1986; Belleville, Rouleau, & Caza, 1998; Rouleau & Belleville, 1996; Salthouse, Fristoe, Lineweaver, & Coon, 1995). Very few of the above studies have provided data in young subjects that would support the specificity of the impairment, yet finding tasks on which only DAT and not normal aging impairs performance would be very helpful from a clinical perspective.

Finally, the majority of studies have relied on group data. Yet, one of the major advances in research over the recent years has been to demonstrate the heterogeneity of DAT at both the neurobiological and cognitive level (Della Sala, Muggia, Spinnler, & Zuffi, 1995; Joanette, Ska, Béland, & Poissant, 1992; Martin, 1990; Martin et al., 1986; Neary et al., 1986; Ritchie & Touchon, 1992). This has major consequences because it suggests that relying only on averaged group data risks masking significant individual performance levels. The current description of DAT's WM decline might thus be inadequate for many of those who suffer from the disease. Some researchers have examined the different DAT patient performance profiles on WM tasks and concluded that the results suggest heterogeneity within WM. Grossi and collaborators (Grossi, Becker, Smith, & Trojano, 1993) reported a normal visuo-spatial span in some patients and impaired performance in others. Becker (1988) and Baddeley, Della Sala & Spinnler (1991) reported cases of DAT patients with pronounced central executive impairment. They also reported patients who exhibited only verbal or spatial span deficiency. When examining the different components of WM in DAT patients (Belleville et al., 1996) we observed that most patients (80%) were impaired on the adapted Brown-Peterson procedure, whereas a substantial proportion was also impaired in tasks measuring the phonological loop (40%). Thus, there is fair evidence for heterogeneous WM profiles. This heterogeneity may be found among different tasks of central executive as well. One goal of this study was to assess the presence of heterogeneity within executive tasks.

In both experiments, an analysis of the distribution of individual performances follows the group analysis to identify patients with divergent patterns of performance. We also wished to assess the relationship between individuals' performance on the two tasks. If the central executive is a monolithic component, there should be a strong relationship between performance on each task in individual patients. If there is a division of the central executive, the two tasks might be dissociated at the group level. Thus, DAT patients might be impaired on one task, but not on the other. Furthermore, performance should also be dissociated at the individual level: impairment on one task should not be related to impairment on the other task in individual subjects. In summary, this study provides new informative data relative to the effect of dementia on WM. First, it assesses working memory functions that have not been investigated in the past and that are possibly dissociated in DAT. Second, it investigates individual differences among DAT patients, which represents crucial information for both clinical and theoretical reasons. Finally, it provides data that can ascertain whether normal aging and DAT lie on a continuum of severity, which is a major issue.

EXPERIMENT 1:ALPHABETICAL RECALL

Manipulation capacity was measured with the alphabetical span procedure (Belleville et al., 1998; Craik, 1986) whereby subjects are presented with a random series of words, which they have to rearrange mentally and report in alphabetical order. In the procedure, care was taken to control for a phonological storage deficiency. Indeed, manipulation operations are certainly more difficult to perform on weak phonological memory traces than on strong ones (Waters, Rochon & Caplan, 1992; Belleville et al., 1998; Loftus, 1978; Salthouse, 1988). The subjects were thus tested with lists that corresponded to their span minus one item. Since the sequence length was individually adjusted to the subject's serial recall capacities, performance on the direct recall condition was not expected to differ between groups. In light of our previous studies of normal aging (Belleville et al, 1998), we predicted that alphabetical recall would be comparable in normal aged and young subjects. However, if the manipulation capacities are deficient in DAT patients, their performance in alphabetical recall should be impaired relative to age-matched controls.

Method

Participants

Sixty one participants, 23 DAT patients, 23 elderly normal subjects and 15 young adult subjects took part in the experiment. The young adults (7 males and 8 females) ranged in age from 18 to 30 years (M = 24.6, SD= 3.98) and had a mean of 13.5 years of education (SD = 2.03). Elderly normal subjects (19 females and 4 males) ranged in age from 62 to 83 years (M = 71.35, SD = 5.59) and had a mean of 11.00 years of schooling (SD = 3.67). The DAT patients (17 females and 6 males) had a mean age of 72.8 years (SD = 5.88) (range 64-87) and an average of 10.34 years of education (SD = 3.52). Patients and normal aged controls were individually matched on both age and education. There was no difference in formal education between age-matched controls and DAT patients, t_{44}= -.6148; p=.5417, two-tailed. However the difference in education was significant between normal aged and young subjects, t_{36}= -2.4038; $p<0.05$, two-tailed. This difference corresponds to the increase in the average educational level in Québec between the two generations concerned (Statistics Canada, 1994). Subjects all reported normal hearing and had normal or corrected vision.

Patients were selected from a pool of volunteers who desired to participate in medical, neurological and neuropsychological investigations at two hospitals (Research Centre of the Institut Universitaire de Gériatrie de Montréal and Hôpital Universitaire de Liège). The patients were referred by neurologists or medical practitioners as suffering from DAT. The patients were then tested using an extensive neuropsychological battery with the goal of documenting all components of cognition. The majority of subjects also underwent a complete clinical examination (e.g.: PET, functional MRI, and blood analysis). Their diagnosis was then confirmed as probable (n=20) or possible (n=3) DAT, according to the NINCDS-ADRDA criteria (McKhann et al., 1984). The severity of their disease ranged from mild to moderate on the basis of the neuropsychological investigation. Their average score on the Mini-Mental State Examination (Folstein, Folstein, & McHugh, 1975) was 22.57/30 (range= 18-29).

Young and normal elderly participants were drawn from a pool of volunteers living in the same community as DAT patients. They had no history of neurological disease, psychiatric disorder, or general anesthesia in the past year. They did not use medication known to affect memory or other cognitive functions. Elderly subjects completed a battery of tests to exclude participants with early signs of dementia. These tests included the Mini-Mental State Examination (Folstein et al., 1975), which is used to screen for major cognitive defects, and the Mattis Dementia Rating Scale (Mattis, 1976), which provides an estimate of attention, initiation, construction, concepts, and memory (an equivalent battery was used in four patients). In this experiment and the following one, subjects' consent was obtained according to the declaration of Helsinki and the Ethical Committee of the Institution in which the work was performed has approved it.

Materials

Two hundred and eleven monosyllabic words were selected. These words were frequent (Baudot, 1992) and imaginable substantives. They were not ambiguous with respect to the print-to-sound correspondence of their first letter. For example, a word like *scie* in French (which is pronounced /si/) would have been excluded because its first sound can also be written with an initial c. Finally, words having homophones of a higher frequency were not used when this homophone started with different letters (for example, the word *fard* is the homophone of a more frequent word, *phare*).

Sequences of words, the length of which ranged from two to eight items (to be used with subjects with a span size from 3 to 9), were constructed with these words. There were 20 different sequences for each length, 10 to be used in the direct condition and 10 to be used in the alphabetical condition. Words included in a sequence differed according to their first letter and had no phonological or semantic similarity. Mean word frequency was equivalent across sequence length**,** as well as for the direct and alphabetical conditions at a given list length. None of the words were repeated across different sequences for a given length.

