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Mental flexibility impairment in drivers with early Alzheimer's disease: A simulator-based study

Virginie Etienne [a,*], Claude Marin-Lamellet [a], Bernard Laurent [b]

[a] IFSTTAR-LESCOT, 25 Avenue François Mitterrand, 69675 BRON cedex, France
[b] CHU Bellevue — Service Neurologie, Pavillon 12, 42055 Saint Etienne, France

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ABSTRACT

After memory impairment, one of the most common troubles of early Alzheimer's disease (AD) is the impairment of executive functioning. However, it can have major consequences on daily life, notably on the driving activity. The present study focused on one important executive function involved in driving: mental flexibility; and considered how this impairment can affect driving. Ten patients with early AD were matched with 29 healthy older drivers. All participants were given an evaluation of mental flexibility through neuropsychological tests and an experimental test developed on a static driving simulator. The experiment was divided in two conditions; one without mental flexibility and another condition with a mental flexibility demand. AD patients showed impairments in the neuropsychological tests evaluating mental flexibility. These deficits are linked to the deficits they showed in the driving simulator flexibility tests. This study contributes to the understanding of mental flexibility mechanisms and on their role in driving activity. It also confirms that the driving simulator is a suitable tool to explore cognitive disorders and driving ability.

1. Introduction

Cognitive functions, as well as perceptual functions, are fundamental to driving. Driving is a complex task and relies strongly on intact cognitive abilities, including the ability to monitor and attend to the road environment, anticipate hazards and respond accurately and quickly to relevant information. This everyday activity requires many different cognitive processes, of which some are automatic but it also requires from the driver a large panel of high level cognitive functions, and it involves the executive system, especially the mental flexibility [1,2]. Older drivers are known to be at higher risk than all other age groups for motor vehicle accidents on a per-mile basis [3,4], and older individuals with early dementia crash risk are two to five times than that of unimpaired older drivers [5]. Moreover, neuropsychological studies on fitness to drive of older drivers and/or impaired drivers have for the most part neglected or limited the assessment of executive functioning.

Executive functions (EF) are very high-level abilities. They allow individuals to anticipate and adapt their behavior to changing situations, and to new situations. For example, attentional control, planning, organization, and mental flexibility, are executive functions [6]. Miyake et al. [7] suggested that the executive system is a global system divided in three components and three main executive functions, — inhibition of automatic responses, updating the content of working memory, and mental flexibility. In the present research, we focused on the mental flexibility component, which seems to be very important component to drive safely [8]. It refers to the ability to switch between cognitive tasks or mental sets [9]. It is an intentional disengagement process of the attention from a situation or a strategy which is not relevant anymore and an engagement towards a new and more adapted situation/strategy. It is sometimes called "mental shifting", "attention switching" or "mental flexibility" [7]. However, some authors prefer to distinguish these concepts [10]. Indeed, it seems that the "mental shifting" refers to the shift of visual attention from one location to another (Posner's paradigm [11]) [12], whereas the "mental flexibility" refers to the concept of displacement towards another pattern of answer (like in the WCST [13,14]) or towards another mental set [10]. In the present study, we refer to this second concept.

Alzheimer's disease (AD) is the most common cause of abnormal cognitive decline in older adults. AD is firstly characterized by deficits in declarative memory, but also by a variety of impairments in high level cognitive abilities. It progressively affects cognitive functions like attention, judgment, reasoning [15], and principally, executive functioning [16]. In the early stages of the dementia, patients are not aware of their

