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# Saccadic Eye Movements and Attentional Control in Alzheimer's Disease

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**Abstract**

**Objective:** Several studies have demonstrated saccadic eye movement (SEM) abnormalities in Alzheimer's disease (AD) when patients performed prosaccade (PS) and antisaccade (AS) tasks. Some studies have also showed that SEM abnormalities were correlated with dementia rating tests such as the Mini Mental State Evaluation (MMSE). Therefore, it has been suggested that SEMs could provide useful information for diagnosis. However, little is known about predictive saccades (PreS)—saccades triggered before or very quickly after stimuli appearance—and their relationships with cognition in AD. Here, we aimed to examine the relationships between our usual dementia screening tests and SEM parameters in PS, AS, and also PreS task.
**Method:** We compared SEMs in 20 patients suffering from AD and in 35 healthy older adults (OA) in PS, AS, and PreS task. All participants also completed a neuropsychological evaluation.
**Results:** We showed that AD patients had higher latency and latency variability regardless the tasks, and also higher AS cost, in comparison with OA. Moreover, AD patients made more uncorrected AS and took more time-to-correct incorrect AS. In PreS task, AD patients showed higher gain and gain variability than OA when they made anticipated saccades. Close relationships were found between the majority of SEM variables in PS, AS, and PreS tasks and dementia screening tests, especially the MMSE and episodic memory measures.
**Conclusion:** Our findings, in agreement with previous studies, demonstrated that AD affects several SEM parameters. SEM abnormalities may reflect selective and executive-attention impairments in AD.

*Keywords:* Dementia; Attention; Executive functions

## Introduction

Recent literature reviews have outlined robust findings demonstrating saccadic eye movement (SEM) abnormalities in Alzheimer's disease (AD) (Kaufman, Pratt, Levine, & Black, 2010; Molitor, Ko, & Ally, 2015; Pereira, Camargo, Aprahamian, & Forlenza, 2014). Most of these findings are relative to well-known prosaccade (PS) and antisaccade (AS) tasks. These tasks are particularly popular because of their simplicity for the participants and their potential measures of cognitive capacities. Indeed, instructions are easily understood by participants: the latter are typically instructed to first fix their gaze on a central dot. Then, they have to stare as quickly as possible at a target dot appearing at the periphery of the central dot (PS task), or to direct their gaze to the direction opposite to the target dot location (AS task). Applied to AD study, SEM tasks can provide useful tools in the evaluation of cognitive impairments and in the diagnosis of AD especially at an early stage. In this paper, we propose to test the capacity of SEM tasks to discriminate AD patients from healthy older adults (OA). More particularly, we measured several SEM parameters in order to examine the impact of AD on each of them and their


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relationships with several neuropsychological tests, routinely used in our hospital center as parts of a practical test battery for screening dementias (Ferreira et al., 2010; Galmiche et al., 2005).

Triggering (or not) a saccade involves a time-dependant decisional process (Carpenter, 1981; Hutton, 2008). This decisional process has typically been measured through saccade latency (i.e., the time between target and saccade onsets). Importantly, previous studies have demonstrated that SEM latency can be associated with cognitive processes (Hutton, 2008). For instance, the time needed to trigger a PS can depend on attentional process in PS task (Clark, 1999; Pratt, Lajonchere, & Abrams, 2006). We have recently shown that information processing speed is involved in saccade latency as well as in the ability to trigger a correct or corrected AS, and that AS task especially involves executive-attention (Noiret, Vigneron, Diogo, Vandel, & Laurent, 2016). AS task requires participants to remember instructions in order to inhibit the visually guided exogenous saccade toward the target, and to trigger a saccade in the direction opposite to the target (Munoz & Everling, 2004). Executive-attention allows maintaining task goals and managing the potential conflict between two competitive responses when usual responses can compete with unusual responses relevant for the goals of the current task (Engle & Kane, 2004, Cohen, 2014). Therefore, executive-attention likely plays a key role in AS performances. Additionally, one of the characteristics of saccade latency is its wide variability (Sumner, 2011). Although the wide latency distribution has no consensual explanation, Kapoula and colleagues (2010) have suggested, based on their own work and previous studies, that latency variability would be a good index of attentional fluctuation when participants perform SEM tasks. Indeed, patients suffering from dementia with Lewy body (a disease leading to attentional fluctuation) had higher latency variability than aged controls (Kapoula et al., 2010). Moreover, Mostofsky, Lasker, Singer, Denckla, and Zee (2001) showed that latency variability in PS was greater in boys with Tourette syndrome (TS) associated with attention-deficit hyperactivity disorder (ADHD) than in boys with TS without ADHD or in controls.

Several studies on AD demonstrated that AD patients showed increased latency associated with greater latency variability in comparison to healthy OA, regardless the SEM tasks performed (Boxer et al., 2006; Bylsma et al., 1995; Crawford et al., 2005, 2013; Fletcher & Sharpe, 1986; Garbutt et al., 2008; Hershey et al., 1983; Pirozzolo & Hansch, 1981; Shafiq-Antonacci, Maruff, Masters, & Currie, 2003; Yang, Wang, Su, Xiao, & Kapoula, 2013). Alzheimer's disease patients also showed more incorrect AS (i.e., saccade triggering toward the target) and fewer corrected AS (i.e., saccade redirecting toward the opposite target location after triggering incorrect AS) (Boxer et al., 2006, 2012; Crawford et al., 2005, 2013; Garbutt et al., 2008; Heuer et al., 2013; Kaufman, Pratt, Levine, & Black, 2012; Shafiq-Antonacci, et al., 2003). The time needed to correct AS errors was also higher in AD patients than in healthy controls (Crawford et al., 2005, 2013).

These results are compatible with others which have demonstrated the role of the parietal and frontal cortex in the PS performances as well as in the visual attention processes (Clark, Squire, Merrikhi, & Noudoost, 2015; Domagalik, Beldzik, Fafrowicz, Oginska, & Marek, 2012; Pierrot-Deseilligny, Milea, & Müri, 2004) which are affected by AD (Levinoff, Li, Murtha, & Chertkow, 2004; Parasuraman, Greenwood, Haxby, & Grady, 1992). The ability to inhibit and maintain task goal in AS task is associated with the dorsolateral prefrontal cortex (DLPFC, Domagalik et al., 2012; Munoz & Everling, 2004; Pierrot-Deseilligny et al., 2004) which is itself associated with working memory and executive-attention functioning (Crawford et al., 2013; Cohen, 2014), also impaired in AD (Belleville, Peretz, & Malenfant, 1996; Stopford, Thompson, Neary, Richardson, & Snowden, 2012). Moreover, several studies have found relationships between SEM and neuropsychological test scores such as the Mini Mental State Evaluation (MMSE; Folstein, Folstein, & McHugh, 1975) in both PS and AS tasks, as well as between SEM and inhibition and working memory tests in AS task (Bylsma et al., 1995; Crawford et al., 2005, 2013; Fletcher & Sharpe, 1986; Heuer et al., 2013; Yang et al., 2013).

