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Phonological loop and central executive functioning in Alzheimer's disease

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Abstract

The phonological loop and central executive functioning were examined in patients with Alzheimer's disease (AD) and in normal elderly subjects. AD patients showed abnormal functioning of the phonological loop and decreased performance on tasks assessing the central executive. However, when AD patients were separated into two groups on the basis of their span level, both groups showed deficits of the central executive but only patients with the lower span level presented a dysfunction of the phonological loop as well as impaired performance in tasks of phonological discrimination, articulation rate and speed of processing. These results are interpreted in terms of progression of the disease, with high-span level patients being less severely demented and displaying deficits only in higher-level cognitive functions (such as manipulation of information stored in working memory) whereas patients with a low span level have impairments encompassing a series of more basic processes.

Keywords*:* Alzheimer's disease; Working memory; Phonological loop; Central executive; Heterogeneity

1. Introduction

Working memory deficits have been shown in AD patients across different types of materials and procedures. Several studies reported a reduced span for words [9, 27, 38], letters [9, 18, 52], digits [9, 14, 30, 40, 45] and spatial locations [21, 26, 45, 47, 52]. Substantial deficits were also found in the Brown-Peterson task in which the subjects have to retain three items in memory during variable periods of time with and without distraction [9, 30, 39]. Finally, the recency effect was also reduced in AD patients [12, 13, 35, 46, 51, 52, 55].

There have been some attempts to explain the AD working memory deficits, mainly in the light of the working memory model developed by Baddeley [1]. According to Baddeley, working memory refers to a limited capacity system which is responsible for temporary storage and processing of information. This model comprises a modality-free controlling central executive which is helped by a number of peripheral slave systems ensuring temporary maintenance of information. Two such systems have been more thoroughly explored: the phonological loop and the visuo-spatial sketchpad. The phonological loop system provides temporary storage for speech-based material and is composed of two subsystems : a passive phonological input store and an active articulatory rehearsal process. The visuo-spatial sketchpad system is assumed to be involved in setting up and maintaining visuo-spatial material. Recently, Logie [31] proposed a model of the sketchpad system comprising a visual temporary store which is subject to decay and interference from new incoming information, and a spatial temporary subsystem which can be used to plan movement and also to rehearse the contents of the visual store. The central executive is assumed to be an atten-tional control system responsible for strategy selection, control and co-ordination of the various processes involved in short-term storage and more general processing tasks. Baddeley [1] has suggested that the supervisory attentional system component of the attentional control of action model proposed by Norman and Shal-lice [44] might be an adequate approximation of the central executive system.

The first studies assessing span deficit in AD with the working memory model evaluated the integrity of the different subcomponents of the phonological loop using the standard variables of phonological similarity, word length and articulatory suppression. In order to inves-
tigate the phonological store, Morris [38] measured the size of the phonological similarity effect using immediate recall for lists of phonologically similar and dissimilar letters. With both auditorily and

visually presented letters, the phonological similarity effect was undiminished in the AD group, despite an overall decline in memory span. In the same study, Morris also evaluated the efficiency of the articulatory rehearsal system by means of the word-length effect. Memory span was measured using either mono- or pentasyllabic words. An equivalent word-length effect in both groups was found, indicating that the articulatory rehearsal mechanism was functioning normally. In a more recent study, Collette et al. [16] have also found a normal word-length effect (by comparing recall performance for short and long words) and a normal phonological complexity effect (with a non-word repetition task). Another way to evaluate the functioning of articulatory rehearsal is to measure the degree to which concurrent articulation reduces memory span. Morris [40] compared digit span with and without concurrent articulation, and showed that span reduction was similar in control subjects and AD patients. The rate at which AD patients can cycle verbal material through the articulatory loop has also been investigated. Morris [41] measured articulation rate in AD patients by requiring subjects to read a series of digits or to count aloud from one to 10 as rapidly as possible. The AD patients read the digits at the same rate as the controls but were significantly slower when required to count. For Morris, the undiminished reading rate is indicative of a normal articulation rate, because this is a better measure of the articulation rate than the counting aloud from one to 10, which is dependent on retrieval from semantic memory. Taken together, these results suggested that reduction in verbal span was not caused by an impairment affecting the phonological store or the articulation rehearsal system but rather by dysfunction of the central executive system [42, 43]. Moreover, recent PET studies [8, 15] showed that verbal short-term memory processes (that is the phonological loop components) are subserved by a similar network of cerebral regions in AD patients and in controls subjects, although these areas can be hypo-metabolic in AD patients.

In this perspective, several studies have more directly showed deficits affecting the central executive in AD. Most of these studies used a dual-task paradigm and found that AD patients were particularly impaired when they had to perform simultaneously two different tasks, which according to Baddeley [5] constitutes one of the most important functions of the central executive. A series of studies indicates very substantial impairment in remembering small amounts of information for short periods, when the attention of the patient is distracted by a subsidiary task. The Brown-Peterson paradigm [9, 39] investigated divided attention capacity by means of various interfering tasks and showed that a simple distractor such as finger tapping was sufficient to cause considerable forgetfulness in AD patients. Moreover, Baddeley et al. [2] have administered to AD patients and normal (young and elderly) control subjects a dual task composed of a pursuit tracking, requiring the patient to maintain a light pen over a moving stimulus on a computer screen, and a digit repetition task. The difficulty of both tasks was adjusted between patients and control subjects so as to equate performance across the groups when the tasks were performed alone. When both tasks were performed simultaneously, the deterioration in performance shown by AD patients was particularly marked, contrary to control subjects. A follow-up study investigated the same patients after 6 months [3]. It revealed that the dual-task performance deteriorated significantly, whereas the single-task performance remained stable. Deficits of the central executive have also been found in AD patients in an alphabetical span task which requires simultaneous storage and manipulation of information [11]. This task consists in presenting word lists whose length corresponds to the span minus one of each individual. In the first condition, subjects have to recall the words in serial order. In the second condition, the words have to be recalled in alphabetical order. The storage requirement being equated between the two conditions, the only difference concerns the intervention of the central executive during alphabetical recall. Although AD patients and control subjects display a similar performance when they have to perform serial recall of information, AD patients show a much poorer performance than control subjects when they have to recall information in alphabetical order.