* Corresponding author at: IFSTTAR-MA, 304 Chemin de la Croix Blanche, 13300 Salon de Provence, France. Tel.: +33 4 90 57 79 83.
E-mail addresses: virginie.etienne@ifsttar.fr (V. Etienne), claude.marin-lamellet@ifsttar.fr (C. Marin-Lamellet), bernard.laurent@chu-st-etienne.fr (B. Laurent).
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deficits and continue their daily life as if they were not impaired at all [17]. It is estimated that around one-third of drivers with dementia continue to drive [18]. While healthy older drivers are able to adopt self-regulatory driving behaviors [19], it seems that AD patients, because of anosognosia, could not adopt safe behaviors like avoiding high traffic situations or driving at night. Carr [20] explained in a literature review that the studies on crash risk in drivers with dementia are limited in terms of conclusions because of the small number of participants, the use of self-assessment questionnaires, and by the lack of matched controls participants. However, all the studies surveyed by Carr showed an increase in the number of accidents among drivers with Alzheimer's disease. Another study also showed that drivers with AD, even in the early stages of the disease are at a greater risk of crashes compared to cognitively preserved drivers at the same age [21]. The studies including an neuropsychological assessment and an evaluation of the fitness to drive tend show that the executive functions' impairment are the most correlated with the impairments in driving [8,22].

The literature concerning the impairment of the mental flexibility in AD is quite important. Perry, Watson and Hodges [23], Siri et al. [24] and also Souchay, Isingrini and Gil [25] reported impairment in mental flexibility in the early stages of dementia. However, its impairment could have major consequences in daily life, notably on the driving activity [26]. Some studies have also reported that mental flexibility is one of the two major features of attention which seems to be particularly impaired in AD, with the inhibitory mechanisms [10]. Inhibitory and mental flexibility mechanisms are often associated in the literature on executive functioning. However, several studies showed that these two features of executive functions were not completely linked. Miyake et al. showed that they are linked but independent in their functioning and Collette et al. [27] showed that the neural substrates of these functions were different. The present study focused on mental flexibility because the literature is not as abundant as for inhibition.

Daigneault, Joly, and Frigon [1] suggest that executive abilities are important determinants of driving ability among older drivers. Indeed, they showed that older drivers with a history of accidents present impairments on several executive tests compared to participants who do not crash.

A recent review article [28] reported that in the last decade at least sixty-nine articles had been published on the role of executive functions in driving. However, the literature concerning the link between executive disorders in AD and driving is finally not very abundant compared to available studies on the others cognitive impairments, like attention, spatial orientation, etc. [8,29]. However the executive functions are quite impaired in AD and particularly in the early stages of the dementia. The difficulty of showing correlation between neuropsychological evaluation and driving evaluation could be explained by the fact that executive functioning, and more particularly mental flexibility, are not sufficiently taken into account in the studies. Indeed, depending on the driving's characteristics and on the fact that it involves a lot of different cognitive processes, neuropsychological tests that are very focused on only one cognitive function cannot show correlations; hence the importance to include executive functioning evaluations that introduce the concept of cognitive control.

The main goal of the present study is to evaluate the impairment of mental flexibility which occurs in the early stages of AD and its consequences on the driving activity. This work will contribute to improve the knowledge of the role of mental flexibility and of executive functions in general, in the driving activity. The research comprises a twin-approach which combined a neuropsychological evaluation and a driving experiment in a driving simulator. Both the neuropsychological evaluation and the driving experiment involved a mental flexibility activity. The aims of the research are first, to evaluate the level of impairment of mental flexibility in AD, secondly, to assess the mental flexibility in a driving situation, and lastly to evaluate the relationship between the neuropsychological evaluation and performance in the driving simulator.

We chose the driving simulator method for various reasons. First of all, the simulator provides controlled and reproducible situations, which is not possible with real driving situations. Furthermore, other studies [30,31], as well as the authors' previous research protocol [32] verified that experiments on driving simulators were possible both with older drivers and with neurologically impaired patients. Korteling and Kaptein [33] also suggested that experiments on driving simulator should be developed because of the overly wide variability of the real situation studies. Based on this earlier work it was hypothesized that impairment of mental flexibility would have consequences on the flexibility needed for safe driving.

2. Method

2.1. Participants

Ten early Alzheimer's disease (AD) patients took part to the experiment. Their age varied between 65 and 81 years (mean = 74.86, SD = 5.36). In order to include only early AD patients, a Mini Mental State Examination (MMSE, [34]) score of 24 or higher was required for study entry (mean = 24.8, SD = 1.48). All the AD patients still drove their own car at least once a week (minimum of 3000 km/year).

