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INTERFERENCE AND NEGATIVE PRIMING IN NORMAL AGING AND IN MILD ALZHEIMER'S DISEASE

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Most studies that have administered interference and negative priming tasks to patients with Alzheimer's disease (AD) and healthy elderly subjects have demonstrated inhibitory dysfunction in AD patients, and mixed results in the elderly. In the present study, we re-explored these two effects in these populations by administering two tasks that allow assessing interference and negative priming effects. Results on both tasks showed (1) the presence of an interference effect in AD and elderly adults, that can be explained by cognitive slowing in the case of elderly controls; (2) the preservation of negative priming abilities in the two groups. These surprising results for AD patients were interpreted by proposing that AD patients have a preserved ability to suppress the representation of a distracter, but specific inhibitory deficits when they have to resolve a selection conflict at the stage of response production (i.e., when competing stimuli have been fully processed).

Introduction

The interference and negative priming effects are commonly used to assess inhibitory functioning in clinical and non-clinical populations. The interference effect is the consequence of a failure to suppress task-irrelevant processes and representations, while the negative priming effect refers to the deleterious effect of an item previously processed on the processing of the next item.

A classical way to explore the interference effect is the Stroop task (Stroop, 1935). In the typical version of the task, subjects are presented with colour words printed in an incongruent colour (e.g., GREEN printed in red ink) and they are asked to name the ink colour as quickly and accurately as possible while ignoring the word. Typically, subjects take more time and make more errors in naming incongruent stimuli than congruent (e.g., GREEN printed in green ink) or neutral (e.g., colour patch) ones. Another effect related to Stroop interference is facilitation (or the congruency effect),

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characterised by faster response times for congruent stimuli than for neutral ones. Both effects are explained by a greater automaticity of word reading as compared to colour naming and by a difference in the processing speed for colours and words, with the latter being processed faster (see MacLeod, 1991, for a complete discussion).

With regard to the negative priming effect, one of the classical procedures consists in presenting simultaneously to subjects a target and a distracter stimulus (i.e., stimulus and distracter are superimposed) and asking them to respond as quickly and accurately as possible to the target while ignoring the distracter. The negative priming effect refers to the fact that subjects take more time to respond to the target of the probe trial when it served as the distracter in the prime trial than when the prime and probe targets are unrelated. Given that it apparently has the opposite effect to the well-known priming effect, this phenomenon was named negative priming (Tipper, 1985; see also Fox, 1995; May, Kane, & Hasher, 1995, for reviews).[1] The dominant explanation of the negative priming effect proposes that it is due to the active suppression (inhibition) of irrelevant information (the distracter), executed to allow easier processing of the target information. Because this suppression lasts for a relatively long time (at least a few seconds), the inhibited representation becomes less available for the next trial, resulting in a delay in response production when the irrelevant stimulus becomes a target one (Neill, 1977; Tipper & Cranston, 1985; see also May et al., 1995, for a discussion of alternative explanations). According to this theoretical framework, the presence of a negative priming effect can then be considered as proof of efficient inhibitory functioning.[2]

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[1]When negative priming is manifested because subjects are asked to select the target by means of a physical feature (e.g., colour), the effect is called identity negative priming. However, negative priming can also be observed when subjects are asked to respond to the target according to its spatial location (Tipper, Brehaut, & Driver, 1990).

[2]An alternative explanation in terms of episodic retrieval was also proposed to account for the existence of the negative priming effect (Neill, 1997; Neill, Valdes, Terry, & Gorfein, 1992). This explanation presupposed that the presentation of a stimulus automatically induces the retrieval of the most recent episode associated to that stimulus. In the case of a negative priming task, this means that the previous distracter and its tag ("to-be-inhibited") are automatically retrieved once the next trial is processed, inducing a conflict because of the opposite requirement in the current trial ("to-be-produced"); the resolution of this conflict resulting in a delayed response. However, the existence of retrieval processes does not exclude a role for inhibitory mechanisms (Milliken, Tipper, & Weaver, 1994; Tipper & Milliken, 1996), and it is not clear whether such automatic retrieval operates at a conscious level. Moreover, according to some authors, both inhibitory mechanisms and episodic retrieval processes can be the source of the negative priming effect, depending on the contextual variables of the task (Kane, May, Hasher, Rahhal, & Stoltzfus, 1997; May et al., 1995). More specifically, episodic retrieval processes are assumed to be the source of the effect under difficult perceptual conditions (such as when test stimuli are degraded or when the exposure duration of test stimuli is limited) and when test stimuli are successively repeated across the task, because these conditions trigger the retrieval of previous episodes.

Even if interference and negative priming effects are classically assessed with Stroop and superimposed pictures naming tasks, respectively, it must be emphasised that the two tasks can be adapted to assess simultaneously each kind of effect. Indeed, in the Stroop task, a negative priming effect will be observed when the ink colour to name corresponds to the word that had to be inhibited in the previous trial, while in the picture naming task, the interference effect refers to the slowing of reaction time when the target is presented with distracting information in comparison to a condition without any distracter.