In addition to PS and AS tasks, the predictive saccade (PreS) task has been developed to capture other cognitive processes. The PreS task is as simple as the PS task, but less employed than PS in AD patients. In the PreS task, participants are instructed to first fix their gaze on a central dot. They have to stare as quickly as possible at two similar target dots appearing alternatively between two spatial locations with a fixed temporal frequency. Although instruction typically asks participants to engage their gaze on the target when it appears, participants often anticipate the onset of the target and therefore initiate saccades before the second target appearance. These PreS can be measured by the number of saccade triggering before, or very shortly after the target onset, and they found to be more hypometric than non-PreS (Bronstein & Kennard, 1987).

This anticipation of target onset leads to the general assumption that saccades in PreS task are not visually but rather internally guided (Hutton, 2008). By using functional magnetic resonance imaging, Simo, Krisky, and Sweeney (2005) demonstrated that anticipatory behavior in PreS task is supported by a memory-guided system, which involves "executive prefrontal centre" and "spatial memory-related circuits". These authors argued that process switches from a first sensory-guided system to a memory-guided system. Other authors have also argued that top-down cognitive process such as working memory system would be involved in target anticipation (Hutton et al., 2001) in order to keep in mind the alternation characteristic of trials, the spatial location and the temporal frequency of the target dot.

As regards AD patients, Shafiq-Antonacci et al. (2003) carried out experiment using PreS task and they did not find any significant difference between AD and controls concerning saccade anticipation or accuracy (i.e., comparison between the

saccade amplitude and the target eccentricity). Explanations could be that, despite executive and memory process impairments, in this simple PreS task, the switching behavior from sensory- to memory-guided system is still operational in AD patients. This may explain why there were similar anticipated saccades in AD patients and controls. The same assumption may explain the similar saccade accuracy in AD patients and controls. However, concerning the latter measure, one possible limit is that anticipated and non-anticipated saccades were gathered together to compute saccade accuracy measure in Shafiq-Antonacci et al. (2003) study. As already mentioned, anticipated saccades have not the same accuracy than non-anticipated saccades in general population—probably because the former are underlain by working memory whereas the latter are triggered when the dot are present on the screen. Measuring the saccade accuracy without distinguishing between anticipated and non-anticipated saccades would lead to hide potential saccade accuracy reduction in AD patients. Therefore, it is possible that anticipated saccades are less accurate than non-anticipated saccades in AD patients in that working memory process is impaired.

Overall, by carrying out PS, AS and PreS tasks on AD patients and healthy control participants, we expected to clarify which cognitive-related SEM parameters are specifically altered in AD and also found relationships between these parameters and neuropsychological tests performed by all participants. Based on previous findings described above, we hypothesized that attentional process impairments in AD patients should lead to increase latency in all the three tasks in comparison with control participants. Greater latency variability should also reflect higher attentional fluctuation in AD patients. Moreover, AS cost (i.e., the difference between correct AS and PS latencies) should be higher in AD than in control participants, reflecting difficulty to inhibit attentional capture of the target dot and triggering saccade in the opposite direction. The ability to maintain the goal of the task, inhibit saccade triggering toward the target and also rapidly correct a saccade triggered toward the target requires efficient executive-attention system in working memory. As AD leads to working memory impairment, we expected that AD patients would make fewer correct AS than controls. For the same raisons, patients should have more difficulty to correct incorrect AS, which should be reflected in fewer corrected AS and also longer correction time when incorrect AS are corrected.

As regards PreS task, although we predicted no difference between AD patients and control participants concerning the number of anticipated saccades, we hypothesized that AD patients should be less accurate than controls when they anticipate the target dot. According to previous literature cited above, we suggested that AD would not cancel the switching from exogenously sensory-guided system to endogenously memory-guided system but that AD would decrease the capacity to keep efficient target dot representation in working memory and therefore decrease the saccade accuracy when saccades are anticipated.

Finally, we expected that SEM parameters and neuropsychological tests used to detect dementia would show close relationships. More particularly, we hypothesized that tests reflecting dementia impairments such as the MMSE, the Memory Impairment Screen (MIS: Buschke, et al., 1999) and the Free and Cueing Selective Recall Test (FCSRT: Grober, Buschke, Crystal, Bang, & Dresner, 1988; Van der Linden et al., 2004) would be correlated with SEM parameters. Other tests such as the Trail Making Test part A (TMTA: Bowie & Harvey, 2006; Reitan, 1958) and the Crossing Off Test (COT: Goldman, Baty, Buckles, Sahrmann, & Morris, 1999) that give information about information processing time, should be positively (TMTA) and negatively (COT) correlated with SEM latency. The Trail Making Test part B (TMTB: Bowie & Harvey, 2006; Reitan, 1958) and the Isaac Set Test (IST: Isaacs & Kennie, 1973) that served as measures of executive function efficiency, should be positively (TMTB) and negatively (IST) correlated with the time-to-correct incorrect AS and with the proportion of corrected AS.

## Materials and Methods

### *Participants*

Forty participants aged over 65 years were included in the study. Twenty inpatients (11 females, age: 69–86 years, $M = 79$ years, $SD = 5.93$) with the diagnosis of probable AD, according to the recommendations from the National Institute on Aging and the Alzheimer's Association (NINDS-ADRDA, McKhann et al., 2011), were recruited in the psychiatry unit of University Hospital and in a healthcare and rehabilitation center in Besançon, France. Diagnosis of AD—as well as exclusion of patients suffering from other dementia—were done by a psychiatrist using systematic clinical interviews as well as medical files, previous neuropsychological interviews and brain imaging analyses when available. Mini Mental State Evaluation was used as a screening measure to determine the severity of AD. Patients had to have a MMSE score > 18 in order to exclude moderate to severe AD. During the study, patients were taking psychotropic medications (anxiolytics $N = 4$; antidepressants $N = 4$; antipsychotics $N = 5$; anticholinesterases $N = 6$).

The control group consisted of 20 healthy volunteers (11 females, age: 68–79 years, $M = 71$ years, $SD = 3.71$) recruited from relatives of members of the research department and through advertisements in an extended learning program in the university. These participants had to have no cognitive alterations. None of the control participants were taking psychotropic medications.

Patients and controls did not present ophthalmological or other neuropsychiatric disorders. None of them did have major depressive disorder. All had a Montgomery and Asberg Depression Rating Scale (MADRS: Montgomery & Asberg, 1979) score < 25. They had normal or corrected-to-normal vision. The study was approved by the local ethics committee for the protection of individuals ("Comité de protection des personnes Est 2"). All participants gave their written informed consent prior to inclusion in the study.

### *Complementary neuropsychological and psychiatric measures*

In order to consolidate initial clinical diagnosis, complementary tests were performed.

The MADRS as well as the Beck Depression Inventory II (BDI-II: Beck, Steer, & Brown, 1996) were used as depression measures for our study. The former consisted of 10 items that allow assessing the presence of depressive symptoms and the latter consisted of 21 items measuring the presence and severity of cognitive, affective, motivational, and physiological symptoms of depression.

