The term “theory of mind” (ToM) refers to the cognitive ability to represent one’s own and other people’s mental states – for instance, in terms of thinking, believing or pretending. Interestingly, the term was first used by a primatologist and a psychologist: Premack and Woodruff (1978). ToM is also referred to as “mentalizing” (Frith, Morton, & Leslie, 1991), “mind-reading” (Frith & Happe, 1994; Singer, 2006; Vogeley et al., 2001), “social intelligence” (Baron-Cohen, O’Riordan, Stone, Jones, & Plaisted, 1999), and “cognitive” (Lepage, 2002) or “affective” (Frith & Happe, 1994) ToM subcomponents. The present results suggest that the deficit in ToM only occurs in the more advanced stages of the disease. In conclusion, our results suggest that the dopaminergic pathways are not involved in ToM.

Abbreviations: PD, Parkinson’s disease; ToM, theory of mind; HC, healthy controls; DRT, dopamine replacement therapy.

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and “Machiavellian intelligence” (Brune, 2001). ToM is thought to have distinct functional subcomponents (Brothers & Ring, 1992; Coricelli, 2005). Depending on task demands, ToM may require emotional (“affective ToM”) or cognitive (“cognitive ToM”) perspective-taking, or both. Cognitive aspects of ToM are referred to as “cold”, and correspond to knowledge about others’ beliefs or intentions, whereas affective aspects of ToM are referred to as “hot”, and correspond to the appreciation of the others’ emotional states.

A number of neuroimaging studies have examined the neural systems engaged during the representation of other people’s mental states, compared with situations requiring no such representation (Brunet, Sarfati, Hardy-Bayle, & Decety, 2000; Calarge, Andreassen, & O’Leary, 2003; Fletcher et al., 1995; Gallagher & Frith, 2003; Goel, Graffman, Sadato, & Hallett, 1995; Harris, Todorov, & Fiske, 2005; Hynes, Baird, & Grafton, 2006; Vollm et al., 2006). Similarly, impaired ToM has been described in adult patients with focal lesions in the frontal lobe (Bird, Castelli, Malik, Frith, & Husain, 2004; Farrant et al., 2005; Happe, Malhi, & Checkley, 2001; Mazza et al., 2006; Rowe, Bullock, Polkey, & Morris, 2001; Shamay-Tsoory & Aharon-Peretz, 2007; Shamay-Tsoory, Tomer, Berger, & Aharon-Peretz, 2003; Stuss, Gallup, & Alexander, 2001) and in the amygdala (Fine, Lumsden, & Blair, 2001; Shaw et al., 2004; Stone, Baron-Cohen, Calder, Keane, & Young, 2003), as well as in patients with neurodegenerative pathologies known to involve the orbitofrontal and cingulate frontostriatal loops, together with the mesolimbic dopaminergic system which modulates the activity of these loops: the frontal variant of frontotemporal dementia (Elsinger et al., 2006; Lough, Gregory, & Hodges, 2001; Lough et al., 2006; Snowden et al., 2003; Torralva et al., 2006), Huntington’s disease (Snowden et al., 2003) and Parkinson’s disease (PD) (Mengelberg & Siegert, 2003; Mimura, Oeda, & Kawamura, 2006; Saltzman, Strauss, Hunter, & Archibald, 2000).

These studies have highlighted the role played by the superior temporal sulcus and temporal poles, the amygdala, the prefrontal cortex (especially the paracingulate cortex) and the “orbitofrontal” and “cingulate” loops (Cummings, 1993) in the representation of other people’s mental states. Neuroimaging (Hynes et al., 2006; Vollm et al., 2006) and lesion studies (Shamay-Tsoory & Aharon-Peretz, 2007; Shamay-Tsoory, Tomer, Berger, Goldsher, & Aharon-Peretz, 2005) have also provided evidence for the existence of a dissociation between the cognitive and affective aspects of ToM. Using fMRI, Hynes et al. (2006) demonstrated that the orbitofrontal cortex is involved in affective, rather than cognitive, perspective-taking. Lastly, it has also been suggested that the mesolimbic and nigrostriatal dopaminergic systems, which modulate the activity of the two loops, may be involved in ToM (Owen, 2004; Pezze & Feldon, 2004).