Taken as a whole, these data are indicative that AD patients exhibit impaired abilities to perform two tasks simultaneously and to manipulate information maintained in working memory, which is compatible with impairments at the level of the central executive system. Although the central executive interpretation of AD working memory deficits has been widely favoured in the literature [42, 43], other studies underscored a phonological loop impairment in AD patients. Miller [36] observed that the magnitude of the phonological similarity effect was significantly smaller in AD patients than in normal elderly controls in both verbal and visual modalities. More recently, Belleville, Peretz and Malen-fant [9] explored the phonological similarity effect and word-length effect at the span level of the subjects and showed a decreased phonological similarity effect in AD patients, but a normal word-length effect. Finally, Hulme, Lee and Brown [27] reported a lower memory span in AD patients as well as a slower speech rate, and they suggested that a reduced rate of rehearsal within working memory may be responsible for the verbal short-term impairment found in AD patients. Moreover, they also postulated a deficit affecting the contribution of long-term memory mechanisms to span

performance.
Finally, some data attested the heterogeneity of the impaired and preserved working memory functions in Alzheimer's disease. Baddeley, Delia Sala and Spinnler [4] described an AD patient with a relatively pure deficit of the central executive and another patient with a predominant deficit of verbal short-term memory. Similarly, Belleville et al. [9] performed an individual case analysis of AD patients in the earlier stages of the disease. The authors showed that eight of the 10 patients had a deficit at the level of the central executive, but only half of the patients presented a phonological loop dysfunction.
Given the controversial data and interpretations in the literature about working memory deficits in Alzheimer's disease, the aim of this study was to re-examine the nature of span deficits in a group of mildly to moderately affected AD patients. The subcomponents of the phonological loop were assessed by means of the phonological similarity and complexity effect as well as the word-length effect and articulation rate. The central executive functioning was investigated in its aspects of dual-task coordination and manipulation of information abilities.

2. Method

2.1. Subjects

Two groups of subjects participated in this study: patients with dementia of the Alzheimer type (AD) and normal elderly subjects. The AD group consisted of 20 patients (3 men and 17 women) who met the NINCDS-ADRDA criteria for probable or possible Alzheimer's disease [34]. All patients had suffered from progressive worsening of memory problems for at least 6 months. The diagnosis of AD was based on general medical, neurological and neuropsychological examination. Patients' age ranged from 65 to 84 years (mean age = 72 ± 5.15 years) and their mean MMSE score was 21.80 ± 4.75. Sixteen of the 20 patients also underwent PET scan at rest, and brain metabolism distribution was compatible with AD [48].
Twenty normal elderly subjects matched for age, sex and sociocultural level served as controls. The normal controls were non-institutionalised, alert, and had no history of neurological problems, alcohol abuse or psychiatric disorders. They had normal or corrected vision and normal or corrected hearing. The average age for the control group was 71.75 + 4.83 years. These control subjects did not differ from AD patients according to their age ($t(38) = 0.15$, ns) and their schooling level (f(38) = 1.16, ns). The Mattis dementia rating scale (DRS, [33]) was administered to AD patients and control subjects. All controls had a total score superior to 130 on this scale, which constitutes a cut-off score to discriminate normal aging from dementia [37]. Overall performance on the
Mattis dementia rating scale was significantly lower for AD patients than for controls subjects ($t(38) = 5.82$, $P < 0.00001$). The results of AD patients and control subjects on the different sub-tests are described in Table 1.

2.2. Cognitive assessment

2.2.1. Phonological store

The integrity of the phonological store in AD patients was evaluated by comparing their phonological similarity effect to that of control subjects. A non-word repetition task was also administered in order to remove the influence of long-term lexical representations [7, 24].
The phonological similarity effect was assessed by comparing span level for phonologically similar and dissimilar words. Two sets of nine words each were used for constructing the sequences of similar and dissimilar items. Three sequences of words were presented for each length. The sequences were presented in increasing number, starting with two-word sequences. Subjects had to recall the sequences immediately in the correct order. Testing was interrupted when the subject failed to recall correctly at least two of the three sequences. The span was the longest sequence in which at least two sequences had been correctly recalled.
The standard span procedure described above may, however, not be sufficiently sensitive to determine the phonological similarity effect, and another method (a constant-length span procedure), adapted from Belleville et al. [9] was used. This method consisted in administering a series of sequences of constant length determined by the subject's span calculated with the short and dissimilar words. The phonological similarity effect was assessed by comparing the performance at the span-level length for phonologically similar and dissimilar words. Five trials with similar and dissimilar words were administered.
The phonological store was also assessed by using a non-word repetition task [24]. Unlike familiar

items, non-words have no long-term lexical representations which could be used to supplement phonological short-term memory [28]. Consequently, the repetition of non-words is likely to be more sensitive to phonological short-term memory skills. The task was designed in such a way as to rule out as much as possible any long-term memory contribution to phonological short-term memory performance. It consisted of 45 non-words: 24 items composed of consonant-vowel syllables (CV; 3 non-words each containing 1, 2, 3, 4, 5, 6, 7 and 8 syllables) and 21 items composed of consonant-consonant-vowel syllables (CCV; 3 non-words each containing 1, 2, 3, 4, 5, 6 and 7 syllables). None of the syllables corresponded to any morpheme in French, although the phoneme sequences in each non-word conformed to the phonotactic rules of French. Each non-word was spoken by the experimenter. The set of CCV items followed the set of the CV items and in each set, the items were presented in ascending order.

The subject had to listen and then to repeat each item immediately. All the procedure was recorded on an audio cassette recorder. A response was scored as incorrect if it differed phonemically from the target non-word. However, one transformation of one articulatory feature was considered as correct. The measure taken was the percentage of CV and CCV syllables correctly recalled.