The neuropsychological evaluation consisted of eight tests. These tests were part of the neuropsychological test battery of the regional network for diagnostic aid and management of patients with cognitive impairment in the Franche-Comté, France, geographical area (RAPID battery), which includes neuropsychological tests calibrated on the same participant sample (Ferreira et al., 2010). These tests included "verbal episodic memory": the MIS, the FCSRT; "language": a picture naming test with 30 items (PN30: Galmiche et al., 2005); "information processing speed": the TMTA, the COT; "executive functions and attention": the Isaacs set test (IST), the TMTB; and "visual-perceptive abilities": a test of coping geometric figures as part of the BEC96 (Signoret et al., 1998). All means and statistical analyses are shown in Table 1.

### *Apparatus*

Participant's eye movements were recorded with a chinrest eye-tracking system (ASL EYE-TRACK®6; Applied Science Laboratories; Bedford, MA) with a sampling rate of 120 Hz and a gaze position accuracy of 0.5° of visual angle. When the participant's right eye was correctly detected by the eye-tracking system, a nine-point calibration was started. Once the calibration was successfully completed, the tasks began. Stimuli were presented using "Inquisit 3.0.6.0" computer software (Millisecond Software; Seattle, WA), on an "Intel Pentium Dual Core 2.50 GHz" desktop computer, and were projected on a 19-inch monitor, with a resolution of 1,280 × 1,024 pixels and a screen refresh rate of 60 Hz.

**Table 1.** Mean (standard deviation) and statistical tests for neuropsychological data as a function of groups

| | Controls | Patients | *F* | *U* | *p* | Cohen's *d* |
|---|---|---|---|---|---|---|
| Age | 71.75 (3.71) | 79 (5,93) | | 51.50 | <.001 | 1.53 |
| Sex F/M | 11/9 | 11/9 | | | | |
| Education | 10.55 (3.02) | 8.6 (2,62) | 38.02 | | =0.03 | 0.69 |
| Psychiatric scales | | | | | | |
| MADRS | 2.05 (2.14) | 6.07 (4,10) | | 58.00 | =0.004 | 1.23 |
| BDI-II | 5.60 (3.87) | 5.31 (4,68) | 0.04 | | =0.85 | 0.07 |
| Neuropsychological measures | | | | | | |
| MMSE | 28.80 (1.32) | 21.68 (3,51) | | 9.00 | <.001 | 2.69 |
| MIS 2 min | 7.60 (0.68) | 3.72 (1,99) | | 21.00 | <.001 | 2.61 |
| MIS 10 min | 7.85 (0.37) | 2.89 (2,83) | | 14.5 | <.001 | 2.46 |
| IST | 42.80 (7.67) | 26.74 (8,33) | 41.39 | | <0.001 | 2.01 |
| Clock test | 1.90 (0.31) | 1.42 (0,77) | | 137.00 | =0.09 | 0.82 |
| FCSRT IR | 15.25 (1.07) | 12.09 (2,89) | | 34.00 | <.001 | 1.45 |
| FCSRT FR | 26.30 (5.31) | 9.93 (8,98) | 48.59 | | <0.001 | 2.22 |
| FCSRT TR | 45.20 (3.30) | 29.40 (11,78) | | 19.50 | <.001 | 1.83 |
| COT | 210.90 (43.99) | 161.95 (43,82) | 12.76 | | <0.001 | 1.11 |
| TMTA | 32.95 (10.18) | 59.67 (21,05) | | 76.00 | <.001 | 1.62 |
| TMTB | 115.80 (54.08) | 196.86 (78,50) | 13.70 | | <0.001 | 1.20 |
| Coping figure | 5.95 (0.22) | 5.26 (1,33) | | 128.50 | =0.01 | 0.72 |
| PN30 | 29.75 (0.55) | 28.31 (2,45) | | 104.50 | =0.01 | 0.81 |

*Notes:* BDI-II, Beck Depression Inventory II; COT, Crossing Off Test; FCSRT, Free and Cueing Selective Reminding Test; IR, Immediate Recall; FR, Free Recall; TR, Total Recall; IST, Isaac Set Test; MADRS, Montgomery and Asperg Depression Rating Scale; MIS, Memory Impairment Screen; MMSE, Mini Mental State Evaluation; PN30, Picture Naming 30 items; TMT, Trail Making Test. Values for the ANOVA *F*-tests are indicated in the *F* column. If the data did not comply with the ANOVA parameters (heterogeneity and normality), we use Mann–Withney *U*-tests as non-parametric statistical test (*U* column).

*Eye movement paradigms*

*PS task.* Each trial started with a central fixation-point (0.5° of visual angle) on a gray background (RGB: 128, 128, 128). After 2,000 ms a red target-point (0.5° of visual angle) appeared for 2,000 ms. The target-point was displayed with a central dot eccentricity of ±4°, ±6°, ±8°, or ±10° of visual angle in the horizontal or the vertical plane. The target-point offset was followed by an inter-trial of 2,000 ms. Then a new central fixation-point appeared to signal the start of the next trial. Participants were instructed to keep their gaze on the central fixation-point until the peripheral target-point appeared. At this time, they had to look at the target-point as accurately and quickly as possible.

*AS task.* The task was similar to the PS task except for the instructions given to the participants. Participants were similarly instructed to keep their gaze on the central fixation-point until the peripheral target-point appeared. However, after the onset of the target-point, they had to direct their gaze in the opposite direction to the target-point as quickly and accurately as possible.

*PreS task.* Each trial started with a central fixation-point (0.5° of visual angle). After 2,000 ms a red target-point (0.5° of visual angle), namely "Dot1" appeared at ±4°, ±6°, ±8°, or ±10° of visual angle in the horizontal or the vertical plane. This target-point disappeared after 1,000 ms and was suddenly followed by a second target-point, namely "Dot2", which appeared for 1,000 ms at the exact central fixation-point symmetry of the dot1 in the horizontal or the vertical plane. Participants were required to keep their gaze on the central fixation-point until the peripheral target-point appeared. At this time, they had to keep watching the target points as accurately and quickly as possible.

*Procedure*

The experiment was divided into two sessions for each participant. In one session, participants took the neuropsychiatric interview by a trained psychiatrist and neuropsychological assessment by a trained neuropsychologist for about 2 h and within a month before the SEM tasks. In the other session, participants performed the SEM tasks for about 45 min.

On the day of the SEM task session, participant was seated in a quiet room, 60 cm in front of the screen. Each participant performed the three tasks. There were 64 trials in each task, for a total of 192 trials, with a 10-min break between the tasks to avoid fatigue. Before each task, a new calibration was started and instructions were given to participants, both via the computer monitor and verbally by the experimenter. Then, four practice trials were performed to ensure that participants understood the upcoming task.

*Data analysis*

Saccade onset and offset were defined by a fixed velocity threshold of 30°/s (Crawford et al., 2005, 2013). The direction of a saccade was identified by the eye position difference between the start and the end of the saccade. Trials were excluded when the eye tracker failed to record the eye coordinates (e.g., eye blink, loss of pupil, or corneal reflection). Correct saccades were defined as saccades directed toward the target in PS and PreS tasks and in the opposite direction in AS tasks. Saccades directed toward the target in AS task were defined as incorrect AS. If there was a subsequent saccade in the opposite direction, AS error was categorized as corrected AS error. If the saccade was not corrected, incorrect AS was categorized as uncorrected AS. Saccades directed toward the target dot2 before or <100 ms after its appearance were defined as anticipatory saccades in PreS task.

