

## **Inference of mental states in patients with Alzheimer's disease**

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*Introduction.* The ability to determine what someone thinks or knows often requires an individual to infer the mental state of another person, an ability typically referred to as one's "theory of mind". The present study tests this ability in patients with mild-to-moderate Alzheimer's disease (AD).

*Methods.* Three theory of mind tests and three standardised neuropsychological tests were presented to a group of patients with AD ( $n = 25$ ) and a group of healthy elderly controls ( $n = 15$ ).

*Results.* On the first two theory of mind tasks, the performance of the AD patients was nearly perfect and did not differ from that of the controls: AD patients showed no difficulties in either attributing a false belief to another person, or in recognising their own previous false beliefs. On the third theory of mind task, where the key information was embedded in a story narrative, AD patients performed significantly worse than controls. However, their performance on this task was similar to the control condition, which used a similar story but which did not involve beliefs.

*Conclusions.* These results, as well as those involving correlations between the neuropsychological tests and performance on the third task, suggest that the AD patients' difficulty may be secondary to their cognitive impairments, rather than a primary impairment in theory of mind.

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The ability to infer mental states in others is often referred to as one's "theory of mind", since it involves a number of assumptions about how mental states are formed and used to interpret reality (e.g., Leslie, 1987; Wellman, 1985). Developmental studies indicate that the ability to correctly infer the mental state of another individual is present in healthy humans across many cultures by age 4 (Wimmer & Perner, 1983; Zaitchik, 1990). Thus, it has been hypothesised that this ability may be species-universal (Avis & Harris, 1991) and innately specified, and may have a dedicated cognitive mechanism that is brain based (Leslie, 1987).

Recent work has shown that high functioning autistic individuals (Baron-Cohen, Leslie, & Frith, 1985, 1986; Baron-Cohen, Tager-Flusberg, & Cohen, 1993; Tager-Flusberg & Sullivan, 1994), middle-aged patients with focal right hemisphere damage (e.g., Brownell, Pincus, Blum, Rehak, & Winner, 1997; Winner, Brownell, Happe, Blum, & Pincus, 1998), and patients with fronto-temporal dementia (FTD) (Gregory et al., 2002) show selective impairments in theory of mind. In contrast, no such deficit is evident in normal elderly individuals (Happe, Brownell, & Winner, 1998), in patients with Down Syndrome (Baron-Cohen et al., 1985), and in patients with very mild, early-onset AD (Gregory et al., 2002). It is still unknown whether AD patients with late-onset AD of mild-to-moderate severity show impairments in the basic ability to attribute mental states.

It is noteworthy that the neurologic populations that show selective deficits on tasks that assess theory of mind, also show marked impairment in their social functioning (Baron-Cohen et al., 1985, 1986; Brownell et al., 1997; Gregory et al., 2002; Tager-Flusberg, & Sullivan, 1994; Winner et al., 1998). This is consistent with the hypothesis that successful social interaction requires an intact ability to make inferences about mental states in others (Fodor, 1987).

To date, theory of mind research has focused almost exclusively on non-emotional states, such as beliefs and desires. However, the successful prediction and explanation of human action sometimes requires understanding how people feel, as well as what they know or believe or desire. Although there are generally behavioural cues to emotions (e.g., facial expressions, gestures), these behaviours are considered indicators of internal states. To that degree, emotions (like beliefs and desires) must be inferred by others.

A number of studies have investigated the ability to identify emotions in patients with Alzheimer's disease (AD) (Albert, Cohen, & Koff, 1991; Allender & Kaszniak, 1989; Cadieux & Greve, 1997; Koff, Zaitchik, Montepare, & Albert, 1999). What is interesting about these studies, in the context of the theory of mind literature, is that patients with AD are not impaired in processing emotional information in general, but they are impaired on several tasks that require inference of emotion from situational information. One interpretation of these findings is that these deficits are part of a specific difficulty representing and making inferences about mental states. Such difficulties would include processing of mental affective information (e.g., sadness) and mental nonaffective information (e.g., knowledge) but not nonmental information (e.g., physical attributes). For example, an individual might have difficulty making an inference

about whether another individual knows a particular fact, or is sad in a particular situation, but have no difficulty inferring whether a person is cold or hungry.

