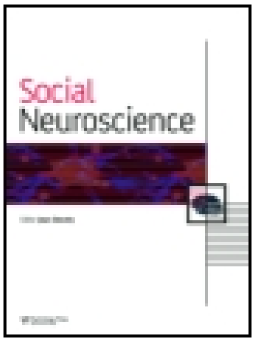

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Theory of Mind and social reserve:

Alternative hypothesis of progressive Theory of Mind decay during different stages of Alzheimer's Disease

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Abstract

Although Theory of Mind (ToM) is thought to be impaired in Alzheimer Disease (AD), it remains unclear whether this impairment is linked to the level of task complexity, the heterogeneity of studied patients, or the implication of executive dysfunctions. To elucidate this point, forty-two AD patients, divided into 2 subgroups [moderate AD patients (n = 19) and early AD patients (n = 23)], and 23 matched healthy older subjects were enrolled. All participants were given (1) a false-belief task (cognitive ToM), (2) a revised version of the ‘‘Reading the Mind in the Eyes’’ test (affective ToM), and (3) a composite task designed to assess ToM abilities with minimal cognitive demands. Participants were also given executive tasks assessing inhibition, shifting, and up-dating processes. We observed a significant impairment of cognitive and composite ToM abilities in early AD patients compared with moderate AD patients. There was no impairment of affective ToM. Stepwise regression revealed that measures of global efficiency and executive functions were the best predictors of progressive decay of ToM scores. These results indicate that cognitive aspects of ToM are more sensitive to AD progression than affective tasks. They also show that ToM abilities are more affected by dementia severity more than by task complexity. One explanation of our results is the presence of compensatory mechanisms (social reserve) in AD.

Keywords: Social cognition; Alzheimer’s Disease; Theory of Mind; Executive Functions, Compensatory mechanisms; Social reserve.

Introduction

Nowadays, researches in social cognition focus on a key aspect of the social functioning, called Theory of Mind (ToM), which involves the ability to understand, predict, and infer other's mental states, such as thoughts, beliefs, and feelings (Baron-Cohen, Leslie, & Frith, 1985).

Current cognitive conceptions of ToM suggest distinguishing between ‘‘cognitive’’ and ‘‘affective’’ components of ToM (Shamay-Tsoory & Aharon-Peretz, 2007). The “Cognitive ToM”, or “Cold” mentalizing, corresponds to inferences based on others’ knowledge or beliefs, without any personal or emotional involvement. The “Affective ToM”, or “hot” aspect of ToM, implies inferences about the emotional states of others (feelings, emotions) on the basis and the comprehension of our own emotions (Brothers & Ring, 1992; Shamay-Tsoory, Tomer, Berger, & Aharon-Peretz, 2003; Coricelli, 2005).

Few studies investigated the effects of neurological diseases on ToM subcomponents, especially in patients with dementia. An impaired ToM ability was described in neurodegenerative pathologies, in particular those involving the orbitofrontal and cingulate regions (frontotemporal dementia, FTD: see for example Eslinger *et al.*, 2007; Torralva, Roca, Gleichgerrcht, Bekinschtein, & Manes, 2009; Bertoux, Volle, de Souza, Funkiewiez, Dubois, & Habert, 2014)

The results of these works suggest that ToM is significantly impaired in FTD. In fact, a recent meta-analysis (Schurz, Radua, Aichhorn, Richlan, & Perner, 2014) suggested the implication of the medial prefrontal cortex and the temporal parietal junction in explicit interpretation of others’ mental states. As these regions appeared to be harshly damaged in FTD (see Adenzato, Cavallo, & Enrici, 2010), meta-analytic reviews of ToM in FTD found a severe, global, and primary deficit in mentalizing ability in this disease (Schurz *et al.*, 2014; Henry, Philips, & von Hippel, 2014). The comparison of ToM abilities in FTD and Alzheimer’s disease (AD) (Bora, Walterfang, and Velakoulis, 2015) confirmed that the evaluation of ToM abilities allows distinguishing between both disorders. In FTD, ToM deficit concerned both cold and hot aspects, and was especially marked for complex aspects of ToM such as recognition of Faux Pas and sarcasms. These primary dysfunctions of ToM seem to be more severe than general cognitive deficits in FTD, and are present early in the course of the disease, unlike ToM impairment in AD.

ToM evaluation in AD is underdeveloped with respect to FTD. Obvious lesions were demonstrated in the orbitofrontal regions (Van Hosen, Parvizi, and Chu, 2000) so it was suggested that ToM deficits may also be present in AD patients, responsible for patients' difficulties in making and using appropriately mental state inferences in social interactions (Hodges, 2013). However, few studies were conducted in these patients, and their results remain controversial.

Concerning cognitive ToM abilities, available descriptions in AD suggested that there was no specific deficit in cold mentalizing. Indeed, patients with AD were able to attribute first-order False Beliefs (FB1: Gregory *et al.*, 2002; Fernandez-Duque, Baird, & Black, 2009). By contrast, AD patients showed difficulties to infer second-order FB (FB2: Cuerva, Sabe, Kuzis, Tiberti, Dorrego, & Starkstein, 2001; Gregory *et al.*, 2002). Based on available literature, it was assumed that AD patients performed worse than control subjects on ToM tasks because of the important cognitive demands of classical ToM tasks (Shany-Ur *et al.*, 2012; Kemp, Després, Sellal & Dufour, 2012; Poletti, Enrici, & Adenzato, 2012). Thus, the success on 2nd order FB tasks depends on many cognitive abilities such as verbal comprehension or naming (Cuerva *et al.*, 2001), abstract thinking (Zaitchik, Koff, Brownell, Winner, & Albert, 2004; 2006), and working memory (Gregory *et al.*, 2002). It is notwithstanding to note that these abilities are usually impaired in AD patients.

As far as affective ToM is concerned, prior studies suggested that AD patients were quite efficient to perform affective tasks. Gregory *et al.* (2002) reported that AD patients only failed the memory and comprehension questions of the Faux Pas test (Stone, Baron-Cohen, & Knight, 1998). In addition, they performed the Reading Mind in the Eyes test (RME; Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001) as adequately as healthy controls (Gregory *et al.*, 2002; Modinos, Obiols, Pousa, & Vicens, 2009). These results are consistent with those found by Zaitchik *et al.* (2006). AD patients showed difficulties to make emotional inferences only when complex cognitive demands were required.

Note however, that recent studies displayed a number of converging lines of evidence questioning these consensuses. In fact, studies conducted on cold aspects of ToM by Laisney, Bon, Guiziou, Daluzeau, Eustache, and Desgranges (2013) or by Freedman, Binns, Black, Murphy, and Stuss (2013) revealed significant deficits on FB1 tasks in AD patients.

In their study, Laisney *et al.* (2013) reported a significant group effect (16 AD versus 15 matched controls) and a significant order effect (FB1 versus FB2), suggesting impaired ToM ability in AD patients for all FB situations. AD patients showed poor performances on FB1 order inferences without any comprehension or memory difficulties. Correlation with global cognitive functioning was also noted, indicating that FB1 inference difficulties increased as the disease progresses. According to these authors, the heterogeneity of included patients may explain controversial results between their study and past findings reporting spared FB1 functioning in early AD patients.

Thanks to an original methodology, Freedman *et al.* (2013) confirmed the existence of specific deficit in FB1 tasks in AD. These authors compared their group of AD patients with a group of patients suffering from behavioral variant frontotemporal dementia (bvFTD) and with a group of healthy subjects. Impairments were found for the FB1 and FB2 stories in both clinical groups. These findings challenge the consensus that mentalizing ability on FB tasks is spared in AD.

Regarding affective ToM, Laisney *et al.* (2013) reported a significant effect of AD on a revised version of the RME test (Baron-Cohen *et al.*, 2001). This impairment was correlated with a global cognitive functioning score. Such findings are on line with the assumption that difficulties on both affective and cognitive ToM are related to disease severity.