Interference and negative priming effects are often used indiscriminately to assess inhibitory functioning in the selective attention field. However, several data support the hypothesis that the interference and negative priming effects specifically tap two distinct inhibitory processes. Indeed, if they were truly separate indices of the same level of inhibitory functioning, the size of the negative priming effect should be inversely proportionate to the size of the interference effect. However, such a negative correlation between interference and negative priming effects has not been found systematically (see May et al., 1995, for a review). Another argument comes from the observation of a selective impairment of the interference effect, associated with a spared negative priming effect in patients with multiple sclerosis (Vitkovitch, Bishop, Dancey, & Richards, 2002), and of the reverse dissociation in patients with schizophrenia (Salo, Henik, Nordahl, & Robertson, 2002). In addition, several behavioural studies have shown that negative priming effect can be experimentally dissociated from the interference effect within the same task in normal young adults (Catena, Fuentes, & Tudela, 2002; Mari-Beffa, Estévez, & Danziger, 2000). In that context, Catena et al. (2002) suggested that the priming effect observed on negative priming trials might reflect an early stage of processing (i.e., the success of a stimulus in activating its representation in memory), whereas interference might reflect competition in gaining control over response production, a stage of processing that does not occur until competing stimuli have been fully processed. Although the authors did not discuss if such priming effects are associated to activation of the representation of the stimulus at a perceptual or a semantic level, several data suggest that the distracter is semantically processed in negative priming tasks (Mari-Beffa, Fuentes, Catena, & Houghton, 2000; Tipper & Driver, 1988). For example, a negative priming effect was observed despite physical changes in stimulus type from prime to test trials (e.g., Driver & Baylis, 1993; Driver & Tipper, 1989; Tipper & Driver, 1988). This supports the view that inhibition intervenes after selection to prevent irrelevant information from being reactivated (Stoltzfus, Hasher, Zacks, Ulivi, & Goldstein, 1993; Tipper, Weaver, Cameron, Brehaut, & Bastedo, 1991), rather than during selection to reduce interference from irrelevant items, as it

was originally suggested (Neill & Westberry, 1987; Tipper, 1985; Tipper & Baylis, 1987).

To summarise, some data suggest that interference and negative priming effects refer to separate inhibitory processes. More specifically, it is plausible to consider the negative priming effect as an index that reflects a subject's ability to inhibit the representation of distracting information, while the interference effect may be considered as an index reflecting the subject's ability to inhibit the response code activated by the distracting information. This is in accordance with the proposal that inhibition is composed of a series of independent and specific processes rather than a single unitary mechanism, as discussed recently by several authors (e.g., Friedman & Miyake, 2004; Nassauer & Halperin, 2003; Nigg, 2000).

Inhibition in healthy elderly adults

Numerous studies have explored inhibitory functioning in normal aging and found age-related impairments (see Zacks & Hasher, 1994, for a review), consistent with the inhibitory deficit hypothesis put forward by Hasher and Zacks (1988).

With regard to the Stroop task, elderly adults' performance is generally characterised by an increase in the interference effect, as evidenced both by response times (Cohn, Dustman, & Bradford, 1984; Hartman & Hasher, 1991; Kieley & Hartley, 1997; Panek, Rush, & Slade, 1984; Spieler, Balota, & Faust, 1996) and errors (Kieley & Hartley, 1997; West & Alain, 2000). These results have long been interpreted as indicative of an inhibitory deficit, with the idea that interference increases with age due to a selective attention impairment, making older adults less able to suppress the influence of the reading process when they are confronted with Stroop items. However, some authors have suggested that this impairment may arise from a general slowing of information processing, which has exponential consequences with any increase in task difficulty. Indeed, age-related differences in the Stroop interference effect disappear when processing speed is controlled for in the statistical analyses (e.g., Salthouse & Meinz, 1995; see also Verhaeghen & De Meersman, 1998a, for a meta-analysis).

Early experiments exploring identity negative priming[3] in normal aging have shown that, contrary to young adults, older adults experience a reduction or an absence of the negative priming effect with pictures (Tipper, 1991), letters (Hasher, Stoltzfus, Zacks, & Rypma, 1991; Stoltzfus et al., 1993), and

[3]In this paper, we discuss only experiments exploring identity negative priming. But it is important to know that negative priming for spatial locations appears to be spared in normal aging (Connelly & Hasher, 1993; Simone & McCormick, 1999).

words (Kane, Hasher, Stoltzfus, Zacks, & Connelly, 1994). These specific observations were also confirmed by a meta-analysis (Verhaeghen & De Meersman, 1998b). However, numerous studies have also shown normal negative priming effects (Buchner & Mayr, 2004; Gamboz, Russo, & Fox, 2000; Kramer & Strayer, 2001; Langley, Overmier, Knopman, & Prod'Homme, 1998; Pesta & Sanders, 2000; Schooler, Neumann, Caplan, & Roberts, 1997; Sullivan & Faust, 1993; Sullivan, Faust, & Balota, 1995), and these findings were confirmed in a recent updated meta-analysis (Gamboz, Russo, & Fox, 2002). According to Kane, May, Hasher, Rahhal, and Stoltzfus (1997), such presence of normal negative priming is due to the use of tasks that induce the intervention of retrieval processes rather than inhibitory processes *per se* (for example, under conditions of degraded stimuli or when the prime-display target is repeated as the subsequent test-display target), which may help elderly adults to compensate for their inhibitory difficulties. However, at least two studies, which have used a procedure neutralising the impact of episodic retrieval on performance, found normal negative priming in the elderly (Gamboz et al., 2000; Schooler et al., 1997). Together, these discrepant results suggest that the reason for preserved/impaired negative priming in normal elderly subjects is not totally clear at this time and may depend on task specificities (e.g., differences in the material used) and procedures (e.g., are the different types of items presented in blocks or intermixed?) that need to be made explicit.