The difficulty of manipulation was controlled in the sequences that were used in the alphabetical condition. This was done first by measuring the distance between the first letter of the words in a sequence. Indeed, according to a pilot study from our laboratory, it is generally easier to judge the alphabetical order of letters that are farther apart in the alphabet. The position in the alphabet of the first letter of the words was also controlled since letters at the beginning of the alphabet are easier to arrange in alphabetical order. Finally, the total number of manipulations to perform in each sequence was controlled (e.g. there is one manipulation in the series *bloc, pneu* and *crabe* but two manipulations in the series *rose, pomme* and *lune*). By using these criteria, the manipulation requirement was made equivalent for the different sequence lengths.

Procedure

Pre-experimental phase. As a first step, the short-term memory capacity of each subject was assessed with a classical word span procedure. The words chosen for the span procedure fit the same criteria as those on the experimental list in terms of length, frequency, and imageability, but differed from those used in the experimental phase. The items were chosen without replacement. Sequences of words were read at the rate of one item per second, starting with sequences of two words. The length of the sequences was increased by one word every two trials. However, if an error occurred on one of these two trials, the subjects were given two additional trials. Subjects were instructed to report items orally in serial order. Testing was interrupted when subjects failed to report correctly two of the four sequences of a particular length. The word span was defined as the longest sequence correctly recalled on 50% of the trials. This span was later used to determine the list length on which subjects were tested in the experimental phase.

Experimental phase. In this phase, subjects were assessed in both the direct and alphabetical conditions of recall. Words were read to the subjects at the rate of one item per second and subjects recalled the words orally. In the direct condition, subjects performed an immediate serial recall of the words. In the alphabetical condition, they were asked to mentally rearrange and recall the words in their alphabetical order. For example, the words *route-nappe-poivre* should be recalled *nappe, poivre, route* in this condition. Ten sequences of words were recalled in each condition. The number of words to be recalled in a sequence corresponded to the subjects' span minus one item. Thus, a subject with a span of 6 was tested with sequences of 5 items in both conditions. At the beginning of our study, we tested a few patients with sequences corresponding to their span. However**,** under these conditions**,** alphabetical recall was virtually impossible for the patients, who tended to withdraw from the task. It was thus decided to test subjects with sequence lengths corresponding to their span minus one item. The order of presentation of the direct and alphabetical conditions followed an ABBA design, starting with the direct condition. This allowed us to control for the possible effects of fatigue and/or practice. The complete procedure was performed within a single testing session.

Results and Discussion

As a first step, a preliminary analysis was performed that compared the pre-experimental span size in young participants, elderly participants, and DAT patients. There was a significant group effect, $F(2,58) = 14.14$, $P < 0.001$. A post-hoc test with Tukey's HSD ($p < 0.05$) revealed that DAT subjects had a smaller average span than elderly subjects ($M = 3.74$, $SD =$

0.69; and M = 4.26, SD = 0.54; in DAT and normal elderly subjects respectively), and that young subjects (M = 4.8, SD= 0.56) differed from elderly controls ($p < 0.05$) on the same measure. A second preliminary analysis was done to assess the effect of the order of presentation due to the ABBA design. A 3 (Group: young, old, DAT) x 2 (Order: first, second) x 2 (Recall: direct, alphabetical) ANOVA was thus conducted. The main effect of Order was marginally significant, $F(1,58) = 3.66$, MSE = 0.597, $p = 0.06$, due to the fact that all subjects improved their performance slightly over trials. More importantly, however, there were neither Group by Order nor Group by Order by Recall interactions ($F<1$ in both cases). This indicates that the order of presentation of the conditions had no significant influence on the critical interactions, namely, those concerning Group. For this reason, the data from the two orders of presentation were pooled in the subsequent analyses.

Figure 1 shows the number of sequences recalled correctly in both conditions. As expected, alphabetical recall yielded a decreased performance in comparison to direct recall. More importantly, the reduction in performance with alphabetical recall was much larger in DAT than in the control groups. This is confirmed by a 3 (Group: young, old, DAT) x 2 (Recall: direct, alphabetical) ANOVA. The analysis revealed a significant main effect of Recall, $F(1,58) = 93.74$, MSE = 1.522, $p < 0.0001$, confirming the reduced performance level in the alphabetical condition. There was a significant Group effect, $F(2,58) = 10.48$, MSE = 3.300, $p<0.001$. Importantly, the interaction was highly significant, $F(2,58) = 13.50$, MSE = 1.522, $p<0.0001$. Analysis of the interaction effect revealed that the Group difference was only apparent in the alphabetical condition, $F(2,58) = 13.50$, MSE = 3.698, $p<0.0001$. In this condition, DAT patients differed from elderly and young subjects ($p<0.01$ in both cases) whereas the latter groups did not differ one from another ($p=0.74$). There was no group effect in the direct condition, $F<1$. The Greenhouse-Geisser procedure, used to control for unequal variances, did not modify the results.

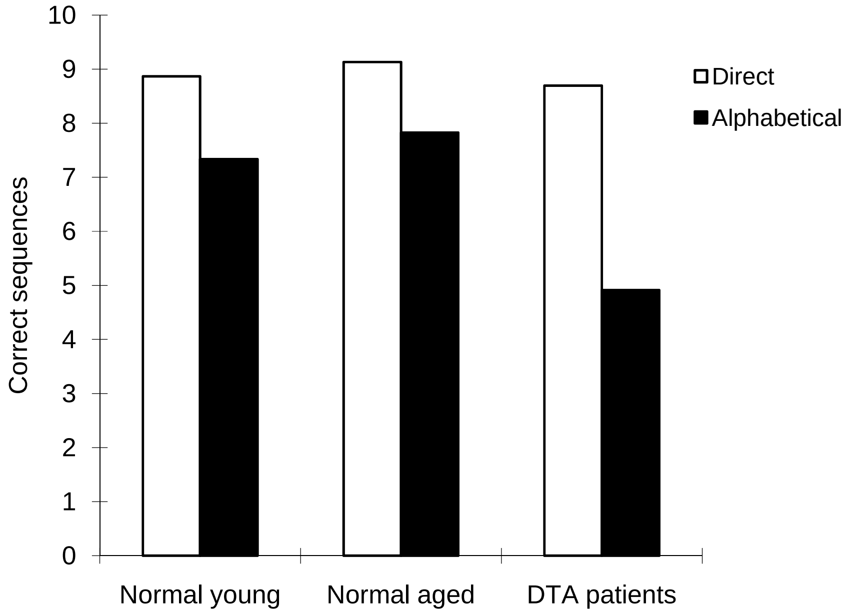


Figure 1

To assess heterogeneity, we derived a manipulation score for each individual subject. The score was calculated according to the formula (D-A/D). This represents the memory reduction experienced by each subject when performing alphabetical recall relative to direct recall. Figure 2 shows the distribution of manipulation cost for each subject. It is worth noting that the scores for the two control groups (young and elderly) approximated normal distributions and overlapped one another. In contrast, the distribution of the scores for the DAT patients was bi-modal. Whereas many patients were severely impaired, a portion of them (about 25 %) overlapped the distribution of normal elderly subjects and were thus unaffected. This difference is not merely related to severity of the disease. We performed a median-split on manipulation cost and compared the MMS score of the most and least impaired patients. Patients that were the most impaired on manipulation showed an average MMS score of 21.82, whereas patients that were least impaired patients exhibited a MMS score of 23.25. This difference was not significant, $t_{(21)} = -1.320$; p=.2012, two-tailed.