As PD is a neurodegenerative affection involving both the nigrostriatal and mesocorticolimbic dopaminergic systems, it offers an opportunity to study the possible influence of dopaminergic pathways on cognitive functions such as ToM. Three previous studies of PD patients seem to have yielded preliminary evidence of impaired ToM. However, the patients included in these studies were not accurately described and the PD group was not homogeneous in terms of age, severity of the disease, duration of the disease and dopa sensitivity. In addition, the PD patients included in these studies displayed major dysexecutive syndromes and mood disorders, making it difficult to determine whether the ToM deficits were due to a specific dopaminergic deficit or to an overall cognitive deterioration in the advanced stages of the disease, owing to the extension of the lesions to non-dopaminergic pathways (Braak et al., 2003).

In this context, several questions remained unanswered: do the ToM deficits observed in PD stem from the progression of the disease and the cortical extension of the lesions rather than from specific dopaminergic depletion? If ToM deficits can indeed be observed in PD, which subcomponents of ToM are impaired: the affective one, the cognitive one or both?

The aim of our study was to explore the involvement of the dopaminergic pathways in ToM by studying PD patients at different stages of the disease: newly diagnosed patients (early PD) and patients with advanced pathology (advanced PD), but also early PD patients with and without dopamine replacement therapy (DRT), compared with healthy controls (HC).

We sought to re-examine previous results highlighting ToM in PD by using two ToM tasks. The first task (Reading the Mind in the Eyes (Baron-Cohen et al., 2001)) was intended to reflect the “affective” subcomponent of ToM, while a second task (faux pas recognition task (Baron-Cohen, Jolliffe, Mortimore, & Robertson, 1997)) was intended to reflect both the “cognitive” and “affective” subcomponents of ToM.

## 2. Methods

### 2.1. Participants

Two groups of PD patients at different stages of the disease (early and advanced PD groups) and a healthy control (HC) group took part in the study.

The characteristics of the two patient groups and the HC group are presented in Table 1.

### 2.1.1. PD patients (Table 1)

Inclusion criteria for PD patients were idiopathic PD (Hughes et al., 1992), preserved dopa reactivity, lack of dementia (score > 130 on the Mattis Dementia Rating Scale) (Mattis, 1988) and, for the early PD group only, the ability to be tested not only in the “on” dopa condition (maximum therapeutic effect of dopaminergic treatment) but also in the “off” dopa condition (after approximately 12 h of therapeutic withdrawal).

The early PD group consisted of 17 non-demented patients with PD. Severity of the disease was rated using both the revised Hoehn & Yahr disability scale (H&Y, Hoehn & Yahr, 1967) and the Schwab & England scale (S&E, Schwab & England, 1969).

The early PD group was examined in two conditions: a medicated condition and an unmedicated one. Note that the terms “medicated” and “unmedicated” only refer to daily DRT for PD (levodopa preparations and/or dopamine receptor agonists). In the medicated condition, all patients were receiving anti-Parkinsonian medication and all were stable on their medication and good responders. Medication intake was defined as the DRT, calculated on the basis of correspondences adapted from Lozano et al. (1995). For the unmedicated condition, patients were asked to abstain from taking their medication the night before the assessment was scheduled to take place. Levodopa is eliminted from plasma with a half-life of 1–2 h (Gancher, Nutt, & Woodward, 1987).

The advanced PD group consisted of 27 non-demented patients with PD. Severity of the disease was also rated using both the revised Hoehn & Yahr disability scale (H&Y, Hoehn & Yahr, 1967) and the Schwab & England scale (S&E, Schwab & England, 1969). All patients were receiving anti-Parkinsonian medication, which was defined in the same way as for the early PD group (DRT).

### 2.1.2. HC participants (Table 1)

The HC group consisted of 26 healthy individuals who had no history of neurological disease, head injury or alcohol abuse, and no signs of dementia as attested by their scores on the MMSE (Dérouesné, 2001).

All groups were comparable for age and education level. After they had been given a full description of the study, written informed consent was obtained from each participant, and the study was conducted in accordance with the Declaration of Helsinki.

### 2.2. Theory of mind (ToM) tasks

Two ToM tasks were used in the experiment. The first task (i.e. the faux pas recognition task (Baron-Cohen et al., 1997)) is thought to reflect both the “cognitive” and “affective” subcomponents of ToM. The second task (i.e. the Reading the Mind in the Eyes test (Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001)) is thought to reflect solely the “affective” subcomponent of ToM.