Inhibition in Alzheimer's disease

Previous studies suggest that, when compared to elderly controls, AD patients systematically show larger interference effect as assessed by Stroop task (Amieva, Lafont, Auriacombe, Le Carret, Dartigues, & Orgogozo, 2002; Amieva, Lafont, Rouch-Leroyer, Rainville, Dartigues, & Orgogozo, 2004; Bondi, Serody, Chan, Eberson-Shumate, Delis, & Hansen, 2002; Fisher, Freed, & Corkin, 1990; Grady, Haxby, Horwitz, Sundaram, Berg, & Schapiro, 1988; Koss, Ober, Delis, & Friedland, 1984; Spieler et al., 1996), picture naming tasks (Sullivan et al., 1995) and letter naming tasks (Langley et al., 1998). Moreover, AD patients show a less reliable or absent negative priming effect with picture naming tasks (Amieva et al., 2002; Sullivan et al., 1995) but a normal negative priming effect when letter naming tasks are used (Langley et al., 1998). To our knowledge, negative priming effect has never been explored in AD patients with Stroop items.

Together, these results suggest an impairment of inhibitory control in AD patients. However, it should be emphasised that impaired performance in inhibitory tasks may be due to a variety of cognitive deficits because of the multi-component nature of these tasks (e.g., Burke, 1997; McDowd, 1997).

More specifically, a slowing down of information processing could also be responsible of the poorer performance of AD patients on inhibitory tasks tapping interference and negative priming effects. Although slower processing speed does not seem to be a good explanation of AD patients' increased interference effect on Stroop tasks (Amieva, Phillips, Della Sala, & Henry, 2004; Bondi et al., 2002; Koss et al., 1984; Spieler et al., 1996), there is to our knowledge no data that can exclude the influence of this factor on the negative priming performance of these patients. On the contrary, some data are indicative that a slowing down may affect negative priming performance. For example, Verhaeghen and De Meersman (1998b) demonstrated that the difference in negative priming effects between young and elderly adults is reduced when slowing down is statistically controlled. Moreover, the literature on hyperpriming in AD has shown that this phenomenon can sometimes be explained as a consequence of cognitive slowing (Balota, Watson, Duchek, & Ferraro, 1999; Nebes, Brady, & Huff, 1989). Then, because early AD patients are slower than elderly adults on processing speed tasks (see for example Nestor & Parasuraman, 1991), a significant influence of such slowing down on negative priming performance seems plausible.

The present study

To sum up, an impaired performance on measures of interference was systematically observed in normal aging and Alzheimer's disease, and was attributed to a slowing down of processing speed in healthy elderly only. However, results concerning the negative priming effects in these two populations remain controversial. Consequently, the aim of the present study is to re-explore interference and negative priming using a Stroop and a naming task in order to determine the generality of the deficits observed in normal and pathological aging on these tasks. More specifically, we were interested to explore if the effect of normal aging and AD are consistent across different tasks allowing to assess both interference and negative priming effects. For that purpose, the Stroop task was adapted to allow the measurement of the negative priming effect, by including trials for which the correct response was the response to be inhibited in the previous trial, and we also administered a picture naming task classically used to explore interference and negative priming effects.

We predict for the two groups an increase in interference effects on both tasks, and hypothesise that this increase might be explained by a slowing of processing speed for elderly adults (Verhaeghen & De Meersman, 1998a) but not for AD patients (Amieva, Lafont et al., 2004; Bondi et al., 2002; Koss et al., 1984; Spieler et al., 1996). Moreover, we tentatively explore the influence of processing speed onto the negative priming effect since several studies

have yielded an influence of cognitive slowing on priming effects (Balota et al., 1999; Nebes et al., 1989; Verhaeghen & De Meersman, 1998b). The influence of processing speed was statistically controlled by computing ratio scores for both the interference and the negative priming effects.

Method

Subjects

The selected AD group consisted of 23 patients diagnosed with probable AD by a neurologist following the criteria of the National Institute of Neurological and Communication Disorders – Alzheimer's Disease and Related Disorders Association (NINCDS – ADRDA; McKhann, Drachman, Folstein, Katzman, Price, & Stadlan, 1984). All patients had suffered from progressive memory impairment for at least 6 months. The diagnosis was based on general medical, neurological, and neuropsychological examinations. Exclusion criteria were a premorbid history of major psychiatric or neurological illness, or drug or alcohol abuse. Computed tomography (CT) scans showed mild atrophy, at most. Six patients were excluded from the analyses because they encountered difficulties to complete the Stroop and negative priming tasks (some were enable to perceive the stimuli of the picture naming task, while other made too many errors to allow valid analysis). The age of the 17 remaining AD patients ranged from 58 to 88 years (M = 76.12 years old; SD = 6.47), and their educational level ranged from 3 to 20 years of education (M = 11.18 years; SD = 4.33). Their mean score on the Mattis Dementia Rating Scale (DRS; Mattis, 1988) was 124.94 (range: 104 - 139; SD = 8.06).

Twenty healthy older participants (7 men and 13 women) who were matched for age and educational level served as controls. The healthy controls were not institutionalised and were subject to the same exclusion criteria as the AD group. The mean age and educational level of the control group were, respectively, 74.4 years (SD = 4.01) and 11.25 years (SD = 4.56). These control participants did not differ from the AD patients in terms of age [$t(35) = -0.95$, $p = .35$] or education level [$t(35) = 0.09$, $p = .93$]. All controls had a total DRS score greater than 129 (M = 139.32; range = 135 - 142; SD = 2.69), which is considered as the cut-off score to discriminate typical aging from dementia (Monsch, Bondi, Salmon, Butters, Thal, Hansen, Wiederholt, Cahn, & Klauber, 1995). The AD patients' overall performance on the DRS was significantly lower than the healthy controls' [$t(35) = 6.82$, $p < .0001$].