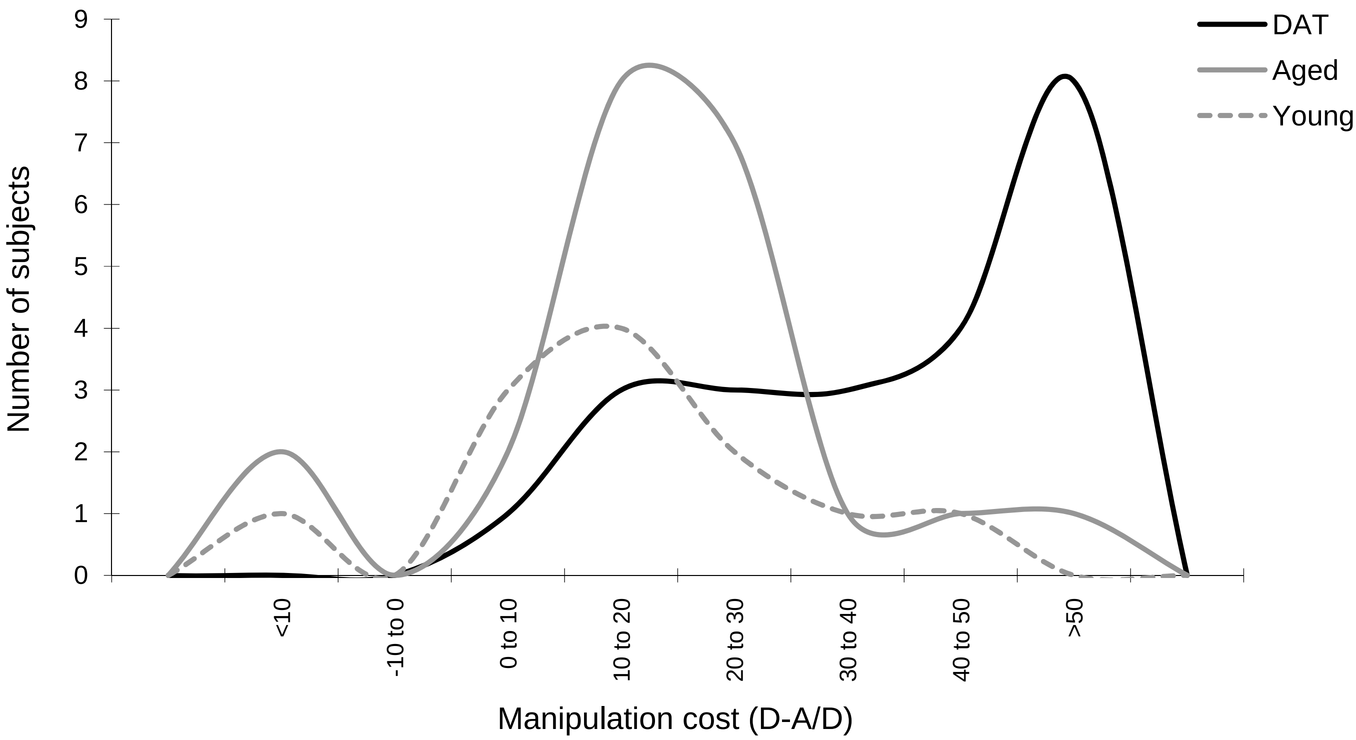


Figure 2

In sum, alphabetical recall yields a decreased performance level, which suggests that there is a cost to the manipulation requirement of the task. Elderly and young normal subjects did not perform differently in the alphabetical condition. This suggests that manipulation is not particularly difficult for normal elderly people as long as basic storage is controlled. In contrast, DAT patients are dramatically impaired in the alphabetical condition even if basic storage demand is equated. Examination of individual scores indicates a bi-modal distribution in DAT patients, with some subjects' scores overlapping with those of normal elderly subjects. Yet a substantial subset of DAT patients were excessively impaired on the task. These differences were independent of disease severity.

EXPERIMENT 2: RECALL WITH INTERFERING NOISE

In this experiment, immediate recall of lists of visually presented digits was measured in French-speaking DAT patients, aged controls and young subjects in the presence of irrelevant verbal and non-verbal backgrounds. French and

Romanian versions of a text (familiar and unfamiliar languages, respectively) were used as verbal distracters. White noise was used as a non-verbal distracter. There was also a baseline condition in which subjects performed in silence. Again, the length of the lists to recall was individually adjusted to isolate inhibition from storage deficiencies. On the basis of previous studies, we predicted that recall should remain unaffected by the presence of non-verbal noise, but should decrease in the presence of both familiar and unfamiliar verbal noise. Indeed both verbal noises should yield similar interference effects, as a large body of evidence has shown that interference effect on immediate serialr recall relates to the phonological content, not the semantic content of the verbal material (Colle & Welsh, 1976; Salamé & Baddeley, 1982; 1986; 1989; Jones & Morris, 1992). All groups were expected to show an irrelevant speech effect, however, we predicted that DAT patients would be more impaired by familiar and unfamiliar verbal backgrounds than normal aged controls. On the basis of our previous study, we did not expect inhibition deficits in normal aged subjects irrespective of the background noise used (Rouleau & Belleville, 1996).

The irrelevant speech effect has been suggested to occur at the level of the phonological store of WM (Colle & Welsh, 1976; Rouleau & Belleville, 1996; Salamé & Baddeley, 1982; Vallar, DiBetta & Silveri, 1997). The articulatory procedure transfers the visually presented digits in the phonological store of WM. Since simultaneous auditory speech has a direct and obligatory access to the phonological store, it would compete for space with digits. Given that the irrelevant speech effect occurs in the phonological store, a phonological loop deficit might also result in an abnormal irrelevant speech effect. For this reason, we included measures of the phonological similarity effect. This effect, defined as the better recall of phonologically dissimilar items over similar items, is frequently used in neuropsychology as a means to assess the phonological loop (e.g.: Belleville et al., 1992; Vallar & Baddeley, 1984; Waters, Rochon, & Caplan, 1992). The effect has been explained as reflecting the fact that subjects maintain verbal material in a phonologically based store. When subjects try to recall the rhyming letters, the similar features of the letters interfere with each other, thus reducing recall.

Method

Participants

Forty-eight participants; 16 young normal subjects, 16 elderly normal subjects, and 16 patients suffering from Alzheimer's disease, took part in the experiment. Of the 16 patients, eleven had participated in the previous experiment. For these eleven subjects, the timing of the two experiments was separated by no more than two weeks. The young normal subjects (7 males and 9 females) ranged in age from 19 to 30 years (M = 23.1) and had a mean of 14.0 years of schooling (SD = 1.97).

The elderly subjects (7 males and 9 females) ranged in age from 62 to 80 years (M = 70.5) and had a mean of 11.6 years of schooling (SD = 2.5). The patients were diagnosed as suffering from probable DAT, according to the NINCDS-ADRDA criteria (McKhann et al., 1984). The severity of their disease ranged from mild to moderate on the basis of an extensive neuropsychological assessment. The patients had a mean age of 72.6 years old (SD = 6.5) (range 64-87) and an average of 11.3 years of education (SD = 3.6). Patients and normal elderly controls were individually matched on age, sex, and education. There was no significant difference between patients and age-matched controls in terms of age, $t_{(30)} = 1.049$, $p=0.3023$, and formal education, $t_{(30)} = -0.2838$, $p=0.7785$. The difference in formal education between the young normal subjects and elderly subjects was significant, $t_{(30)} = -3.0239$, $p<0.01$. Participants spoke French as their mother tongue and had no knowledge of Romanian, the language employed in the non familiar speech condition. Young and normal elderly participants were selected using the same inclusion and exclusion criteria as in Experiment 1. The young and aged normal participants completed the Mill Hill Vocabulary test. Their scores did not differ (34.81/44, SD = 4.98 and 34.25, SD = 6.25 in elderly and young subjects respectively).