A control group of 29 healthy older drivers (MMSE: mean = 29.65, SD = 0.66) was matched in terms of age (mean = 70.83, SD = 2.95) and education. Participants with medical, substance abuse, neurologic or psychiatric disorders which could account for their cognitive compromise were all excluded.

Participants were excluded if they had suffered a cerebrovascular accident (stroke), traumatic brain injury, or any other type of dementia, or if there was suspicion of dementia for the healthy control group. People with motion sickness or epilepsy were also excluded. All participants had a normal or corrected visual acuity sufficient for driving (binocular acuity >5/10° according to French legislation).

2.2. Procedure

The study presented here is a part of a longer research protocol (for reference: [35,36]). Participants were administered with the neuropsychological tests and the experiment in the driving simulator at IFSTTAR the same day. Institutional review board approval was obtained for all components of the study; information forms were given to the participants.

2.2.1. Neuropsychological evaluation of flexibility

The mental flexibility was assessed by one neuropsychological test: The Plus–Minus Test [37], which consists of 3 lists of 30 two-digit numbers on a single sheet of paper. For the first list, the participants are instructed to add 3 to each number and to write their answers. For the second list, they were instructed to subtract 3 from each number. Finally, for the third list, the participants were required to alternate between adding 3 and subtracting 3 from the numbers. The participants were asked to complete each list as quickly and as accurately as possible.

In this situation, three dependent measures were defined:

✗ *Response time* (RT, in seconds) to complete the lists of operation: Plus-RT, Minus-RT, Plus/minus-RT,
✗ *Number of calculation errors* (E) in the completion of the lists (max = 30): Plus-errors: number of errors recorded during the task of addition, Minus-errors: number of errors recorded during the task of subtraction, Plus/minus-errors: number of errors recorded during the alternance task.
✗ *Shift cost* calculated as the difference between the time to complete the alternating list and the average of the times to complete the addition and subtraction lists.

2.2.2. Driving simulator evaluation of flexibility

In order to assess mental flexibility, a specific driving simulator scenario has been designed [38]. There were two conditions in this task. In the condition without alternation (a 13.8 km scenario), participants had to state the shape of the road sign (rectangular, triangular, square or round) placed on the right-hand side of the road (session 1). They then had to state the dominant color of the road sign (blue, green, red or brown) placed on the left-hand side of the road (session 2). The road signs were reproduced from real French national road signs, with respect to shape and their size was augmented to a ratio of 1.5 in order to avoid any visibility difficulty for participants (simulator characteristics). Each session included three practice trials and 16 tests. In the condition with alternation (session 3, requiring mental flexibility), a 10.9 km scenario, participants were asked to state the shape of the road sign if it was placed on the right-hand side, and to indicate the color of the road sign if it was located on the left. Signs were placed alternately on the right or left of the road. The condition with alternation included four practice trials and 32 tests. Flexibility cost constituted our mental flexibility measure; this was obtained by calculating the difference between mean reaction times of correct trials in the condition with alternation and mean reaction times of correct trials from the first two sessions in which no flexibility was required. The participant had to give the answer into a microphone as quickly as possible. The reaction times (RT) between the appearance of the target and the answer were recorded for each target. The target remained visible until the participant reached this point of the road, thus the time of appearance depended on the driving speed. The cost of shifting was calculated as the difference between the mean time for the third condition and the average of the times for the first and second condition. The mean vehicle speed was also recorded throughout the experiment, and was also analyzed. The participants were asked to respect the legal speed limit on French national roads (i.e., 90 km/h). The mean vehicle speed was the only variable acquired for this experiment because the main objective remained to measure mental flexibility in a driving context. Adding other driving situations (intersections, interactions, curves …) would have added an irrelevant level of complexity.

In this situation, three measured variables were thus defined:

- ✗ *Mean reaction time* (RT, in ms) between the target's appearance and the participant's answer,
- ✗ *Number of errors* (E) made by the participants (max = 32 for each condition),
- ✗ *Mean vehicle speed* (VS) recorded during each condition (in km/h).