On the basis of these categorizations, we derived the following saccade parameters (Fig. 1): the latency and latency standard deviation (SD) of saccades in a PS task, of correct AS and incorrect AS in AS task, and of saccades for dot1 and saccades for dot2 in PreS task. We also measured the proportion (i.e., percentage of the total number of saccades) of correct AS and corrected among incorrect AS in AS task, and the proportion of anticipatory saccades in PreS task. The time-to-correct AS errors in AS task and the anticipation time (i.e., the time between the anticipatory saccade onset and the dot2 onset) in PreS task were also computed. The gain (i.e., the ratio between saccade amplitude and dot2 eccentricity) was also calculated for anticipated and non-anticipated saccades in PreS task. Finally, the difference between correct AS latency and PS latency was calculated to obtain the AS cost.

Preliminary statistical analyses showed that, whatever the dependent variables, the group effects did not depend on eccentricity (all $F < 1.70$, all $p > .17$) or direction (all $F < 3.49$, all $p > .07$). These results allowed us to collapse the data across eccentricity and direction conditions to simplify statistical analyses and obtain the statistical plan described below. In the first

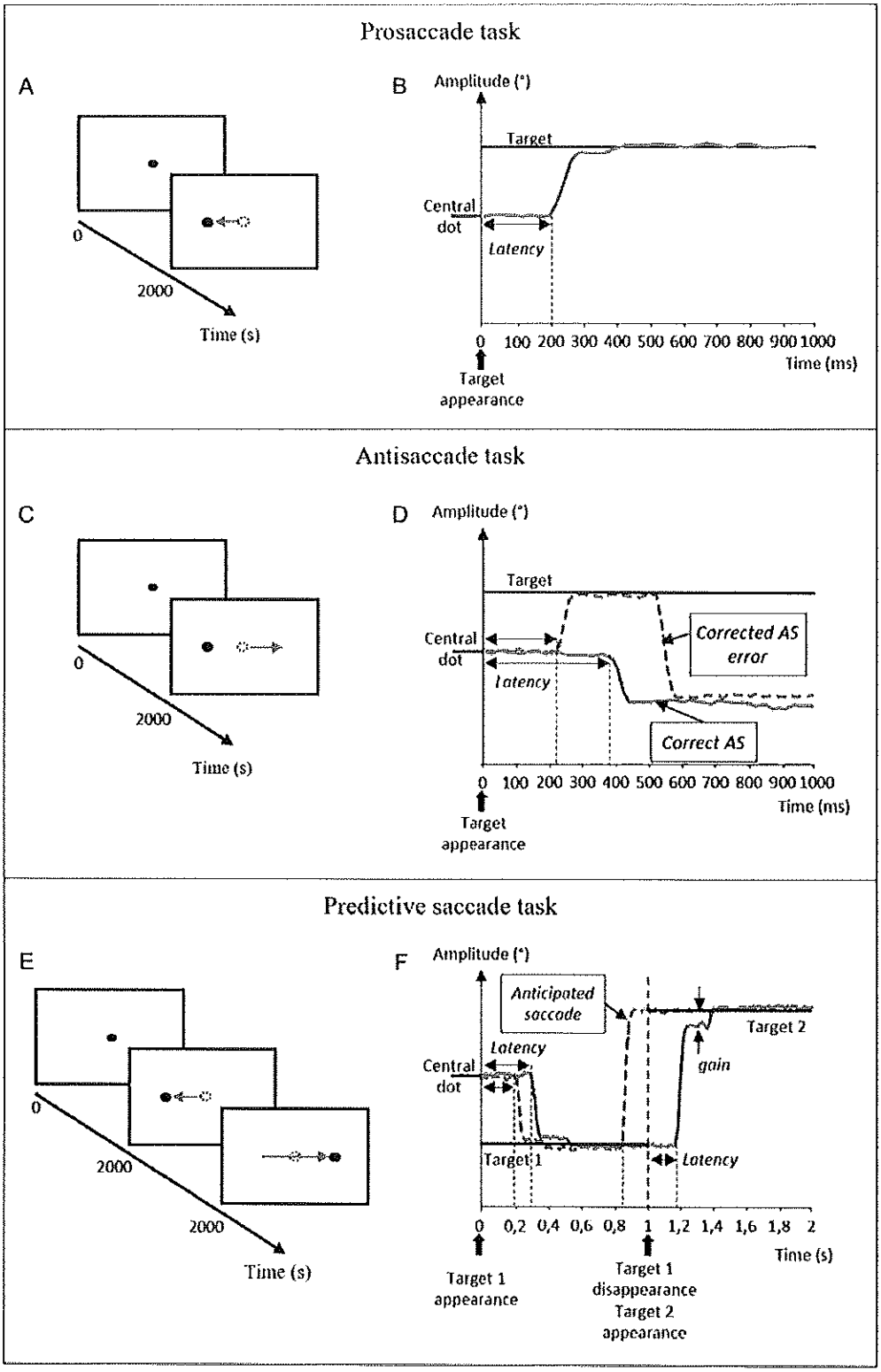


**Fig. 1.** Illustration of one trial in the prosaccade (PS) task (A), the antisaccade (AS) task (C), and the predictive saccade (PreS) task (E). Saccadic dynamics as a function of time in PS task (B), AS task (D), and PreS task (F).

step, these parameters were analyzed using analyses of variance (ANOVA) with group (patients vs. controls) as a between-subjects factor. When the distributions were not normal and/or the variances not homogeneous, we used non-parametric Mann–Whitney test. As illustrated in Table 1, patients had different age, education and scores in comparison with controls. In order to take into account the possible covariations, we carried out Pearson's r correlations analyses and parametric or non-parametric analyses of covariance (ANCOVA) with each potential covariate such as age, education and each neuropsychological test or psychiatric scale for which group difference was found.

## Results

### *PS task*

Patients had longer latency ($F[1, 38] = 4.28$, $p = .04$) greater latency variability ($F[1, 38] = 34.03$, $p < .001$) than controls (Table 2). Latency was not correlated with any neuropsychological or psychiatric scale scores. Latency variability was correlated with age and scores of MADRS, MMSE, MIS, IST, FCSRT, COT, and TMTA and B (Table 3).

When we ran ANCOVA with the MMSE, the MIS, the FCSRT, the TMTA or B, or the IST as covariates, latency difference between patients and controls was not statistically significant ($p_s > .11$). As regards latency variability, difference between patients and controls was not statistically significant when the MMSE, MIS, and TMTB were used as covariates ($p > .06$). The other scores used as covariates did not change statistical difference for latency variability ($p_s < .05$).