Eighteen young subjects also participated in this experiment in order to explore the effect of normal aging on interference and negative priming

effects. The young participants (M = 24.12 years old; SD = 4.61) were mostly undergraduate students. Young and elderly subjects performed similarly on the French adaptation of the Mill Hill vocabulary test [Deltour, 1993; young subjects: M = 23.55; SD = 3.5; elderly adults: M = 24.6; SD = 4.68; $t(36) = 0.77$, $p = .45$]. However, the young adults had a higher educational level than the elderly subjects [young subjects: M = 14.35 years; SD = 1.79; $t(36) = -3.19$, $p = .004$]. All subjects had normal or corrected-to-normal visual acuity. Written informed consent was obtained for all participants and their caregivers (where appropriate), and the study was approved by the Ethical Committee of the University Hospital of Liège.

Materials and procedure

Stroop task

Four different colours (red, blue, yellow and green) were used to create three sets of stimuli: coloured strings of %%%, congruent stimuli and incongruent stimuli. The incongruent stimuli were created by printing each of the four colour names in the three other ink colours (e.g., RED printed in green ink). The congruent stimuli were created by printing each of the four colour names in its own colour (e.g., RED printed in red ink). These sets of stimuli were combined in order to create five different types of stimulus: 36 congruent stimuli or Fa (facilitator items), 36 neutral stimuli or N (%%%), 72 incongruent stimuli that were not primed or I (interferent items), 36 incongruent stimuli that were positively primed or I+ (positive priming items; the colours of the stimuli on trials n-1 and n were the same, but the colour names were different), and 36 incongruent stimuli that were negatively primed or I- (negative priming items; the irrelevant word on trial n-1 was the same as the relevant colour on trial n). The I stimuli were always followed by either I+ or I- stimuli, and this prime-probe couplet was always followed by a neutral stimulus (72 in total) that served as a filler. These filler trials were included in the task to eliminate an unwanted priming effect that may have spread from trial to trial and distorted performance. The whole task was therefore composed of 288 stimuli divided into two equivalent blocks of 144 items. Trials in each block were sorted pseudo-randomly, with the exception that no stimulus type occurred in more than three consecutive trials.

Subjects sat in front of and approximately 50 cm away from a computer screen. They were asked to say aloud, as quickly and accurately as possible, the ink colour in which each stimulus was printed, while ignoring the word itself. Stimuli were presented individually in the centre of a black background (54-point Arial) and were preceded for 500 milliseconds (msec) by a sound. Each stimulus remained on the screen until the subject gave his or her response (the experimenter pressed a mouse button as soon as the subject

responded). In order to minimise loss of trials and inaccurate reaction time measurement due to hesitation in subject responses, a correction method was developed that allows us to avoid the problems inherent in the use of a vocal key. More specifically, subject responses were recorded with a voice recorder and were corrected later with Sound Forge 7.0. (Sony®), which allowed us to generate the waves of the warning sound and the subject's response for each trial in order to determine response time with millisecond accuracy. We preferred this technique to the classic vocal key because the latter is less accurate since the first sound uttered by the subject is systematically recorded as the response. Thus, with a vocal key, every trial for which the subject hesitated (by saying, for example, 'ehhhhh' or 'gre…red') before responding correctly is generally lost, while this was not the case with our technique, which allowed us to accurately identify the start of the wave associated with the correct response (in the example: '…red'). Subjects were given a seven-trial practice run before the start of the task and the first four trials of the two test blocks were also excluded as practice. The two test blocks were separated by a pause that lasted at most 5 minutes. Moreover, trials with incorrect responses and trials following an error were also excluded from the reaction time analysis. The Stroop interference effect was assessed for each subject by comparing the median reaction time associated with the N items to the median reaction time associated with the I items. The facilitation effect was assessed for each subject by comparing the median reaction time associated with the Fa items to the median reaction time associated with the N items. Finally, the negative priming effect was assessed by comparing the median reaction time associated with the I- items to the median reaction time associated with the I items, and the positive priming effect by comparing the median reaction time associated with the I items to the median reaction time associated with the I+ items.

Picture naming task

This task was adapted from Sullivan et al.'s (1995) procedure. Five pictures of semantically unrelated objects were printed in red and in green, and each picture in one colour was then superimposed over every picture in the other colour until all the possible combinations were obtained (20 superimposed pictures). These superimposed pictures were then combined in pairs to create 30 positive priming trials (the target picture for the prime and probe trials is the same), 30 negative priming trials (the target picture for the probe trial is the distracter for the prime trial) and 30 neutral trials (the prime and probe pictures are unrelated). Trials were sorted pseudo-randomly to form two equivalent blocks, with the exception that no stimulus type occurred in more than three consecutive trials. As was the case for the Stroop task, all these test trials were separated by filler superimposed pictures in order to

neutralise the possible spreading of a priming effect from trial to trial. For that purpose, three pictures that were semantically unrelated to the test pictures were also printed in red and in green, and combined two by two.

Subjects sat in front of and approximately 50 cm away from a computer screen. First, the different pictures were presented one at a time and named by the experimenter. Then, the subject had to do the same without any display time or response time constraints. This naming exercise was repeated until the subject was able to name all the pictures quickly and accurately. Following this control task, participants were presented with the single pictures and were asked to say aloud, as quickly and accurately as possible, the name of each picture (i.e., baseline condition). Each picture was presented 12 times pseudo-randomly, for a total of 60 trials. The single pictures were printed either in red or in green, depending on the condition in which the subjects were placed. After they had experienced the baseline condition, subjects were presented with the superimposed pictures condition, that is, 30 positive, 30 negative and 30 neutral trials presented pseudo-randomly.