2.3. Statistical Analysis

According to the distribution's normality of the defined variables, *t*-tests of Student or *U*-tests of Mann–Whitney were used. A significance threshold of 0.05 was accepted ($p < 5\%$).

3. Results

3.1. Neuropsychological evaluation of mental flexibility

The main results of the neuropsychological evaluation of mental flexibility (PMT) are given in Table 1. These results showed that AD patients are significantly impaired in the PMT. The mean comparison analysis of reaction times (RT) showed that there was a significant difference between AD patients' performances and older controls' performances, in both conditions, without mental flexibility demand (Plus-RT: $t(37) = 4.31$, $p < 0.001$; Minus-RT, $t(37) = 3.99$, $p < 0.001$) and with mental flexibility demand (Plus/minus-RT: $t(37) = 4.31$, $p < 0.001$). These results show that AD patients are significantly slower than older controls to make the test and the “shift cost” is significantly higher for AD patients compared to older controls (Shift cost, $t(37) = 4.75$, $p < 0.01$). The non-parametric analysis of errors also revealed a significant difference between AD patients and controls: AD patients made more errors than controls in the condition with flexibility demand (Plus/minus-errors, $U = 35.1$, $p < 0.001$).

Table 1
Performances of Alzheimer's disease patients (AD) and control group in the Plus–Minus Test (PMT).

	AD patients (n = 10) mean (SD)	Older controls (n = 29) mean (SD)	*p*
Plus–Minus Test			
Plus-RT (s)	81.10 (32.94)	48.59 (14.49)	<0.001
Plus-errors	1.40 (3.17)	0.24 (0.64)	n.s.
Minus-RT (s)	141.00 (61.24)	61.55 (24.22)	<0.001
Minus errors	1.50 (2.76)	1.41 (5.65)	n.s.
Plus/minus-RT (s)	138.80 (46.26)	73.45 (21.4)	<0.001
Plus/minus-errors	5.80 (6.03)	0.69 (1.49)	<0.001
Shift cost	27.75 (18.70)	18.37 (12.38)	<0.01

3.2. Evaluation of flexibility with the driving simulator

3.2.1. Analysis of the mean reaction times (RT)

To explore Alzheimer's disease-related modifications in flexibility, a two (Group: AD/Control) × two (condition: with and without mental flexibility) analysis with repeated measures analysis of variance (ANOVA) was carried out on the mean RT (Table 2).

This analysis yielded a global significant group effect [$F(1,37) = 87.04$, $p < 0.001$], showing that AD patients are slower than the older controls; a significant condition effect [$F(1,37) = 20.42$, $p < 0.001$], indicated further that participants were slower in the condition with mental flexibility. The analysis yielded a significant interaction between group and conditions [$F(1,37) = 4.93$, $p < 0.05$], demonstrating that AD patients were significatively more impaired than controls in the condition with mental flexibility. Moreover, the shift cost (calculated in the same way as for the PMT) is significantly higher for the AD patients than for the older controls (Shift-cost, $t(37) = 2.47$, $p < 0.05$).

3.2.2. Analysis of flexibility task: errors

In the conditions without mental flexibility, AD patients showed slower answers than healthy older controls. However, a non parametric test (Mann–Whitney) showed that in this simple condition, the number of errors was not significantly different between AD patients and controls [$U(10, 30) = 47.85$, $p > 0.05$]. On the other hand, in the condition requiring mental flexibility, the Mann–Whitney test indicated that AD patients made significantly more alternance errors than the healthy controls [$U(10,30) = 23.5$, $p < 0.001$].

3.2.3. Analysis of vehicle speed

Analysis of the vehicle's mean speed also gave interesting results. The two (Group: AD/control) × two (condition: with and without mental flexibility) repeated measures ANOVA yielded no global effect of condition [$F(1,37) = 0.178$, $p > 0.05$], which means that the

Table 2
Flexibility performances (mean RT) in the driving situation for the two experimental conditions in the AD patient and the older controls.