Table 1 Mean performance of AD patients and control subjects in the different sub-tests of the DRS

	AD	Controls	/ test
Attention	34.05(4.05)	36.30(0.65)	$t(38) = -2.45$, $P < 0.05$
Verbal-motor initiation	27.7(7.15)	34.90(3.23)	$t(38) = -4.10$, $P < 0.0005$
Construction	4.90(2.07)	5.85(0.67)	$t(38) = -1.95$, P = 0.058
Concept	33.35(6.21)	38.50(0.83)	$t(38) = -3.68$, $P < 0.001$
Memory	14.45(4.50)	24.45(1)	$t(38) = -9.70$, $P < 0.00001$
DRS overall score	114(19.62)	140.15(4.31)	$t(38) = -5.82$, $P < 0.00001$

2.2.2. Articulatory rehearsal system

The integrity of the articulatory rehearsal system was evaluated in AD patients by comparing their word-length effect and articulation rate to those of control subjects.

The word-length effect was assessed by comparing performance on a span task for short- and long-words. Two sets of nine words were constructed to generate sequences of short- and long-words. Words of each set were matched according to the frequency of occurrence. From these two sets, separate series of randomly selected sequences were created. The span procedure was similar to that described for assessment of the phonological similarity effect.

As for the phonological similarity effect, the word-length effect was also assessed with the constant-length span procedure adapted from Belleville et al. [9]. The procedure was similar to that described for the assessment of the phonological similarity effect. The performance recall for short- and long-words was compared for five sequences, length of which corresponded to the individual subject's span for short and dissimilar words.

Finally, the articulation rate was assessed for short (1-syllable), medium (3-syllable) and long (5-syllable) words. Subjects were presented with a pair of items and were instructed to repeat them continuously as fast as possible, until asked to stop. The time taken for five repetitions of the pair was recorded. From these values, the mean number of syllables articulated per second was calculated. Two sets of pairs of 1-, 3- and 5-syllables words were constructed. One pair of each length was presented but if the subject failed to repeat it (forgetting or transforming of the words), the other pair was given. The influence of storage requirements in this task was minimised by asking (before the measure of articulation rate) the subjects to repeat the pair of words until they could recall it without any difficulties.[1]

2.2.3. Influence of long-term memory on span performance

The contribution of information stored in long-term memory on span performance [28] was evaluated by comparing performance with words and non-words by means of a span and a constant-length span procedure.

In the span procedure, one set of words and one set of non-words were constructed. Each set was composed of nine short and dissimilar items. Non-words were chosen in order not to call to mind any French words. Three sequences of items were presented for each length. The sequences were presented in increasing number, starting with two-item sequences. The task was to report immediately the sequences in the correct order. Testing was interrupted when the subject failed to recall correctly at least two of the three sequences. The span was the longest sequence in which at least two sequences had been correctly recalled. Long-term memory contribution was assessed by comparing span level for words and non-words.

In the constant-length span procedure adapted from Belleville et al. [9], five series of sequences of a constant length, determined by the subject's span for short and dissimilar words, were administered. Long-term memory contribution was assessed by comparing the total number of sequences correctly recalled on five trials for words and non-words.

2.2.4. Assessment of the central executive

Two tasks, designed to assess the central executive of working memory, were used. The first task, the α span task [10], investigated the ability to manipulate information stored in working memory. The second task, the dual-task paradigm [2, 25], assessed the ability to coordinate the simultaneous realisation of two tasks.

The α span task compares the recall of information in serial order (implicating only storage of information) or in alphabetical order (implicating storage and manipulation of information). Firstly, a classical word span procedure was administered in order to assess the span level of each subject. Sequences of words were read to the subject at the rate of one item per second, starting with short sequences of two words. The length of the sequences was progressively increased. Two trials were administered at each level. If one 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 at a particular length. The word span was defined as the longest sequence correctly recalled on 50% of the trials. Following the span measurement, subjects were assessed in two conditions: direct and alphabetical recall. In the direct condition, subjects performed an immediate serial recall of the words. In the alphabetical condition, they were asked to recall the words in their alphabetical order. Ten sequences of words were administered in each condition. The number of words to be recalled corresponded to the subject's span minus one item. In order to control for possible practice or fatigue effects, five trials in the direct condition were firstly administered, followed by the 10 trials of the alphabetical condition, and lastly the five remaining trials of the direct condition.

The dual task consists in a paper-pencil version of the dual-task paradigm proposed by Baddeley et al. [2, 3]. This paradigm compares the performance in a verbal and a motor task carried out separately to the performance when the two tasks are carried out simultaneously [25]. Firstly, digit span of each subject was determined by administering digit strings of increasing length. Three sequences were presented per length. Testing was interrupted when the subject failed to recall correctly at least two of the three sequences. The span was the longest sequence in which at least two sequences had been correctly recalled. Following this span measurement, the verbal and motor tasks were presented successively. During the digit recall task, sequences of digits at the subject's span level were continuously given for 2 min and the number of correct sequences was determined. For the motor task, the subjects were presented with a trail of boxes, and were required to put a cross on each box following the trail as quickly as possible during 2 min. The second part of the paradigm was then administered, in which the subjects were required to put crosses on the boxes in the trail while simultaneously being presented with sequences of digits to repeat.

2.2.5. Speed of processing

This task was administered in order to assess general processing speed and to examine the possible contribution of a reduction of processing speed to working memory deficits in AD patients. Speed of processing was assessed with a letter comparison task which is a computerised version of the task initially proposed by Salt-house and Babcock [49]. Participants were presented with pairs of letters and their task was to decide as rapidly and accurately as possible whether the letters were the same or different, by pressing a key-response. The test comprised 60 trials, with 30 'same' and 30 'different' pairs. The selected measure was the mean correct latency for 'same' pairs.

2.2.6. Phonological analysis

This task was administered in order to examine the possible contribution of a reduction of basic phonological analysis to phonological short-term memory deficits in AD patients. The phonological

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analysis abilities were assessed by asking subjects to perform a 'same-different' judgement task with orally presented syllables [19]. The material comprises 148 pairs of tape-recorded syllables with a consonant-vowel-consonant structure. None of the syllables correspond to any word in French. Half of the syllables are similar (e.g., lid-lid) and the other half are dissimilar (e.g., biz-siz). The pairs were presented at a rate of about one pair every 4 s and the two syllables of a pair were separated by a 1 s interval.