### *AS task*

Correct AS latency was higher ($F[1, 38] = 22.98$, $p < .001$) in patients than in controls whereas incorrect AS latency was not statistically different between the two groups ($F[1, 38] = 0.003$, $p = .95$). Latency variability was higher in patients than in controls for correct AS ($U = 76.00$, $p < .001$) but not for incorrect AS ($F[1, 38] = 1.90$, $p = .18$). The AS cost was also higher in patients than in controls ($U = 73.00$, $p < .001$). As regards the proportions of correct and incorrect AS, patients made fewer correct AS than controls ($F[1, 38] = 13.07$, $p < .001$). The proportion of corrected AS was also lower in patients

**Table 2.** Means (M), standard deviations (SDs), and confidence intervalles ([±95% CI]) of saccadic eye movement (SEM) variables in prosaccade (PS), antisaccade (AS), and predictive saccade (PreS) task as a function of groups

| SEM variables | Controls | | Patients | | Cohen's *d* |
|---|---|---|---|---|---|
| | *M* (SD) | [±95% CI] | *M* (SD) | [±95% CI] | |
| PS task | | | | | |
| PS latency* | 240.15 (25.07) | [228.84, 251.89] | 258.55 (30.90) | [244.09, 273.02] | 0.65 |
| PS latency SD*** | 44.67 (9.99) | [39.99, 49.34] | 70.21 (16.84) | [62.33, 78.10] | 1.84 |
| AS task | | | | | |
| Correct AS latency*** | 372.22 (45.16) | [351.08, 393.35] | 473.55 (83.06) | [434.68, 512.42] | 1.52 |
| Correct AS latency SD*** | 79.64 (27.60) | [66.73, 92.56] | 164.81 (117.99) | [109.59, 220.03] | 0.99 |
| Incorrect AS latency | 240.74 (37.39) | [223.25, 258.24] | 241.52 (45.60) | [220.18, 262.87] | 0.02 |
| Incorrect AS latency SD | 52.73 (22.25) | [42.32, 63.15] | 64.90 (32.59) | [49.65, 80.16] | 0.44 |
| Proportion of correct AS*** | 56.09 (28.95) | [42.55, 69.64] | 26.39 (22.63) | [15.80, 36.98] | 1.14 |
| Proportion of corrected AS*** | 97.01 (5.36) | [94.50, 99.52] | 72.17 (32.83) | [56.80, 87.53] | 1.06 |
| Time-to-correct AS*** | 255.98 (10.50) | [206.82, 305.14] | 501.32 (226.90) | [395.12, 607.51] | 1.53 |
| AS cost*** | 133.32 (55.02) | [107.57, 159.08] | 247.71 (186.37) | [156.49, 330.94] | 0.83 |
| PreS task | | | | | |
| Latency dot1* | 235.07 (26.34) | [222.74, 247.39] | 258.84 (38.26) | [240.93, 276.75] | 0.72 |
| Latency SD dot1*** | 42.19 (14.55) | [35.38, 49.00] | 67.49 (25.97) | [55.34, 79.65] | 1.20 |
| Non-anticipated latency dot2** | 231.14 (32.54) | [215.91, 246.37] | 267.75 (41.88) | [248.15, 287.36] | 0.98 |
| Non-anticipated latency SD dot2*** | 49.48 (13.12) | [43.35, 55.62] | 91.58 (35.41) | [75.01, 108.15] | 1.58 |
| Proportion of anticipated saccades | 18.35 (16.06) | [10.83, 25.87] | 19.34 (12.76) | [13.35, 25.31] | 0.07 |
| Anticipated latency dot2 | −101.93 (88.57) | [−143.38, −60.47] | −94.75 (82.68) | [−133.44, −56.05] | 0.08 |
| Anticipated latency SD dot2 | 130.73 (56.08) | [104.49, 156.98] | 138.44 (73.71) | [103.94, 172.94] | 0.12 |
| Non-anticipated saccade gain | 0.76 (0.08) | [0.72, 0.80] | 0.80 (0.08) | [0.74, 0.84] | 0.50 |
| Non-anticipated saccade gain SD | 0.26 (0.09) | [0.22, 0.30] | 0.28 (0.08) | [0.24, 0.32] | 0.23 |
| Anticipated saccade gain* | 0.67 (0.08) | [0.68, 0.63] | 0.74 (0.10) | [0.70, 0.78] | 0.77 |
| Anticipated saccade gain SD*** | 0.17 (0.05) | [0.15, 0.19] | 0.30 (0.11) | [0.25, 0.35] | 1.52 |

*Notes:* Statistically significant differences between controls and patients: *$p < .05$, **$p < .01$, ***$p < .001$.

**Table 3.** Correlations between saccadic eye movements (SEMs) in prosaccade (PS) task, age, education, MADRS, and neuropsychological tests

| | PS latency | PS latency SD |
|---|---|---|
| Age | 0.02 | 0.40** |
| Education | −0.01 | −0.12 |
| MADRS | 0.13 | 0.54*** |
| MMSE[a,b] | −0.22 | −0.68*** |
| MIS 2 min[a,b] | −0.24 | −0.61*** |
| MIS 10 min[a,b] | −0.28 | −0.52*** |
| IST[a] | −0.20 | −0.51*** |
| FCSRT IR[a] | −0.13 | −0.45** |
| FCSRT FR[a] | −0.28 | −0.61*** |
| FCSRT TR[a] | −0.18 | −0.53*** |
| COT | −0.07 | −0.41** |
| TMTA[a] | 0.10 | 0.44** |
| TMTB[a,b] | 0.18 | 0.54*** |
| Coping figure | 0.03 | −0.26 |
| PN30 | −0.12 | −0.21 |

*Notes:* COT, Crossing Off Test; FCSRT, Free and Cueing Selective Reminding Test; IR, Immediate Recall; FR, Free Recall; TR, Total Recall; IST, Isaac Set Test; MADRS, Montgomery and Asperg Depression Rating Scale; MIS, Memory Impairment Screen; MMSE, Mini Mental State Evaluation; PN30, Picture Naming 30 items; TMT, Trail Making Test; SD, Standard deviation. Statistically significant correlation: $^{**}p < .01$, $^{***}p < .001$.

[a]Exponents represent the significant effect of the covariant when ANCOVAs were computed on the PS latency.

[b]Exponents represent the significant effect of the covariant when ANCOVAs were computed on the PS latency SD.

than controls ($U = 79.50$, $p = .001$) and, therefore, patients had more uncorrected AS than controls. When they were able to correct incorrected AS, patients took more time than controls to correct incorrect AS ($U = 50.00$, $p < .001$) (Table 2).

Correct AS latency as well as correct AS latency variability were correlated with all scores except education, FCSRT, the coping figure test, PN30, and MADRS for correct AS latency variability (Table 4). Incorrect AS latency was not correlated with any scores whereas incorrect AS latency variability was correlated with MADRS, TMTA, and PN30. The proportion of correct AS as well as the proportion of corrected AS were correlated with age, MMSE, MADRS, MIS, IST, FCSRT, TMTB, and COT. The proportion of correct AS was also negatively correlated with TMTA and the proportion of corrected AS was also positively correlated with the coping figure test. The time-to-correct AS errors as well as the AS cost were correlated with all scores, except level of education and PN30 for the former, and age and level of education for the latter.

