

Specificity of inhibitory deficits in normal aging and Alzheimer's disease

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Abstract

Deficits of suppression abilities are frequently observed in normal aging and Alzheimer's disease. However, few studies have explored these deficits in the two populations simultaneously using a large battery of tasks. The aim of the present study was to explore if the pattern of performance presented by elderly subjects and AD patients is in agreement with theoretical frameworks [Wilson, S.P., Harnishfeger, K.K., 1998. The development of efficient inhibition: Evidence from directed forgetting tasks. *Dev. Rev.* 18, 86–123; see also Nigg J.T., 2000. On inhibition/disinhibition in developmental psychopathology: views from cognitive and personality psychology and a working inhibition taxonomy. *Psychol. Bull.* 126, 220–246], distinguishing between the concepts of inhibition (a voluntary suppression of irrelevant information) and interference (an automatic suppression process occurring prior to conscious awareness). The results obtained demonstrated that (1) there is an alteration of the inhibitory process in normal elderly subjects; (2) inhibitory and interference resolution processes are quantitatively less efficient in AD, since these patients present a correct performance only for information which leaves weak traces in memory.

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1. Introduction

Inhibition (or suppression abilities) is a basic aspect of cognitive and emotional functioning, which is involved in the performance of numerous tasks and processes (Arbuthnott, 1995; Bjorklund and Harnishfeger, 1995; Clark, 1996; Dagenbach and Carr, 1994; Dempster and Brainerd, 1995; Nigg, 2000). Recently, several theoretical frameworks have been proposed to explain the inhibitory effects reported in the literature in various normal and pathological populations. For instance, inhibition was specifically related to working memory by Hasher, Zacks, and May (Hasher et al.,

1999, 2001), who described three general inhibitory functions that operate at different times in the information processing sequence: the *access* function, preventing access to irrelevant information; the *deletion* function, suppressing information that either is or becomes irrelevant; and the *restraint* function, which operates when strong responses are triggered by a familiar cue but do not have to be produced. Other authors viewed inhibition as a general process operating in various cognitive domains. In that context, Dempster and Corkill (Dempster and Corkill, 1999a; Dempster and Corkill, 1999b) have suggested making a distinction between perceptual, motor and verbal inhibition. Inhibitory tasks were also classified according to the following three dimensions: (1) intentional *versus* unintentional, (2) behavioral *versus* cognitive, and (3) inhibition *versus* interference (Harnishfeger, 1995). More generally, Nigg (2000) suggested dissociating effortful inhibitory processes (for example, cognitive

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inhibition, behavioral inhibition and oculo-motor inhibition) from automatic inhibition of attention (concerning inhibition of irrelevant spatial localizations or of recently inspected stimuli). Finally, Harnishfeger (Harnishfeger et al., 1993; Harnishfeger, 1995; Wilson and Harnishfeger, 1998), on the basis of task-analyses, proposed to distinguish between the concepts of inhibition and interference. In that theoretical framework, inhibitory control corresponds to a voluntary suppression of the information, and interference resolution represents a gating mechanism preventing the processing of distracting information. More precisely, Harnishfeger proposed that interference resolution consists in an automatic process occurring prior to conscious awareness while inhibition results when a stimulus is classified as irrelevant for the ongoing task and is then consciously suppressed.

It must nevertheless be emphasized that the terms “inhibition” and “interference resolution” were used in slightly different ways by authors interested in suppression processes. For example, the *access* inhibitory function proposed by Hasher, Zacks, and May (Hasher et al., 1999, 2001) could be considered as an interference resolution process in the context of the Harnishfeger proposal (Wilson and Harnishfeger, 1998). Similarly, performance on the Stroop task was considered as reflecting sensitivity to interference although the task requires the voluntary suppression of an irrelevant cognitive process. In this paper, the term “inhibition” will be used to refer to functions that are voluntary and require cognitive control whereas the term “interference resolution” will refer to functions that are more automatic and require no (or less) cognitive control.

Changes in inhibitory/interference resolution abilities have been reported across the entire life span (e.g., Harnishfeger et al., 1993; Harnishfeger, 1995). During normal aging, larger Stroop effects were observed, indicating difficulties suppressing an overlearned response (e.g., reading) in order to produce a less-practiced response (e.g., naming) (Dulaney and Rogers, 1994; Hartley, 1993; Houx et al., 1993; Klein et al., 1997; Spieler et al., 1996). Similarly, lesser negative priming effects have often been demonstrated in elderly subjects in comparison to young subjects, indicating a less efficient suppression of the irrelevant dimension of the stimulus (Hasher et al., 1991; Kane et al., 1994; McDowd and Oseas-Kreger, 1991; Stoltzfus et al., 1993; Tipper, 1991). With regard to semantic processes, difficulties inhibiting the reading and processing of irrelevant information embedded in a text (Connelly et al., 1991; Duchek et al., 1998; Hamm and Hasher, 1992), suppressing no longer relevant information produced following a reading task (Hartman and Hasher, 1991) or restraining the production of a word that is strongly induced by the context of a sentence (Andrès and Van der Linden, 2000) have frequently been reported. Motor inhibition deficits were also observed on the stop-signal task (Kramer et al., 1994; May and Hasher, 1998), the go/no-go task (Nielson et al., 2002) and the antisaccade task (Butler et al., 1999). Finally, decreased directed forgetting abilities in working and episodic memory have

also been reported (Andrès et al., 2004; Zacks et al., 1996). However, a negative effect of aging on suppression abilities has not been systematically observed (see Kieley and Hartley, 1997, for the Stroop task; Connelly and Hasher, 1993; Kramer et al., 1994; Langley et al., 1998; Sullivan et al., 1995; Verhaeghen and De Meersman, 1998b, for negative priming and Hartley and Kieley, 1995, for inhibition of return), or is sometimes explained by more basic cognitive variables, such as a decrease in processing speed (Salthouse and Meinz, 1995; Salthouse et al., 1997; Verhaeghen and De Meersman, 1998a), fluid intelligence abilities (Shilling et al., 2002) or circadian preferences (Intons-Peterson et al., 1998; Yoon et al., 2000).

Inhibitory and interference resolution deficits have also been frequently reported in the first stages of Alzheimer's disease (AD) (for reviews, see Amieva et al., 2004a; Balota et al., 2001; Collette and Van der Linden, 2002). Typically, the Stroop effects (assessed by response times and response accuracy) are considerably larger in AD patients in comparison to healthy elderly controls, even after adjustment of suppression scores for processing speed (Amieva et al., 2004b; Bondi et al., 2002; Fisher et al., 1990; Koss et al., 1984; Spieler et al., 1996). Similarly, a less reliable or absent negative priming effect has been observed in these patients (Amieva et al., 2002; Sullivan et al., 1995; see, however, Langley et al., 1998). With regard to semantic inhibition, Collette et al. (1999) observed a weaker ability to suppress semantically related but task-irrelevant responses on the Hayling task (Burgess and Shallice, 1996), and Duchek et al. (1998) found that AD patients are disproportionately influenced by semantically related distracting information during a reading task. Finally, perseverations (Fox et al., 1998; Fuld et al., 1982; Sebastian et al., 2001) and intrusion errors (Amieva et al., 1998; Bandera et al., 1991; Cahn et al., 1997; LeMoal et al., 1997) are frequently produced by AD patients during list recall performance, indicating an impairment of the suppression processes associated with explicit memory tasks.