3. Results

3.1. Phonological store assessment

Classical span and constant-length span performance for phonologically similar and dissimilar words, as well as performance in the non-word repetition task and the phonological discrimination task, are showed in Table 2.

Span performance for similar and dissimilar words was assessed by an ANOVA with group (AD, controls) as a between-subject factor and type of words (similar, dissimilar) as a within-subject factor. The analysis revealed a group effect ($F(1,38) = 21.59$, $P < 0.00005$) and a phonological similarity effect ($F(1,38) = 86.27$, $P < 0.000001$). There was also an interaction between group and phonological similarity effect ($F(1,38) = 9.58$, $P < 0.005$), with AD patients having a smaller phonological similarity effect than control subjects (Newman-Keuls post hoc test).

Similar results were obtained with the number of correctly recalled similar and dissimilar words at the individual word span level: a significant group effect, ($F(1,38) = 7.28$, $P<0.05$), a phonological similarity effect ($F(1,38) = 146.43$, $P < 0.00001$) and a significant interaction between group and type of words ($F(1,38) = 8.11$, $P < 0.01$), confirming a weaker phonological similarity effect (Newman-Keuls post hoc test).

In the non-word repetition task, the percentage of correctly recalled simple and complex syllables was analysed by an ANOVA with group (AD, controls) as a between-subject factor, and type of syllables (simple, complex) as a within-subject factor.

The analysis revealed a significant group effect ($F(1,37) = 12.53$, $P < 0.005$), with control subjects showing better performance than AD patients. There was also a phonological complexity effect ($F(1,37) = 100.45$, $P< 0.0001$), with simple syllables being recalled better than complex syllables. No significant interaction between group and type of syllables was found ($F(1,37) = 1.34$, $P > 0.1$).

Table 2 Performance of both groups in tasks assessing the phonological store

	AD	Controls
Dissimilar-word span (classical)	3.5(0.83)	4.9(0.85)
Similar-word span (classical)	2.90(0.64)	3.60(0.75)
Dissimilar-word span (constant length)	4.1(0.78)	3.95(0.89)
Similar-word span (constant length)	2.15(1.53)	0.80(1.05)
Simple syllable recall (%)	66.97(18.83)	85.58(9.64)
Complex syllable recall (%)	48.65(20.17)	62.47(11.98)

3.2. Articulatory rehearsal system assessment

The performance of AD patients and control subjects (classical span and constant-length span performance for short and long words and articulation rate) are described in Table 3.

The span level for short and long words was analysed using an ANOVA with group (AD, controls) as a between-subject factor and word length (short, long) as a within-subject factor. The analysis showed a main group effect ($F(1,38) = 21$, $P < 0.00005$) and a significant effect of word length ($F(1,38) = 122.58$, $P < 0.00001$). There was also an interaction between group and word length ($F(1,38) = 11.03$, $P < 0.005$), with AD patients having a smaller word-length effect than control subjects (New-man-Keuls post hoc test).

A similar analysis was performed with the number of short- and long-words correctly recalled at the word-span level of each individual. The analysis again revealed a significant word-length effect ($F(1,38) = 151.11$, $P < 0.00001$) but there was no group effect any longer ($F(1,38) = 1.51$, $P>0.1$) and no interaction between group and type of words ($F(1,38) = 0.89$, $P > 0.1$). However, given the very low performance

of both groups in the recall of long words, this absence of interaction could be due to a floor effect.
The articulation rate (number of syllables articulated per second) was analysed using an ANOVA with group (AD, controls) as a between-subject factor and word length (one, three, five syllables) as a within-subject factor. The analysis revealed a main group effect ($F(1,33) = 7.33$, $P < 0.05$) and a significant word-length effect ($F(2,66) = 125.82$, $P < 0.00001$). Finally, there was also an interaction between group and word length ($F(2,66) = 5.10$, $P<0.01$). Newman-Keuls post hoc tests show that the number of items articulated per second increases from the one- to the three-syllable words in both groups, but only in the control subjects group for the three- to the five-syllables words.

3.3. Influence of long-term memory on span tasks

The performance of AD patients and control subjects in classical span and constant-length span tasks implicating words and non-words is described in Table 4.
The scores for both types of items were analysed using an ANOVA with group (AD, controls) as a between-subject factor and type of items (words, non-words) as a within-subject factor. The analysis revealed a significant group effect ($F(1,38) = 18.87$, $P < 0.0001$) and a main type of item effect ($F(1,38) = 383.04$, $P < 0.00001$).

An interaction between group and type of items was also found ($F(1,38) = 26.27$, $P < 0.00001$), with control subjects showing a larger decrease of performance from words to non-word than AD patients (Newman-Keuls post hoc test).
The number of correctly recalled words and non-words at each individual word span level was not analysed because both groups showed a floor effect in the non-word recall.

Table 3 Performance in tasks assessing the articulatory rehearsal system

	AD	Controls
Short-word span (classical)	3.55(0.83)	4.09(0.85)
Long-word span (classical)	2.85(0.81)	3.60(0.60)
Short-word span (constant length)	4.10(0.79)	3.95(0.89)
Long-word span (constant length)	1.7(1.59)	1.15(1.04)
Number of syllables articulated per second (one syllable words)	2.47(1.27)	3.28(0.95)
Number of syllables articulated per second (three syllable words)	4.36(1.92)	5.93(1)
Number of syllables articulated per second (five syllable words)	4.77(2.08)	6.63(1.53)
Mean articulation rate	3.60(1.71)	5.28(1.04)

Table 4 Performance of AD patients and control subjects in word and non-word span tasks

	AD	Controls
Word span (classical)	3.55(0.83)	4.09(0.85)
Non-word span (classical)	2(0.46)	2.25(0.44)
Word span (constant length)	4.10(0.79)	3.95(0.89)
Non-word span (constant length)	0.2(0.41)	0(0)

3.4. Central execufive assessment

From our sample of 20 AD patients, three patients were unable to perform the *α.* span task or the dual-task paradigm.