When we ran ANCOVA with MMSE, MIS, the free or the total recalls of FCSRT as covariates, correct AS latency difference between patients and controls was not statistically significant ($p_s > .07$). As regards correct AS latency variability, ANCOVA with MMSE, MIS, IST, FCSRT, COT, and TMTA and B as covariates, group difference was not statistically significant ($p_s > .08$). Age, education, MADRS, and the other neuropsychological scores as covariates did not change statistical difference for latency ($p_s < .04$) and latency variability ($p_s < .03$). Incorrect AS latency as well as incorrect AS latency SD remained statistically similar between the two groups when we ran the ANCOVA adjusting dependent variable means for differences in age, education, MADRS, or neuropsychological scores ($p_s > .10$).

ANCOVA with MMSE, IST, MIS, FCSRT, or TMTA and B as covariates did not reach statistical significance for the proportion of correct AS ($p_s > .11$). Using age, MADRS, or the other neuropsychological scores as covariates did not change previous results ($p_s < .05$). The proportion of corrected AS errors was not different between the two groups when we ran ANCOVA with age, MMSE, MIS, FCSRT, COT, or TMTA or B as covariates ($p_s > .06$). Using MADRS or the other neuropsychological scores as covariates did not change previous results ($p_s < .05$).

Differences for the time-to-correct AS errors was not statistically significant when ANCOVA was computed with MMSE, MIS, the immediate and free recall of FCSRT or TMTA and B ($p_s > .17$). Finally, when we ran ANCOVA with MMSE, MIS, STI, FCSRT, or TMTA as covariates, AS cost difference between patients and controls was not statistically significant ($p_s > .09$). ANCOVA with age, MADRS, or the other scores as covariates did not change previous results on the time-to-correct AS errors ($p_s < .04$) and on AS cost ($p_s < .05$).

### *PreS task*

Patients had higher latency than controls for dot1 ($F[1, 38] = 5.28$, $p = .03$) as well as for dot2 when saccades were not anticipated ($F[1, 38] = 9.53$, $p = .004$). Latency variability was also greater in patients than in controls for dot1 ($F[1, 38] = 14.44$, $p < .001$) and dot2 ($U = 38.00$, $p < .001$). The proportion of anticipated saccades did not statistically differ between

Table 4. Correlations between saccadic eye movements (SEMs) in antisaccade (AS) task, age, education, MADRS, and neuropsychological test

| | Correct AS latency | Correct AS latency SD | Incorrect AS latency | Incorrect AS latency SD | Proportion of correct AS | Proportion of corrected AS | Time-to-correct AS | AS cost |
|---|---|---|---|---|---|---|---|---|
| Age[f] | 0.57*** | 0.32* | −0.03 | 0.06 | −0.39* | −0.38* | 0.34* | 0.26 |
| Education | −0.31* | −0.28 | 0.10 | −0.06 | 0.18 | 0.10 | −0.19 | 0.19 |
| MADRS | 0.42** | 0.22 | −0.05 | 0.35* | −0.45** | −0.36* | 0.50** | 0.48** |
| MMSE[a,b,e,f,g,h] | −0.64*** | −0.44** | 0.02 | −0.17 | 0.52*** | 0.35* | −0.50*** | −0.61*** |
| MIS 2 min[a,b,e,f,g,h] | −0.55*** | −0.42** | 0.01 | −0.13 | 0.60*** | 0.38* | −0.59*** | −0.46** |
| MIS 10 min[a,b,e,f,g,h] | −0.59*** | −0.58*** | 0.01 | −0.10 | 0.49** | 0.35* | −0.57*** | −0.43** |
| IST[b,e,h] | −0.55*** | −0.46** | 0.05 | −0.14 | 0.61*** | 0.32* | −0.53*** | −0.59*** |
| FCSRT IR[b,e,f,g,h] | −0.51** | −0.27 | 0.01 | −0.16 | 0.47** | 0.38* | −0.56*** | −0.54*** |
| FCSRT FR[a,b,e,f,g,h] | −0.63*** | −0.44** | −0.02 | −0.17 | 0.61*** | 0.52*** | −0.64*** | −0.41* |
| FCSRT TR[a,b,e,f] | −0.52** | −0.38* | 0.10 | −0.15 | 0.49** | 0.49*** | −0.58*** | −0.47** |
| COT[b,e,f] | −0.47** | −0.30* | −0.03 | −0.12 | 0.56*** | 0.30* | −0.43** | −0.57*** |
| TMTA[b,e,f,g,h] | 0.57*** | 0.31* | 0.03 | 0.33* | −0.48** | −0.25 | 0.40* | 0.45** |
| TMTB[b,e,f,g] | 0.45** | 0.32* | 0.01 | 0.26 | −0.58*** | −0.32* | 0.51** | 0.39* |
| Coping figure | −0.26 | −0.06 | −0.03 | −0.08 | 0.19 | 0.32* | −0.33* | −0.62*** |
| PN30 | −0.32* | −0.23 | −0.04 | −0.35* | 0.12 | 0.09 | −0.29 | −0.36* |

*Notes:* COT, Crossing Off Test; FCSRT, Free and Cueing Selective Reminding Test; IR, Immediate Recall; FR, Free Recall; TR, Total Recall; IST, Isaac Set Test; MADRS, Montgomery and Asperg Depression Rating Scale; MIS, Memory Impairment Screen; MMSE, Mini Mental State Evaluation; PN30, Picture Naming 30 items; TMT, Trail Making Test; SD, Standard deviation. Statistically significant correlation: $^{*}p < .05$, $^{**}p < .01$, $^{***}p < .001$.

[a]Exponents represent the significant effect of the covariant when ANCOVAs were computed on the correct AS latency.

[b]Exponents represent the significant effect of the covariant when ANCOVAs were computed on the correct AS latency SD.

[c]Exponents represent the significant effect of the covariant when ANCOVAs were computed on the incorrect AS latency.

[d]Exponents represent the significant effect of the covariant when ANCOVAs were computed on the incorrect latency SD.

[e]Exponents represent the significant effect of the covariant when ANCOVAs were computed on the proportion of correct AS.

[f]Exponents represent the significant effect of the covariant when ANCOVAs were computed on the corrected AS.

[g]Exponents represent the significant effect of the covariant when ANCOVAs were computed on the time-to-correct AS.

[h]Exponents represent the significant effect of the covariant when ANCOVAs were computed on the AS cost.

patients and controls ($F[1, 38] = 0.05$, $p = .83$). There was also no statistical difference between the two groups concerning anticipated saccades' latency ($F[1, 38] = 0.07$, $p = .79$) and latency variability ($F[1, 38] = 0.14$, $p = .71$) for dot2. When we considered non-anticipated saccades, gain ($F[1, 38] = 1.45$, $p = .24$) as well as gain variability ($F[1, 38] = 0.40$, $p = .53$) did not differ between the two groups. However, anticipated saccades' gain ($F[1, 38] = 5.21$, $p = .03$) and gain variability ($F[1, 38] = 22.20$, $p < .001$) were higher in AD patients than in controls (Table 2).

Latency for dot1 was not correlated with any neuropsychological scores and latency variability for dot1 was only correlated with MMSE (Table 5). Latency and latency variability for dot2 did not correlate with any scores when saccades were anticipated. When saccades were non-anticipated, latency for dot2 was correlated with age and MIS, and latency variability for dot2 was correlated with age, MMSE, MADRS, MIS, IST, FCSRT, and TMTB. The proportion of anticipated saccades did not correlate with any scores. Finally gain and gain variability were correlated with education when saccades were not anticipated. Gain variability was also correlated with COT when saccades were not anticipated. When saccades were anticipated, gain did not correlate with any scores whereas gain variability was correlated with education, MMSE, MIS, and IST.