Materials

Memory task. The experimental task was based on the one reported in Rouleau & Belleville (1996). Series of randomly selected digits (1 to 9) were constructed. The length of the series ranged from 2 to 9 digits. Forty lists were constructed for each sequence length, with 10 lists for each experimental condition. Digits were presented on a Macintosh monitor, in the center of the screen, using a program written with SuperLab (version 1.5.9) (Cedrus Corporation, 1992).

Noises and irrelevant speech sources. The white noise consisted of electronically generated FM modulations. The familiar noise was an excerpt from Madame de Staël's novel Corinne ou l'Italie read in French, the participant's mother tongue. The unfamiliar noise was the same text read in Romanian. Romanian was chosen because it is a Roman language like French and thus contains numerous phonological similarities. Romanian contains vocalic and consonantic sounds that are not found in French and that come from geographically closer languages. In that respect, it is not the Roman language that is the most phonologically similar to French. Nevertheless, it was chosen over other Roman languages because it is unfamiliar to most French speakers, unlike more common Latin languages such as Italian and Spanish. This ensured that lexemes were not recognised by listeners. Thus, the two verbal noises used were phonologically similar but differed at the lexico-semantic level in that one was comprehensible to participants. A professional translator produced the Romanian version of the original French text. A female reader fluent in both French and Romanian was used for the recordings to have a voice with similar acoustic qualities in both versions, thereby ensuring a better comparison of the verbal conditions. The reader was instructed to read both versions in a steady rhythm without long pauses, while maintaining steady prosody and volume. This last control measure was taken to avoid possible orienting responses elicited by sudden variations in prosody or tone of voice. Each version lasted approximately 8 minutes. The auditory stimuli were played on a Sony tape recorder (TMC-5000) and presented binaurally through Sony headphones (MDR-006). Noise intensity was 75 dB on average. A level of 75 dB is well within the range of normal hearing for both young and older adults (Corso, 1977).

Procedure

Short-term memory (STM) span measure. STM capacity for visually presented digits was measured using a classic span procedure. Digits were presented one at a time for 750 ms, with a 250-ms inter-stimulus interval, in the center of a computer monitor screen. Testing began with sequences of two digits randomly selected from 1 to 9. The length of the sequences was increased by one digit every four trials. A 2-s visual warning (Ready) in the centre of the screen preceded each sequence. At the end of a sequence, a table containing the digits 1 to 9 was displayed on the screen. The position of the digits in the table was randomized to prevent participants from using spatial cues. Participants were required to reproduce the entire sequence in correct order by pointing to each item serially with a finger. Participants were instructed to point to a question mark appearing on the right of the screen whenever they could not remember a digit. Testing ended once participants failed to report correctly at least two of four same-length sequences. STM span was defined as the longest sequence recalled correctly on 50% of the trials.

Experimental testing. Experimental testing lasted approximately thirty minutes, including a 10-min pause after half of the conditions were completed. The digit recall procedure was the same as that used in the STM span measure, except that participants were tested only with digit sequences length-adjusted to their individual STM span. In other words, the number of digits a participant had to recall in each condition corresponded to his or her own span. Participants wore headphones in each noise condition, including the silent condition. They were instructed to ignore distracting noises and focus their attention on memorizing digits. Noise began 10 s before presentation of the first digit in a particular condition and continued until participants finished recalling the last sequence in the condition. Ten sequences were presented in each condition. The experiment thus assessed recall under four auditory backgrounds: silence, non-verbal noise, familiar verbal noise, and unfamiliar verbal noise. The effect of order of presentation of the conditions was counterbalanced using a Latin Square design.

Phonological loop testing. The effect of the phonological similarity of words on short-term retention was measured in both the visual and auditory modalities of presentation. Recall of phonologically similar (rhyming such as B-D-G) and dissimilar (non-rhyming) letters was tested separately. Order of presentation of the material was counterbalanced across subjects. Subjects were tested with 10 sequences in each condition. The length of the sequences to recall corresponded to each subject's digit span as measured with the Côte-des-Neiges memory battery (Belleville et al., 1992; Chatelois et al., 1993).

Results and Discussion

A preliminary analysis was performed first on the digit span data with a one-way ANOVA. There was a main Group effect, $F(2,45)= 22.53$, $MSE = 40.646$, $p<0.0001$. Post-hoc comparisons with a Tukey HSD test indicated that young subjects (average span= 7.50) performed significantly better than normal elderly subjects (average span= 5.88, $p<0.01$). Normal elderly subjects had a larger span than DAT patients (average span= 4.31, $p<0.01$). An analysis was also performed to assess the effect of the Latin square on performance. An ANOVA was used with Group as a between-subject factor, and Noise and Order as repeated factors. The main effect of Order was not significant, $F(3,36)= 2.04$, $MSE = 601.870$, $p= .125$. Furthermore, there were neither Group by Order, $F(6,36)= 2.04$, $MSE = 601.870$, $p= .313$ nor Group by Noise by Order interactions, $F(18,108)= 2.04$, $MSE = 77.709$, $p= .258$. This indicates that the order of presentation of the conditions had no significant influence on the results. Thus, the data were pooled across Latin square orders.

A 3 (Group) by 4 (noise) one factor repeated measures ANOVA was then performed using percent correct recall as the dependent variable. The data are represented in Figure 3. Results showed a significant effect of noise, $F(3,135)= 32.27$, $MSE = 77.515$, $p<0.0001$. Post-hoc comparisons with a Tukey HSD test indicated that the silence and white noise conditions were comparable ($p=0.82$) and that Romanian and French did not differ from each other ($p=0.98$). However both French and Romanian impaired recall relative to white noise ($p< 0.0001$ in both cases). The Group effect was not significant, $F(2,45)=1.84$, $MSE = 662.340$, $p=0.17$. Importantly, the Noise by Group interaction was not significant ($F<1$). Results were not modified when adjusted by the Greenhouse-Geisser procedure for heterogeneous variance.