Nevertheless, not all inhibitory/interference resolution processes appear to be impaired by AD. Little evidence of dysfunction has been found in tasks assessing motor response inhibition (Amieva et al., 2002; Collette et al., 2002). Similarly, tasks requiring suppression processes considered to be more automatic (e.g., Nigg, 2000) also appear to be preserved, since normal inhibition-of-return effects have been observed (Danckert et al., 1998; Faust and Balota, 1997; Langley et al., 2001). In the episodic memory domain, no effect of AD was found on a retrieval-induced forgetting task (Moulin et al., 2002).

Taken as a whole, these results indicate that not all suppression processes are affected by normal aging or AD. However, at this time, very few studies have explored a series of inhibitory/interference resolution processes in the same group of subjects in order to formally determine the generality of impairments in these populations. In that context, Kramer et al. (1994) observed that elderly subjects had more difficulties than young subjects in stopping an overt response

and adopting new rules in a categorization task, although both groups produced equivalent negative priming effects, response compatibility effects, spatial precuing effects, and self-reported cognitive failures. More recently, Charlot and Feyereisen (2004, 2005) assessed inhibitory/interference resolution functioning in working memory using tasks exploring the access, deletion and restraint functions, and demonstrated that the effects of aging are weaker on the access function than on the other two suppression functions. With regard to AD, Amieva et al. (2002) investigated the effects of mild AD on four suppression tasks: the negative priming paradigm, the Stroop test, the go/no-go task and the stop-signal task. Impaired performance was observed on the negative priming and Stroop tasks, but not on the go/no-go task, and only limited impairment was observed on the stop-signal task, suggesting that motor response inhibition could be relatively spared in that group of patients. However, Collette et al. (2002) showed a worse performance in AD patients on the go/no-go task, as well as on the Stroop and Hayling tasks. Finally, Belleville et al. (2006) assessed verbal suppression processes using the Stroop and the Hayling tasks in normal elderly and Alzheimer's disease, and demonstrated impaired performance on both tasks in healthy elderly and patients.

In summary, studies of inhibition/interference resolution abilities in normal aging and AD indicate that, although both populations exhibit deficits on a large range of tasks, they do not present a general suppression dysfunction. In a comprehensive review, Amieva et al. (2004a) showed that the effect of Alzheimer's disease was obvious on tasks requiring controlled inhibition processes (e.g., the Stroop), but not on tasks requiring more automatic inhibition (e.g., inhibition of return). So, on the basis of the taxonomy proposed by Nigg (2000), the authors concluded that AD patients were impaired only on tasks requiring conscious cognitive control. The observation of the performances obtained by elderly subjects evidenced a similar pattern of results, suggesting also a selective deficit of controlled inhibitory mechanisms in normal aging. The only difference observed between the patterns of results associated to each population concerns a specific deficit in normal aging on motor inhibitory tasks. However, tasks used to assess motor inhibition in normal aging studies are characterized by a lower frequency of withholding responses than that administered to AD patients, which would place more substantial demands on controlled inhibition (Houghton and Tipper, 1994). It seems thus that the pattern of preserved/impaired inhibitory tasks in normal aging can be related, as in AD patients, to a specific impairment of inhibitory processes requiring conscious cognitive control.

To the best of our knowledge, there exists very few studies that explored the specificity of inhibitory/interference resolution dysfunctions in these populations with reference to theoretical models proposed in the literature (see however Charlot and Feyereisen, 2004), nor that directly compare the effect of AD and normal aging on suppression abilities (see however Belleville et al., 2006). Consequently, the

aim of the present study was to formally explore if the pattern of performance presented by elderly subjects and AD patients is in agreement with the theoretical framework proposed by Harnishfeger (Harnishfeger et al., 1993; Harnishfeger, 1995; Wilson and Harnishfeger, 1998), distinguishing between the concepts of inhibition and interference. As indicated previously, inhibitory control corresponds to a voluntary/conscious suppression of the information classified as irrelevant for the ongoing task, and interference resolution represents an automatic gating mechanism occurring prior to conscious awareness and preventing the processing of distracting information. The exploration of the adequacy of this theoretical framework to suppression deficits in normal aging and Alzheimer's disease was motivated by two arguments. First, developmental data attests that inhibition and interference resolution mechanisms can be dissociated. Indeed, younger children were less efficient than older children and adults at consciously suppressing information while young and old children and adults showed a similar performance when the task required automatic inhibition of competing items (Teresa Lechuga et al., 2006). Second, the performance of elderly subjects and AD patients on various suppression tasks suggest the existence of an impairment of controlled inhibitory processes while more automatic processes are preserved.

Consequently, a series of four tasks requiring either inhibitory or interference processes was administered to young subjects, healthy elderly subjects and AD patients. With regard to interference resolution tasks, a correct performance will be obtained only if subjects prevent other information to interfere with the processing of the target information. In the probe recency task (Jonides et al., 1998), subjects were required to judge whether a probe letter was a member of a set of previously presented items. In some trials, the probe letter was not member of the target set but was presented just before, and thus this distracting information interfered with the recognition process in the current trial. In the flanker task (Shaw, 1991), three words were presented (one central target and two flankers), with the instruction to semantically categorize the central word by pressing one of two key-responses. In some trials, the target and distracting information belong to separate target semantic categories, and were thus associated to different key-responses, leading to interference at the level of response production (namely, to suppress the motor response associated to the distracting category). In these two tasks, subjects were not informed of the presence of distracting information on some trials (probe recency *versus* response incompatibility), and post-hoc questioning confirmed that they were not aware of that experimental manipulation. On the contrary, the exploration of inhibitory control (assessed with a directed forgetting task (Reed, 1970) and the Hayling task (Burgess and Shallice, 1996)) required to actively suppress an information that is or became irrelevant for the ongoing task. In the directed forgetting working memory task, one or two series of letters were successively presented and, on some trials, an instruction to

forget was explicitly given following the presentation of the second series. The performance recall for the last series was compared between the different conditions. In the Hayling task, subjects have to complete sentences in which the last word is omitted, but has a particularly high probability of one specific response, by any word unrelated to the sentence. So, subjects have to explicitly suppress a mandatory response in order to produce a less automatic response.

The exploration of suppression abilities in normal aging and Alzheimer's disease in relation to the distinction between controlled inhibition and automatic interference resolution (Wilson and Harnishfeger, 1998) appears to be particularly worth investigating. Indeed, a dominant theory to explain cognitive changes associated to normal aging is that the cognitive resources available to perform mental operations decrease with age (Park and Hedden, 2001). Since controlled processes are considered to require more attentional resources than automatic ones, we expect a lower inhibitory performance in the group of elderly (by comparison to young subjects) for the tasks requiring a conscious suppression of some information, but a similar performance in the two groups with regard to tasks requiring automatic interference resolution processes. We also expect a further and specific decrease of performance in AD patients (by comparison to healthy elderly subjects) on inhibitory tasks requiring controlled processes. Indeed, it is now well acknowledged that the various cognitive deficits presented by AD patients in the early stages of the disease are characterized by an impairment of controlled processes associated to a preservation of the automatic ones (Adam et al., 2005; Fabrigoule et al., 1998; Salthouse and Becker, 1998).