3.4.1. α span task

The subjects' results are described in Table 5. Firstly, the AD patients' word span was inferior to that of control subjects ($t(38) = -3.04$, $P < 0.005$). The scores for serial and alphabetical recall were then separately analysed using an ANOVA with group (AD, controls) as a between-subject factor and type of recall (serial, alphabetical) as a within-subject factor. The analysis revealed a significant group effect ($F(1,35) = 5.65$, $P < 0.05$), and a condition effect ($F(1,35) = 71.58$, $P < 0.00001$). A significant interaction between group and type of recall was also found ($F(1,35) = 18.34$, $P < 0.0005$), with AD patients showing a more important decrease of performance from direct to alphabetical recall than control subjects, despite a similar performance in direct recall (Newman-Keuls post hoc test).

Table 5 Performance of AD patients and control subjects in the α span task

	AD	Controls
Word span	3.6(0.99)	4.45(0.76)
Serial recall	9.35(0.61)	9.05(1)
Alphabetical recall	5.23(2.61)	7.70(1.87)
Serial recall 1-5	4.65(0.49)	4.45 (0.60)
Serial recall 6-10	4.71 (0.47)	4.60(0.68)
Alphabetical recall 1-5	2.29(1.31)	3.50(1.15)
Alphabetical recall 6-10	2.94(1.60)	4.20(1.24)
Manipulation score	44.43 (26.28)	15.49(18.05)

A manipulation score was also derived for each individual subject. This score was calculated according to the formula ((direct-alphabetical)/ direct) x 100. This represents the performance reduction experienced by each subject when performing the alphabetical recall relative to the direct recall. The diminished performance of AD patients appears more important than that of control subjects ($t(35) = 3.95$, $P < 0.0005$). In order to assess an eventual effect of fatigue or practice, we explored the performances on the first five and last five items in each condition using an ANOVA with group (AD, control) as a between-subject factor, type of recall (serial, alphabetical) and trials (items 1-5 vs items 6-10) as a within-subject factor. There was no significant interaction between group, task and time ($F(1,35) = 0.006$, $P > 0.5$).

3.4.2. Dual-task paradigm

The subjects' results in the single- and dual-task conditions are described in Table 6. The digit span performance was lower in AD patients than in control subjects ($f(38) = -3.24$, $P < 0.005$).
The proportion of correctly recalled sequences in single- and dual-task conditions was then analysed using an ANOVA with group (AD, controls) as a between-subject factor and condition (single, dual) as a within-subject factor. The analysis revealed a significant condition effect ($F(1,35) = 10.64$, $P < 0.005$), with digits in the single condition being recalled better than in dual condition. There was neither a group effect ($F(1,35) = 0.16$, $P > 0.5$), nor interaction between group and condition ($F(1,35) = 0.002$, $P > 0.5$).
A similar analysis was performed with the number of crosses put on the boxes which revealed a significant group effect ($F(1,35) = 10.30$, $P < 0.005$) and a significant condition effect ($F(1,35) = 76.44$, $P < 0.00001$). An interaction between group and condition was also found ($F(1,35) = 4.70$, $P < 0.05$), with AD patients showing a more important decrease of performance than control subjects from the single to the dual condition (Newman-Keuls post hoc test).
Finally, a global measure was computed expressing an individual's dual-task performance as a percentage of single-task performance, the contribution of the two tasks being equally weighted. This measure is defined as: (1-((digit repetition single-digit repetition dual) + (motor task single-motor task dual)/motor task dual)/2) x 100 [6].

Table 6 Performance of both groups in the dual-task paradigm

	AD	Control
Digit span	4.50(0.95)	5.55(1.10)
Decrease of performance from single to dual condition	74.22(13.93)	84.27(16.26)
Digit repetition task, single	73.96(16.99)	76.07(16.74)
Motor task, single	108.71 (40.52)	139.40(34.43)
Digit repetition task, dual	61.44(18.48)	63.21(21.37)
Motor task, dual	67.29(34.15)	111.45(34.32)

Performance of AD patients appears marginally inferior to that of control subjects. ($t(35) = -1.99$, $P = 0.053$).

3.5. Processing speed and phonological discrimination abilities

Performance of both groups are described in Table 7. With regard to the processing speed, mean response times for correct responses on 'same' items were compared between groups. A similar analysis was also computed with the logarithmic value of this measure (Log) in order to reduce variability between subjects. AD patients had slower response times than control subjects, for the raw score (t(37) = 2.23, $P < 0.005$) and for the logarithmic value (t(37) = 2.93, $P < 0.01$). The comparison of the error score in the phonological discrimination task also revealed impaired performance in AD patients (t(34) = 2.32, $P < 0.05$).

3.6. Correlation analysis

Measures assessing the phonological store and the articulatory rehearsal system (with the classical span procedure), the central executive, the speed of processing, the articulation rate and the phonological discrimination abilities were separately correlated in AD patients and control subjects (Table 8). Significant correlations were found in AD patients between phonological discrimination abilities and similar/dissimilar word span as well as with the non-word repetition performance; between mean articulation rate and short/long word span; between speed of processing and short/long word span as well as decrease of performance on the dual task and articulation rate; between word span level and overall score at the DRS. The significant correlations in control subjects were found between span level and central executive functioning (with only a tendency for the α span task); between phonological discrimination abilities and non-word repetition performance, and between speed of processing and articulation rate.

3.7. Performance of AD patients with low and high span level

Previous analyses showed that taken as a whole group the AD patients have smaller phonological similarity and word-length effect as well as impaired performance on tasks assessing the central executive. However, their span performance ranged from 2 to 5 and we could hypothesize that a deficit affecting the phonological loop is present in AD patients with a low span, since a previous study showed that the presence of phonological similarity and word-length effect is highly correlated with verbal span size [32]. Consequently, AD patients were divided into two groups related to their span level for short and phonologically dissimilar words : a group of AD patients with a span level between the mean span of control subjects and 2.5 standard deviations (AD+ patients, *1N* = 11) and a group of AD patients with a span level inferior to the mean span level of control subjects minus 2.5 standard deviations (AD— patients, N = 9).

Phonological similarity and word-length effects for each patient group were compared to those of control subjects. Both classical span and constant-length span procedures were used because an absence of phonological similarity or word-length effect in span tasks could be in fact due to a floor effect in the group with a low span. Performance of the three groups on central executive tasks was also examined, as well as measures of phonological discrimination, articulation rate and speed of processing. Furthermore, the influence of long-term memory on span task was assessed in the three groups. Results are presented in Table 9.