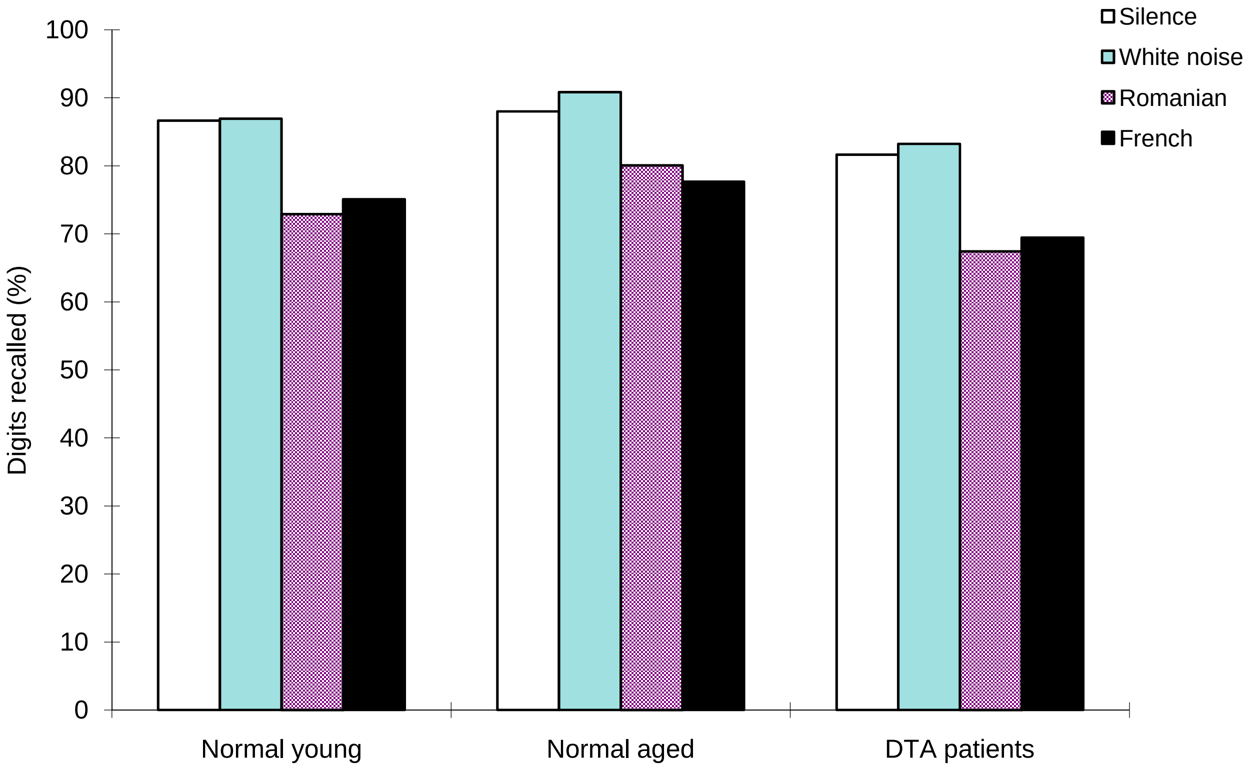
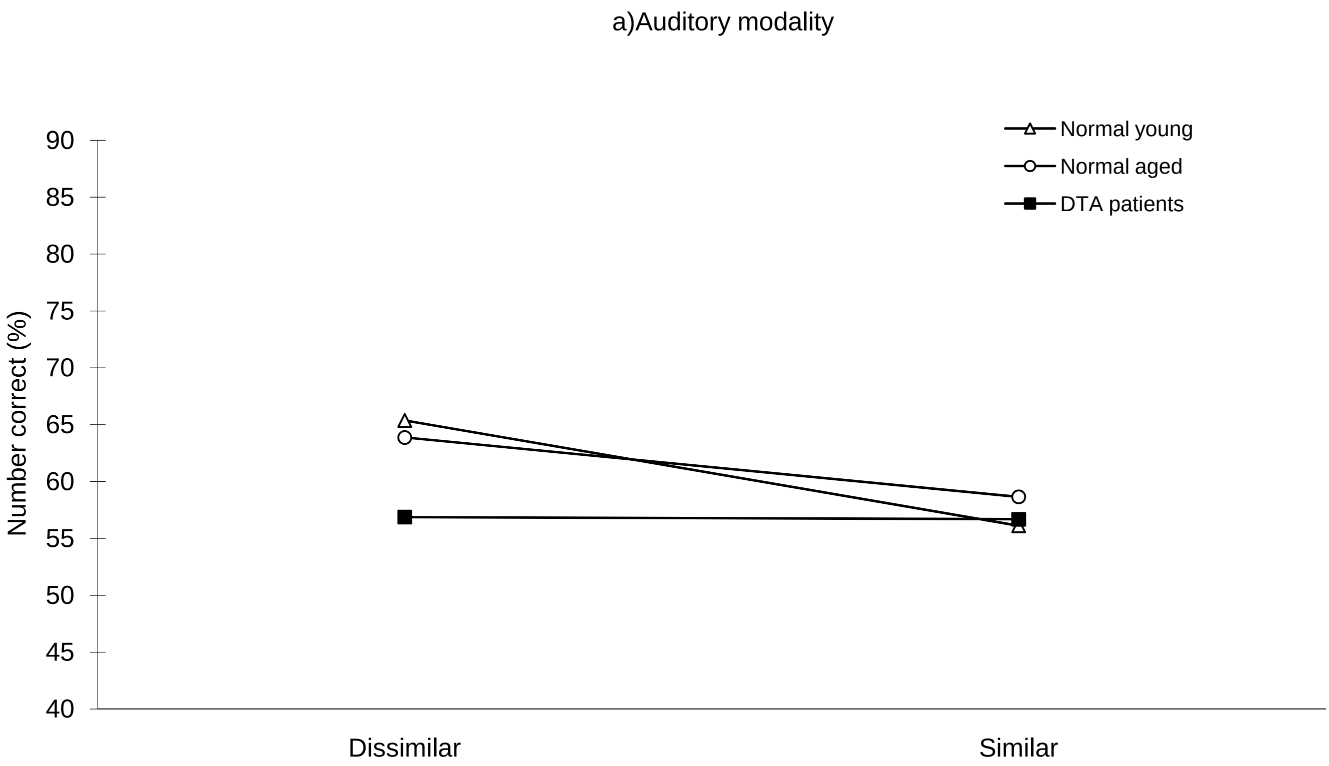

Silence
White noise
Romanian
French
100
90
80
70
60
50
40
30
20
10
0
Digits recalled (%)
Normal young
Normal aged
DTA patients

Figure 3


a)Auditory modality
Normal young
Normal aged
DTA patients
Number correct (%)
90
85
80
75
70
65
60
55
50
45
40
Dissimilar
Similar