Nonetheless, Castelli *et al.* (2011) proposed another explanation to interpret controversial data. They suggested that decay of ToM reasoning increased according to task complexity. In fact, these authors submitted 16 AD patients and 16 matched controls to a ToM battery including ToM precursor’s tasks, FB1 and FB2 tests, the RME test, and a strange stories task. Results showed faulty ToM abilities in complex tasks while the basic ones were still functional. These findings support the assumption of "*progressive decay of ToM abilities in AD patients starting from more complex ones backwards to the simpler ones*" (Castelli *et al.*, 2011).

By contrast, Poletti and Bonuccelli (2013) recently reported an alteration of hot mentalizing in amnestic mild cognitive impairment subjects, as measured by the RME. This empirical evidence of a faulty affective ToM in individuals with high risk of developing probable AD is not consistent with previous findings (Castelli *et al.*, 2011; Laisney *et al.*, 2013) suggesting a lesser degree of impairment on the cognitive dimension than on the affective one. Therefore further studies on the topic are needed.

Furthermore, the implication of the frontal lobe in ToM abilities led some authors to propose a relationship between executive dysfunctions and ToM deficits, especially since impairments of mental state inference was explained by more general difficulties (Poletti *et al.*, 2012; Kemp *et al.*, 2012).

In fact, some experimental evidences led to think that ToM performances could be correlated to more general cognitive decline. In normal aging, German and Hehman (2006), for example, showed that non-specific cognitive abilities, and especially on executive resources contributed most to explaining mental inference deficits. A recent review (Sandoz, Démonet, & Fossard, 2014) argued that general cognitive resources are involved in ToM performances on AD. In fact, these authors suggested that mentalizing abilities were relying on different executive components, especially inhibition process that totally mediated ToM scores, as well as flexibility and up-dating processes involved in ToM performances (see Sandoz *et al.*, 2014 for a detailed review).

Although many researches had documented executive dysfunctions in AD (Amieva, Phillips, Della Sala, & Henry, 2004; Allain, Etcharry-Bouyx, & Verny, 2013), the link between executive functions (EF) and ToM is not yet fully studied in AD patients by means of a theoretical approach of EF (Aboulafia-Brakha, Christe, Martory, & Annoni, 2011). In fact, to our knowledge, only very few studies assessed correlations between ToM performances and EF. In one hand, studies by Zaitchik *et al.* (2004; 2006) showed that performances on ToM tests were significantly correlated with performances on WAIS Similarities subtest that assess abstraction ability. In the other hand, Laisney *et al.* (2013) found significant correlations only between FB2 inference and inhibition (Stroop test), shifting (phonemic verbal fluency), and working memory (backward digit span), suggesting that these dysfunctions contributed to the deterioration in the more complex aspects of cognitive ToM abilities.

In sum, available literature on ToM abilities in AD remains controversial, for both cognitive and affective dimensions of ToM reasoning. The implication of non-specific cognitive abilities (especially EF) on these performances remains understudied in AD. These divergent data could be explained either (a) by the multiplicity of methodologies used in these studies, especially the complexity of some ToM tasks (Castelli *et al.*, 2011), (b) by the heterogeneity of the AD patients included in terms of disease severity (Laisney *et al.*, 2013), (c) or by the involvement of decreased general cognitive resources in AD on mentalizing abilities (Sandoz *et al.*, 2014).

Therefore, the original aim of the present study was to propose a ToM protocol assessing cognitive (FB task) and affective (RME test) subcomponents of ToM abilities in AD patients classified into two distinct groups according to the stage of AD (early versus modorate AD). In addition, this protocol includes a composite ToM task developed to asses ToM ability with minimal cognitive demands (judgment of preferences task). The second goal was to assess the implication of EF deficits on ToM performances in our two AD groups. For this purpose, EF was assessed according to the approach of Miyake, Friedman, Emerson, Witzki, Howerter, and Wager (2000). Our main research hypotheses were: (a) if ToM abilities are sensitive to general cognitive functioning, we can expect to observe significant differences between our two AD groups, with lower performances on all ToM tasks, regardless of the task complexity, in the group of patients having moderate AD. Correlations of ToM scores with general cognitive functioning indicator should also support this assumption; (b) we also expect to highlight a significant difference between scores on well-documented ToM tasks and the composite ToM task with minimal cognitive demands in both AD patients groups. Higher correlations between global executive indicator and ToM scores of complex tasks should support this hypothesis; (c) Finally, we aimed at looking for the implication of executive disorders on faulty mentalizing abilities. Correlations between general cognitive resources and ToM scores will be assessed in order to discuss more specifically an integrated conception of ToM performances in AD groups.

Methods

Participants

Forty-two French-speaking AD patients and 23 healthy older subjects (HO) took part in this study. In order to take into account progressive decay of ToM reasoning in the course of AD, we formed 2 subgroups of AD patients: moderate AD patients and early AD patients. Informed consent was obtained from all subjects, or from substitute decision-makers, in compliance with research standards for human research for participating institution, and in accordance with the Helsinki Declaration.

AD patients

Moderate AD patients (mAD)

Nineteen patients suffering from mAD (14 females and 5 males; mean age: 79.3 years; mean years of education: 7.7 years) were included. For all subjects, diagnosis was made according to the international criteria of DSM-5 (American Psychiatric Association, 2013) and fulfilling the recommendation of the National Institute on Aging (Albert *et al.*, 2011; McKhann *et al.*, 2011). Patient’s medical history, neurological examination, brain imaging, and laboratory tests provided assurance that dementia symptoms could not be attributed to an illness other than moderate AD. The level of global cognitive performance was based on the Mini Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975); mAD was considered when the MMSE score was between 18 and 22 (m = 19.8, SD = 1.4).

Early AD patients (eAD)

The group of patients with eAD included 23 individuals (12 females and 11 males; mean age: 77.7 years; mean years of education: 9.2 years). All subjects fulfilled the same clinical criteria (Albert *et al.*, 2011; McKhann *et al.*, 2011; American Psychiatric Association, 2013) for probable AD. Patient's medical history, neurological examination, brain imaging, and laboratory tests provided assurance that dementia symptoms could not be attributed to an illness other than early AD. MMSE scores were comprised between 23 and 27 (*m* = 24.3, *SD* = 1.2).

Healthy Older subjects (HO)

The 23 HE subjects consisted of 11 men and 12 women. Their mean age was 77.9 years (*SD* = 9.9; range: 45-91). Their educational level ranged from 6 to 13 years of schooling (*m* = 8.6; *SD* = 2.1). The HO subjects had no history of neurological or psychiatric diseases, brain damage, or global cognitive deterioration as documented by the MMSE (*m* = 28.9; *SD* = 1; range: 27–30).

Brief neuropsychological assessment

As previously mentioned, global efficiency was evaluated using the MMSE. A short global executive functions assessment was also performed using the Frontal Assessment Battery (FAB; Dubois, Slachevsky, Litvan, & Pillon, 2000), which consists of 6 subtests exploring conceptualization, mental flexibility, motor programming, sensitivity to interference, inhibitory control, and environmental autonomy. It takes approximately 10 minutes to administer. Neuropsychological scores are presented in Table 1. These measures were selected because they have been shown to be the most commonly used cognitive screening tool of general cognitive functioning (MMSE) and executive functioning (FAB) in AD patients (Woodford & George, 2007).

Executive functioning:

In addition to a brief global assessment of executive functioning according to the FAB (Dubois *et al.*, 2000), the main executive components were assessed on the basis of the study of Miyake *et al.* (2000), which made the distinction between the following elementary executive processes: "shifting" process, "inhibition" process, "updating" process, and evaluation of central executive components of working memory. We investigated these functions by employing the following standard tests:

Shifting process: *the plus/minus test* consisting of 3 lists of numbers. Participants had to add 1 to each number (list 1), to subtract 1 (list 2), then to alternately add or subtract 1 to each presented number (list 3). Time necessary to complete this task, and errors number were taken into account. For the statistic analysis, we focused on the "errors shifting score" (average errors made on the 3rd list - average errors made on the 2 simple conditions).