The short and dissimilar word span level was significantly different between the three groups (F(2,37) = 30.46, $P < 0.0000$ 1).Newman-Keuls post hoc tests showed that control subjects had the higher span level, followed by the AD + group, with the AD — group having the lowest span level. Similar results were found for the DRS overall score ($F(2,37) = 31.98$, $P < 0.0001$).

Table 7 Performance of AD patients and control subjects in the processing speed and the phonological discrimination tasks

	AD	Controls
Response time (RT)	2289.08(2640.71)	966.98(213.88)
LogRT	3.20(0.34)	2.97(0.10)
Phonological discrimination performance (number of errors)	17.42(8.85)	11.55(4.38)

Table 8 Correlation analysis in AD patients and control subjects

	AD	Controls
Phonological discrimination and dissimilar word span	r= -0.52, $P< 0.05$*	r= -0.44, $P> 0.05$
Phonological discrimination and similar word span	r= -0.56, $P< 0.05$*	r= -0.31, $P> 0.1$
Phonological discrimination and syllables correctly recalled on the non-word repetition task	r= - 0.68, $P< 0.005$*	r= - 0.46, $P < 0.05$*
Short word span and mean articulation rate	r = 0.58, $P< 0.01$*	r = 0.41, $P> 0.05$
Long word span and mean articulation rate	r = 0.61, P< 0.005*	r = 0.37, $P> 0.1$
Speed of processing and short word span	r = -0.50, $P < 0.05$*	r= -0.37, $P> 0.1$
Speed of processing and long word span	r= -0.56, $P < 0.05$*	r = -0.43, $P> 0.05$
Speed of processing and manipulation score in the α span task	r = 0.37, P>0.1	r= -0.11, $P> 0.5$
Speed of processing and decrease of performance in the dual task	r= -0.58, $P < 0.05$*	r = 0.34, $P> 0.1$
Speed of processing and mean articulation rate	r= -0.49, $P < 0.05$*	r= -0.46, $P< 0.05$*
Decrease of performance in the α span and dual task	r= -0.07, $P> 0.5$	r= -0.27, $P> 0.1$
Digit span and decrease of performance in the dual task	r = 0.11,P>0.5	r= -0.64, $P< 0.05$*
Word span and decrease of performance in the α span task	r = 0.17, P> 0.5	r = 0.39, $P > 0.05$
Word span and DRS overall score	r=0.76,$P< 0.0001$*	r = 0.23, $P> 0.1$

3.7.1. Phonological store

Span performance for phonologically similar and dissimilar words was assessed using an ANOVA with group (AD —, AD +, controls) as a between-subject factor and type of words (similar, dissimilar) as a within-subject factor. The analysis revealed a group effect ($F(2,37) = 21.57$, $P< 0.00001$), a type of word effect ($F(1,37) = 67.90$, $P< 0.00001$) and an interaction between group and type of words ($F(2,37) = 9.71$, $P < 0.0005$). Analysis of the interaction with planned comparison showed that the phonological similarity effect was smaller in the AD — patient group compared to control subjects ($F(1,37) = 19.39$, $P < 0.0001$) while the AD + patient group and control subjects had a similar phonological similarity effect ($F(1,37) = 1.72$, $P>0.1$).

A similar analysis with the number of correctly recalled phonologically similar and dissimilar words at the individual word span level revealed a similar pattern of results. There was a main type of word effect ($F(1,37) = 140.66$, $P < 0.00001$), a significant group effect ($F(2,37) = 6.08$, $P < 0.01$) and a significant interaction effect ($F(2,37) = 12.37$,$P < 0.0001$), with a smaller phonological similarity effect in the AD — patient group compared to control subjects ($F(1,37) = 23.92$, $P < 0.00005$) while the AD+ patient group and control subjects showed a similar phonological similarity effect ($F(1,37) = 0.59$, $P> 0.1$).
The percentage of simple and complex syllables correctly recalled was investigated using an ANOVA with group (AD +, AD —, controls) as a between-subject factor and type of syllables (simple, complex) as a within-subject factor. The analysis disclosed a significant group effect ($F(2,36) = 15$, $P < 0.0001$), with control subjects and AD + patients having a performance superior to that of AD— patients. There was also a task effect ($F(1,36) = 80.21$, $P < 0.0001$), with a better recall of simple syllables. No interaction between group and task was found.

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Table 9 Performance of patients with low and high span level

	AD- patients(N= 9)	AD+ patients (N = 11)	Control subjects *(N* = 20)
DRS overall score (without span tasks)	95.78(21.54)	116.55(9.91)	132.70(4.05)
Short and dissimilar word span (classical)	2.78 (0.44)	4.18(0.41)	4.90(0.85)
Long-word span (classical)	2.33(0.71)	3.27(0.65)	3.60(0.60)
Similar-word span (classical)	2.56(0.53)	3.18(0.60)	3.60(0.75)
Short and dissimilar word span (constant length)	4(0.87)	4.18(0.75)	3.95(0.89)
Long-word span (constant length)	2.56(1.67)	1(1.18)	1.15(1.04)
Similar-word span (constant length)	3.11(1.27)	1.36(1.29)	0.80(1.05)
Non-word span (classical)	1.78(0.44)	2.18(0.40)	2.25(0.44)
Phonological discrimination performance (total of errors)	21.83(7.41)	15(8.93)	11.55(4.38)
Mean articulation rate (number of syllables per second)	2.66(1.30)	4.37(1.65)	5.28(1.04)
Speed of processing (log value)	3.39(0.39)	3.06(0.22)	2.97(0.10)
Simple syllable recall (%)	55.10(17.48)	77.67(13.03)	85.58(9.64)
Complex syllable recall (%)	38.68(18.57)	57.63(17.84)	62.47(11.98)
a span, manipulation score	43.15(24.49)	45.12(28.35)	15.49(18.05)
Dual task, performance decrease	74.52(18.45)	74.05(11.84)	84.27(16.56)

3.7.2. Articulatory rehearsal system

Span performance for short and long words was assessed by an ANOVA with group (AD —, AD +, controls) as a between-subject factor and type of words (short, long) as a within-subject factor. The analysis revealed a group effect ($F(2,37) = 25.06$, $P < 0.00001$), as well as a word-length effect ($F(1,37) = 91.23$, $P < 0.00001$) and a significant interaction effect between group and type of words ($F(2,37) = 7.62$, $P < 0.005$). Analysis of the interaction with planned comparison showed that the word-length effect was smaller in the AD— group compared to control subjects ($F(1,37) = 14.83$, $P < 0.0005$) while the AD+ group and control subjects had a similar word-length effect ($F(1,37) = 3.54$, $P > 0.05$).