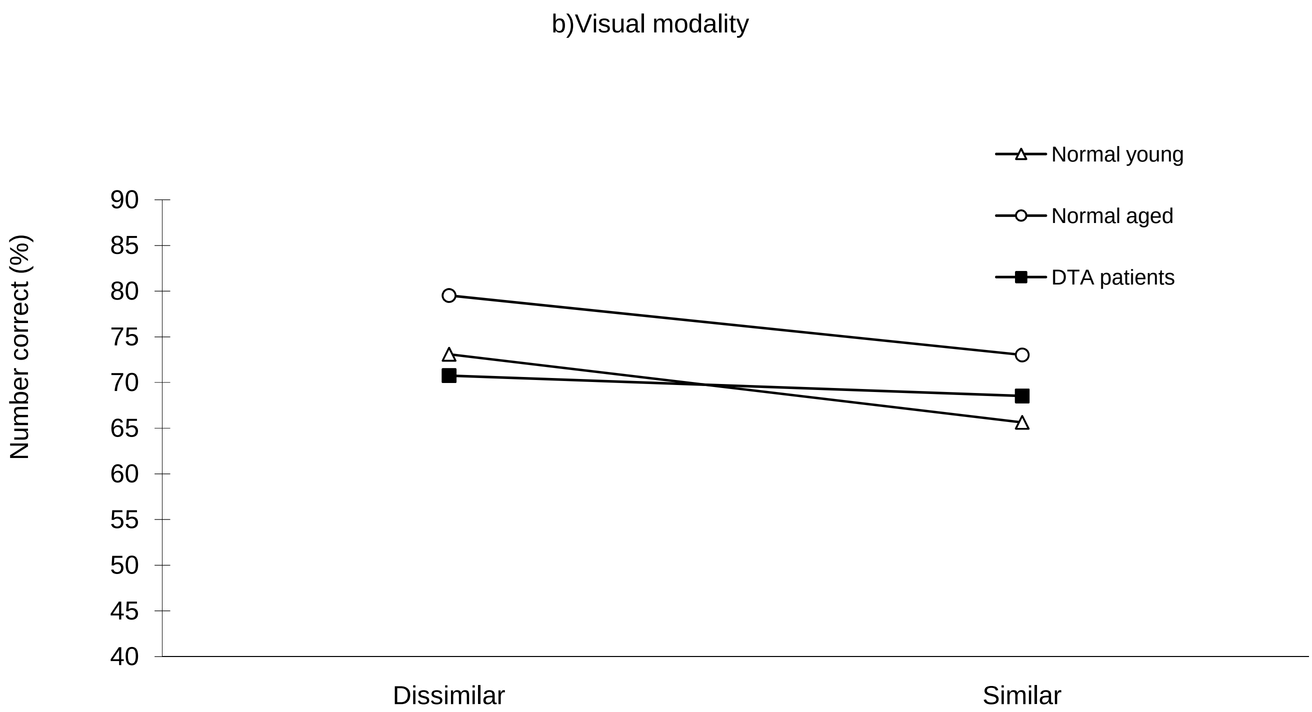

b)Visual modality
Normal young
Normal aged
DTA patients
Number correct (%)
90
85
80
75
70
65
60
55
50
45
40
Dissimilar
Similar

Figure 4

The effect of phonological similarity was also assessed by comparing recall of similar to dissimilar letters in both the auditory and visual modalities of presentation (Figure 4). A three-way ANOVA was used with Group, Modality and Similarity as factors. Results of the analysis showed a significant Modality effect, F(1,45)= 23.951, MSE = 296.368, p<0.0001 as visual presentation yielded higher recall performance than auditory presentation. As predicted, non rhyming letters were recalled more accurately than rhyming letters, F(1,45)= 12.30, MSE = 103.27, p=0.001. Inspection of Figure 4 suggests that the phonological similarity effect is smaller in DAT patients than in the other two groups, particularly with auditory presentation. However, none of the other interactions reached significance, including Group by Similarity, F(2,45)= 2.04, MSE = 103.27, p=0.142, and the three-way interaction, F<1.

Individual scores were calculated to assess the level of performance on the interference task for each subject. Scores of interference costs were determined using the formula ([(% recall in Silence - [(% recall in Romanian+% recall in French)/2]) / [(% recall in Silence]. This corresponds to the reduction in recall incurred by verbal noise relative to silence. The distribution of individual data is presented in Figure 5, which shows young normal and elderly normal performances as a normal distribution. The distribution of DAT patients overlaps with that of the controls, however, two patients were severely impaired (cost was larger than 40%). Again, a median-split was conducted to compare the MMSE of the patients with the largest and smallest interference cost. Patients with the largest interference cost had an average MMSE score of 21.5 whereas patients with the smallest interference cost showed a MMSE score of 22.75 on average. This difference was not reliable, $t_{(14)}$= -.8704; p=.3988, two-tailed.

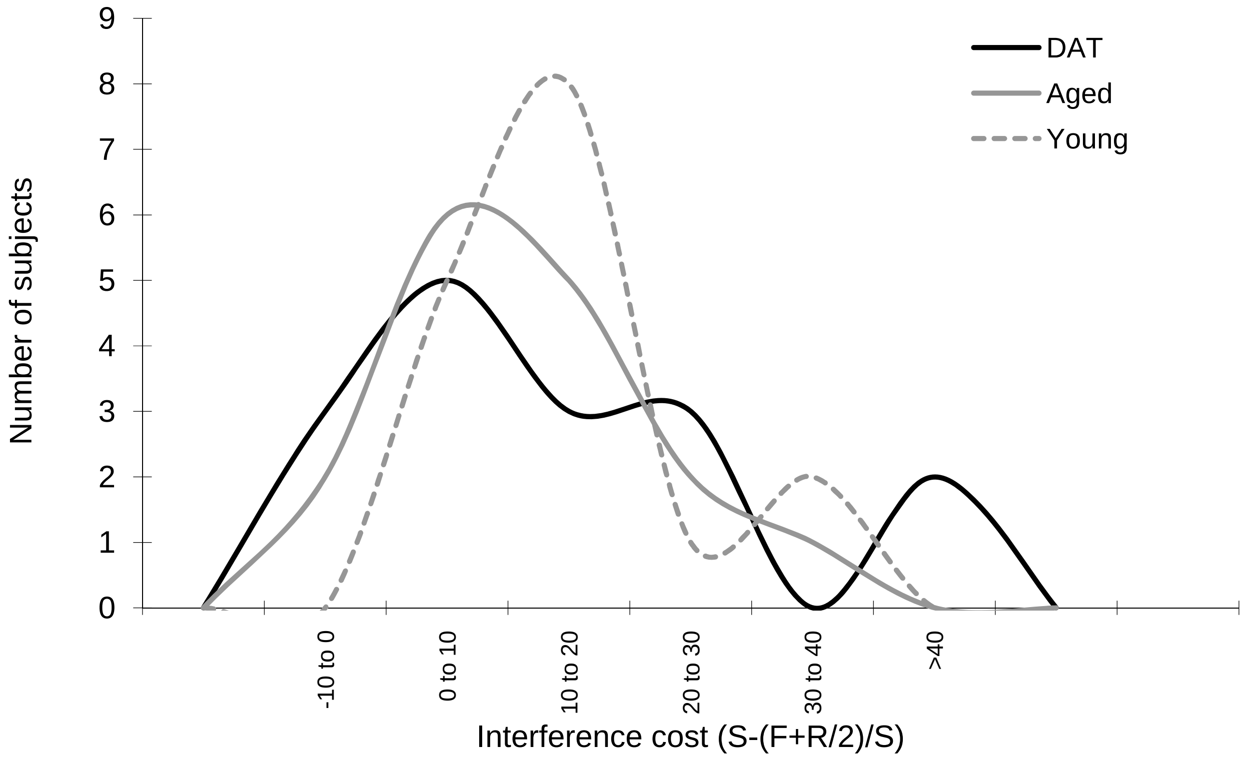


Figure 5

We tested whether some patients exhibited a phonological loop impairment that would interfere with their performance on that task. This is a reasonable suggestion because we have shown in another sample of DAT patients that up to 50% of them have an impaired phonological loop (Belleville et al., 1996). As mentioned previously, the irrelevant speech effect occurs within the phonological store of WM. Auditory verbal noise has direct access to the store whereas visually presented digits access the store only via the rehearsal procedure. Patients with rehearsal deficits might fail to show the effect: if digits are not transferred to the phonological store, their retention should not be disrupted by auditory verbal noise. Nothing is known about the effect of phonological storage impairment on the effect. However, an impaired phonological store might result in subjects becoming even more affected by the presence of irrelevant speech.

Using the phonological similarity effect tested these two possibilities. If rehearsal is impaired, visual material will not be transferred to the phonological store and the phonological similarity effect will not be observed in the visual modality. If the phonological store is impaired, the similarity effect should be absent in both modalities of presentation. We thus expect a different pattern of performance with regard to modalities of presentation in the case of a phonological store or rehearsal impairment. If the variability in the irrelevant speech effect relates to a rehearsal or a phonological store deficit, there should be a systematic relationship between the amount of impairment and the size or presence of a phonological similarity effect. Specifically, patients with a smaller irrelevant speech effect should exhibit a smaller phonological similarity effect in the visual modality (or rehearsal deficit). In contrast, patients with a larger irrelevant speech should exhibit a smaller phonological similarity effect in the auditory modality.