	AD patients (n = 10 Mean (SD)	Older controls (n = 29) Mean (SD)
Condition 1: without flexibility		
RT (ms)	4150.28 (942.33)	1651.09 (716.01)
Errors	1.55 (1.42)	0.00 (0.00)
VS (km/h)	100.15 (12.44)	104.99 (10.34)
Condition 2: with flexibility		
RT (ms)	4781.39 (1301.07)	1942.92 (781.88)
Errors	4.66 (3.81)	0.31 (0.66)
VS (km/h)	96.79 (7.16)	109.03 (12.34)
Shift cost	631.11 (567.93)	291.81 (326.87)

participants did not drive slower in the condition with mental flexibility. A significant effect of the group [F (1,37) = 23.60, p < 0.001], confirmed that AD patients drove slower (mean = 97.31, SD = 10.79) than older controls (mean = 107.01, SD = 11.31). The analysis also yielded a significant interaction between group and condition [F (1,37) = 7.88, p < 0.01], suggesting that the AD patients drove significantly more slowly than the controls in the condition with flexibility, whereas the older controls drove more quickly in this condition (Fig. 1).

In summary, both evaluations of flexibility indicate that this executive component is significantly impaired in AD. Moreover, both assessments of flexibility were significantly correlated (r = 0.409, p < 0.05).

4. Discussion–conclusion

The aim of the present study was to examine how the mental flexibility function can be impaired in the early stages of Alzheimer's disease (AD), and whether this impairment can evaluated in a driving context. This evaluation had been conducted with, on the one hand, a neuropsychological evaluation of the mental flexibility, and on the other hand, with an experiment evaluating flexibility in a driving simulator. The hypothesis that the impairment of mental flexibility could have consequences on the flexibility needed in a driving context was confirmed.

Mental flexibility impairment has previously been assessed in studies on executive dysfunction in AD [39,40]. The results presented here are consistent with these previous researches, and reveal a particular significant impairment of mental flexibility in AD, evaluated with the Plus–Minus Test (PMT). AD patients had significatively lower performances in this test concerning their reaction times (RT) and the number of errors. The difference between AD patients and controls was also more significant for the condition with shift (third list), which means that the AD patients are impaired in the flexibility needed to complete the test correctly. This is confirmed by the statistically significant difference between AD patients and controls in the number of errors. However, this impairment cannot be linked with impairments in speed of processing, as it has been previously stated [41], because of the significant higher level of perseverative errors made by the AD patients. Other studies had previously showed that the mental flexibility is impaired in the early stages of dementia [23,25]. However most of these studies did not study directly the mental flexibility; they used mental flexibility tests only in the aim of assessing executive functioning and the tests used were very complex for cognitively impaired participants [42]. Sorel and Pennequin [43], using the Plus–Minus test demonstrated that the mental flexibility is preserved in the "early" normal cognitive aging, but the performances of older old participants were impaired (after 75 years). It seems that the mental flexibility is an executive function that deteriorates slowly and that the impairments speed up with dementia.

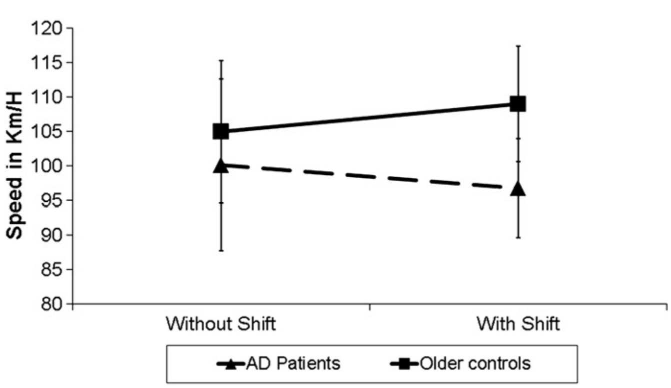

Fig. 1. Mean speed (in km/h) in the driving situation for the two experimental conditions in the AD patients and the older controls.