Inhibition process: *the Stroop test* was considered as a measure of inhibition of automatic responses. We were interested in the difference between uncorrected errors on the 3rd condition (interference condition) and errors made on the 1st condition (color denomination).

Updating process: We used the *2-back test* consisting of a list of orally presented 30 letters, at a rate of one letter per 2 seconds. Participants were asked to identify whether the last letter heard was identical to the last but one. The scores considered were the number of errors made.

Central executive components of working memory: Complementary measures of the central executive system of working memory were obtained using the *classic dual task*. In the simple conditions, a digit-span task was presented to participants who had to immediately recall the series in the same order, and then the box-crossing task consisted of traversing a chain of squares with crosses. The dual condition task consisted of the simultaneous execution of both tasks and the performance was estimated by "mu" (Baddeley, Bressi, Della Sala, Logie, & Spinnler, 1991), a composite index that is supposed to reflect the subject's capacity to coordinate the separate tasks.

ToM tasks

All participants completed 3 non-verbal ToM tasks (Duval, Piolino, Bejanin, Eustache, & Desgranges, 2011). Each one contained a ToM condition and a control condition, to fairly link poor performances on these tasks to difficulties in making mental inferences.

Cognitive ToM task: False-beliefs Task (FB)

This task was a revised version of the Wimmer and Perner's FB (Wimmer & Perner, 1983). It assessed the ability to attribute 1st and 2nd order epistemic mental states to others. This task was thought to reflect solely the “cognitive” subcomponent of ToM, without an emotional involvement (Duval *et al.*, 2011; Desgranges *et al.*, 2012). It consisted of 15 short comic strips, each comprising 3 pictures with a short written description. These comic strips assessed the ability to solve problems involving FB1 (8 situations) and FB2 (7 situations). The stories were everyday situations involving a character, which took knowledge of described information. The situation changed without her/his knowledge. We then asked questions about the expected reactions of the person carrying FB about his environment. There were two conditions. In the ToM condition, a question about the belief of one of the characters in the story was proposed. In the control condition, the same cartoons were used, but the question probed participants’ understanding of the reality of the cartoon scenario. For each question, only two answers were possible. In order to reduce working memory load, the pictures, the written descriptions, and the possible answers remained visible throughout the task. The percentages of correct responses in each condition were considered as dependent variables.

Affective ToM task: The Eyes/Faces Test (EFT)

The EFT was inspired by the RME test (Baron-Cohen *et al.*, 2001). It assessed understanding of other people’s mental states from their eyes. It consisted of 20 black-and-white photographs of the eye region of a female actor who was asked to produce different facial expressions. Ten of the photographs depicted primary emotions (happiness, surprise, *etc.*). Ten photographs depicted complex emotions (guilt, thoughtful, flirting, *etc.*). Under each picture, three adjectives (a target and two foils) describing emotions were written. Participants were asked to identify which adjective best described the person’s mental state. This task is thought to measure emotion recognition in the basic emotions condition (control condition) and affective ToM in the complex emotions one (ToM condition). The percentages of correct responses in each condition were used as dependent variables.

Composite ToM task: Preference Judgement Task: (PJ)

The third task, inspired by Snowden *et al.* (2003), could be considered as a composite task because it involves the ability to judge the preference (or thoughts) of a central character, named Tom (referring to cognitive ToM), on the basis of its facial expression (pouting or smiling, referring to affective ToM). This task is supposed to engage minimal cognitive demands (Snowden *et al.,* 2003; Duval *et al.,* 2011). We used it in order to test our hypothesis of the implication of task complexity on ToM performances in AD patients.

The material consisted of 16 cards drawings on separate sheets, each showing a figure in a central position, either smiling or pouting, in order to express Tom's preferences (affective ToM component). Tom's gaze was directed towards a balloon containing the picture of an object (*e.g.* biscuits), expressing his thoughts (cognitive ToM component) meaning, for example, that he likes biscuits. For each ToM situation, a short scenario with an ending question was orally presented to put it in a social context (*e.g.* ‘‘imagine that you have kindly invited Tom to your house for tea or coffee. What would you serve with the tea or coffee?’’). Then, the experimenter showed four possible response pictures, chosen for their degree of relevance: (1) correct response taking both Tom's preference and the context into account (madeleines), (2) incorrect response only taking the context into account (chocolates), (3) incorrect response only taking Tom's preference into account (salted crackers), and (4) unsuitable response taking neither Tom's preference nor the context into account (oysters). Once the participant had answered, he was asked to justify his choice for each item. These answers were coded as “preference” if the participant took into account Tom's preference in the correct context; “self” if he/she responded according to his/her own preference; “context” if he/she chose the response suitable only to the history context and “random” for other motivations. In a second condition (control condition), the same 16 Tom's faces were presented, without social situations or possible responses. The participant was asked to interpret the facial expression of Tom to check the good understanding of facial cues. The dependent measure was the percentage of correct answers (according to both Tom's preference and context) in the first (ToM) condition. We also looked for the distribution of each type of erroneous response (preference, self, context, random).

Statistical analysis

All statistical analyses were performed using Statistica 10 (StatSoft, Inc., Tulsa, OK, USA). The threshold of significance was set at $p = .05$. Factorial ANOVA were carried out to compare the demographical and general neuropsychological data of the 3 groups. Factorial ANOVA were also conducted to analyze ToM and EF scores. Follow-up *post-hoc* comparisons were conducted with Tukey's Honestly Significant Difference tests. A chi-square test was used to test whether the AD patients had specific patterns of errors in the PJ task. Then, we carried out correlation analysis and stepwise regression analysis in order to determine the best ToM measure predictors. Regression analysis used the MMSE score, the FAB score, EF scores, the number of years of education, and age as independent factors, and ToM scores as dependent factors.

Results

Demographic characteristics and neuropsychological performances of AD patients and HO subjects are shown in Table 1. The 3 groups did not differ significantly in age ($F(2,62) =.17$; $MSE = 14.1$), or educational level ($F(2,62) =1.4$; $MSE = 11.6$). Chi-square tests revealed that they were also matched with respect to sex (*Chi-square* = 2.56; $df = 1$; $p = .27$).

Table 1 about here

Complementary cognitive assessment

Both AD groups performed below the normal range on short neuropsychological measures, suggesting diminished general cognitive functions and executive abilities. In fact, AD patients performed poorly as compared to control subjects on the MMSE ($F(2,62) =307.4$; $MSE = 430.3$; $p < .0001$). A group effect also emerged for the FAB ($F(2,49) =23.3$; $MSE = 222.5$; $p < .0001$). All *post-hoc* analyses reported significant differences between the 3 groups, with HO subjects performing significantly better than eAD and mAD patients (both $p < .0001$). In addition, consistent with our methodological choices, eAD patients performed significantly better than mAD patients on MMSE ($p < .0001$) measure and on FAB score ($p < .001$).

Executive performances:

For the executive functions (Table 2), we reported a group effect on inhibition process ($F(2,60) = 3.6$; $MSE = 427.5$; $p = .03$), and on shifting process ($F(2,60) = 9.4$; $MSE = 99.2$; $p = .0002$). *Post-hoc* analyses indicated a significant difference between the mAD and the HO groups (Inhibition: $p < .03$; Shifting: $p < .0002$), and a non-significant difference between the eAD and the HO groups, which demonstrates the progressive deterioration of these processes in AD. The difference between the two AD groups was significant for the shifting process ($p = .02$) but not for the inhibitory process ($p = .09$).

As far as up-dating process was concerned, we only noted a tendency to significance ($F(2,60) = 2.8$; $MSE = 47.3$; $p = .07$). Finally, regarding the dual task, no difference was reported on "mu" score ($t(30) = .7$; $p = .5$) between our two AD groups.