In the baseline and superimposed picture conditions, each stimulus was preceded by a sound for 500 msec. Stimuli were then presented individually during 250 msec, and were followed by a pattern mask displayed during 100 msec. The pattern mask consisted of a pseudo-figure composed by randomly scrambling the test pictures. Once the stimulus and the pattern mask had been presented, a black screen remained until the subject gave his or her response (the experimenter pressed a mouse button as soon as the subject responded), and a response-stimulus interval of 250 msec began, followed by the sound that announced the next stimulus. The single and superimposed pictures were presented in the centre of a black screen in a 7 x 7 cm white square. In the superimposed picture condition, subjects were asked to say aloud, as quickly and accurately as possible, the name of each red picture (or green picture, depending on the condition to which the subject was assigned), while attempting to ignore the green (or red) pictures. Subjects were given a seven-trial practice before the start of the task and two trials were added to the beginning of each test block as fillers. The two test blocks were separated by a pause lasting at most 5 minutes. Moreover, the reaction time for the prime and probe trials was excluded from the reaction time analysis if the subject made an error on either the prime or the probe trial. This picture naming task was administered after the Stroop task. The interference effect was assessed for each subject by comparing median reaction times to the probe in the neutral condition to median reaction times in the baseline condition (in which targets were presented without distracters). The negative priming effect was assessed by comparing median reaction times to the probe in the negative priming condition to median reaction times to the probe in the neutral condition. Finally, the positive priming effect was assessed by compar-

ing median reaction times to the probe in the neutral condition to median reaction times to the probe in the positive priming condition.

Results

Reaction time in the Stroop task

All effects were assessed for significance at the $p < .05$ level. No subject was excluded from the analyses based on reported awareness of the relationship between prime (I) and probe trials (I- or I+). A 3 (young, old, AD) x 5 (Facilitator, Incongruent, Incongruent-, Incongruent+, Neutral) within-subjects ANOVA was performed on the median reaction time for correct responses. Means for the median reaction times on the five types of items according to group are presented in Table 1. The results of this analysis yielded a significant group effect [$F(2, 51) = 22.54$, $p < .00001$], indicating slower response times in AD patients and elderly adults, and an effect of the type of item [$F(4, 204) = 97.84$, $p < .00001$]. The two-way interaction between group and type of item was also significant [$F(8, 204) = 11.24$, $p < .00001$]. Planned comparisons revealed a significant interference effect (assessed by comparing I and N items) for all three groups (all $F > 11$), which was greater for AD patients than for healthy elderly adults [$F(1, 51) = 19.8$, $p < .0001$], and greater for elderly adults than for young subjects [$F(1, 51) = 4.39$, $p = .041$]. Planned comparisons also revealed a significant negative priming effect (assessed by comparing I and I- items) for all three groups (all $F > 5$), which was greater for AD patients than for healthy elderly adults [$F(1, 51) = 7.85$, $p = .0072$], but did not differ between elderly and young subjects [$F(1, 51) = 0.37$, $p = .54$]. Planned comparisons revealed a significant reverse facilitation effect (namely, a slowing down of reaction times for congruent stimuli compared to neutral ones; all $F > 7$), except for young adults ($F = 2.48$). This effect was greater for AD patients than for healthy older adults [$F(1, 51) = 6.02$, $p = .017$]. Finally, planned comparisons revealed a significant positive priming effect (assessed by comparing I and I+ items) for all three groups (all $F > 20$), which was greater for AD patients than for older adults [$F(1, 51) = 4.17$, $p = .046$], but equivalent for young and elderly adults [$F(1, 51) = 0.0007$, $p = .98$].

In order to take into account the possible influence of processing speed slowing down onto interference, facilitation, negative priming and positive priming effects, we finally computed ratio scores for all these effects [(I-N)/N for interference effect, (N-I+)/N for facilitation effect, [(I-)-I]/I for negative priming effect and (I-I+)/I for positive priming effect]. A one-way ANOVA revealed a significant effect of group for the interference effect [$F(1,$

51) = 18.15, $p < .0001$]. Planned comparisons revealed that the interference effect was equivalent between young and older adults [$F(1, 51) = 3.59$, $p > .05$], while it was significantly different between elderly adults and AD patients [.36 *versus* .62; $F(1, 51) = 17.43$, $p < .001$]. A one-way ANOVA revealed a significant effect of group on the facilitation effect [$F(1, 51) = 3.55$, $p < .05$]. Planned comparisons revealed that the facilitation effect was equivalent between young and older adults [$F(1, 51) = .19$, $p > .05$], while it was significantly different between elderly adults and AD patients [-.09 *versus* -.18; $F(1, 51) = 4.49$, $p < .05$]. A one-way ANOVA failed to reveal any significant effect of group for the negative priming effect [$F(1, 51) = 1.81$, $p > .05$]. Indeed, planned comparisons revealed that the negative priming effect was equivalent between young and older adults [$F(1, 51) = .05$, $p > .05$], and between elderly adults and AD patients [$F(1, 51) = 2.46$, $p > .05$]. Finally, a one-way ANOVA failed to reveal any significant effect of group for the positive priming effect [$F(1, 51) = 1.05$, $p > .05$]. Indeed, planned comparisons revealed that the positive priming effect was equivalent between young and older adults [$F(1, 51) = 2.10$, $p > .05$], and between elderly adults and AD patients [$F(1, 51) = .50$, $p > .05$].