2. Methods

2.1. Subjects

Seventy adults volunteered to participate in this study. All subjects had normal or corrected vision and normal or corrected hearing. The 30 younger adults (14 men and 16 women) had an average age of 22.4 years (range = 19–26). The 20 normal elderly subjects (5 men and 15 women) had an average age of 72.3 ± 5.1 years (range = 63–80). These elderly participants were non-institutionalized, alert, and had no history of neurological problems, alcohol abuse or psychiatric disorders. To assess crystallized verbal ability, each young and elderly participant was administered the Mill-Hill Vocabulary Scale (multiple-choice form; a French-language adaptation (Deltour et al., 1993)). No significant difference was found between the scores of the younger (26.10 ± 3) and older (27.03 ± 4.95) subjects [$t(38) = 0.25$, $p > 0.5$]. All participants were native speakers of French and did not report any medical, neurological or sensory defects, or use of medication likely to alter cognitive functioning.

A total of 20 patients attending the Day Care Center for Memory Disorders in Elderly (CHU Liège) also partici-

pated in this study. The patients (6 men and 14 women) met the NINCDS-ADRDA criteria for probable Alzheimer's disease (McKhann et al., 1984) and suffered from Alzheimer's disease at a mild stage. All patients had suffered from progressively worse memory problems for at least 6 months. The diagnosis of AD was based on general medical, neurological and neuropsychological examination. Structural neuroimaging showed only slight atrophy or mild leukoaraiosis. Patients' age ranged from 58 to 83 years (mean age: 74 ± 5.8 years). No patients suffered from any other medical or neurological condition nor did they take medication that would be likely to adversely affect cognitive performance. They were able to hear and see adequately and follow instructions. The normal elderly subjects were matched as accurately as possible for age, sex and sociocultural level to the AD patients. These control subjects did not differ from AD patients according to age [$t(38) = 0.98$, $p > 0.5$] or education level [$t(38) = 0.33$, $p > 0.5$]. The elderly participants and AD patients were also administered the Mattis Dementia Rating Scale (Mattis, 1973), which is widely used to screen for dementia. All control subjects had a total score superior to 130 on this scale, which constitutes a cut-off score to discriminate normal aging from dementia (Monsch et al., 1995). Overall performance on the Mattis dementia rating scale was significantly lower for AD patients than for control subjects [$t(38) = 9.08$, $p < 0.00001$; AD patients = 119.6 ± 8.9 ; control subjects = 139.1 ± 3.3].

2.2. Procedure

The participants were tested individually in a two-hour session in a quiet room. Most of the tasks were presented on a microcomputer. In order to avoid practice and weariness effects, two orders for the administration of the tasks were defined and were randomly assigned to participants. Computerized tasks were presented on a PC-compatible computer interfaced with a 14-inch SVGA color monitor using E-Prime software version 1.0 (Schneider et al., 2002). They were seated in front of the computer screen so that their eyes were approximately 70 cm from the display.

3. Cognitive tasks

3.1. Interference control

3.1.1. Probe recency task

The design of this task was similar to that used in neuroimaging studies by Jonides et al. (1998) and D'Esposito et al. (1999). Each subject completed 80 trials of an item recognition memory task (four sessions of 20 trials separated by short periods of rest) in which they were required to judge whether a test probe item was a member of a set of previously studied items. In each trial, four consonants were simultaneously presented in the center of a computer screen for 1500 ms. After a retention delay of 3000 ms, the

probe letter was presented and the subjects had to decide, and indicate by a key-press, whether the probe was one of the four letters previously presented in that trial. The probe letter remained displayed for a maximum of 2000 ms or until the subject responded. Practice trials were administered before the beginning of each session. The task was composed of four conditions: (1) Recent Negative trials, in which the probe did not match any items in the target set of the present trial but did match an item from the target set of one of the two previous trials (and thus required a “no” response); (2) Nonrecent Negative trials, in which the probe matched items from neither the current nor the two previous target sets (and thus required a “no” response); (3) Recent Positive trials, in which the probe matched an item that was presented in the current target set (and thus required a “yes” response) and in one of the two previous target sets; and (4) Nonrecent Positive trials, in which the probe matched an item that was presented in the current target set (and thus required a “yes” response) but not in any of the two previous target sets. The four kinds of trials were randomly administered across the four sessions, with the restriction that no more than three trials of the same type were presented in succession (the order of presentation being similar for all subjects). Subjects were not informed about the manipulation of probe recency.

3.1.2. *The flanker task*

This task was a French adaptation of that used by Shaw (1991). The material consisted of 16 target words (8 *metal* words and 8 *furniture* words) and 16 neutral flanker items (8 *vehicles* and 8 *fishes*) taken from Brulex (Content et al., 1990) and representing the most frequent category exemplars. The mean number of graphemes in the words in each of the four categories was similar [$F(1, 12) = 0.05$; $p > 0.9$]. In each trial, the stimuli were three words (one central target and two flankers) presented on a single column in uppercase letters on a computer screen. The task was described to participants as a study of reading and categorization of the centrally presented information and they were told not to pay any attention to the flanker words. The subjects were given 128 trials in four sessions of 32 trials each separated by short rest periods. Practice trials were administered before the beginning of each session. At the outset of each trial, a blinking arrow appeared for 600 ms in the location in which the first letter of the target word was to appear. As the fixation point disappeared, it was immediately replaced by the target and flanker words. These stimuli were removed immediately after the participant responded. On each appearance, the target word was flanked, above and below, by an additional word. Participants pressed one of two response-keys to indicate the category of each target word. Each of the four experimental conditions was determined by the relation between the target and flanker words. For two of the conditions, the target and flanker words were associated with compatible responses (namely, the same response-key): in the same-word (SW) condition, the target word appeared three times on the screen, because the flanker word was identical to the target; in the same-category (SC)

condition, the target and flanker words were two exemplars of the same category. In the third, or neutral-response (NR) condition, the flanker was one of the neutral words (and thus was not associated with any response-key). In the different-response (DR) condition, the target and flanker words were from separate target categories and were therefore associated with incompatible responses.

The flanker task requires in fact several suppression processes. Indeed, subjects were given the instruction to ignore the flanker words and to concentrate on the central target word. Although the instruction to ignore some information can be related to controlled inhibitory processes, some data (see Shaw, 1991) are indicative that the flanking information is nevertheless processed, leading to a phenomenon of perceptual interference. Moreover, some output interference comes also from the association of the target and flanker words to different key responses in the different-response condition. Controlled inhibition is required in a similar way in each condition, and consequently this effect will disappear with the comparison of the different conditions. On the contrary, the automatic perceptual and output interference effects are more important in the different-response condition, and will be evidenced by the comparison of that condition to the other ones. Subjects were not warned that, in the different-response condition, the relationship between targets and flankers leads to interference at the level of response production.