Table 2 about here

ToM tasks

FB task

For the FB task (Table 3), data were submitted to a 3 x 3 ANOVA with group (mAD, eAD, HO) as the between-subjects factor, and FB task condition (control condition, FB1, FB2) as the within-subjects factor. The main effect of group was highly significant, $F(2, 62) = 7.8$; $MSE = 6640.3$; $p < .0001$. *Post hoc* tests revealed that, all conditions combined, mAD patients (mean percentage of correct responses: 59.8% ± 30.5) performed significantly worse ($p = .001$) than HO subjects (mean: 79.4% ± 19.5), but equally ($p = .56$) to eAD patients (mean: 65.2% ± 24.8). The group difference between eAD patients and HO subjects was also significant ($p = .02$).

There was also a main effect of FB task condition, ($F(2, 62) = 65.4$; $MSE = 16431.3$; $p < .0001$). Independently of group, the proportion of correct answers was significantly higher in the control condition (mean 84.1% ± 16.1) than in the FB1 condition (mean: 68.2% ± 24) and the FB2 condition (mean: 52.1% ± 27) (both $p < .0001$). In addition, the difference between the FB1 condition and the FB2 condition also reached significance ($p < .0001$).

The group × condition interaction was also significant ($F(4, 62) = 2.9$; $MSE = 735.2$; $p = .02$), indicating that the groups' patterns of performance varied across conditions. Subsequent one-way ANOVA computed for each group revealed that the mean proportion of correct answers differed significantly across condition (control condition, FB1, FB2) in all groups [mAD patients: $F(2, 36) = 16.8$; $MSE = 6913.3$; $p < .0001$; eAD patients: $F(2, 44) = 43.6$; $MSE = 8511.5$; $p < .0001$; HO subjects: $F(2, 44) = 12.7$; $MSE = 2233.9$; $p < .0001$]. As can be seen in Table 2, the percentage of correct responses in all groups was higher in the control condition than in the FB1 condition and the FB2 condition, and higher in the FB1 condition than the FB2 condition. In mAD patients, *post hoc* tests indicated that the difference of performance between the control condition and the two FB conditions was significant (both $p < .004$), but that the difference between FB1 and FB2 conditions did not reach significance ($p = .07$). On the other hand, eAD patients and HO subjects had similar patterns of performance, with significant difference between control condition and the FB1 condition, and between the FB1 and the FB2 conditions (all $p < .04$). Additionally, one-way ANOVA computed for each type of percentage of correct responses revealed no significant difference between groups in the control condition, $F(2, 62) = 2$; $MSE = 482.9$, indicating that both AD groups were as good as HO subjects to answer comprehension questions. Conversely, between group differences were significant for FB1 ($F(2, 62) = 5$; $MSE = 2558.2$; $p = .009$) and FB2 ($F(2, 62) = 8.5$; $MSE = 5069.5$; $p = .0005$). Concerning FB1, subsequent *post hoc* tests showed that mAD patients performed significantly worse than HO subjects ($p = .007$). No significant difference emerged between eAD patients and HO subjects ($p = .21$), or between our two AD groups ($p = .27$). Finally, *post hoc* analyses for FB2 showed that both groups of AD patients performed worse than

HO subjects (both p < .002), and that the difference in percentage of correct answers between the patients groups was marginal (p = .93).

Table 3 about here

EFT task

Concerning affective ToM, the results for the EFT test showed no significant main effect of group, $F(2, 51) = .7$; $MSE = 311.4$. Nevertheless, a significant effect of condition was observed, $F(3, 51) = 12.3$; $MSE = 2909.6$; $p < .0001$, suggesting different performances in all groups between control and ToM conditions. No interaction group × condition, $F(6, 153) = 1.4$; $MSE = 321.3$ was found.

PJ task

Finally, the ANOVA conducted for PJ task revealed a significant main effect of group, $F(2, 61) = 12.2$; $MSE = 3127.4$; $p < .0001$. *Post hoc* tests indicated that mAD patients performed significantly worse (mean 50.3% ± 16) than eAD patients (mean 55.4% ± 16) and HO subjects (mean 73.4% ± 16) on this task (both p' < .0001). The difference between eAD patients and HO subjects was also significant (p = .001).

Further analysis comparing the proportions of each type of errors in our groups was conducted with Chi square test. The proportions of error rates did not differ (p = .25) between the two AD groups (mAD patients: 17%, 52%, 27%, and 4% for "preference", "context", "self", and "random", respectively; eAD patients: 22%, 42%, 32%, and 4%, respectively). As shown in figure 1, significant differences emerged between HO subjects (41%, 35%, 23%, and 1%, respectively) and mAD patients (p < .0001), and between HO subjects and eAD patients (p = .0001).

Figure 1 about here

To summarize, AD has deleterious effects on general ToM abilities. However, this effect mainly concerns cognitive and composite ToM performances, while affective ToM appears to be spared. In the cognitive task, while the FB1 is spared in eAD patients, the FB2 is affected by both eAD and mAD. In the composite task, both groups of AD present faulty preference judgments, with a pattern of error that differs from HO subjects. Depending on the task, eAD patients differ either from mAD patients or from HO subjects, suggesting a progressive and non-unitary ToM ability decay.

Relationship between ToM and general and executive functioning within the patients' groups

Correlation analyses

To assess the links between EF and ToM tasks, simple correlation analyses were carried out. First analyses were conducted for the two AD groups together, then for each group independently. The results are detailed in Table 4.

Results showed no significant correlations between ToM tasks and EF when they were assessed in the mAD group only (for all Pearson correlation coefficients $p > .05$).

Second, in the eAD group, we pointed out significant correlations between up-dating and cognitive ToM [FB1 score ($r = -.81$; $p = .004$); FB2 task ($r = -.65$; $p = .04$)]. As affective ToM was concerned, a unique significant correlation was reported between the complex emotions-eyes score and Stroop interference score ($r = -.63$; $p = .04$). Composite ToM measure was also correlated to global FAB score ($r = -.56$; $p = .004$), and to shifting ($r = -.81$; $p = .04$).

Finally, in the whole AD group, we showed very few negative significant correlations, on one hand between the FB1 and up-dating ($r = -.54$; $p = .03$), and on the other hand between the FB2 score and shifting ($r = -.54$; $p = .03$).

Table 4 about here

Regression analyses

To go one step further, we conducted a set of upward stepwise regression analyses to identify the best predictor(s) of intergroup differences in ToM performance in the whole AD group. We selected as predictors: age; educational level, MMSE, FAB, and executive measures. Results are outlined in Table 5. They showed that performances on FB1 task were mainly predicted by up-dating and MMSE scores. Educational level and FAB score were the best predictors of the FB2 reasoning (proportion of variance R^2 = 57%) and of the affective ToM measures (proportion of variance R^2 = 43%).

Table 5 about here

To sum up, cognitive and affective ToM were both correlated to EF scores. Specifically, cognitive ToM was mainly related to up-dating and shifting process, whereas, affective ToM was correlated to inhibition. As far as composite ToM was concerned, few correlations were pointed out, except for shifting process. However, the relationship between ToM indicators and EF scores seems to be explained, at least partly, by demographic (age and educational level) and global cognitive data (MMSE and FAB).

Discussion

The main goal of the present study was to discuss the implication of task complexity and AD severity in performing cognitive and affective ToM tasks. For this purpose, we assessed two groups of AD patients at different stages of disease (moderate AD patients and early AD patients), and a matched control group of HO subjects using two classical tasks designed to explore cognitive (1st and 2nd False Beliefs task) and affective (Eyes/Faces Test) mental states attribution. We also included a third task appreciating both affective and cognitive ToM with minimal cognitive load (Preference Judgments task). Overall, we observed a progressive decrease of ToM abilities (except for affective task) regardless the complexity of tasks.

First of all, as far as 1st order cognitive ToM is concerned, our findings throw more light upon this topic. To date, this study is the first to demonstrate a significant difference in ToM performance between two groups of AD patients at different stages of disease. Only mAD patients displayed difficulties in detecting FB1. Patients with eAD had equal performances to HO subjects but showed poorer global cognitive performances (as documented by the MMSE). This original finding confirms that cognitive ToM abilities decrease progressively over the course of disease (Laisney *et al.*, 2013). Regression analysis confirmed this assumption since we observed that up-dating process and disease severity (MMSE score) were the best predictors of FB1 deficits.