Table 1
Means for median reaction times on the five types of items in the Stroop task according to group

	Fa	I	I–	I+	N
Young adults	643 (127)	745 (137)	798 (158)	588 (85)	599 (101)
Old adults	813 (194)	1009 (214)	1082 (226)	851 (185)	742 (137)
AD patients	1014 (318)	1376 (405)	1538 (477)	1120 (362)	851 (212)

Note. Reaction times are expressed in msec; numbers in parentheses are standard deviations.

Response accuracy in the Stroop task

A 3 (young, old, AD) x 5 (Fa, I, I-, I+, N) within-subjects ANOVA was performed on the proportion of correct responses. The proportions of correct responses associated with the five types of items according to group are presented in Table 2. The results of this analysis yielded a significant effect of group [$F(2, 51) = 4.35$, $p = .018$], and of type of item [$F(4, 204) = 22.38$, $p < .00001$]. The two-way interaction between group and type of item [$F(2, 51) = 1.50$, $p = .16$] was not significant. Planned comparisons tentatively revealed that AD patients made more errors than healthy elderly subjects [$F(1, 51) = 6.55$, $p = .013$], while young and elderly adults did not differ [$F(1, 51) = 0.02$, $p = .90$]. Planned comparisons also revealed a significant interference effect [$F(1, 51) = 36.09$, $p < .00001$], and a nearly significant

negative priming effect [$F(8, 204) = 3.14$, $p = .082$]. The overall facilitation effect [$F(1, 51) = 7.16$, $p = .0099$] and the positive priming effect were also significant [$F(1, 51) = 27.87$, $p < .0001$].

Table 2
Proportions of correct responses associated with the five types of items in the Stroop task according to group

	Fa	I	I–	I+	N
Young adults	.995 (.011)	.962 (.055)	.943 (.102)	.990 (.022)	.997 (.009)
Old adults	.997 (.009)	.959 (.037)	.949 (.045)	.981 (.033)	.993 (.012)
AD patients	.993 (.021)	.911 (.075)	.894 (.124)	.939 (.081)	.977 (.037)

Note. Numbers in parentheses are standard deviations.

Reaction time in the picture naming task

No subject was excluded from the analyses based on reported awareness of the relationship between prime and probe trials, but four AD patients were excluded because of problems processing the stimuli due to the short display duration. A 3 (young, old, AD) x 4 (baseline, negative, neutral, positive trials) within-subjects ANOVA was performed on the median reaction time for correct probe responses. Means for median reaction times on the four types of items according to group are presented in Table 3. This analysis revealed a significant effect of group [$F(2, 45) = 10.76$, $p = .0001$], indicating that AD patients and elderly adults are slowed, and of type of item [$F(3, 135) = 81.06$, $p < .00001$], indicating overall significant positive and negative priming effects; there was a significant two-way interaction between group and type of item [$F(6, 135) = 7.63$, $p < .00001$]. Planned comparisons revealed a significant interference effect for all three groups (all $F > 5$), which was greater for AD patients than for healthy elderly adults [$F(1, 45) = 9.3$, $p = .0038$], but equivalent between elderly adults and young subjects [$F(1, 45) = 2.09$, $p = .155$]. Planned comparisons also revealed a significant negative priming effect for all three groups (all $F > 4$), which was equivalent for AD patients and healthy elderly adults [$F(1, 45) = 0.32$, $p = .57$]. Similarly, elderly adults showed an equivalent negative priming effect compared to young subjects [$F(1, 45) = 0.36$, $p = .55$]. Finally, planned comparisons revealed a significant positive priming effect for all three groups ($F > 9$), which was greater for AD patients than for older adults [$F(1, 45) = 6.77$, $p = .0125$], and was equivalent for young and elderly adults [$F(1, 45) = 3.75$, $p = .059$].

In order to take into account the possible influence of processing speed slowing down onto interference, negative priming and positive priming effects, we finally computed ratio scores for all these effects [(Neutral-

Baseline)/Baseline for interference effect, (Negative-Neutral)/Neutral for negative priming effect, and (Neutral-Positive)/Neutral for positive priming effect]. A one-way ANOVA revealed a significant effect of group for the interference effect [$F(1, 45) = 9.43$, $p < .001$]. Planned comparisons revealed that the interference effect was equivalent between young and older adults [$F(1, 45) = 1.88$, $p > .05$], while it was significantly different between elderly adults and AD patients [.25 *versus* .50; $F(1, 45) = 9.36$, $p < .01$]. A one-way ANOVA failed to reveal any significant effect of group for the negative priming effect [$F(1, 45) = .79$, $p > .05$]. Indeed, planned comparisons revealed that the negative priming effect was equivalent between young and older adults [$F(1, 45) = 1.53$, $p > .05$], and between elderly adults and AD patients [$F(1, 45) = .13$, $p > .05$]. Finally, a one-way ANOVA revealed a significant effect of group for the positive priming effect [$F(1, 45) = 8.32$, $p < .001$]. Planned comparisons revealed that the positive priming effect was different between young and older adults [.09 *versus* .14; $F(1, 45) = 5.99$, $p < .05$], but it was equivalent between elderly adults and AD patients [$F(1, 45) = 3.27$, $p > .05$].

Table 3
Means for median reaction times on the four types of items in the picture naming task according to group

	Baseline	Negative	Neutral	Positive
Young adults	551 (56)	681 (94)	632 (89)	573 (66)
Old adults	606 (77)	793 (152)	759 (123)	647 (97)
AD patients	629 (87)	993 (303)	944 (290)	758 (182)

Note. Reaction times are expressed in msec; numbers in parentheses are standard deviations.