In a recent study (Gregory et al., 2002), FTD patients' performance on theory of mind tasks was compared to that of AD patients. In order to be equivalent in age and overall level of cognitive function, as measured by scores on the Mini-Mental State Exam (MMSE; Folstein, Folstein, & McHugh, 1975), the AD patients had early-onset AD (mean age = 66.5 years) and were quite high functioning. In fact, the overall level of cognitive functioning of the AD group (mean MMSE = 27.1) was not statistically different from that of a group of the healthy elderly controls (mean MMSE = 28.7).

Another recent study (Garcia Cuerva et al., 2001) demonstrated that AD patients were impaired in their ability to make inferences of second order beliefs (second order belief inferences are those in which one must infer one person's belief about another person's belief, i.e., what one person thinks another person believes to be true). However, tests of second order beliefs are typically long, complex and place demands on memory ability. It is therefore still unknown whether late-onset AD patients of mild-to-moderate severity show impairments in the basic ability to attribute mental states.

The present study therefore looks specifically at the ability of mild-to-moderately impaired AD patients to infer mental states. We administered the most basic tasks in the theory of mind literature to these patients. All of these tasks, which were initially designed for use with preschool children, make minimal demands on language, memory, and attention. Nevertheless, they tap an understanding of three properties that appear to be central to an individual's theory of mind. These properties are: (1) that perceptual experience leads to belief; (2) that things may appear to us other than as they are; and that (3) therefore we may hold beliefs that are false. In other words, to have an accurate "theory of mind" one must assume: (1) that beliefs are representations we form in our mind; (2) that beliefs are based on other representations in the mind (e.g., by what one sees or hears); and (3) that, insofar as beliefs are only representations, they may be incorrect.

Based on the hypothesis that the AD patient's ability to infer a belief would be similar to their ability to infer an emotion, we hypothesised that there would be no primary deficit in the patients performance, compared to controls; that is, there would be no deficit that appeared on all tasks across the board. Instead, we predicted evidence of secondary deficits—deficits that derived from the specific demands of the task in question, rather than from an underlying impairment in making inferences about mental states in others.

## METHODS

### Participants

This study was conducted at the Hebrew Rehabilitation Center for Aged, a long-term care facility in Boston. A total of 40 residents gave informed consent to

participate in the study; 15 were cognitively normal controls (2 men and 13 women) and 25 were patients with AD (2 men and 23 women). Since success on basic theory of mind tasks appears to be virtually universal among healthy individuals of both sexes by age 4 (as mentioned above), the small number of male subjects was not considered problematic. The mean ages of the two groups were 88.47 ( $SD = 6.70$ ) and 88.96 ( $SD = 5.75$ ) years, respectively, which did not differ significantly from one another.

The cognitive status of each member of the control group was carefully reviewed with an informed source—a close friend or family member—to determine that there was no history of progressive cognitive decline. Laboratory tests to determine general medical health were also given (e.g., SMA-20, vitamin B<sub>12</sub> and folate levels, serologic tests, and thyroid function tests). Since the controls were residents in a long-term care facility, they had a variety of chronic medical illnesses (e.g., arthritis). However, none of the controls had conditions known to cause cognitive deficits (e.g., vitamin deficiency, electrolyte imbalance) or a history of severe head trauma, alcoholism, or psychiatric illness. The hearing and vision for the participants was also evaluated, and all had adequate hearing and visual abilities for the task demands. To corroborate the adequacy of the participants' cognitive status, the MMSE was administered. The mean MMSE of the controls was  $28.9 \pm 1.28$ .