Regarding FB2 task, our results are in line with those of previous studies on AD (Gregory *et al.*, 2002; Fernandez-Duque *et al.*, 2011; Laisney *et al.*, 2013; Freedman *et al.*, 2013). In fact, regardless the disease severity, AD patients presented a faulty cognitive ToM ability. There was no more differences between both groups of AD patients.

Interestingly, we showed that the best predictor of FB2 performance was the educational level. This indicator reflects premorbid cognitive resources. Indeed, in line with the assumption of Laisney *et al.* (2013), we observed a general effect of crystallized intelligence on cognitive ToM performance. Similar finding was also previously reported in healthy aging (Maylor, Moulson, Muncer, & Taylor, 2002), and in fv-FDT (Torrelva *et al.*, 2009). This was never experimentally tested in AD patients until today.

Our results are consistent with other current researches on ToM. They confirm the integrative conception of ToM performances in normal aging (German & Hehman, 2006), and in AD population as it was recently suggested (Sandoz *et al.*, 2014). This assumption implies that ToM reasoning is relying on both cognitive resources (*e.g.* executive process) and mentalizing ability. Hence, decreased performances on ToM tasks could reflect, in part, a general cognitive decline. We can then speculate that our eAD patients had similar performances on ToM tasks as did subjects of the control group because of better cognitive resources that offset the decreasing mentalizing reasoning. These aspects of compensatory mechanisms could operate until cognitive resources become too reduced to deal with the complexity of FB2 tasks.

In the FTD, Eslinger and his colleagues had already developed a neural model of social cognition; the social executors framework (Eslinger *et al.*, 2007; Eslinger, Moore, Anderson, & Grossman, 2011). In this model, social breakdowns result from the interaction between social knowledge and executive resources (for more details see Eslinger *et al.*, 2007). Accordingly, and due to the fact that executive decline in AD appears later in the course of disease (Sandoz *et al.*, 2014), our results can be explained on the basis of compensatory mechanisms: cognitive ToM reasoning in early stages of AD continues to be efficient because of the alternative use of non-specific executive resources.

Second, with regard to affective ToM, results showed that both AD groups as well as control subjects had similar performances on the EFT. These findings are not entirely in accordance with the recent study of Laisney *et al.* (2013) who found, using the same methodology, an impairment of complex affective mental states understanding in AD. Moreover, unlike Laisney *et al.* (2013) we did not observe a correlation between EFT scores and the severity of dementia, but, a correlation between affective ToM and educational level and global FAB score was found. As these two indicators are reflecting global cognitive resources, we can suggest that AD patients are able to infer correct affective states to others thanks to a correct comprehension of the situation. Since decoding of facial emotions becomes impaired over the course of the disease due to the decline of general cognitive resources (see for example Klein-Koerkamp, Beaudoin, Baciu, & Hot, 2012), the affective ToM may decrease.

In fact, this is consistent with the finding of Castelli *et al.* (2010) who submitted two healthy groups (young versus older) to an fMRI scanning while realizing the RME test. Although the authors did not report any difference in behavioral performances between the two groups, they showed differences in activated mentalizing circuits. In fact, if the youngest group activated the superior temporal sulcus and the temporal poles, old people showed a relevant bilateral activation of frontal areas and a stronger involvement of the linguistic components of the mirror neuron system, reflecting according to Castelli *et al.* (2010), compensatory mechanisms.

In the current study, we did not perform neuroimaging studies so we could only speculate on a possible link between our divergent results and compensatory mechanisms on hot mentalizing. Further studies are needed to explore if activated circuits differ between AD patients showing frontal damages (Van Hoesen *et al.*, 2000; Carrington & Bailey, 2009) and HO subjects.

Third, in order to test the implication of task severity, we included a composite ToM task (PJ task), with minimal cognitive demands, to test mental reasoning without involving more general cognitive aspects (Snowden *et al.*, 2003; Duval *et al.*, 2011; Laisney *et al.*, 2013). Our results showed that both AD groups performed worse than HO subjects on the composite ToM task. These results are not consistent with the task complexity assumption.

We also observed participants' significant error patterns. Indeed, mAD and eAD patients produced more personal justifications (52% and 42%, respectively) than HO subjects (35%). HO subjects took into account Tom's taste better than their own preference. Our result supports the proposition, made by Castelli *et al.* (2011) without experimental verification, that AD patients' choices were driven by their own preferences. This pattern of justifications leads us to interpret personal taste salience as a compensatory mechanism. In fact, patients tend to rely on personal elements, which are always available, to cope with their failure to take into account others' perspectives.

The present results may also be interpreted in accordance with prior studies depicting faulty perspective taking in AD (Ruby *et al.*, 2009; Freedman *et al.*, 2013). In fact, the PJ test presents a conflict between two perspectives (own perspective vs. third-person perspective). Participants had to (a) inhibit their salient perspectives; (b) shift attentional focus on the third-person perspective; and (c) infer others' perspectives (Samson, Apperly, Kathirgamanathan, & Humphreys, 2005; Samson, 2009). The extant data (Bora *et al.*, 2015; Le Bouc *et al.*, 2012) suggest that mentalizing disturbances in AD are the consequence of difficulty to infer beliefs to others (mainly subtended by a dysfunction of the temporo-parietal junction, see Le Bouc *et al.*, 2012). This difficulty is distinct from ToM dysfunction in FTD associated with difficulty to inhibit their own perspective, which mainly depends on the lateral prefrontal cortex (see for a review Henry *et al.*, 2015; Bora *et al.*, 2015).

The second main aim of the present study was to examine the association between ToM performance and executive dysfunction in AD people.

We showed that while moderate AD patients were impaired on spontaneous flexibility (plus/minus test) and inhibition (Stroop), but not on up-dating (2-back) nor on allocation of attention in working memory (dual task) the early AD patients did not differ from HO group on any of these executive tasks. These results further support the idea of a progressive executive decline in AD patients (see for example Carter, Caine, Burns, Herholz, & Lambon Ralph, 2012).

The progressive decay of both ToM ability and executive functioning in AD patients at different stages of disease, allows us to consider EF as a “scaffold” (Apperly, Samson, Humphreys, 2009) to a successful ToM reasoning. When EF deficits appear, the ability to interpret mental state decreases, reflecting individual discrepancy to deal with brain damages and cognitive demands of mentalizing tasks. These results are consistent with the idea that ToM performances result from an integrative reasoning: specialized mentalizing abilities and non-specific resources such as executive selection (Sandoz *et al.*, 2014). As it was demonstrated in normal aging (German & Hehman, 2006), faulty ToM performances in our patients were, in part, linked to a decline in executive selection abilities due to AD.

As reported by Stern (2009; 2012), we hypothesized that compensatory mechanisms could allow functional social interacting in AD patients, even if some ToM performances were declined. These mechanisms could be called “social reserve”. On the basis of the same principle of cognitive reserve (individual differences to tolerate, over at least, brain changes and still maintain functional cognitive performance, Stern, 2012), premorbid cognitive level, as well as global resources, can act as moderators between pathological lesions in AD and social outcome. Social reserve can be defined as the ability of early AD patients to maintain efficient mentalizing reasoning relying on spared cognitive general resources. This reserve allows AD patients to adapt their social behaviors in real interactions, despite poorer ToM scores. So, individuals with high social reserve would better cope with brain dysfunction due to higher general cognitive recourses. When, cognitive deficits reach a critical threshold, social symptoms will start to appear.

However, in the current study, caution is needed as regard the assumption of the alternative hypothesis of social reserve due to the lack of neuroimaging data to confirm behavioral data (Carrington & Bailey, 2009) as well as the absence of functional indicators of real behavioral disturbances. In addition, we did not use clinical scales (as Clinical Dementia Rating Scale) for staging AD and our neuropsychological protocol would have to include more cognitive processes influencing ToM in AD (Sandoz *et al.*, 2014). For instance, measures of vocabulary level, logical reasoning, and episodic memory were not considered in this paper. In line with the social reserve hypothesis, further studies are needed for (a) examining the performance of amnestic mild cognitive impaired patients, considered as a pre-clinical condition (see for example Moreau *et al.*, 2015); and (b) testing AD patients in situation of real interaction to assess the use of social knowledge in dynamic interaction.