When we ran ANCOVA with age, education, MMSE, MIS, FCSRT IR, FR, or TMTB as covariates, latency difference between patients and controls for dot1 was not statistically significant ($p_s > .06$). As regards latency variability for dot1, difference between patients and controls was not statistically significant when age or TMTB were used as covariates ($p_s > .07$). The other scores used as covariates did not change statistical difference for latency ($p_s < .05$) and latency variability ($p_s < .04$). ANCOVA with age, FCSRT, or TMTB as covariates removed the significant difference between patients and controls for non-anticipated saccades' latency for dot2 ($p_s > .07$). Using MADRS or the other neuropsychological scores as covariates did not change previous results ($p_s < .03$). Non-anticipated saccades' latency variability remained statistically different between groups whatever the covariates used ($p_s < .05$). Anticipated saccades' latency for dot2 remained statistically similar between the two groups when we ran ANCOVA with age, education, MADRS, or neuropsychological scores ($p_s > .07$). However, ANCOVA with MIS or FCSRT RL as covariates reached statistical significance for the variability of anticipated saccade latency for dot2 ($p_s < .03$). The other scores used as covariates did not change previous results for the anticipated latency variability ($p_s > .13$).

When we ran ANCOVA with MADRS, MMSE, IST, FCSRT, COT, TMT, coping figure test, or PN30 as covariates, anticipated saccades' gain difference between patients and controls was not statistically significant ($p_s > .10$). The other scores used as covariates did not change statistical difference for anticipated gain ($p_s < .05$).

Proportion of anticipated saccades ($p_s > .41$) as well as non-anticipated saccades' gain ($p_s > .30$) and gain variability ($p_s > 0.56$) remained statistically similar between the two groups when we ran ANCOVA with age, education, MADRS, or neuropsychological scores. Anticipated saccades' gain variability remained statistically different between groups whatever the covariates used ($p_s < .02$) (Table 5).

## Discussion

By using PS, AS, and PreS paradigms, we have provided evidence for abnormal SEMs in patients suffering from AD in comparison with healthy OA. Alzheimer's disease patients showed longer latency whatever the task performed. They also showed greater latency variability in comparison with controls. Interestingly, in AS task AD patients and controls had similar latency when they made incorrect AS. Alzheimer's disease patients also made fewer correct AS than controls and they had more difficulty to correct saccade direction when they made incorrect AS. Finally, when they succeeded in correcting AS errors, AD patients took more time to correct them. Our results concerning PreS showed that gain as well as gain variability were higher in AD patients than in controls.

In agreement with a large majority of previous studies, we showed that AD patients took more time to trigger a saccade (Boxer et al., 2006; Bylsma et al., 1995; Crawford et al., 2005, 2013; Fletcher & Sharpe, 1986; Garbutt et al., 2008; Hershey et al., 1983; Pirozzolo & Hansch, 1981; Shafiq-Antonacci et al., 2003; Yang et al., 2013). According to studies that have demonstrated that saccade latency depends on attentional processes (Clark et al., 2015; Domagalik et al., 2012; Pierrot-Deseilligny et al., 2004) and others that showed that these processes are impaired in AD (Levinoff et al., 2004; Parasuraman et al., 1992), saccade latency increase could be related to attentional impairment in AD patients. We also found higher latency variability in AD than in controls participants. These results add an argument for attentional processes impairment in AD in that higher latency variability can be related to higher attentional fluctuation (Kapoula et al., 2010; Mostofsky et al., 2001).

**Table 5.** Correlations between saccadic eye movements (SEMs) in predictive saccade (PreS) task, age, education, MADRS, and neuropsychological test

| | Non-anticipated saccades | | | | | | Anticipated saccades | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Latency dot1 | Latency SD dot1 | Latency dot2 | Latency SD dot2 | Gain | Gain SD | Latency dot2 | Latency SD dot2 | Proportion (%) | Gain | Gain SD |
| Age[a,b,c] | 0.27 | 0.31* | 0.34* | 0.43** | 0.35* | 0.09 | 0.22 | −0.01 | 0.06 | 0.15 | −0.30 |
| Education[a] | −0.22 | −0.33* | −0.10 | −0.08 | −0.17 | −0.17 | 0.05 | −0.13 | −0.10 | −0.03 | −0.35* |
| MADRS[j] | −0.05 | 0.20 | −0.22 | 0.45** | 0.18 | 0.10 | −0.09 | −0.10 | 0.06 | 0.23 | 0.16 |
| MMSE[a,j] | −0.17 | −0.35* | −0.24 | −0.44** | −0.14 | 0.01 | 0.01 | 0.05 | 0.05 | −0.15 | −0.43* |
| MIS 2 min[a,h] | −0.20 | −0.25 | −0.33* | −0.52*** | −0.18 | −0.13 | −0.07 | 0.16 | 0.02 | −0.16 | −0.33* |
| MIS 10 min[a,h] | −0.25 | −0.33* | −0.25 | −0.47** | −0.17 | −0.10 | −0.07 | 0.17 | −0.08 | −0.19 | −0.39* |
| IST[j] | −0.18 | −0.28 | −0.15 | −0.35* | −0.30 | −0.29 | 0.01 | 0.15 | −0.02 | −0.24 | −0.40* |
| FCSRT IR[a,c,j] | 0.04 | 0.03 | −0.10 | −0.32* | 0.01 | −0.12 | 0.15 | 0.03 | 0.06 | −0.02 | −0.23 |
| FCSRT FR[a,c,h,j] | −0.24 | −0.26 | −0.31 | −0.52*** | −0.19 | −0.20 | 0.03 | 0.16 | −0.06 | −0.09 | −0.28 |
| FCSRT TR[c,j] | −0.10 | −0.13 | −0.15 | −0.47** | 0.01 | −0.10 | 0.15 | 0.05 | −0.07 | −0.10 | −0.09 |
| COT[j] | −0.14 | −0.18 | −0.10 | 0.16 | −0.34* | −0.18 | −0.09 | 0.16 | −0.09 | −0.25 | −0.22 |
| TMTA[j] | 0.20 | 0.13 | 0.14 | 0.25 | 0.30 | 0.19 | 0.12 | −0.15 | −0.03 | 0.40* | 0.39* |
| TMTB[a,b,c,j] | 0.23 | 0.21 | 0.30 | 0.37* | 0.32* | 0.20 | −0.01 | −0.20 | −0.14 | 0.11 | 0.19 |
| Coping figure[j] | 0.23 | −0.05 | 0.08 | −0.02 | −0.20 | −0.20 | 0.10 | −0.05 | −0.02 | −0.34* | −0.25 |
| PN30[j] | 0.06 | 0.09 | 0.14 | 0.01 | 0.09 | 0.08 | 0.19 | −0.04 | 0.15 | −0.10 | −0.10 |

*Notes:* COT, Crossing Off Test; FCSRT, Free and Cueing Selective Reminding Test; IR, Immediate Recall; FR, Free Recall; TR, Total Recall; IST, Isaac Set Test; MADRS, Montgomery and Asperg Depression Rating Scale; MIS, Memory Impairment Screen; MMSE, Mini Mental State Evaluation; PN30, Picture Naming 30 items; TMT, Trail Making Test; SD, Standard deviation. Statistically significant correlation: *$p < .05$, **$p < .01$, ***$p < .001$.