The diagnosis of AD was based on a neurologic, psychiatric, and neuropsychologic evaluation. Participants met the National Institute of Neurological Disorders and Stroke/Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA) criteria for probable AD (McKhann et al., 1984). Medical conditions known to produce dementia were excluded. A large number of laboratory tests (e.g., SMA-20, vitamin B<sub>12</sub>, and folate levels, serologic tests, and thyroid function tests) were given to rule out various neoplastic, infectious, or metabolic causes for dementia. As with the controls, individuals with a record of severe head trauma, alcoholism, or serious psychiatric illness were excluded. All AD participants received an ischaemic score of 4 or less on the Ischaemic Scale for assessing the likelihood of multi-infarct dementia (Hachinski, 1978). The hearing and vision of the AD participants was also evaluated, and all had adequate hearing and visual abilities for the task demands. The mean MMSE of the AD patients was  $19.64 \pm 3.51$ ; some were mildly impaired and some were moderately impaired.

### Assessment of theory of mind

Three tasks were used to assess the participants' ability to infer mental states. All are well established in the theory of mind literature and have been successfully used in a number of studies that have primarily examined normal children or children with neurologic disorders, such as mental retardation and autism (Tager-Flusberg & Sullivan, 1994). As mentioned above, the tasks are designed to minimise demands on language skills and memory, but nevertheless have been shown to effectively assess the ability to infer mental states.

*Task 1: The appearance/reality task.* In the appearance/reality task, based on Flavell, Green, and Flavell (1986), the stimulus is a single real object that remains in view throughout the test. The object is a “sponge-rock”; a piece of sponge that is shaped and coloured to look like a rock. The experimenter points to the “sponge-rock”, which is lying out of reach of the subject, and asks the first of three questions. (1) Question 1: Initial Belief Question—What is this? Since this task is designed to provide each participant with the experience of being deceived, only those participants who report that the object is a rock continue with the task. Since the sponge-rock is quite convincing, the vast majority of participants do, in fact, report that it is a rock. After this occurs, the experimenter hands the sponge-rock to the subject to feel, and then asks the following test questions. (2) Question 2: Reality Question—What is it really? and (3) Question 3: Appearance Question—What does it look like? To be given credit for succeeding on this task, the subject must answer both of these questions correctly (i.e., responding that the object is really a sponge, but it looks like a rock). Task 1 thus assesses one property of mental states, the ability to understand that things may appear differently from how they are.

*Task 2: The false belief/real object task.* The false belief/real object task, based on Astington and Gopnik (1988), assesses the ability to correctly identify one’s own previously held false belief, as well as the ability to correctly infer a false belief in someone else. The subject is first shown a container (i.e., a Band-Aid box). The subject is then asked the first of four questions. (1) Initial Belief Question—What do you think is inside the box? The experimenter then opens the box and shows the subject its contents, which are not what is usually found in the box (i.e., paper clips rather than Band-Aids). After the subject has seen the contents of the box, he/she is asked the second question: (2) Reality Question—What is really in the box? Then the third and fourth questions, which are about false beliefs, follow: (3) Former False Belief Question—What did you think was in the box before we opened it? and (4) Other’s False Belief Question—If I bring another person into the room and show him the box all closed up like I first showed it to you, what will he think is in the box? To be credited with the ability to report on one’s own former false belief, the subject must correctly respond to both the second and third questions, the Reality Question and the Former False Belief Question. To be credited with the ability to infer another person’s false belief, the subject must correctly respond to the second and fourth questions, the Reality Question and the Other’s False Belief Question. Task 2 assesses the subject’s understanding of all three properties of mental states: (1) that things may appear to us other than as they are; (2) that beliefs are sometimes formed by perceptual experience; and (3) that we may hold beliefs that are false. As in Task 1, there is a single stimulus, a real object, and the discrepancy between belief and reality is based on first-hand experience.