3.2. *Inhibitory control*

3.2.1. *Directed forgetting in working memory*

We used a procedure adapted from Reed's (1970) study and similar to that used by Andr s et al. (2004). In this task, trigrams composed of consonants were presented for 2000 ms on a computer screen and subjects were asked to read aloud and memorize the trigrams presented. Three experimental conditions were administered. In the single-trigram condition (control condition), a single trigram (three consonants) was presented for retention. In the retroactive interference condition, a second (interfering) trigram was presented for retention immediately after the first one. In the directed forgetting (or inhibition) condition, two trigrams were also presented consecutively. However, immediately after the presentation of the second trigram, a screen displayed the message “to be forgotten” for 500 ms, which prompted participants to forget the trigram as they would not be required to recall it later. Immediately after the presentation of the trigram(s), an interpolated activity was presented that consisted of reading strings of numbers aloud for 10 s. Next, the participants were asked to recall the three letters of the trigram(s), with no time constraint. In the inhibition condition, only the first trigram had to be recalled while in the interference condition, subjects have to recall the first and second trigrams. Three practice trials, one per condition, were given prior to the beginning of the task. Participants were then presented with 30 trials, 10 per experimental condition.

The trials belonging to the three conditions were presented in an intermixed way, but the same pre-established order was administered to all participants.

A criticism that could be made to the directed forgetting task concerns its susceptibility to proactive interference building across trials. However, since the trials belonging to the different conditions were randomly presented, the susceptibility to proactive interference, even if not similar between the three groups, should be proportionally of the same amplitude for the three conditions. So, proactive interference should not influence the comparison of performance between the three conditions across the groups.

3.2.2. *The Hayling task*

This task assesses the capacity to suppress (inhibit) a habitual response and was initially devised to examine both initiation and inhibition processes (Burgess and Shallice, 1996). The Hayling task consists of 30 sentences in which the final word is omitted but has a particularly high probability of one specific response. The task is composed of two sections (A and B), each containing 15 sentences. In section A (initiation), sentences are read aloud to subjects who have to complete each sentence with the missing word. In section B (response suppression), sentences are read aloud to subjects who this time have to complete the sentence not with the expected word but with a word unrelated to the sentence. If at any time during this stage of the test, subjects give a sentence completion rather than an unrelated word, they are told that the word is too closely related to the sentence, and the task instructions are repeated. If a subject does not produce a word within 30 s, that trial is terminated and a response latency of 30 s is recorded. Different measures of response suppression abilities were used in the analysis. First, section B latencies minus section A latencies were considered for each subject, which presumably represents the additional thinking time required in having to produce a novel word rather than a straightforward sentence completion. Secondly, a semantic score was devised for section B whereby the overall semantic relationship of each response to its stimulus sentence was measured: three points were given if the word was a straightforward completion of the sentence, one point for a word semantically related to the sentence in some way and no score when the response successfully fulfilled the task requirements (namely, no relationship was found between the word produced and the remaining of the sentence).

3.3. *Additional measures*

3.3.1. *Processing speed*

This task was administered in order to assess general processing speed and examine the possible contribution of a reduction in processing speed to the inhibitory abilities of normal elderly subjects and Alzheimer's patients. Processing speed was assessed with a letter comparison task, which is a computerized version of the task initially proposed by Salthouse and Babcock (1991). The interest of this task is

that it induces no distraction from task-irrelevant information, susceptible to deteriorate the speed performance of elderly subjects (Lustig et al., 2006). Participants were presented with pairs of letters and their task was to decide as quickly and accurately as possible whether the letters were the same or different, by pressing a response-key. The test comprised 60 trials, with 30 "same items" and 30 "different items" trials. The selected measure was the mean correct latency for "same items" trials.

3.3.2. *Digit span task*

Since three of the tasks required maintenance of information in working memory (the probe recency task, the directed forgetting task and the Hayling task), a digit span task was administered to examine the possible contribution of a reduction in short-term memory capacity to the inhibitory abilities of our subjects. Forward digit span was tested in auditory modality. Lists of two to nine digits were read by the examiner at the rate of one digit per second. Three sequences of each length were presented until the subject failed on three sequences with a particular length. The longest sequence correctly recalled on at least two of the three trials represented the subject's digit span.

3.3.3. *Pyramid and palm tree test*

This matching task (Howard and Patterson, 1992) was administered in order to assess semantic memory in Alzheimer's disease and examine the possible contribution of impaired semantic representations to the inhibitory abilities of these patients. Three pictures are simultaneously presented (the target one on the top and two other pictures on the bottom). The task requires the patient to select the one of the two bottom pictures that is connected with the target picture. Fifty-two trials were administered. Measure of performance was the number of correct matching.

4. *Results*

Statistical analyses consisted of three-way ANOVAs on the groups of young subjects, elderly controls and AD patients. Planned comparisons were used to compare (1) the performance of young and elderly subjects and (2) the performance of elderly controls and AD patients. A statistical level of $p < 0.05$ was used for all analyses, and logarithmic values were used to reduce between-groups variability. Inhibitory and facilitation abilities were measured by both response times and response accuracy, and the influence of processing speed and span size on these abilities was assessed by covariance analyses.

4.1. *Additional measures*

With regard to processing speed, mean response times (in ms) for correct responses on "same items" trials were compared between groups. A significant difference between

the three groups was found [$F(2, 67) = 25.78, p < 0.0001$], with a slowing down in elderly subjects by comparison to young subjects, as well as in AD patients by comparison to matched control subjects (young: 721 ± 204 ; elderly: 859 ± 181 ; AD: 1296 ± 536). With regard to the digit span, there was also a significant difference between the three groups [$F(2, 67) = 12.34, p < 0.0001$], with a higher span in young subjects than in elderly ones, and in elderly controls compared to AD patients (young: 6.2 ± 0.9 , elderly: 5.5 ± 1.0 ; AD: 4.8 ± 1.0).

4.2. Interference resolution

4.2.1. Probe recency task

4.2.1.1. Results. Mean response times (RT) for correct responses and accuracy of responses in the four conditions (Nonrecent Negative, Recent Negative, Nonrecent Positive, Recent Positive) are presented in Table 1. The critical features of behavioral performance concern the comparison of the Recent Negative trials to the Nonrecent Negative trials (interference effect) and the comparison of the Recent Positive trials to the Nonrecent Positive trials (facilitation effect). Difference scores were computed to test these two effects: [Nonrecent Negative – Recent Negative] for the interference effect and [Nonrecent Positive – Recent Positive] for the facilitation effect.

The comparison of the interference effect on RT between the three groups demonstrated no significant differences [$F(2, 67) = 0.57, p > 0.5$], and this was confirmed by planned comparisons [young *versus* elderly: $F(1, 67) = 0.34, p > 0.5$; elderly *versus* AD: $F(1, 67) = 0.18, p > 0.5$]. Similar results were observed for response accuracy [comparison between the three groups: $F(2, 67) = 1.34, p > 0.1$; young *versus* elderly: $F(1, 67) = 1.10, p > 0.1$; elderly *versus* AD: $F(1, 67) = 0.22, p > 0.5$].