Concerning the simulator experiment, the three measured variables were concordant, showing that AD patients are impaired in their flexibility. Indeed, AD patients had significant lower RT in both conditions, without and with shift, and the repeated measures ANOVA showed that there was a significant interaction between the groups (AD patient versus controls) and the condition ("without" versus "with" flexibility). It was also interesting to observe that even in the condition without flexibility, the AD patients performed relatively slowly; their mean RT being more than two times slower than the controls' mean RT. Thus, even when the situation does not require mental flexibility, AD patients still need more time to react. This result is consistent with a neuropsychological result obtained with the same group of patients and controls, in a test assessing simple reaction times [44]. The participants were asked to react to the appearance of a stimulus as quickly as possible. No differences were found between young and older adults, and only a mild significant difference was found between older controls and AD patients (p = 0.04). This indicates that AD patients have slower reaction times on the whole. This time penalty was far more important in the driving simulator situation, and again more in the condition requiring mental flexibility, showing that the AD patients are not only impaired in their speed of processing, but also concerning their executive system that allows mental flexibility. This result was also supported by the significant difference observed on the test scores obtained by the participants. In the condition without flexibility, AD patients did not make more errors than the controls; while in the condition requiring mental flexibility, they made more perseverative errors (they forgot to alternate) than controls.

The results obtained concerning the driving speed in the condition of flexibility indicate that AD patients, because they needed more time to give their answer, developed a compensatory strategy by reducing their speed which allowed them to have more time to give their answer. The results revealed that the difference between AD patients and controls was small (and not significant) in the condition without flexibility ($\Delta = 6.39$ km/h), but larger (and significant) in the condition with flexibility ($\Delta = 12.99$ km/h). AD patients engaged an adaptive behavior in order to get more time to process the information. This phenomenon could be explained by the behavioral data from the video recording which showed that most of AD patients removed their foot from the accelerator at each traffic-sign to have time to give the answer. However, as the inertia of the driving simulator dynamic model was not exactly the same as in a real car, it has produced a limited difference in the mean speed recorded. It can be expected that this difference would have been greater in a real car. Moreover, correlations between neuropsychological evaluation and in-driving evaluation of flexibility support the hypothesis of the role of flexibility in the driving activity. Indeed, the more the mental flexibility performance is impaired in neuropsychological tests, the more it would be impaired in the driving activity, in real conditions. The consequences could, for example, present some difficulties in managing the situation in high traffic conditions, and in information processing, which results in difficulties choosing relevant cues in the driving scene.

Another important consequence of these difficulties for road safety could be an increase of the numbers of unexpected slowing potentially hazardous for other drivers in the traffic. Moreover, Uc, Rizzo, Anderson, Shi and Dawson [45] obtained similar results in a real driving situation. These results showed that, while doing a visual search task in the driving scene, early AD patients made more critical driving errors, like slowing and inappropriate braking, than the controls. The early detection of flexibility impairments, in normal aging or in mild cognitive impairment can be proposed as a good criterion in the assessment of fitness to drive framework. This is at least a relevant issue as it is estimated that around one third of drivers with dementia continue to drive after getting the diagnosis of dementia [18]. Some of the unsafe behaviors reported by Eby et al. [46] like impaired signaling, decrease comprehension of traffic could be linked with mental flexibility impairment. However, as observed in the current study, Eby et al. found in their naturalistic driving study that drivers with early dementia drove slower than the surrounding traffic. The question is to know if this compensatory strategy is consciously adopted or if it is a spontaneous behavior adopted to face the slowing of information processing and difficulties to shift attention. Such question should be investigated by empirical research in real driving situations as well as research in the area of driving assistance systems, which could also be an option to monitor driver activity and develop safe adaptive behaviors.

In conclusion, this paper addressed the important issue of how to assess executive dysfunction in a driving context. The mental flexibility was chosen in a context of driving simulation because it appears to be a relevant function for safe driving. The results lead us to address new research questions, specifically the links with fitness to drive and about the perspectives on real driving assessments and adaptations.

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