*Task 3: The false belief/false picture story task.* Unlike Tasks 1 and 2 above, Task 3, based on Wimmer and Perner (1983), and Zaitchik (1990), does not use real objects to generate first-hand experience of false beliefs in the participants. In the false belief/false picture story task, the subject must infer the false beliefs of story characters. To make it easier for participants to understand and remember the stories, each story is illustrated by a set of four simple line drawings depicting the main events in the story. The experimenter reads each story aloud, pointing to the relevant characters in the illustrations. The task contains two conditions: the “mental state condition” and the “control condition”. In the “mental state condition” the subject must make a conclusion about a false belief in another person. In the “control condition”, the subject must make a conclusion about a false pictorial representation (e.g., drawing, photograph). In both instances, the subject him/herself knows what is true. In the “mental state condition”, to respond correctly the subject must understand that another person’s belief will depend on that person’s perceptual experience (e.g., where he saw the object) and therefore that the person might have a false belief. Notwithstanding the fact that the subject knows the real state of affairs, he or she must be able to infer a false “mental state” in another individual. In the “control condition”, to respond correctly the subject must be able to understand that a picture can represent events that are no longer true (and, in that sense, that the picture is “false”). In both conditions, the characters in the stories interact with objects or people, and the length of the stories, the language quality, and the number of illustrations are equivalent (Zaitchik, 1990).

*The mental state condition.* In the mental state condition, there are four stories, each pertaining to a character who has a false belief about the location or identity of an object (Wimmer & Perner, 1983; Zaitchik, 1990, 1991). For example, in one story, a woman puts a set of keys in her pocketbook; in the woman’s absence, a man takes the keys out of the pocketbook and places them in his briefcase. The subject is then asked two questions: (1) Reality Question—Where are the keys really? and (2) False Belief Question—Where does the woman think the keys are? To be scored correct in the mental state condition, the subject must correctly answer both the reality and the false belief question of that story, demonstrating the understanding that beliefs can conflict with reality.

*The control condition.* In the control condition, there are also four stories, each pertaining to a character who either takes a photograph or draws a picture; something then happens so that the photograph (or picture) no longer reflects the current reality (Zaitchik, 1990). For example, in one story, a woman puts a vase of flowers on the dining room table. The woman then takes a photograph of the vase. She then leaves the house. While she is gone, a man takes the vase off the table and places it on the windowsill. The subject is then asked two questions: (3) Reality Question—Where is the vase now? and (4) False Picture Question—

Where is the vase in the photo? To be scored correct in the control condition, the subject must correctly answer both the reality and the false picture question of the story, demonstrating an understanding that pictorial representations can conflict with reality (e.g., that the vase is on the table in the photo but the vase is now on the windowsill). The control condition is structurally identical to the mental state condition but it involves pictorial rather than mental representations; it is designed to test whether a subject's difficulty on the mental state condition is due to an impairment in understanding mental representations or a problem in understanding representations in general.

**Neuropsychological assessment**

Three standardised neuropsychological tests were administered to all participants. The neuropsychological tests were: (1) The Mini-Mental State Exam (MMSE; Folstein et al., 1976), a standard measure for assessing the patients' overall level of cognitive impairment, which was also used to corroborate the adequacy of the mental status of participants in the control group. (2) The figure copying subtest from the CERAD battery that assesses spatial ability (Morris et al., 1989), administered because of the possible influence of spatial skill on participants' understanding of the story illustrations included in Task 3. (3) The Similarities subtest of the WAIS-R (Wechsler, 1981), which assesses one aspect of executive function, concept formation.

**RESULTS**

*Task 1: The appearance/reality task.* The participants in both groups performed perfectly on the task that is, all responses to both question 1 (the Appearance Question) and question 2 (the Reality Question) were correct. (Note that five AD patients and one healthy control were not initially deceived by the sponge-rock; therefore they were not asked the second question and their data were not included.)

*Task 2: The false belief/real object task.* On this task, the normal controls received a perfect score, but the AD participants did not. Table 1 shows the percentage of correct trials for each condition (Former False Belief condition

TABLE 1  
 Percentage of correct trials on the false belief/real object task (Task 2), by condition, for the AD patients (AD) and controls (NC)

	<i>Former False Belief</i>	<i>Other's False Belief</i>
AD	96	92
NC	100	100

and Other's False Belief condition), for each subject group. (As mentioned above, for a trial to be scored correct, the subject had to respond correctly to both the reality question and the relevant false belief question.)