### 2.2.1. Faux pas recognition test (“Cognitive” and “affective” verbal ToM task)

In this test, participants are read a story which may or may not contain a social faux pas (Baron-Cohen et al., 1999; Farrant et al., 2005; Stone et al., 2003; Stone, Baron-Cohen, & Knight, 1998). A faux pas story could feature someone being rude about a wedding gift, forgetting that they are speaking to the person who gave...
it to them (see example below). The story is placed in front of participants so that it may be referred to if necessary, thereby reducing the demands made on working memory (Stone et al., 2003). We used a shortened version of the test, comprising 5 stories with a faux pas and 5 control scenarios without a faux pas. A second equivalent version of this test was used to assess the early PD patients in the unmedicated condition. After each story, participants were asked the following questions:

1. “Did anyone say something s/he should not have said or something awkward?” (faux pas detection test). If the participants answered “yes”, they were asked the following questions:

2. “Who said something s/he should not have said or something awkward?” (faux pas comprehension test).

3. “Why shouldn’t s/he have said it or why was it awkward?” (faux pas comprehension test).

4. “Why do you think s/he said it?” (faux pas comprehension test).

5. “Did X know that Y . . .?” (test for realising that the faux pas was unintentional).


Questions 7 and 8 were control questions to check that participants understood the details of the story. Participants were asked a question about some important detail of the story, such as “What had Jeanette given Anne for her wedding?”

Example: Jeanette bought her friend Anne a crystal bowl for a wedding gift. Anne had a big wedding and there were a lot of presents to keep track of. About a year later, Jeanette was over one night at Anne’s for dinner. Jeanette dropped a wine bottle by accident on the crystal bowl, and the bowl shattered. “I’m really sorry, I’ve broken the bowl,” Jeanette said. “Don’t worry,” said Anne, “I never liked it anyway. Someone gave it to me for my wedding.”

Questions 2–6 were only asked if participants detected the faux pas, i.e. if they answered “Yes” to Question 1. If not, the experimenter skipped to Questions 7 and 8 (the control questions). In order to realise that a faux pas has occurred, participants have to represent two mental states. First that the person making the remark does not realise that they have said something inappropriate, and that the listener (the person hearing it) is bound to feel hurt or insulted (“affective” ToM; emotion attribution score). Second, that the person making the remark does not realise that they have said something inappropriate, and that the listener (the person hearing it) is bound to feel hurt or insulted (“cognitive” ToM; intentionality score. Second, that the person making the remark does not realise that they have said something inappropriate, and that the listener (the person hearing it) is bound to feel hurt or insulted (“affective” ToM; emotion attribution score) (Shamay-Tsoory & Aharon-Peretz, 2007).

Scoring: we adopted the scoring system used by Stone et al. (1998), whereby performances on each component of the test are calculated separately as follows (Stone et al., 1998):

1. Correct hits score: for each story with a faux pas, one point was given for each correct answer. The maximum “correct hits” score on the test was therefore 30 (6 questions × 5 faux pas stories, maximum = 30), and scores were converted into a percentage of correct responses.

2. Correct rejects score: for each neutral story, two points were given for each correct answer. The maximum “correct rejects” score on the test was therefore 10 (1 question × 5 neutral stories, maximum = 10), and scores were converted into a percentage of correct responses.

3. Correct faux pas story control score: for each story with a faux pas, one point was given for each correct answer to the two control questions. The maximum “correct faux pas story control” score on the test was therefore 10 (2 control questions × 5 faux pas stories, maximum = 10), and scores were converted into a percentage of correct responses.

4. Correct neutral story control score: for each neutral story, one point was given for each correct answer to the two control questions. The maximum “correct neutral story control” score on the test was therefore 10 (2 control questions × 5 neutral stories, maximum = 10), and scores were converted into a percentage of correct responses.

Several composite scores and subscores were also calculated. The correct hits score was broken down into four subscores as follows:

1a) Detection score (question 1 × 5 faux pas stories, maximum = 5),
1b) Explanation score (questions 2 to 6 × 5 faux pas stories, maximum = 25),
1c) Intention attribution score (question 5 × 5 faux pas stories, maximum = 5),
1d) Emotion attribution score (question 6 × 5 faux pas stories, maximum = 5).