In conclusion, and notwithstanding these limitations, the current study provides the first empirical evidence of a progressive decay of cognitive ToM abilities in AD. Cognitive ToM seems to be spared in the early stage of AD. Disorganized behaviors and breakdown in everyday life relationships appear when the social reserve is exhausted. These findings need further empirical and neuroimaging confirmations. This original neuropsychological study also suggests the importance to include ToM evaluation in neuropsychological assessments (Adenzato & Poletti, 2013) in order to better understand behavioral changes in real interpersonal interactions (Hodges, 2013).

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References

Aboulafia-Brakha, T., Christe, B., Martory, M. D., & Annoni, J. M. (2011). Theory of Mind tasks and executive functions: A systematic review of group studies in neurology. *Journal of Neuropsychology*, *5*(1), 39-55. doi:10.1348/174866410X533660

Adenzato, M., & Poletti, M. (2013). Theory of Mind abilities in neurodegenerative diseases: An update and a call to introduce mentalizing tasks in standard neuropsychological assessments. *Clinical Psychiatry, 10*(5), 226-234. Retrieved from http://www.psych.unito.it/csc/pers/adenzato/adenzato.html

Adenzato, M., Cavallo, M., & Enrici, I. (2010). Theory of mind ability in the behavioral variant of frontotemporal dementia: an analysis of the neural, cognitive, and social levels. *Neuropsychologia*, *48*(1), 2‑12. doi:10.1016/j.neuropsychologia.2009.08.001

Albert, M. S., DeKosky, S. T., Dickson, D., Dubois, B., Feldman, H. H., Fox, N. C., … Phelps, C. H. (2011). The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*, *7*(3), 270-279. doi:10.1016/j.jalz.2011.03.008

Allain, P., Etcharry-Bouyx, F., & Verny, C. (2013). Executive functions in clinical and preclinical Alzheimer's disease. *Revue Neurologique*, *169*(10), 695-708. doi:10.1016/j.neurol.2013.07.020

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders (5th ed.)*. Washington, DC: Author.

Amieva, H., Mokri, H., Le Goff, M., Meillon, C., Jacqmin-Gadda, H., Foubert-Samier, A., … Dartigues, J.-F. (2014). Compensatory mechanisms in higher-educated subjects with Alzheimer's disease: a study of 20 years of cognitive decline. *Brain: A Journal of Neurology*, *137*(Pt 4), 1167-1175. doi:10.1093/brain/awu035

Apperly, I. A., Samson, D., & Humphreys, G. W. (2009). Studies of adults can inform accounts of theory of mind development. *Developmental Psychology*, *45*(1), 190-201. doi:10.1037/a0014098

Baddeley, A. D., Bressi, S., Della Sala, S., Logie, R., & Spinnler, H. (1991). The Decline of Working Memory in Alzheimer's Disease. *Brain*, *114*(6), 2521‑2542.

doi:10.1093/brain/114.6.2521

Baron-Cohen, S., Leslie, A. M., & Frith, U. (1985). Does the autistic child have a « Theory of Mind »? *Cognition*, *21*(1), 37-46. Retrieved from http://www.sciencedirect.com/science/article/pii/0010027785900228

Baron-Cohen, S., Wheelwright, S., Hill, J., Raste, Y., & Plumb, I. (2001). The « Reading the Mind in the Eyes ». Test revised version: A study with normal adults, and adults with Asperger syndrome or high-functioning autism. *Journal of Child Psychology and Psychiatry, and Allied Disciplines*, *42*(2), 241-251. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11280420

Bertoux, M., Volle, E., de Souza, L. C., Funkiewiez, A., Dubois, B., & Habert, M. O. (2014). Neural correlates of the mini-SEA (Social cognition and Emotional Assessment) in behavioral variant frontotemporal dementia. *Brain Imaging and Behavior*, *8*(1), 1-6. doi:10.1007/s11682-013-9261-0

Bora, E., Walterfang, M., & Velakoulis, D. (2015). Theory of mind in behavioural-variant frontotemporal dementia and Alzheimer's disease: a meta-analysis. *Journal of Neurology, Neurosurgery, and Psychiatry*. doi:10.1136/jnnp-2014-309445

Brothers, L., & Ring, B. (1992). A neuroethological framework for the representation of minds. *Journal of Cognitive Neuroscience*, *4*(2), 107-118. doi:10.1162/jocn.1992.4.2.107

Carrington, S. J., & Bailey, A. J. (2009). Are there Theory of Mind regions in the brain? A review of the neuroimaging literature. *Human Brain Mapping*, *30*(8), 2313-2335. doi:10.1002/hbm.20671

Carter, S. F., Caine, D., Burns, A., Herholz, K., & Lambon Ralph, M. A. (2012). Staging of the cognitive decline in Alzheimer's disease: insights from a detailed neuropsychological investigation of mild cognitive impairment and mild Alzheimer's disease. *International Journal of Geriatric Psychiatry*, *27*(4), 423-432. doi:10.1002/gps.2738

Castelli, I., Baglio, F., Blasi, V., Alberoni, M., Falini, A., Liverta-Sempio, O., … Marchetti, A.

(2010). Effects of aging on mindreading ability through the eyes: an fMRI study. *Neuropsychologia*, *48*(9), 2586-2594. doi:10.1016/j.neuropsychologia.2010.05.005

Castelli, I., Pini, A., Alberoni, M., Liverta-Sempio, O., Baglio, F., Massaro, D., … Nemni, R. (2011). Mapping levels of theory of mind in Alzheimer's disease: a preliminary study. *Aging & Mental Health*, *15*(2), 157-168. doi:10.1080/13607863.2010.513038

Coricelli, G. (2005). Two-levels of mental states attribution: from automaticity to voluntariness. *Neuropsychologia, 43*(2), 294-300. doi:10.1016/j.neuropsychologia.2004.11.015.

Cuerva, A. G., Sabe, L., Kuzis, G., Tiberti, C., Dorrego, F., & Starkstein, S. E. (2001). Theory of Mind and pragmatic abilities in dementia. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology*, *14*(3), 153-158. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11513098

Desgranges, B., Laisney, M., Bon, L., Duval, C., Mondou, A., Bejanin, A., Fliss, R., Beaunieux, H., & Eustache, F. (2012). TOM-15: Une épreuve de fausses croyances pour évaluer la théorie de l'esprit cognitive. *Revue de Neuropsychologie, 4*(3), 216‑220

Dubois, B., Slachesvsky, A., Litvan, I., & Pillon, B. (2000). The FAB: A frontal assessment battery at bedside. *Neurology, 55*, 1621–1626. doi:10.1212/WNL.55.11.1621.

Duval, C., Piolino, P., Bejanin, A., Eustache, F., & Desgranges, B. (2011). Age effects on different components of Theory of Mind. *Consciousness and Cognition*, *20*(3), 627-642. doi:10.1016/j.concog.2010.10.025

Eslinger, P. J., Moore, P., Anderson, C., & Grossman, M. (2011). Social cognition, executive functioning, and neuroimaging correlates of empathic deficits in frontotemporal dementia. *The Journal of Neuropsychiatry and Clinical Neurosciences*, *23*(1), 74-82. doi:10.1176/appi.neuropsych.23.1.74

Eslinger, P. J., Moore, P., Troiani, V., Antani, S., Cross, K., Kwok, S., & Grossman, M. (2007). Oops! Resolving social dilemmas in frontotemporal dementia. *Journal of Neurology, Neurosurgery, and Psychiatry*, *78*(5), 457-460. doi:10.1136/jnnp.2006.098228

Fernandez-Duque, D., Baird, J. A., & Black, S. E. (2009). False-belief understanding in frontotemporal dementia and Alzheimer's disease. *Journal of Clinical and Experimental Neuropsychology*, *31*(4), 489-497. doi:10.1080/13803390802282688

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). « Mini-mental state ». A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research*, *12*(3), 189-198. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/1202204

Freedman, M., Binns, M. A., Black, S. E., Murphy, C., & Stuss, D. T. (2013). Theory of Mind and recognition of facial emotion in dementia: challenge to current concepts. *Alzheimer Disease and Associated Disorders*, *27*(1), 56-61. doi:10.1097/WAD.0b013e31824ea5db.