[a]Exponents represent the significant effect of the covariant when ANCOVAs were computed on the latency for dot1.

[b]Exponents represent the significant effect of the covariant when ANCOVAs were computed on the latency SD for dot1.

[c]Exponents represent the significant effect of the covariant when ANCOVAs were computed on the non-anticipated saccades' latency for dot2.

[d]Exponents represent the significant effect of the covariant when ANCOVAs were computed on the non-anticipated saccades' latency SD for dot2.

[e]Exponents represent the significant effect of the covariant when ANCOVAs were computed on the non-anticipated saccades' gain for dot2.

[f]Exponents represent the significant effect of the covariant when ANCOVAs were computed on the non-anticipated saccades' gain SD for dot2.

[g]Exponents represent the significant effect of the covariant when ANCOVAs were computed on the anticipated saccades' latency for dot2.

[h]Exponents represent the significant effect of the covariant when ANCOVAs were computed on the anticipated saccades' latency SD for dot2.

[i]Exponents represent the significant effect of the covariant when ANCOVAs were computed on the proportion of anticipated saccades for dot2.

[j]Exponents represent the significant effect of the covariant when ANCOVAs were computed on the anticipated saccades' gain for dot2.

[k]Exponents represent the significant effect of the covariant when ANCOVAs were computed on the anticipated saccades' gain SD for dot2.

As regards AS task, our findings showed that AS cost was higher in AD patients than in controls. Moreover, AD patients presented difficulty to make correct AS and to correct incorrect AS. These results are also in agreement with those of previous studies (Boxer et al., 2006, 2012; Crawford et al., 2005, 2013; Garbutt et al., 2008; Heuer et al., 2013; Kaufman et al., 2012; Shafiq-Antonacci et al., 2003). In comparison with PS task, the difficulty to perform correct AS are assumed to reflect supplementary cognitive processes in that participants have to inhibit (or correct) saccades toward the target, which also imply to keep in mind the goal of the task (Noiret et al., 2016; Munoz & Everling, 2004; Sumner, 2011). These findings support our hypothesis that AD affects executive-attention functioning. The relationships between AS, executive-attention and the DLPFC (Cohen, 2014; Pierrot-Deseilligny, Muri, Nyffeler, & Milea, 2005; Kaufman et al., 2010), suggest that AS impairments in AD were due to DLPFC damage.

Otherwise, another interesting finding was that there was no latency difference concerning incorrect AS. Given that PS latency was higher in AD patients than in controls, this suggests that incorrect AS cannot be assimilated to PS. This differentiation supports the idea that PS is not a mere "reflexive saccade" but that supplementary decisional process modulates its latency (Hutton, 2008). In comparison, AS errors would be considered as behavioral outcomes of the attentional capture by the target appearance. This process would be facilitated by the reduction of attention control.

We can speculate that correct saccades in AS and in PS tasks have highlighted attentional control efficiency—firstly focused on the central dot—allowing decisional process to trigger saccades as a function of task goal. Higher saccade latency in AD patients for correct AS as well as PS suggested decline in decisional processing speed in AD. Additionally, difficulty in triggering correct AS suggested attentional control failure and direct attentional capture by the target dot. This assertion is supported by an absence of supplementary delay to trigger incorrect AS in AD patients.

PreS task also provided us some interesting results. As we differentiated anticipated from non-anticipated saccade latency and gain, our results highlight differences between the groups that were not found in Shafiq-Antonacci et al. (2003). Indeed, when saccades were anticipated, there was no latency difference between the two groups whereas non-anticipated saccade latency was higher for AD patients than for controls—like saccades in the other tasks. Although there was no gain difference between the groups for non-anticipated saccades, gain and gain variability was higher in AD patients than in controls for anticipated saccades. Taken together, these results suggested that AD patients were able to anticipate the second target but their anticipated saccades toward the target were more scattered around the target location.

Our correlation and covariant analyses revealed that although several neuropsychological test and psychiatric scale scores correlated with SEM variables, only some of these had an influence on the differences between AD patients and controls. Overall, we found close relationships between the MMSE and all SEM variables, except incorrect AS latency and latency SD, and non-anticipated as well as anticipated saccades' latencies and non-anticipated saccades' gain of dot2 in PreS task. There were also relationships between MIS and SEM variables and between the FCSRT and SEM variables, incorrect AS latency and latency SD, and latencies and gain of dot2 in PreS task. Trail Making Test scores also influenced SEM differences between AD patients and controls in PS, AS and PreS tasks, except for incorrect AS latency and latency SD and anticipated saccades' latency, non-anticipated saccades' gain, proportion of anticipated saccades in PreS task.

Given the difference between patients and controls regarding SEMs as well as the close relationships between SEMs and our dementia screening tests, we suggest that SEMs allow discriminating AD patients from healthy participants as dementia screening tests do. Additionally, our results raise an interesting question: if we consider that SEM variables were mainly dependent on attentional and executive processes, we can question the nature of the process measured in memory tests such as the MIS or the FCSRT. Given that memory capacities were related to executive function, and that the latter was early impaired in AD (Baudic et al., 2006; Collette, Van der Linden, & Salmon, 1999), the active retrieval in memory involving executive function could be impaired, at least partially, because of executive function decline rather than because of memory impairment per se.

## Conclusion

In the present experiment, we showed that SEMs in AD patients and in healthy participants are different. Moreover, we showed that each SEM parameter is not as useful as another and they do not measure exactly the same cognitive process. We assumed that attentional control mainly underlie SEMs. Prosaccade performance can reflect the altered ability in AD patients to rapidly trigger endogenous saccade toward a target while attention is firstly focused on the central dot. AS performance can reflect impairment in executive-attention dysfunction in AD patients. Finally, PreS performances likely reflects AD patients' decreased ability to keep efficient target dot location representation in working memory. Although one of the limits presented in this experiment was the age difference between AD patients and control participants, our statistical analysis showed that the majority of SEM variables did not covariate with age (except the proportion of corrected saccades in AS task, latency for

dot1 and non-anticipated saccades' latency for dot2 in PreS task). Another limit is the relatively small patient sample size ($N = 20$). Larger age controlled sample size should allow increasing statistical power. Finally, although we actually found clear relationships between SEM parameters and basic dementia rating tests, it should be useful to carry out experiments comparing SEM variables with tests measuring specific cognitive process such as inhibition, cognitive flexibility, short-term memory, selective attention, in order to better describe potential additional relationships between SEM alterations and cognitive process impairments in AD.

These preliminary results on AD patients confirm that SEM paradigms can serve as tools to detect and study attentional processes impairments in AD. We should now focus on the potential power of SEM parameters to discriminate AD from other neurological or psychiatric pathologies in order to further evaluate test specificity.

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## Conflict of Interest

None declared.

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