The size of the phonological similarity effect was measured independently in each modality and in each patient using the following formula: Recall of dissimilar letters - Recall of similar letters / Recall of dissimilar letters. This provides a score for the phonological similarity effects in which positive scores represent normal effects. We found that six of the 16 patients failed to show a phonological similarity effect in the visual modality and that eight of them did not show the effect in the auditory modality. The phonological similarity effects of patients with the largest interference cost were compared with those of patients with the smallest interference cost. The score for the visual phonological similarity effect was -4.75 (SD= 16.4) and 2.3 (SD= 52.5) in patients with smallest interference costs and in those with largest interference costs on the ISE, respectively. The scores for the auditory phonological similarity effects were 9.2 (SD= 23.0) and -11.8 (SD= 31.8) in patients with smallest and in those with largest cost on the ISE, respectively. Impaired and unimpaired patients did not differ on either the auditory, $t_{(14)} = 1.36$; $p=0.1955$, two-tailed, or visual phonological similarity effect score, $t_{(14)} = -0.405$; $p=0.6911$, two-tailed.

In sum, French and Romanian speech, but not white noise, impaired recall in young and elderly subjects, as well as in DAT patients. Interestingly, the effect was equivalent across groups. DAT patients were not more impaired than normal elderly subjects, and normal aging was not responsible for any impairment on that task. The finding that unattended speech has no more detrimental effect in DAT patients is consistent with the notion that it occurs at the level of the phonological store (Vallar, DiBetta & Silveri, 1997) even if performance on the two tasks was unrelated. Two DAT patients exhibited a severe deficit on this task and many failed to show the expected phonological similarity effect. Yet, there was no systematic relationship between the size of the phonological similarity effect and sensibility to distraction. However, this result should be interpreted cautiously because of the relatively small number of patients in each subgroup.

As mentioned previously, a proportion (n=11) of the DAT patients were included in both experiments. This provided the opportunity to assess whether the two tasks were related. Figure 6 shows their performance in terms of manipulation cost plotted against performance in terms of interference cost (as defined earlier), and reveals no relationship between the manipulation and interference scores in this subset of patients. This is confirmed by a correlation that was weak and non-significant, $r_{(9)} = 0.07$, NS. Furthermore, there is a double-dissociation between the tasks. Six patients were impaired (impairment is defined as a score that lies more than one SD away from the mean of aged controls) on the alphabetical span but performed normally on the interference task. In contrast, two other patients were impaired on the interference task, yet performed normally on the alphabetical task.

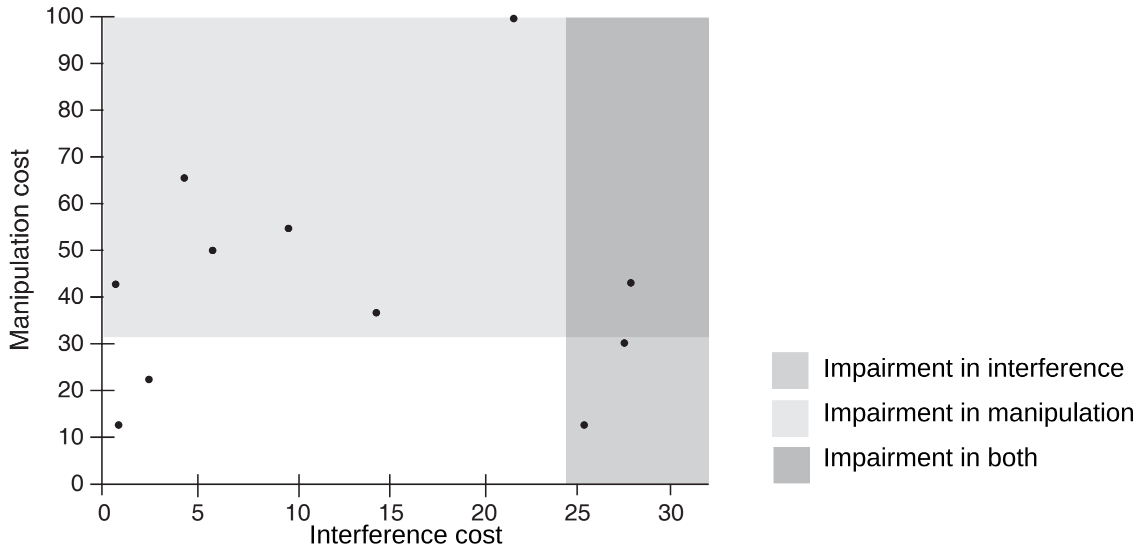


Figure 6

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GENERAL DISCUSSION

This study included two experiments that assessed different components of working memory. Experiment 1 revealed impaired manipulation capacities in a group of patients suffering from DAT. Experiment 2 indicated that in contrast to manipulation, resistance to irrelevant interfering noise is not affected in the early stages of the disease. Both experiments were consistent with our previous data in showing that normal elderly subjects do not differ from young normal subjects in their WM abilities to manipulate information or resist irrelevant interfering speech. In that respect, the manipulation impairment observed here in DAT represents a qualitative difference from normal aging.

This could have implications for our understanding of the relationship between normal aging and dementia. The question of whether there are indeed qualitative differences between normal aging and AD is of acute importance, especially in light of medical research efforts to increase life expectancy. Indeed, the existence of a cognitive continuum between normal aging and DAT may suggest that the two manifestations are on a continuun not only on the cognitive dimension, but neuroanatomically and clinically (Petit, 1982; Drachman, 1983; Bäckman, 1998). A consequence of the continuum conception is that DAT would be an inevitable consequence of normal aging. Although some cognitive components may appear to lie on a continuum when comparing normal and impaired groups (for example, Bäckam, 1998, argues that this is the case for episodic memory), a variety of cognitive components, including WM, may differ qualitatively (see also Nebes and Madden, 1988). The finding of a qualitative difference on the alphabetical recall could also have implications for clinical practice. Indeed, the most powerful tasks for the diagnosis of DAT should be those that measure processes that are normal in neurologically intact elderly persons. Obviously, the alphabetical procedure responds to this criteria.

Numerous studies have reported impaired WM in DAT patients (for a review, Belleville et al., 1996; Morris & Baddeley, 1988) that was explained by a central executive dysfunction (Baddeley, 1986; Baddeley, Bressi et al., 1991; Belleville et al., 1996; Greene, Hodges, & Baddeley, 1995; Morris, 1986), and our experiments corroborate these findings. However, they also circumscribe it by dissociating two putative executive tasks. This dissociation is found both at the group and the patient level. As a group, DAT patients do not show a reduced span in the presence of distraction, but exhibit major difficulties in the on-line manipulation of information. Furthermore, individual patients produced double-dissociations, as some were impaired in alphabetical recall but exhibited normal irrelevant speech effect, whereas at least two patients showed the reverse dissociation. A similar fractionation has been recently reported by Baddeley and collaborators (2001) in DAT. They found impaired performance in the ‘ ability to divided their attention, no impairment in their ability to focus their attention and a deficit in a visual search task.