Response accuracy in the picture naming task

A 3 (young, old, AD) x 4 (baseline, negative, neutral, positive trials) within-subjects ANOVA was first performed on the proportion of correct responses. The proportions of correct responses associated with the four types of items according to group are presented in Table 4. This analysis revealed a significant effect of group [$F(2, 45) = 15.80$, $p < .0001$], indicating that AD patients and elderly adults made more errors than young subjects, and of type of item [$F(3, 135) = 20.81$, $p < .00001$], indicating overall significant interference, positive and negative priming effects. The two-way interaction between group and type of item was also significant [$F(6, 135) = 11.13$, $p < .00001$]. Planned comparisons revealed that AD patients showed a greater interference effect than healthy elderly adults [$F(1, 45) = 13.91$, $p = .0005$], while the negative priming effect was equivalent for the two groups

[$F(1, 45) = 0.69$, $p = .41$]. Elderly adults showed an equivalent interference effect [$F(1, 45) = 0.50$, $p = .48$] and an equivalent negative priming effect [$F(1, 45) = 1.78$, $p = .19$] compared to young subjects. Finally, planned comparisons revealed an equivalent positive priming effect for AD patients and older adults [$F(1, 45) = 0.41$, $p = .53$], and for young and elderly adults [$F(1, 45) = 0.09$, $p = .76$].

Table 4
Proportions of correct responses associated with the four types of items in the picture naming task according to group

	Baseline	Negative	Neutral	Positive
Young adults	.996 (.007)	.996 (.011)	.994 (.018)	.996 (.011)
Old adults	.992 (.017)	.937 (.057)	.959 (.059)	.969 (.035)
AD patients	.974 (.028)	.731 (.21)	.769 (.239)	.795 (.22)

Note. Numbers in parentheses are standard deviations.

Discussion

This study re-examined interference and negative priming effects in Alzheimer's disease and normal aging using a Stroop word-colour task and a superimposed picture naming task.

Our analysis of reaction time data revealed that both AD patients and elderly adults experienced a significant increase in the Stroop interference effect, while only AD patients showed an increase in the interference effect in the picture naming task. Such increased interference effects have been reported in the literature for both groups of subjects (e.g., Amieva, Lafont et al., 2004; Fisher et al., 1990; Hartman & Hasher, 1991; Kieley & Hartley, 1997), and are compatible with the presence of inhibitory difficulties. However, the results of the ratio scores lead us to attribute the increased interference effect to a slowing down of processing speed in elderly subjects rather than to an inhibitory dysfunction *per se* (see also Verhaeghen & De Meersman, 1998a), while this was not the case for AD patients, since the effect of group was still significant after controlling for processing speed on both tasks (see also for similar results Amieva, Lafont et al., 2004; Bondi et al., 2002; Koss et al., 1984; Spieler et al., 1996). Analyses of reaction time also revealed that, for the Stroop task, negative and positive priming effects were equivalent in young and elderly subjects, while these two effects were greater for AD patients compared to healthy elderly subjects. However, such hyper-priming effects was apparently due to a processing speed slowing down since they disappeared when processing speed was taking into account (see Nebes et al., 1989, for similar results).

With regard to the picture naming task, the negative priming effect was equivalent in all three groups of subjects. The observation of normal negative priming for elderly adults is consistent with recent studies (Buchner & Mayr, 2004; Kramer & Strayer, 2001; Langley et al., 1998; Pesta & Sanders, 2000; Sullivan & Faust, 1993; Sullivan et al., 1995; see also Gamboz et al., 2002, for an updated meta-analysis) and suggests that, under some circumstances, this effect is not impacted by normal aging. For instance, some authors have demonstrated that elderly adults show a normal negative priming effect when the methodology allows for the intervention of retrieval processes that compensate for inhibitory dysfunction, while they fail to show normal negative priming when such contamination is avoided (Kane et al., 1997). However, several recent studies, including this one, have tried to minimise the influence of retrieval processes by avoiding using degraded stimuli and repeating the same prime-probe associations successively across the task, and by applying no constraint to the exposure duration of test stimuli (note however that there was an exposure duration constraint in the picture naming task of this study). Despite such minimisation of retrieval processes contribution, they still found a normal negative priming effect in elderly adults (Gamboz et al., 2000; Schooler et al., 1997). The fact that AD patients showed negative priming effects on both tasks is consistent with the idea that episodic retrieval processes are not the main source of the negative priming effect in this study, since one would expect AD patients to have impairments if the effect depended mainly on memory processes (e.g., Bäckman, Small, & Fratiglioni, 2001; Grober, Lipton, Hall, & Crystal, 2000). Then, together, these results suggest that healthy elderly adults do not suffer from an inhibitory dysfunction as assessed with negative priming and interference effects. The presence or absence of negative priming effects from one study to another cannot, then, be due only to variation in the naming processing demands or in retrieval process contamination, and need to be specified.