A similar analysis with the number of correctly recalled short and long words at the individual span level disclosed no group effect ($F(2,37) = 2.32$, $P>0.1$). However, a significant word-length effect ($F(1,37) = 152.60$, $P < 0.00001$) was found as well as an interaction effect ($F(2,37) = 5.77$, $P < 0.01$), with a smaller word-length effect in the AD— group compared to control subjects ($F(1,37) = 7.95$, $P < 0.01$) while the AD+ group and control subjects have a similar word-length effect ($F(1,37) = 0.72$, $P > 0.1$).

The mean articulation rate was also compared using an ANOVA. Again, there were differences ($F(2,37) = 12.91$, $P < 0.0001$) and Newman-Keuls post hoc tests showed that AD— patients had the slower articulation rate, whereas that of AD + patients and control subjects was similar.

3.7.3. Influence of long-term memory on span performance

Span performance for words and non-words was assessed using an ANOVA with group (AD — , AD + , controls) as a between-subject factor and type of items (words, non-words) as a within-subject factor. The analysis revealed a significant group effect ($F(2,37) = 21.88$, $P < 0.0001$), a significant type of items effect ($F(1,37) = 373.44$, $P < 0.0001$) and an interaction between group and type of items ($F(2,37) = 25.13$, $P < 0.0001$). Analysis of the interaction with planned comparison showed that the decrease of performance from words to non-words differed between the three groups (AD- vs controls: $F(1,37) = 49.81$, $P < 0.0001$; AD+ vs controls: $F(1,37) = 8.84$, $P<0.01$; AD+ vs AD-: $F(1,37) = 14.59$, $P < 0.0005$), with the influence of long-term memory being the most important in control subjects, followed by the AD+ patients and being the less important in AD — patients.

3.7.4. Central executive

The manipulation score of the *a* span task was significantly different between the three groups ($F(2,34) = 7.61$, $P < 0.005$); Newman—Keuls post hoc tests showed that the two AD groups did not differ and displayed a larger decrease of performance than the control subjects from the serial to the alphabetical recall. With regard to the dual-task paradigm, a global measure of central executive functioning showed no significant differences between the three groups ($F(2,34) = 2.18$, $P>0.1$).

3.7.5. Speed of processing and phonological discrimination abilities

Speed of processing was also significantly different between the three groups ($F(2,36) = 10.52$, $P < 0.0005$); Newman—Keuls post hoc analysis showed that AD + patients and control subjects displayed a similar performance whereas AD — patients had a slower response time. The analysis of the phonological discrimination abilities revealed similar results ($F(2,34) = 5.88$, $F<0.01$), with AD— patients producing more errors than AD + patients and control subjects.

3.8. Individual-case analysis

Individual profiles of AD patients were examined to assess whether the averaged group pattern described above persists at the individual level (Table 10). This is an important issue due to the heterogeneity of cognitive impairments that have been reported in DAT patients [4, 9]. Individual profiles were examined only for the cognitive processes for which two measures of the subject's performance were available, namely the phonological similarity and word-length effect (with the classical and constant-length span procedure) and the central executive (with the α span task and dual-task paradigm). Scores of each patient were compared to the corresponding mean value in the control group and a cut-off point of 2.5 standard deviations below the control mean was used to define impaired performance. A deficit will be considered affecting the phonological store or the articulatory rehearsal procedure if a patient presents deficits on both the classical span and constant-length span procedure. Finally, an intact functioning of the central executive will be considered when patients have normal performance in both the α span task and the dual-task paradigm.

Analysis of individual profiles of AD patients firstly revealed an important agreement in our classification of AD + and AD — patients, on the basis of word span performance. Indeed, seven of the nine AD — patients showed abnormal phonological similarity and word-length effects and 10 of the 11 AD+ patients displayed normal effects. Several examples of double dissociations were found within the phonological loop system between deficits of phonological storage and articulatory rehearsal mechanism, with some patients showing only deficits of the phonological storage (P6, P12, P14) while other patients displayed isolated dysfunction of the articulatory rehearsal mechanism (P3, P16). With regard to the central executive, six AD patients were impaired in at least one of the two tasks, with a majority of deficits on the α span task (P1, P3, P7, P8, P9, P18). Moreover, three additional patients did not accomplish the executive tasks because of major difficulties (P6, P12, P14). There were also dissociations between the manipulation function and the dual-task co-ordination abilities of the central executive, with one AD patient showing deficits on the dual-task paradigm only (P1) and five patients having specific impairments on the α span task (P3, P7, P8, P9, P18). Moreover, of these nine patients with central executive impairments, five also exhibited impairment at the level of the phonological loop (P3, P6, P8, P12, P14), while three other patients showed a phonological loop deficit without any impairment of the central executive (P11, P13, P16).