With regard to the facilitation effect on response times, although no significant difference was found between the

three groups [$F(2, 67) = 2.83, p > 0.05$], planned comparisons demonstrated a larger facilitation effect for AD than for elderly controls only [elderly *versus* AD: $F(1, 67) = 4.62, p < 0.05$; young *versus* elderly: $F(1, 67) = 0.10, p > 0.7$]. This effect could however be explained by span size and processing speed, since the addition of the covariates into the analysis suppressed the differential facilitation effect between elderly adults and AD patients [$F(1, 66) = 3.56, p > 0.05$; $F(1, 66) = 1.66, p > 0.1$, respectively]. Finally, similar analyses were done to determine the effect of facilitation on response accuracy. No significant differences between the three groups was found for accuracy of responses [$F(2, 67) = 2.11, p > 0.1$] and this was confirmed by planned comparisons [young *versus* elderly subjects [$F(1, 67) = 0.59, p > 0.1$]; elderly *versus* AD [$F(1, 67) = 1.37, p > 0.1$].

4.2.1.2. Discussion. With regard to the probe recency task, interference effects were observed both for responses times and accuracy of responses. These interference effects were similar in size in all three groups of subjects. This task was previously used by Jonides et al. (1998) who found interference effects that were greater in the elderly than the young subjects, indicating an interference resolution deficit. However, unlike to our study, Recent Negative and Nonrecent Negative items were not randomly presented but were presented in blocks composed of half recent and half Nonrecent Negatives items, or Nonrecent Negative items only. Moreover, a combined score with response latency and accuracy was used to compare the performance of young and elderly subjects, while we preferred to use two scores to determine whether specific patterns of deficits could be observed with regard to RTs or response accuracy. Such methodological differences could explain the different pattern of results observed between these two studies. With regard to AD, no specific inhibitory deficit was observed. One could argue that this might be due to very poor performance by these patients in all task conditions, or to a

Table 1
Probe recency task

	Young subjects	Elderly subjects	Alzheimer patients
Response times			
Nonrecent Negative	895 (269)	1376 (255)	2808 (1154)
Recent Negative	953 (280)	1435 (270)	2910 (1373)
Nonrecent Positive	930 (277)	1367 (304)	2487 (1267)
Recent Positive	917 (251)	1369 (304)	2319 (1151)
Interference effect	0.064 (0.08)	0.041 (0.10)	0.023 (0.20)
Facilitation effect	−0.008 (0.09)	0.002 (0.12)	−0.072 (0.12)
Correct responses			
Nonrecent Negative	19.43 (0.90)	19 (1.32)	16.65 (3.1)
Recent Negative	19.33 (0.76)	18.30 (1.52)	15.60 (2.76)
Nonrecent Positive	18.60 (1.65)	17.75 (1.86)	15.25 (3.18)
Recent Positive	18.87 (1.33)	18.45 (1.15)	16.5 (2.91)
Interference effect	−0.005 (0.06)	−0.041 (0.08)	−0.059 (0.20)
Facilitation effect	0.016 (0.08)	0.042 (0.12)	0.086 (0.15)

Response time (in ms; mean \pm standard deviation) and number of correct responses [out of 20; mean (standard deviation)] as a function of group and condition.

rapid decrease in the traces left by previous items, leading to less sensitivity to interference because these items had already completely disappeared from working memory. However, the AD patients' performance was superior to 75% in all conditions; this is considerably above the chance level. Moreover, the presence of a greater facilitation effect suggests the persistence of a memory trace from the previous trials that influences the production of the response. So we can be confident that AD patients present similar interference resolution abilities to elderly subjects in this task.

4.2.2. The flanker task

4.2.2.1. Results. Statistical analyses were performed by grouping together the two facilitation conditions (same word and same category) involved in Shaw's (1991) initial task. This was done to obtain measures of semantic interference and facilitation that could easily be compared to those obtained in the probe recency task. The critical features of behavioral performance concern the comparison of the different response condition to the neutral response condition (interference effect) and the same word and same category conditions to the neutral response condition (facilitation effect). Difference scores were computed to test these effect: [different response – neutral] for the interference effect and [same word/category – neutral] for the facilitation effect. Table 2 shows average response time and number of correct responses as a function of group and condition.

The comparison of the interference effect on response times demonstrated no significant differences between the three groups [$F(2, 67) = 1.93, p > 0.1$], that was confirmed by planned comparisons [young *versus* elderly $F(1, 67) = 1.14, p > 0.1$; elderly *versus* AD $F(1, 67) = 0.62, p > 0.1$]. With regard to the facilitation effect, again no significant differences between the three groups was observed [$F(2, 67) = 2.66, p > 0.05$]. However, planned comparisons demonstrated a larger facilitation effect in AD subjects [young *versus* elderly: $F(1, 67) = 1.36, p > 0.1$; elderly *versus* AD: $F(1, 67) = 5.31, p < 0.05$]. However, when span size and speed

of processing were taken as confounding covariates, this effect disappeared [$F(1, 66) = 4.02, p > 0.05$; $F(1, 66) = 1.98, p > 0.1$, respectively].

With regard to measure of accuracy, the comparison of the three groups demonstrated a similar interference effect [$F(2, 67) = 2.92, p > 0.05$]. However, planned comparisons demonstrated that, while there was no difference between young and elderly subjects [$F(1, 67) = 0.63, p > 0.1$], AD patients presented a larger interference effect than elderly subjects [$F(1, 67) = 5.49, p < 0.05$]. This effect remains significant when span size and processing speed were used as covariates [$F(1, 66) = 4.75, p < 0.05$; $F(1, 66) = 4.26, p < 0.05$, respectively]. Finally, the comparison of the facilitation effect on accuracy of responses demonstrated a significant difference between the three groups [$F(2, 67) = 5.47, p < 0.01$], with a similar effect between young and elderly subjects [$F(1, 67) = 1.14, p > 0.1$], but a larger facilitation effect in AD patients than elderly subjects [$F(1, 67) = 4.86, p < 0.05$]. This effect disappeared when span size and processing speed were used as covariates [$F(1, 66) = 3.22, p > 0.05$; $F(1, 66) = 3.89, p > 0.05$, respectively].