German, T. P., & Hehman, J. A. (2006). Representational and executive selection resources in « theory of mind »: evidence from compromised belief-desire reasoning in old age. *Cognition*, *101*(1), 129-152. doi:10.1016/j.cognition.2005.05.007

Gregory, C., Lough, S., Stone, V., Erzinclioglu, S., Martin, L., Baron-Cohen, S., & Hodges, J. R. (2002). Theory of mind in patients with frontal variant frontotemporal dementia and Alzheimer's disease: theoretical and practical implications. *Brain*, *125*(4), 752-764. doi:10.1093/brain/awf079

Henry, J. D., Phillips, L. H., & von Hippel, C. (2014). A meta-analytic review of theory of mind difficulties in behavioural-variant frontotemporal dementia. *Neuropsychologia*, *56*, 53-62. doi:10.1016/j.neuropsychologia.2013.12.024

Hodges, J. R. (2013). Alzheimer's disease and the frontotemporal dementias: Contributions to clinico-pathological studies, diagnosis, and cognitive neuroscience. *Journal of Alzheimer's Disease, 33*(l1), S211-217. doi:10.3233/JAD-2012-129038.

Kemp, J., Després, O., Sellal, F., & Dufour, A. (2012). Theory of Mind in normal ageing and neurodegenerative pathologies. *Ageing Research Reviews, 11*(2), 199-219. doi:10.1016/j.arr.2011.12.001.

Klein-Koerkamp, Y., Beaudoin, M., Baciu, M., & Hot, P. (2012). Emotional decoding abilities in

Alzheimer's disease: a meta-analysis. *Journal of Alzheimer's Disease: JAD*, *32*(1), 109‑125. doi:10.3233/JAD-2012-120553

Laisney, M., Bon, L., Guiziou, C., Daluzeau, N., Eustache, F., & Desgranges, B. (2013). Cognitive and affective Theory of Mind in mild to moderate Alzheimer's disease. *Journal of Neuropsychology*, *7*(1), 107-120. doi:10.1111/j.1748-6653.2012.02038.x.

Le Bouc, R., Lenfant, P., Delbeuck, X., Ravasi, L., Lebert, F., Semah, F., & Pasquier, F. (2012). My belief or yours? Differential theory of mind deficits in frontotemporal dementia and Alzheimer's disease. *Brain: A Journal of Neurology*, *135*(Pt 10), 3026‑3038. doi:10.1093/brain/aws237

Maylor, E. A., Moulson, J. M., Muncer, A.M., & Taylor, L. A. (2002). Does performance on Theory of Mind tasks decline in old age? *British Journal of Psychology, 93*(4), 465-485. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12519529

McKhann, G. M., Knopman, D. S., Chertkow, H., Hyman, B. T., Jack, C. R., Kawas, C. H., … Phelps, C. H. (2011). The diagnosis of dementia due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & dementia : the journal of the Alzheimer's Association*, *7*(3), 263‑269. doi:10.1016/j.jalz.2011.03.005

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex « Frontal Lobe » tasks: a latent variable analysis. *Cognitive Psychology*, *41*(1), 49‑100. doi:10.1006/cogp.1999.0734

Modinos, G., Obiols, J. E., Pousa, E., & Vicens, J. (2009). Theory of Mind in different dementia profiles. *The Journal of Neuropsychiatry and Clinical Neurosciences*, *21*(1), 100-101. doi:10.1176/appi.neuropsych.21.1.100

Moreau, N., Rauzy, S., Bonnefoi, B., Renié, L., Martinez-Almoyna, L., Viallet, F., & Champagne-Lavau, M. (2015). Different Patterns of Theory of Mind Impairment in Mild Cognitive

Impairment. *Journal of Alzheimer's Disease: JAD*. doi:10.3233/JAD-143021

Poletti, M., & Bonuccelli, U. (2013). Alteration of affective Theory of Mind in amnestic mild cognitive impairment. *Journal of Neuropsychology*, *7*(1), 121‑131. doi:10.1111/j.1748-6653.2012.02040.x

Poletti, M., Enrici, I., & Adenzato, M. (2012). Cognitive and affective Theory of Mind in neurodegenerative diseases: Neuropsychological, neuroanatomical and neurochemical levels. *Neuroscience and Biobehavioral Reviews*, *36*(9), 2147-2164. doi:10.1016/j.neubiorev.2012.07.004

Ruby, P., Collette, F., D'Argembeau, A., Péters, F., Degueldre, C., Balteau, E., … Salmon, E. (2009). Perspective taking to assess self-personality: what's modified in Alzheimer's disease? *Neurobiology of Aging*, *30*(10), 1637‑1651. doi:10.1016/j.neurobiolaging.2007.12.014

Samson, D. (2009). Reading other people's mind: insights from neuropsychology. *Journal of Neuropsychology*, *3*(Pt 1), 3‑16. doi:10.1348/174866408X377883

Samson, D., Apperly, I. A., Kathirgamanathan, U., & Humphreys, G. W. (2005). Seeing it my way: a case of a selective deficit in inhibiting self-perspective. *Brain: A Journal of Neurology*, *128*(Pt 5), 1102‑1111. doi:10.1093/brain/awh464

Sandoz, M., Démonet, J. F., & Fossard, M. (2014). Theory of Mind and cognitive processes in aging and Alzheimer type dementia: A systematic review. *Aging & Mental Health, 18*(7), 815-827. doi:10.1080/13607863.2014.899974

Schurz, M., Radua, J., Aichhorn, M., Richlan, F., & Perner, J. (2014). Fractionating theory of mind: a meta-analysis of functional brain imaging studies. *Neuroscience and Biobehavioral Reviews*, *42*, 9‑34. doi:10.1016/j.neubiorev.2014.01.009

Shamay-Tsoory, S. G., & Aharon-Peretz, J. (2007). Dissociable prefrontal networks for cognitive and affective Theory of Mind: A lesion study. *Neuropsychologia, 45*(13), 3054-3067. doi:10.1016/j.neuropsychologia.2007.05.021

Shamay-Tsoory, S. G., Tomer, R., Berger, B. D., & Aharon-Peretz, J. (2003). Characterization of empathy deficits following prefrontal brain damage: the role of the right ventromedial prefrontal cortex. *Journal of Cognitive Neuroscience, 15*(3), 324-337. doi:10.1162/089892903321593063

Shany-Ur, T., Poorzand, P., Grossman, S., Growdon, M., Jang, J., Ketelle, R., … Rankin, K. P. (2012). Comprehension of insincere communication in neurodegenerative disease: Lies, sarcasm, and theory of mind. *Cortex; a journal devoted to the study of the nervous system and behavior*, *48*(10), 1329-1341. doi:10.1016/j.cortex.2011.08.003

Snowden, J. S., Gibbons, Z. C., Blackshaw, A., Doubleday, E., Thompson, J., Craufurd, D., … Neary, D. (2003). Social cognition in frontotemporal dementia and Huntington's disease. *Neuropsychologia*, *41*(6), 688-701. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12591026

Stern, Y. (2009). Cognitive reserve. *Neuropsychologia, 47*(10), 2015-2028. doi:10.1016/j.neuropsychologia.2009.03.004

Stern, Y. (2012). Cognitive reserve in ageing and Alzheimer's disease. *Lancet Neurology, 11*(11), 1006-1012. doi:10.1016/S1474-4422(12)70191-6

Stone, V. E., Baron-Cohen, S., & Knight, R.T. (1998). Frontal lobe contributions to Theory of Mind. *Journal of Cognitive Neuroscience*, *10*(5), 640-656. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/9802997

Torralva, T., Roca, M., Gleichgerrcht, E., Bekinschtein, T., & Manes, F. (2009). A neuropsychological battery to detect specific executive and social cognitive impairments in early frontotemporal dementia. *Brain: A Journal of Neurology*, *132*(5), 1299-1309. doi:10.1093/brain/awp041.