A second point of interest relates to the selectivity of the executive impairment across the different WM components. Morris proposed that the phonological loop was unimpaired in DAT (Morris & Baddeley, 1988). Consistent with this suggestion, our analysis of DAT patients was not coherent with abnormal phonological similarity effect because the Material effect did not interact with Group. In the present study, abnormal phonological similarity effects were observed in a portion of patients. Previous studies (Belleville et al., 1996; Baddeley et al, 1991) have proposed that a subset of DAT patients may exhibit an impaired phonological working memory deficit even if it is normal in the majority of them. Our results are congruent with this suggestion because a small proportion of our DAT patients exhibit clear signs of an impaired phonological loop. It is conceivable that if only part of the DAT population is phonologically impaired, different studies using different patients and having different statistical power will lead to conflicting statistical outcome. This relates to the important issue of heterogeneity in DAT patients.

As mentioned above, heterogeneity in the performance of DAT patients was observed at the level of the phonological loop, as a proportion of the patients in this study failed to show the expected phonological similarity effects. Furthermore, examination of the individual performance profiles in DAT patients suggests that a general description of impaired manipulation capacities but normal distraction was true for most but not all patients. Although the majority of DAT patients fit the above description (about 55%), two patients exhibited no executive impairment, one had deficits in both tasks and two showed the reverse pattern, with greater interference from irrelevant speech and intact manipulation capacities. This heterogeneity is not a simple exaggeration of the increased variability that occurs as a result of normal aging, as the performance distribution of normal elderly subjects has a normal shape and is much closer to that of young subjects than to that of DAT patients. Therefore, the variable distribution found in DAT patients is likely to reflect differences in underlying pathological processes.

The presence of substantial heterogeneity in the performance of our DAT patients corroborates numerous recent findings. However, the heterogeneity that is usually reported concerns wider domains of knowledge such as language, perception and memory (e.g.: Martin et al., 1986; Neary et al., 1986; but see Baddeley, Della Sala et al., 1991; Becker, 1988; Della Sala et al., 1995). In the present report, we have obtained evidence for the presence of a heterogeneity that extends beyond the large modules to their constituents. The extension of heterogeneity to smaller components of cognition is not surprising. One important hypothesis to explain the presence of heterogeneity in DAT is that different regions of the brain are differently affected by neuropathological alterations (Ritchie & Touchon, 1992). Many authors have suggested that the central executive is located in the pre-frontal cortex, whereas the left pre-motor cortex (Broca's area) is involved in articulatory rehearsal and the left infero-parietal lobule in short-term phonological memory (e.g.: Paulesu, Frith, & Frackowiak, 1993). Consequently, it is no more surprising to observe dissociations in DAT patients between physically distant components of WM - the phonological loop and the central executive - than it is to observe dissociations between language and praxis. The same logic applies to the different executive functions in the hypothesis of frontally located systems. The frontal lobe is a large part of the brain with different cytoarchitectonic regions and it is likely that different parts of the frontal lobe are responsible for different executive functions.

The finding of a dissociation in DAT patients between alphabetical recall and recall under distraction appears to corroborate a subdivision of the central executive. It is necessary to consider alternative interpretations to this dissociation. First, one possible explanation of this dissociation could relate to the difficulty of the task; it is indeed possible that our manipulation task was more difficult than the interference. If the central executive is a single resource component, its impairment is likely to be more apparent on tasks that are more demanding. Whereas this is a possibility, we do not think that it explains our results, as there was a double-dissociation between the two tasks. We have been able to identify patients who are impaired on the inhibition task but perform normally on the manipulation task. This pattern of performance would not be possible if a single component were responsible for the two tasks. Furthermore, there was no correlation between the two tasks in DAT patients: impairment in one executive aspect was not necessarily accompanied by impairment in the other aspect.

We should also point out that the irrelevant speech effect paradigm used here is different from typical measures of inhibition on which impairments were found among DAT patients. For example, Spieler, Balota and Faust (1996) showed the presence of a slightly larger Stroop interference effect and more intrusion errors in DAT patients. Sullivan, Faust and Balota (1995) also found that inhibitory components underlying selective attention are impaired in DAT patients when using the negative priming paradigm. However, whereas those tasks measure the ability to keep salient but inappropriate responses from controlling the action sequence (e.g.: Logan & Cowan, 1984; Norman & Shallice, 1986; Rogers et al., 1998), the processes involved in our task act to sustain attention to task-relevant information in spite of environmental distracters (Houghton &

Tipper, 1994; Klein & Taylor, 1994). Furthermore, there likely exist different control systems dedicated to selective attention in specialized domains (e.g.: spatial, lexical and phonological; Connelly & Hasher, 1993; Rouleau & Belleville, 1996). Our paradigm probably refers to selective attention for phonological properties of irrelevant words. Thus, it is this aspect of attention control that may be more resistant to DAT.

Finally, one must acknowledge the possibility that the processes measured by the irrelevant speech effect paradigm are not under executive control. This last objection echoes the lack of consensus in the literature with respect to the concept of executive function, and to the criteria that should be used to define a task as executive. Some researchers have tended to circumvent this problem by suggesting that executive function may be defined in terms of aspects that implicate the frontal lobe. However, other researchers consider executive function to be a cognitive construct that should thus be defined in cognitive terms. In addition, some authors (D'Esposito & Grossman, 1996; Fuster, 1993; Weinberger, 1993) have proposed that executive control is not strictly dependent on the frontal lobes but requires the integration of information coming from different cerebral areas. As a result of this lack of common criteria, tasks that are considered to be executive are also often those that are the most complex (but see Halford, Wilson, & Phillips, 1998 and Waltz, Knowlton, & Holyoak, 1998 for a neural net model in which relational complexity is proposed to underlie executive processes). Future research should thus be devoted to the formulation of specific criteria that would help categorize tasks as being of or lacking an executive nature. This will only be possible with strong theoretical formulations that can be operationalized (for a recent attempt, see Rabbit, 1997). Yet considering that our finding is consistent with the contention that the existence of a single executive system is not viable (Parkin, 1998) and as executive functions are dissociated into a number of neurologically and psychologically distinct components, the need to refer to a central executive of working memory may be obviated. Instead, the present research may lead us to believe that performance on executive tasks relies on complex interactions between distinct control processes.

In summary, the present study contributes to our knowledge of the cognitive impairments in early DAT 1) by presenting data on WM tasks that have not been typically used in DAT and that were dissociated; 2) by showing that heterogeneity in performance can also be found within executive components, as was found across larger cognitive domains; 3) by showing that there are qualitative differences between the effect of normal aging and DAT on some WM components. This advocates against the idea that normal aging and DAT lie on a continuum of severity.

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Figure Caption

Figure 1. Number of correct sequences in conditions of direct and alphabetical recall of Experiment 1.

Figure 2. Distribution of the manipulation cost in the three groups of subjects (Experiment 1).

Figure 3. Percent correct recall on the irrelevant speech task of Experiment 2.

Figure 4. Effect of phonological similarity in the a) auditory and b) visual modality of presentation (Experiment 2). Subjects are tested with sequences of a length which corresponds to their individual digit span.

Figure 5. Distribution of the interference cost in the three groups of subjects (Experiment 2).

Figure 6. Relation between manipulation and interference cost in eleven DAT patients. Shadows represent the nature of the impairment. Performance is considered as impaired when it stands more than one standard deviation above that of the age-matched control subjects' average. The white area indicates no impairment.

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