4.2.2.2. Discussion. The flanker task (Shaw, 1991) requires to process only the centrally presented information and, in some trials, the relationship between targets and flankers leads to interference at the level of perceptual input and response production. The flanker task did not demonstrate any sensitivity to interference in normal aging or in AD, when assessed by RTs, but a greater sensitivity to interference in AD patients when assessed by response accuracy. Shaw used this task to show that elderly subjects present greater semantic inhibitory effects than young subjects but equivalent semantic facilitation in the time taken to classify target words. However, semantic inhibition deficits were not systematically observed in normal aging (see, for example, Hogge et al., 2004; Paul, 1996). With regard to AD, a slight impairment was found for response accuracy, but not for RTs, and this impairment was not explained by a reduction of span size or a slowing down. In order to test if the inhibitory effect cannot be explained by the semantic deficits frequently

Table 2
Flanker task

	Young subjects	Elderly subjects	Alzheimer patients
Response times			
Facilitation condition	703 (131)	906 (290)	1324 (628)
Interference condition	740 (134)	900 (267)	1484 (974)
Neutral condition	725 (126)	904 (290)	1540 (1086)
Interference effect	−0.020 (0.05)	0.004 (0.06)	0.015 (0.086)
Facilitation effect	0.032 (0.04)	−0.003 (0.04)	0.07 (0.18)
Correct responses			
Facilitation condition	31.35 (0.72)	31.30 (1.17)	31.27 (1.31)
Interference condition	31.27 (1.05)	31.45 (1)	29.05 (4.63)
Neutral condition	31.13 (1.11)	30.70 (0.73)	29.75 (2.07)
Interference effect	−0.004 (0.04)	−0.024 (0.023)	0.040 (0.15)
Facilitation effect	−0.007 (0.03)	−0.019 (0.02)	−0.05 (0.07)

Response time [in ms; mean (standard deviation)] and number of correct responses (out of 32) as a function of group and condition.

observed in the disease (for a review, see Garrard et al., 2004), correlations were computed between performance in the different conditions of the flanker task and performance on the designation task “Pyramid and Palm Tree test” (Howard and Patterson, 1992). No significant correlation was found (all $p > 0.05$), indicating an absence of relationship between the performance on the flanker task and the semantic abilities of the AD patients. So, results obtained are in agreement with the hypothesis that there exists some difficulties in Alzheimer’s disease (expressed by a measure of accuracy only) to control interference coming from distracting information in a semantic decision task.

4.3. Inhibitory control

4.3.1. Directed forgetting

4.3.1.1. Results. Participants’ responses were scored by assigning one point for each letter recalled (regardless of its position within the trigram) (maximum score per condition was therefore 30). In the retroactive interference condition (i.e., presentation of a second, interfering trigram), only recall of the first trigram was scored (as in the inhibition condition). Sensitivity to retroactive interference was measured by the difference in performance between the single-trigram and retroactive interference conditions. Inhibitory capacity was measured by the difference in recall performance between the retroactive interference and directed forgetting conditions (see Table 3). This measure was preferred to the one used by Andr  s et al. (2004) (namely, a comparison between the directed forgetting and control conditions) in order to suppress a putative effect of retroactive interference on the measure of inhibition.

A 3 (group: young, elderly, AD) \times 3 (condition: control, retroactive interference, inhibition) ANOVA was done, and demonstrated a significant group effect [$F(2, 67) = 18.49$, $p < 0.0001$], with a similar performance for young and elderly, and a lower performance for AD; a significant condition effect [$F(2, 134) = 133.39$, $p < 0.0001$], with a better performance in the single trigram condition than in the retroactive interference and inhibition conditions; and a significant interaction between group and condition [$F(4, 134) = 11.35$, $p < 0.0001$]. Planned comparisons revealed a similar decrease in performance between the single trigram and the retroactive

interference condition in young and elderly subjects, and a larger decrease in AD patients than elderly. With regard to the comparison of the retroactive interference and inhibition conditions, planned comparisons demonstrated a greater increase in performance in young subjects than in elderly subjects, but a similar pattern of performance in the elderly and AD groups (namely, no improvement in performance from the retroactive interference to the inhibition condition). When span size and processing speed were taken as confounding covariates, the interaction effect remained significant [span size: $F(4, 132) = 9.08$, $p < 0.0001$; processing speed: $F(4, 132) = 6.51$, $p < 0.0001$]. A directed forgetting score was also calculated by subtracting the performance on the directed forgetting condition from that on the retroactive interference condition. As observed with the ANOVA, between groups differences were also found [$F(2, 67) = 3.51$, $p < 0.05$], with elderly subjects having a larger directed forgetting effect than young subjects [$F(1, 67) = 6.55$, $p < 0.05$], while a similar effect was found between elderly subjects and AD patients [$F(1, 67) = 0.68$, $p > 0.1$]. When span size and processing speed were taken as confounding covariates, the interaction effect remained significant [span size: $F(1, 66) = 11.94$, $p < 0.0001$; processing speed: $F(1, 66) = 15.02$, $p < 0.0005$].

Finally, the different types of errors were analyzed. Significant differences were found for the omission errors (the number of consonants missing) [$F(2, 67) = 13.94$, $p < 0.0001$], with no differences between young and elderly subjects but a difference between elderly subjects and AD patients. This difference remained significant when span size and processing speed were used as confounding covariates [respectively, $F(2, 66) = 7.13$, $p < 0.005$; $F(2, 66) = 5.99$, $p < 0.005$]. Similarly, the number of to-be-forgotten (TBF) errors (corresponding to the number of consonants produced that belonged to the second trigram in the inhibition condition) differs between the three groups [$F(2, 67) = 29.74$, $p < 0.0001$]. Again, young and elderly subjects performed similarly, but AD patients produced more errors than elderly controls. Using span size and processing speed as confounding covariates did not remove the difference between elderly subjects and AD patients [respectively, $F(2, 66) = 7.54$, $p < 0.005$; $F(2, 66) = 15.18$, $p < 0.0001$]. Finally, there was no significant difference between the three groups with regard to the position errors (the number of consonants recalled in an incorrect serial position) [$F(2, 67) = 1.32$, $p > 0.1$].

Table 3
Directed forgetting task

	Young subjects	Elderly subjects	Alzheimer patients
Control condition	29.30 (0.88)	29.75 (0.71)	29 (1.27)
Retroactive interference condition	23.37 (3.31)	25.95 (4.11)	18.40 (5.17)
Inhibition condition	24.53 (3.60)	24.80 (3.90)	18.20 (6.04)
Directed forgetting cost	1.53 (3.46)	−1.15 (3.10)	−0.20 (4.31)
Omission errors (all conditions)	0 (0)	2 (2.4)	5.8 (6.8)
Position errors (all conditions)	0.2 (1.1)	2.10 (2.02)	2.95 (1.93)
Intrusion errors TBF	3.17 (2.71)	3.65 (3.09)	8.95 (6.52)

Number of correct responses and errors [mean (standard deviation)] as a function of group and condition.

4.3.1.2. Discussion. Directed forgetting (as reflected by the difference in correct recall performance between the inhibition and retroactive interference conditions) was more efficient in young than in elderly subjects (and was not explained by a difference in span size or speed of processing), but no difference was found between elderly controls and AD patients. However, AD patients made more omission and intrusion errors than elderly subjects. The existence of an impaired directed forgetting effect in normal aging had already been reported by [Andrès et al. \(2004\)](#). The results obtained in our study indicate that elderly participants and AD patients were less able than young subjects to inhibit no longer relevant information. Moreover, AD patients presented specific difficulties in comparison to normal elderly subjects in recalling information, in the sense that they produced more intrusions of the TBF trigrams, and that these errors were not explained by span size or speed of processing. It has frequently been reported that AD patients produce more intrusions ([Amieva et al., 1998](#); [Bandera et al., 1991](#); [Cahn et al., 1997](#); [LeMoal et al., 1997](#)) and preservation errors ([Fox et al., 1998](#); [Fuld et al., 1982](#); [Sebastian et al., 2001](#)) during word recall tasks. Thus, we can suggest that, unlike normal elderly subjects who only have difficulties completely suppressing TBF items from working memory but clearly distinguish between TBF and TBR items (since they produced no more intrusions than young subjects), AD patients have additional difficulties inhibiting the production of the TBF items. We can hypothesize that the memory traces for TBF items are as strongly activated as those of the TBR items and that, due to the source memory deficit presented by these patients (e.g., [Multhaup and Balota, 1997](#)), the presentation of the recall cue triggers the production of any activated item. Indeed, an influence of source memory failures on the performance in verbal working memory tasks was previously described (see [Hedden and Park, 2003](#)).