A  $2 \times 2$  repeated measures ANOVA (group by condition) on percentage of correct trials showed no significant effect of group:  $F(1, 38) = 1.1, p = .30$ , or condition,  $F(1, 38) = 0.59, p = .45$ . In addition, there was no significant interaction of group by condition:  $F(1, 38) = 0.59, p = .45$ .

*Task 3: The false belief/false picture story task.* Table 2 shows the percentage of correct trials for each group, on each condition, of Task 3. To be credited with a correct trial, a participant had to respond correctly to both the reality question and the inference question of that story.

A  $2 \times 2$  repeated measures ANOVA (group by condition) on percentage of correct trials showed a main effect for group:  $F(1, 38) = 5.13, p < .03$ . There was no significant effect of condition:  $F(1, 38) = 1.34, p = .3$ , and no significant interaction between group and condition:  $F(1, 38) = 0.04, p = 0.8$ . That is, for both control participants and AD patients, performance was similar in the mental state condition and in the control condition, although the AD patients' performance was lower than that of the controls. When the responses of the participants were analysed by question type, that is, pooled reality questions (questions 1 and 3) versus pooled inference questions (questions 2 and 4), a similar pattern was seen (see Table 3). A *t*-test showed that patients' performance on the reality

TABLE 2  
Percentage of correct trials on the false belief/false picture story task (Task 3), by condition, for the AD patients (AD) and controls (NC)

	<i>False Belief</i>	<i>False Picture</i>
AD	76	68
NC	92	87

TABLE 3  
Percentage of correct responses to types of test questions on the false belief/false picture story task (Task 3), by condition, for the AD patients (AD) and controls (NC)

	<i>Mental state condition</i>		<i>Control condition</i>	
	<i>Reality</i>	<i>False Belief</i>	<i>Reality</i>	<i>False Picture</i>
AD	87	79	76	79
NC	98	93	95	90

TABLE 4  
 Raw scores: means, ranges, and (standard deviations) on  
 neuropsychological tests, for AD patients (AD) and controls (NC)

	<i>Mini-Mental State Exam</i>	<i>CERAD Figure Copying</i>	<i>WAIS-R Similarities</i>
AD			
Mean	19.5	6.9	7.7
Range	14–26	2–11	0–21
SD	(3.5)	(2.0)	(5.9)
NC			
Mean	28.9	9.5	15.1
Range	25–30	7–11	8–22
SD	(1.28)	(1.6)	(3.7)

questions (82%) was not significantly better than their performance on the inference questions (79%), ( $t = -0.77, df = 24, p = .45$ ).

It should also be noted that although the performance of the AD patients was worse than the controls on the mental state condition (76% vs. 92%), it was significantly better than chance performance (25%),  $t = 7.1, df = 24, p < .001$ .

Raw scores on the neuropsychological tests appear in Table 4. All tasks were administered by the same highly trained individual. Normal controls performed better than AD patients on the MMSE ( $t = 11.98, df = 33, p = .0001$ ), on the WAIS-R Similarities ( $t = 4.23, df = 38, p = .0001$ ), and on the CERAD Figure Copying test ( $t = 3.96, df = 38, p = .0003$ ).

For each group, Pearson correlations were conducted to determine whether performance on the neuropsychological tests was related to performance on the two conditions of the task. For the control participants, there were no significant correlations between the neuropsychological variables and performance on either condition of Task 3. For the AD patients, performance on the mental state condition was significantly correlated with performance on the WAIS Similarities test ( $r = .55, p < .01$ ), while performance on the control condition was significantly correlated with performance on both the WAIS Similarities ( $r = .68, p < .001$ ) and the MMSE ( $r = .75, p < .001$ ). The AD patients scores on a test of spatial skill (CERAD Figure Copying) was not significantly correlated with performance on either of the test conditions.

### CONCLUSIONS

The present study suggests that AD patients do not have a primary impairment in their ability to make inferences about mental states. On Task 1 (the appearance/reality task) and Task 2 (the false belief/real object task), where task demands are extremely minimal, performance was nearly perfect for both groups. On

Task 3 (the false belief/false picture story task), the AD patients were impaired with respect to controls overall, but they were not selectively worse in the mental state condition than in the control condition.