Van Hoesen, G. W., Parvizi, J., & Chu, C. C. (2000). Orbitofrontal cortex pathology in Alzheimer's disease. *Cerebral Cortex, 10*(3), 243-251. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10731219

Wimmer, H., & Perner, J. (1983). Beliefs about beliefs: Representation and constraining function of wrong beliefs in young children's understanding of deception. *Cognition , 13*, 103-128. Retrieved from http://www.sciencedirect.com/science/article/pii/0010027783900045

Woodford, H. J., & George, J. (2007). Cognitive assessment in the elderly: A review of clinical methods. *QJM: An International Journal of Medicine, 100*(8), 469-484. doi:10.1093/qjmed/hcm051

Zaitchik, D., Koff, E., Brownell, H., Winner, E., & Albert, M. (2004). Inference of mental states in patients with Alzheimer's disease. *Cognitive Neuropsychiatry*, *9*(4), 301-313. doi:10.1080/13546800344000246

Zaitchik, D., Koff, E., Brownell, H., Winner, E., & Albert, M. (2006). Inference of beliefs and emotions in patients with Alzheimer's disease. *Neuropsychology*, *20*(1), 11-20. doi:10.1037/0894-4105.20.1.11

Table 1. Neuropsychological and demographic data of the study population.

	mAD patients (n = 19)		eAD patients (n = 23)		HO subjects (n = 23)		ANOVA *p*-value	*Tukey HSD post-hoc test*		
	mean	*SD*	mean	*SD*	mean	*SD*		eAD/mAD	HO/mAD	HO/eAD
Age	79.3	*9.9*	77.7	*7*	77.9	*9.9*	ns	ns	ns	ns
Sex-ratio (M/F)	5/14		11/12		11/12		ns*		-	
Education level	7.7	*2.6*	9.2	*3.7*	8.6	*2.1*	ns	ns	ns	ns
MMSE	19.8	*1.4*	24.3	*1.2*	28.9	*1*	*< .0001*	*.0001*	*.0001*	*.0001*
FAB	9.5	*4.2*	13.2	*2.7*	17.5	*0.5*	*< .0001*	*.001*	*.001*	*.0001*

note: *SD*= Standard Deviation; HO= Healthy Older subjects; eAD= early Alzheimer's Disease patients, mAD= moderate Alzheimer's Disease patients; M= male; F= female;

MMSE = Mini Mental Sate Examination (Folstein *et al.*, 1975) ; FAB = Frontal Assessment Battery (Dubois *et al.*, 2000).

*Chi square

significant results p < . 05

Table 2. Performances of the groups of AD patients and HO subjects on executive tasks.

	mAD (n = 19)		eAD (n = 23)		HO (n = 23)		ANOVA $F(p)$	*Tukey HSD post-hoc test*	Effect size η^2
	mean	*SD*	mean	*SD*	mean	*SD*			
Stroop interference	10.2	*19.6*	2.9	*3.2*	1.5	*3.6*	3.6 *(.03)*	mAD<HO ; HO = eAD	.11
Plus/Minus Shifting	5.2	*4.5*	2.5	*3.1*	0.8	*1.8*	9.4 *(<.0000)*	mAD<HO ; HO = eAD ; mAD<eAD	.23
2-back up-dating	11.1	*4.1*	8.7	*3.7*	7	*4.4*	2.8 *(ns)*	-	.12
“Mu”	90.5	*14.2*	86.5	*18*	-		.7 *(ns)* *	-	.007

note: *SD*= Standard Deviation; HO= Healthy Older subjects; eAD= early Alzheimer's Disease patients, mAD= moderate Alzheimer's Disease patients

* t student

significant results p < .05

Table 3. Performances of the groups of AD patients and HO subjects on ToM tasks.

	mAD patients (n = 19)		eAD patients (n = 23)		HO subjects (n = 23)		ANOVA *F*(*p*)	*Tukey HSD post-hoc test*	Effect size η^2
	mean	*SD*	mean	*SD*	mean	*SD*			
Cognitive ToM									
1st order FB	57.3	*28*	67.9	*22.2*	79.3	*17.5*	5 *(.009)*	mAD<HO ; HO = eAD	.14
2nd order FB	42.1	*28.8*	44.7	*20.8*	69.6	*23.7*	8.5 *(.0005)*	mAD<eAD<HO	.22
Control FB	80	22.4	82.9	14.2	89.3	10	2 (ns)	mAD = eAD = HO	.05
Affective ToM									
ToM condition	45.7	*18.3*	54.4	*16.5*	48.2	*21.1*	.4 *(ns)*	-	.01
Control condition	55	*18.7*	55.3	*20.4*	64.3	*13.4*	.2 *(ns)*		.02
Composite ToM									
Judgment of preferences	50.3	*16*	55.4	*16.1*	73.4	*15.9*	12.9 *(< .0001)*	mAD<eAD<HO	.29

note: *SD*= Standard Deviation; HO= Healthy Older subjects; eAD= early Alzheimer's Disease patients, mAD= moderate Alzheimer's Disease patients

significant results p < .05

Table 4. Main correlations (Pearson correlation coefficient) between ToM scores and EF in the groups of AD patients

	FAB	Inhibition *Stroop*	Shifting *Plus/Minus*	Up-dating *2-back*	Dual Task *Composite score "mu"*
ToM Cognitive					
1st order FB task	.37	.15	.03	-.48	.21
	.12	.11	-.08	*-.54**	-.05
	-.26	-.31	-.03	*-.81**	-.31
2nd order FB task	.33	.22	-.19	.10	.19
	.28	.09	*-.54**	-.29	-.09
	.17	.10	-.29	*-.65**	-.28
ToM Affective					
Complex Emotions-Eyes	.21	.39	.36	-.29	.21
	.30	.10	.18	.02	-.27
	.41	*-.63**	.21	-.06	-.29
ToM Composite					
Preference Judgments task	-.31	.03	-.31	-.41	.09
	-.31	.03	-.31	-.41	.09
	*-.82**	.01	*-.56**	-.47	.006

note: FAB = Frontal Assessment Battery (Dubois *et al.*, 2000) ;

1st line = correlations on the mAD group only; 2sd line = correlations on the eAD group only; and the 3rd line = correlations on the whole AD group.

**significant results p < .05*

Table 5. Stepwise regression analyses with ToM dependent variables correlated with EF scores.

EF related ToM dependent variable	Steps and predictors	*β**	*p*	R^2	*F*	*p*
	1. Up-dating	- .71*	.002*			
	2. Inhibition	ns	ns			
	3. MMSE	-.53*	.04*			
1st order FB task	4. FAB	ns	ns	.63*	3.9	.02*
	5. Shifting	ns	ns			
	6. Educational level	ns	ns			
	1. Educational level	.47*	.02*			
	2. FAB	.55*	.03*			
	3. MMSE	ns	ns			
2nd order FB task	4.Up-dating	ns	ns	.57*	3.1	.04*
	5. Inhibition	ns	ns			
	6. Shifting	ns	ns			
	1. Educational level	.53*	.02*			
	2. FAB	.60*	.02*			
Complex Emotions-Eyes	3. MMSE	ns	ns	.43*	2.9	.05*
	4.Ihibition	ns	ns			
PJ task	1. Educational level	ns	ns	.12	2.5	ns

note: MMSE = Mini Mental Sate Examination (Folstein *et al.*, 1975) ; FAB = Frontal Assessment Battery (Dubois *et al.*, 2000)

* significant results $p < .05$

Figure 1. Proportion of error rates across error types in the groups of AD patients and HO subjects on PJ task.