4.3.2. The Hayling task

4.3.2.1. Results. Measures of initiation of response consisted of mean response times and number of errors in part A of the task. Measures of inhibition consisted in the raw response latency (mean latencies across 15 trials) when the suppression time was controlled for the initiation time (namely, RTs for part B—part A) and the semantic score (measuring the overall semantic relatedness of the responses to the sentence). The results for the three groups of subjects are presented in [Table 4](#).

The comparison of response time for Part A (requiring only initiation of response) showed a significant difference between the three groups [$F(2, 67) = 7.60, p < 0.005$], with slower RTs for elderly than young subjects and no differences between elderly subjects and AD patients. However, the effect disappeared when span size and processing speed were taken as confounding covariates [respectively, $F(2, 66) = 2.86, p > 0.05$; $F(2, 66) = 1.95, p > 0.1$]. With regard to the inhibition portion, the comparison of RTs (B–A) revealed significant differences between groups [$F(2, 67) = 18.73, p < 0.0001$], with elderly subjects having slower RTs than young subjects, but AD patients performing similarly to elderly subjects. These results were not modified when span size and processing speed were used as covariates [respectively, $F(2, 66) = 13.52, p < 0.0001$; $F(2, 66) = 11.65, p < 0.0001$].

With regard to error score, very few errors were committed in the Part A. However, the semantic relatedness of responses made in Part B differed for the three groups [$F(2, 67) = 24.81, p < 0.0001$], with elderly subjects erroneously providing more related responses to the stimuli than young subjects and AD patients providing more related responses than elderly subjects. When span size was taken as a confounding covariate, the difference between young and elderly subjects remained significant [$F(1, 66) = 10.32, p < 0.0001$] but the difference between AD patients and elderly subjects became marginally significant [$F(1, 66) = 3.65, p = 0.06$]. Similarly after controlling for processing speed, the difference in semantic relatedness between elderly subjects and AD patients remained significant [$F(1, 66) = 11.29, p < 0.005$], but disappeared between young and elderly subjects [$F(2, 66) = 2.98, p > 0.05$].

4.3.2.2. Discussion. Deficits on the Hayling task, not totally explained by span size or speed of processing, were observed in elderly subjects for both RT and semantic relatedness of response. AD patients made more errors than elderly in terms of the semantic relatedness of responses, but this difference became marginally significant after the span size was controlled for. Again, deficits of the patients on this task cannot be related to a potential influence of semantic memory impairment on performance, since no significant correlations were observed between measures on the Hayling task and performance on the Pyramid and Palm Tree test (all $p > 0.05$). Impaired performance on the Hayling task in normal aging had previously been described in the literature ([Andrès and Van der Linden, 2000](#); [Belleville et al., 2006](#); [Bielak et al.,](#)

Table 4
Hayling task

	Young subjects	Elderly subjects	Alzheimer patients
Response time (Part A)	1.03 (0.07)	1.39 (0.93)	1.59 (0.77)
Errors (Part A)	0.03 (0.18)	0.50 (1.47)	0.85 (1.23)
Response time (Part B – Part A)	1.63 (1.17)	4.24 (2.23)	5.61 (4.79)
Semantic relatedness (Part B)	4.33 (2.56)	8.05 (3.63)	14.15 (0.38)

Response time [in s; mean (standard deviation)] and accuracy of response [mean (standard deviation)] as a function of group and part of the task.

2006), and was also partly explained by an influence of processing speed (Andr  s and Van der Linden, 2000). With regard to the AD patients' performance, there were no differences in comparison to control subjects in terms of response speed, but they produced more responses related to the item to be inhibited (for similar results, see Collette et al., 1999). These results indicate that AD patients are able to correctly inhibit the target word but not to restrain the production of the first alternative responses that came in mind, these alternatives being or not semantically related to the target words.

5. General discussion

The aim of our study was to explore the performance of young volunteers, normal elderly subjects and AD patients on a series of suppression tasks assessing interference resolution or active inhibitory control. Very few earlier studies had been interested in evaluating the existence of specific inhibitory/interference resolution dysfunction simultaneously in normal and pathological aging, and those studies did not select suppression tasks with reference to recently proposed theoretical frameworks. In that context, we will first briefly discuss the influence of processing speed and working memory capacity on inhibitory abilities. Next, the main question of this study will be addressed, namely if the pattern of performance observed in normal elderly and AD patients can be interpreted with reference to Wilson and Harnishfeger (1998) hypothesis that controlled inhibition and interference resolution are dissociable cognitive processes.

The results obtained with the battery of tasks are summarized in Table 5 and demonstrate the existence of a dysfunction of suppression abilities in both normal elderly and AD patients. Interestingly, not all tasks were impaired in these two groups. Some authors have proposed that suppression dysfunction in aging represents a side-effect of a general

slowing down of information processing (see Verhaeghen and De Meersman, 1998a for the Stroop task). Thus, a measure of processing speed was included in our battery to test that hypothesis. Moreover, participants' digit span size was also assessed since it had been proposed that working memory resources are a mediator between age and decreased performance on complex cognition tasks (e.g., Park and Hedden, 2001; Van der Linden et al., 1999) and three of the suppression tasks required to maintain information in short-term memory. Interestingly, the suppression deficits presented by normal elderly and AD subjects were not influenced by these two variables, except for the semantic relatedness score on the Hayling task. The absence of any influence by these variables on suppression performance is not due to a lack of sensitivity of the measures, since processing speed and span size are clearly related to measures that assess facilitation effects. Consequently, the impaired performance of elderly and AD subjects can be explained in terms of inhibitory/interference resolution dysfunction, and not as a consequence of slowing down or a reduction of resources in working memory. On the contrary, the facilitation effects we observed disappear when covariates assessing more general aspects of cognition (speed of processing and short-term memory capacity) were used, indicating that these effects cannot be clearly related to the suppression aspects of the tasks only.

The pattern of performance observed on the battery of tasks is in accordance with the hypothesis that the dysfunction of suppression abilities in normal aging and AD is not generalized. More specifically, the aim of this study was to explore whether suppression deficits associated with normal aging and AD can be interpreted in the theoretical framework distinguishing between the concepts of interference resolution and controlled inhibition. Normal elderly subjects clearly demonstrated performances similar to that of young subjects on the two tasks assessing interference resolution but impaired performances when active inhibitory control is required. However, results obtained by AD patient cannot be explained in that theoretical framework. Indeed, interference resolution was preserved in the working memory task while deficits were observed in the flanker task for response accuracy. With regard to the active inhibitory control, the directed forgetting task demonstrated the presence of difficulties to inhibit the production of items that were clearly labeled as "to forget", and this although AD patients present a normal performance on the measure reflecting inhibitory control (the directed forgetting effect). Performance was also altered on the Hayling task, mainly for the error score, that was interpreted as reflecting difficulties to restrain the production of responses strongly activated but that are not totally relevant for the ongoing task.