The AD patients' results are quite surprising concerning the negative priming effects. Indeed, we found a reliable negative priming effect in the Stroop and picture naming tasks, while previous studies mostly failed to show any negative priming effect in AD patients (Amieva et al., 2002; Sullivan et al., 1995; see also Langley et al., 1998). The discrepancies between our results and those of these two earlier studies are surprising since we adapted our procedure from the one used by Sullivan et al. (1995), which is similar to the one used by Amieva et al. (2002). We tentatively propose the following interpretations to these discrepant results. First, the severity of the disease could impact on the negative priming effect. Indeed, the DRS score of AD patients was higher in our sample (125.6, SD = 8.7), than in the Sullivan et al.'s (1995) (121, SD = 9.9) and Amieva et al.'s (2002) (120, SD

= 9.6) samples.[4] In order to explore this possibility, we computed correlational analyses between DRS score of AD patients and their interference and negative priming effects on the two tasks. However, these correlations failed to reach significance (all $p > .05$). Second, slight but important methodological differences between studies might also explain these results. Indeed, previous studies were characterised (contrary to ours) by an absence of filler trials to neutralise unwanted priming effects and also by less accurate response time measurement due to the use of a classic vocal key (and not voice recorder). In our study, we used filler trials between each test trials in order to eliminate unwanted positive and negative priming effects that may have spread trial to trial, while such precaution was not met in the previous studies. Moreover, we recorded subject responses with a voice recorder, and each response time was determined *a posteriori* with millisecond accuracy, without loss of trials or inaccurate measurement due to hesitation in the response production (which are frequent with AD patients). On the contrary, the authors of the discussed above studies used a classical vocal key, in which response time of correct responses preceded by vocalised hesitation are suppressed, or inaccurate if included in the analysis. Since negative priming is a subtle effect that needs a sufficient amount of trials to emerge, it is possible that it was not significant for AD patients in previous studies because of a reduced sensitivity of the task due to inaccurate reaction time measurement or extensive loss of trials. Then, we believe that the absence of negative priming for AD patients in previous studies was due to these two methodological limitations, namely an absence of filler trials that neutralise unwanted priming effects and a response time measurement less accurate than ours. Further studies will be obviously necessary to really understand these differences.

How then to link together these conflicting results (i.e., impaired interference effects associated to spared negative priming effects) regarding the inhibitory functioning of AD patients in this study? Based on several studies which have dissociated interference and negative priming effects (Catena et al., 2002; Mari-Beffa, Fuentes, et al., 2000; Salo, et al., 2002; Vitkovitch et al., 2002), we hypothesised that the negative priming effect is an index reflecting a subject's ability to inhibit the semantic representation of the distracting information, while the interference effect reflects the subject's ability to inhibit the response code activated when the distracting information is fully processed. The comparison of performance in young and elderly subjects clearly indicates that normal aging is not associated with dysfunction of these two inhibitory processes. On the contrary, the dissociation between

[4]However, a test of homogeneity revealed only slightly significant differences from Amieva et al.'s (2002) sample ($p = .0561$), and no significant differences from Sullivan et al.'s (1995) sample ($p = .172$).

normal negative priming effects and the increase in interference effects in the Stroop and picture naming tasks would suggest that AD patients have no difficulty (with our material and under our procedure) inhibiting the representation of a distracter when processing a stimulus, whereas they do encounter difficulties when they have to resolve the production selection conflict.[5] Thus, the results of our study are in agreement with the hypothesis that not all inhibitory processes are impaired in Alzheimer's disease (Amieva et al., 2002; Danckert, Maruff, Crowe, & Currie, 1998; Faust & Balota, 1997). More specifically, our results are compatible with a selective impairment in AD affecting the inhibition of irrelevant verbal responses when several alternatives are available, while the inhibition of the semantic representation of a distracter is spared. Based on the distinction between intentional (effortful) and unintentional (automatic) inhibitory processes made by some authors (e.g., Harnishfeger, 1995), we hypothesise that the dissociation between spared negative priming and impaired interference effects arises because the former is triggered more automatically and the latter more intentionally. According to Conway and Fthenaki (2003), intentional inhibitory processes are modulated by executive control and are triggered voluntarily by the subject to prevent or reduce interference due to activated competing or distracting information. Unintentional inhibitory processes, on the other hand, are triggered automatically during a cognitive activity, and need less modulation of executive control to perform properly. Because of this independence of executive control, unintentional inhibitory processes are assumed to be more resistant to brain damage (see Conway & Fthenaki, 2003; Moulin, Perfect, Conway, North, Jones, & James, 2002, for support for this assumption). Other studies also support this assumption of spared automatic inhibitory processes in AD. Indeed, AD patients do not encounter difficulties in retrieval-induced forgetting and inhibition of return tasks, which are considered to rely onto automatic inhibitory processes (Danckert et al., 1998; Faust & Balota, 1997; Moulin et al., 2002). Otherwise, they are known to suffer from difficulties when inhibition needs to be triggered voluntarily, such as in the antisaccade and go/no-go tasks (e.g., Collette, Van der Linden, Delrue, & Salmon, 2002; Mulligan, Mackinnon, Jorm, Giannakopoulos, & Michel, 1996). However, further studies are needed to confirm that negative priming truly reflects a more automatic inhibitory process than the interference effect.

To sum up, our results suggested that elderly adults and AD patients may show spared negative priming effects. They also confirmed that the increase

[5]It seems important to emphasise that no significant correlations were observed between interference and negative priming effects for each task and within each group. This is a supplementary argument to consider that negative priming and interference effects do not rely on the same inhibitory mechanisms (May et al., 1995).

in interference is not systematic for elderly adults and, when obvious, is merely due to slower processing speed, while this is not the case in AD patients. These contrasting results support the assumption that not all inhibitory mechanisms are impaired in normal aging and in Alzheimer's disease, especially automatic ones. More generally, our results are also compatible with the view that the negative priming effect reflects semantic processing of the distracter, while interference reflects the time taken to resolve the output conflict.

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