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Table 10 Pattern of individual performances of AD patients in tasks assessing the phonological loop and central executive of working memory

	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	P16	P17	P18	P19	P20	SC
Type	AD-	AD-	AD-	AD +	AD +	AD —	AD +	AD-	AD +	AD +	AD-	AD —	AD +	AD-	AD +	AD-	AD +	AD +	AD +	AD +	
Phonological similarity (classic span)	+	+	+	+	+	-	+	-	+	+	-	-	-		+	-	+	+	+	-	SC4
Phonological similarity (constant-length span)	+	+	+	+	+	-	+	-	+	+	+	-	+	-	+	+	+	+	+	+	
Word length (classic span)	+	+	-	+	-	+	+	-	+	+	-	-	-	+	+	-	+	+	+	+	SC5
Word length (constant-length span)	+	+	-	+	+	+	+	-	+	+	+	+	+	+	+	-	+	+	+	+	
α span	+	+	-	+	+		-	-	-	+	+		+		+	+	+	-	+	+	SC4
Dual Task	-	+	+	+	+		+	+	+	+	+		+		+	+	+	+	+	+	SC2

Sign ' + ' indicates a normal performance and sign ' — 'a performance inferior to the mean of control subjects minus 2.5 standard deviations. SC column represents control subjects having a performance inferior to the minus 2.5 standard deviations on a given measure. mea

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4. Discussion

Considered as a group, AD patients present deficits affecting both the phonological loop and the central executive. A phonological loop deficit has also been described in AD patients by Miller [36], Belleville et al. [9] and Hulme et al. [27]. Our results suggest that the phonological loop deficit in AD patients is partly the consequence of impairments affecting more basic factors, namely phonological analysis, articulation rate and processing speed. Indeed, we observed in AD patients only a significant correlation between span performance on the one hand and phonological analysis, articulation rate and speed of processing on the other. A significant correlation was also found in both groups between phonological analysis performance and the number of correctly recalled syllables in the non-word repetition task. A reduction in phonological analysis abilities would lead to less distinctive traces in the phonological store and this reduction would have a more important repercussion on the storage of phonologically similar items. In addition, a decrease of the articulation rate would slow the articulatory rehearsal mechanism and would prevent the rein-troduction of items, especially long words, in the phonological store. It should be noted that the significant correlation observed between articulation rate and processing speed suggests that a slower articulation rate might be the consequence of a more general slowing factor. Furthermore, it appears that the AD patients' span deficit is also due to a less important contribution of long-term memory to span performance. Indeed, the comparison of span performance for words and non-words showed that the superiority of words compared to non-words is higher in control subjects than in AD patients, which suggests that control subjects benefit more than AD patients from long-term memory representations.

To summarize, the phonological loop impairment observed in AD patients seems to be the consequence of several factors, namely an impairment of the phonological store, a slowing of articulation rate, a defective phonological discrimination ability and a less effective contribution of long-term memory.

Concerning the central executive system, the results observed in the α-span task showed that AD patients had more difficulties than control subjects to manipulate stored information, even when basic storage demands were equated. Moreover, the decrease of performance (mainly for the motor task) from the single to the dual condition in the dual-task paradigm also indicated that AD patients are less able to co-ordinate simultaneous processes. This pattern of deficit is consistent with the existence of a central executive impairment. However, different executive processes are involved in the two tasks assessing the central executive. The dual-task paradigm requires mainly co-ordination of cognitive processes while the α-span task requires a series of processes attributed by Baddeley (1996) to the central executive, i.e. the inhibition of serial recall order, the extraction of alphabetical order from long-term memory and the checking of that order to rearrange the sequences of items before producing the response [10]. In that context, the existence of a more important deficit in the α-span task than in the dual-task paradigm in AD patients could result from the fact that the α-span task involves several different executive processes which are susceptible to be affected by the disease. Moreover, the AD patient deficit on the dual-task paradigm could be partly mediated by a more general speed factor as suggested by the significant correlation between dual-task performance and processing speed in AD patients only. Furthermore, no significant correlation was found between the performance on the dual-task paradigm and α-span which suggests that these tasks tap two independent processes. This is consistent with the hypothesis of a central executive fractionation into subsystems or sub-processes [5]. Finally, a negative significant correlation was observed in control subjects only between functioning of the central executive and span performance. This result suggests that span performance in control subjects depends on both the phonological loop and the central executive while in AD patients, span performance is exclusively dependent on the phonological loop system.

The examination of AD patients with a high and low span level revealed that only patients with a low span performance presented deficits affecting the phonological loop. It also appears that span level in AD patients was related to the severity of the disease, as measured by the Mattis DRS score [33]. Such a pattern of performance might help to understand the heterogeneity of results observed in various studies which explored the phonological loop system in AD patients. Indeed, this heterogeneity could be due to the fact that these studies explored patients with various degrees of severity [9, 16, 27, 36, 38, 40, 41]. Another interesting result is that a less important contribution of long-term memory to span performance (measured by means of the word/non-word span task), as well as impaired central executive functioning were found in both high- and low-span level AD patients while only low-span level patients showed deficits in phonological discrimination, articulation rate and processing speed tasks. These data seems to indicate that high-span level patients have impairments affecting high-level executive processes as well as integration of information coming from various cerebral areas while the low-span level patients showed deficits involving a series of more general or basic processes.

Finally, the single-case analysis revealed an important heterogeneity in the patterns of preserved and impaired performance of AD patients. In particular, several examples of double dissociation were observed, namely between phonological store and articulatory rehearsal deficits. Furthermore, with regard to the central executive, it appears that a deficit can affect a specific function, that is manipulation of information or dual task coordination. In addition, even if central executive impairments generally preceded phonological loop deficits, three patients showed deficits affecting the phonological loop without any difficulties on the two tasks assessing the central executive system. Such an heterogeneity has also been observed in the long-term memory and the face recognition domain [4, 20].
As a whole, the present results suggest the existence of a possible trajectory of cognitive impairment in Alzheimer's disease. One of the earliest deficits would frequently concern central executive functioning (along with hippocampal system deficit; e.g., [22]). Two neu-robiological interpretations of this central executive deficit might be proposed. The first one suggests that the central executive deficit is related to frontal lobe dysfunction [50]. However frontal lobe dysfunction does not seem to be a prominent feature in the earlier stages of the disease ([29]; see however [53]). The second interpretation considers that executive control requires the integration of information coming from different cerebral areas [17, 23, 54]. In that perspective, the central executive dysfunction observed in AD patients should be due to a breakdown in connections between the main cortical associations areas [43]. This disconnection process could also explain the isolation of the phonological loop functioning in AD patients. As the disease progresses, the neuropathological changes would also affect specific cortical areas (and not only connections between them), which could explain the existence of phonological loop deficits in the low-span level and more severely demented patients.

Note

[1] Moreover, results showed that the word span performance is superior to two items in all subjects except for one AD patient exhibiting a word span level of two items.

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