Our results with normal aging can be interpreted as reflecting a specific impairment of active inhibitory control processes, associated to a preservation of the mechanism of interference resolution. If we consider that interference resolution in the working memory task is a relatively automatic inhibitory process, these results are similar to those

Table 5
Summary of the inhibitory effects observed in elderly subjects and AD patients for the different tasks

Task	Elderly subjects	AD patients
Probe recency		
Response time	Preserved	Preserved
Accuracy of response	Preserved	Preserved
Directed forgetting		
Recall of TBR consonants	Impaired	No more impaired
TBF intrusions errors	Preserved	Impaired
Flanker		
Response time	Preserved	Preserved
Accuracy of response	Preserved	Impaired
Hayling		
Response time	Impaired	No more impaired
Semantic relatedness	Impaired	Impaired*

* Explained by span size and processing speed.

reported in earlier studies that distinguished between controlled and automatic inhibitory processes in normal aging. [Andrès \(2002\)](#) administered to young and elderly subjects the Stroop interference task (in which subjects have to consciously suppress the prepotent process of reading in order to produce a response) and a negative priming task (supposed to involve automatic inhibitory processes, since subjects were not warned of the relationship between the prime and probe trials). The results indicated an age-related effect on the Stroop task but not on the negative priming task. A similar pattern was observed when performance on inhibition of return (requiring automatic inhibitory processes) was contrasted to that obtained in an antisaccade task (in which subjects are explicitly warned to ignore a spatial cue to orient their gaze towards the opposite side of the screen) ([Andrès, 2003](#)). This selective impairment of controlled inhibitory processes in normal elderly subjects is consistent with some recent theories of cognitive aging. Indeed, one major theory is that the cognitive resources available to perform mental operations decline with aging ([Park and Hedden, 2001](#)), leading to greater age-related differences on tasks that require controlled processes than on those requiring automatic processes ([Hasher and Zacks, 1979](#); [Jennings and Merikle, 1993](#); [Light, 1991](#); [Titov and Knight, 1997](#)).

The pattern of results presented by AD patients is more difficult to interpret in the context of a theoretical distinction between inhibitory control and interference resolution. Indeed, normal performance is observed both for the directed forgetting task and for the probe recency task. One common characteristic of these two tasks is that the information to suppress is not present when the subject produces the response: this information was present in the one of the two previous trials in the interference resolution tasks and was presented 10 s before the presentation of the response in the directed forgetting task. On the contrary, information to suppress remained present in the two tasks impaired in AD patients: the distracting information remained on the screen until the production of a response in the flanker task and we consider that, in the Hayling task, the word to inhibit, as well as the remaining of the sentence, is accessible to consciousness during the search for a semantically unrelated item. So, we can hypothesize that, although AD patients are not able to prevent the processing of distracting information (as evidenced in the Hayling and flanker tasks), these patients are not sensitive to interference from information that was previously processed (as it is the case in the directed forgetting and interference resolution tasks).

The pattern of results we obtained in AD fit particularly well with the proposal of [Houghton and Tipper \(1994\)](#). These authors proposed that the strength of the cognitive processes or representations that have to be suppressed will determine the degree of effort of the mechanisms required to suppress it. In other words, these authors suggest that a very skilled process (e.g., reading for a high-school level adult) or a representation strongly activated (for example, following repeated exposures) will require more cognitive

resources to be suppressed than few skilled processes or less activated representations. Due to their memory problems, AD patients process information less deeply than normal elderly ([Weingartner et al., 1981](#)), or they forget more quickly the information previously encoded (see for a review [Salmon, 2000](#)). Consequently, the memory traces on which suppression will apply will be less strong in AD patients and suppression of that information will require less effort than for normal elderly subjects. So, a similar performance will be observed, not because AD patients have preserved suppression abilities but because their residual suppression abilities are sufficient to process information whose traces were partially decayed. On the contrary, when the information that must be suppressed is present, suppression abilities of AD patients do not allow to prevent the processing of that information. Consequently, the patients present a larger interference/inhibitory effect than healthy elderly. An indirect confirmation of this interpretation is provided by the presence of a larger facilitation effect in AD when the distracting information in the flanker task belong to the same category than the information to suppress. Nevertheless, the design of the present study does not allow to specifically test the relationship between the strength of the memory traces and the degree of suppression necessary to suppress it. So, this interpretation remains tentative and further studies will be necessary to confirm it.

This distinction between an impairment on the suppression of distracting information in the environment but preserved suppression abilities for information previously processed in AD patients can also be tentatively related to the concepts of “access” and “deletion” functions as proposed by [Hasher et al. \(1999\)](#). In the present study, interference resolution in the probe recency and the flanker tasks can be considered as depending on the access function; inhibition in the directed forgetting task as depending on the deletion function; and inhibition in the Hayling task as depending on the restraint function. Our results indicate that, by comparison to elderly subjects, AD patients are no more impaired than elderly subjects on the deletion function, but present a decreased performance when the restraint function was assessed. Nevertheless, the performance on the two interference resolution tasks does not allow to determine if there exists a deficit of the deletion function, since a normal performance on the probe recency task was associated to a decreased performance on the flanker task. So, our data concerning suppression abilities in AD are not completely in agreement with the theoretical framework proposed by [Hasher et al. \(1999\)](#). It must nevertheless be emphasized that the pattern of results observed in elderly (that was previously interpreted as reflecting a specific impairment of controlled inhibitory processes) is also clearly in agreement with the proposal of Hasher et al., and is indicative of a specific preservation of the access function in normal aging.

In conclusion, this study revealed that distinct suppression deficits are observed in normal aging and Alzheimer's

disease. By comparison to young subjects, normal elderly subjects demonstrate a specific impairment of suppression processes requiring an active inhibition of some information, but the ability to resolve interference from distracting information appears preserved. Otherwise, the comparison of performance in elderly subjects and AD patients seems to indicate that suppression processes are quantitatively less efficient in AD, since these patients present a correct suppression performance only when the trace of information is partially decayed. This could indicate that the impaired performance on suppression tasks in AD does not represent a specific alteration of some inhibitory/interference resolution processes (as observed in normal aging) but rather a less efficient functioning of all these processes. From a theoretical point of view, results of this study are indicative that more attention should be paid to the integration of the different inhibitory frameworks proposed in the literature. Indeed, the design of this study was build up to determine if suppression deficits reported in normal aging and Alzheimer can be interpreted as reflecting a deterioration of controlled inhibitory processes associated to a preservation of more automatic interference resolution processes (Wilson and Harnishfeger, 1998). Although in agreement with our initial hypothesis, the pattern of results observed in normal aging, also fits with the proposal of three distinct suppression functions in working memory (Hasher et al., 1999).

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