The finding that AD patients were similarly impaired on both types of questions on Task 3 (i.e., questions related to factual information and questions requiring inference) suggests that the impairment of the AD patients on this task may be related to their difficulty keeping the facts about the stories straight; this is perhaps secondary to problems with both memory and conceptual ability, that is, difficulty handling two conflicting representations (i.e., reality and outdated photo or reality and false belief). In fact, many of the errors made by AD patients involved flipping the responses to the reality question and the inference question (38%). This type of error is consistent with recognising the distinction between reality and inference—and mixing up which is which in the story. Furthermore, the hypothesis that AD patients' difficulty on this task are secondary to problems with memory and conceptual ability is consistent with the correlations observed between performance on Task 3 and the neuropsychological test scores. The correlation between the scores on both conditions of Task 3 and scores on the WAIS Similarities test suggests that difficulty with the flexible manipulation of concepts may be contributing to AD patients' problems with this task. Future studies will further investigate this issue with more extensive testing of executive function ability. In addition, a significant correlation between performance on the control condition and the MMSE suggests that the overall severity of dementia (which in the patients in the current study is particularly influenced by the severity of their memory deficit) also contributes to difficulties on the task. This result is similar to that of Gregory et al. (2002); the only theory of mind task on which the AD group was impaired was one which placed heavy demands on working memory. It is also in line with the recent finding that most AD patients are impaired in their ability to attribute second order beliefs (Garcia Cuerva et al., 2001). Indeed, Garcia Cuerva et al. report that those AD patients who failed the second order task had more severe deficits on tests of verbal memory, verbal comprehension, abstract thinking, and naming than did those AD patients who succeeded on the task. The absence of significant correlations for the controls may be due to ceiling effects.

It is interesting to note that this pattern of results is similar to that seen in studies of inference of emotion. That is, AD patients are often impaired in tests where emotion processing is assessed (Albert, Cohen, & Koff, 1991; Allender & Kaszniak, 1989; Cadieux & Greve, 1997; Koff et al., 1999), but this impairment does not appear to be a primary one; rather it appears in some tasks but not others, and thus may be due to task-specific processing demands unrelated to emotions *per se* (Albert et al., 1991; Allender & Kaszniak, 1989; Cadieux & Greve, 1997; Koff et al., 1999; Lavenu, Pasquier, Lebert, Petit, & Van de Linden, 1999; Moayeri, Cahill, Jin, & Potkin, 2000; Ogrocki, Hills, & Strauss, 2000; Roudier et al., 1998; Zandi, Cooper, & Garrison, 1992). Likewise, in the

present study, performance of AD patients on two of the three tasks showed no impairment, while deficits in performance on the third task appeared to be due to task demands unrelated to reasoning about beliefs *per se*. This suggests that the basic ability involved in theory of mind, the ability to make an inference about beliefs held by another person, remains largely intact under simple conditions in patients with mild-to-moderate AD. The results of this study therefore extend the finding of Gregory et al. (2002) to mild-to-moderately impaired patients with late-onset AD.

The strength of the present study is that participants were evaluated with tasks that assess the basic ability to make inferences about mental states. While these tasks are simple insofar as they make few demands on memory, language, etc., and insofar as young children succeed on them, they are not at all simple conceptually. As mentioned above, to succeed on these tasks requires an understanding that beliefs are representations in the mind, that they are formed by other representations in the mind (e.g., what one sees or hears) and that, insofar as they are only representations, they may be incorrect. Moreover, patients with neurologic disorders other than Alzheimer's (e.g., disease fronto-temporal dementia) do not perform normally on such tasks.

The limitation of the present study is the range of difficulty evaluated. In our everyday lives we are sometimes required to make more complex inferences (e.g., example, the second order inferences mentioned above, where one must infer an individual's belief about another person's belief). A study is therefore underway examining the ability to infer mental states under more complex conditions, such as these, in mild-to-moderately impaired AD patients.

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