A composite “total detection” score was calculated as follows: the detection score plus the correct rejects score (maximum = 15). Lastly, a composite “total control questions” score was calculated as follows: the correct faux pas story control score plus the correct neutral story control score (maximum = 20).

All these additional scores were converted into a percentage of correct responses.

Control tasks: To check that the early processing stages of verbal abilities were intact (abilities required for the faux pas recognition task), the abridged version of the Token Test (De Renzi & Vignolo, 1962) and the verbal modality of the Pyramids and Palm Trees Test (PPTT, Howard & Patterson, 1992) were administered to all participants. The former assesses syntax comprehension and requires participants to point to tokens corresponding to a verbal instruction (e.g. “Touch the large red square”), while the latter measures semantic access from words and requires participants to match one item (word) with one of two others (e.g. a pyramid with a palm tree or a pine tree). None of the participants included in the study presented any deficit in syntax comprehension, as measured by the Token Test, or in semantic access, as measured by the verbal PPTT.

2.2.2. Reading the Mind in the Eyes test (“affective” visual ToM task)

A French adaptation of the revised version of the Reading the Mind in the Eyes test was used (Baron-Cohen et al., 2001; Cohen et al., 2006). We used a shortened, computerised version, comprising 17 photographs of the eye region of the faces of actors and actresses. A second equivalent version of this test was used to assess the early PD patients in the unmedicated condition. The stimuli were depicted on separate slides and presented one after the other. Four adjectives corresponding to complex mental state descriptors (e.g. hateful, panicked) were printed on each slide, with one adjective in each corner and the photo in the middle. One of these words (the target word) correctly described the mental state of the person in the photograph, while the others were included as foils. It was possible for the three foils to have the same emotional valence as the target word. Participants were required to decide which of the four words best described what the individual in the photograph was thinking or feeling, and there was no time limit. Participants were instructed to read the chosen word aloud. This task is regarded as an advanced ToM task, as participants have to try and put themselves in the shoes of the person shown in the photograph and attribute a relevant complex mental state to him/her. As a control
task, participants judged the gender of the person shown in the photograph (gender attribution task). Before the test, participants read through a glossary which contained the meanings of the words describing the mental states. If necessary, the glossary could be used during the assessment (for a detailed description, see Baron-Cohen et al., 2001).

Scoring: The test was scored by totalling the number of items (photographs) that had been correctly identified by the participant, i.e. the number of correctly identified mental states. The maximum “emotion score” on the test was therefore 17, which was converted into a percentage of correct responses. In addition, a control score was calculated by totalling the number of correct responses in the gender attribution task. The maximum “gender score” on the test was therefore 17, and scores were again converted into a percentage of correct responses.

Control task: To check that the early processing stages of face perception were intact, and to supplement the gender attribution task included in the Reading the Mind in the Eyes test, the Benton Facial Recognition Test (Benton, Hamsher, Varney, & Spreen, 1983) was administered to all participants. This task requires participants to match pictures of the same individuals’ faces, taken from different angles and in different lighting conditions. None of the patients included in the study presented any aperceptive prosopagnosia, as measured by the Benton Recognition Test.

2.3. Neuropsychological background and psychiatric assessment

Prior to the ToM assessment, a short neuropsychological and psychiatric battery was administered to the two patient groups (i.e. the advanced PD group and the early PD group in the medicated condition). Performances by the participants on the neuropsychological and psychiatric tests are presented in Table 2.

The battery included the Mattis Dementia Rating Scale (Mattis, 1988) and a series of tests assessing executive functions: the Modified Wisconsin Card Sorting Test (Nelson, 1976), the Trail Making Test (Reitan, 1958), categorical and literal fluency tasks (Cardebat, Doyon, Puel, Goullet, & Jouante, 1990), the action (verb) fluency task (Woods et al., 2005) and the Stroop Test (Stroop, 1935). In the unmedicated condition, only the Mattis Dementia Rating Scale (Mattis, 1988) was administered to the early PD patients. Depression was assessed using the Montgomery–Asberg Depression Rating Scale (MADRS, Montgomery & Asberg, 1979). The MADRS was chosen because of the predominance of psychic over somatic items, thus limiting interference with Parkinson’s symptoms.

2.4. Procedure

In order to avoid a list effect between the “on” dopa and “off” dopa conditions in the early PD patient group, these were counterbalanced in each of the ToM tasks. In the “on” dopa condition, half the early PD patients were assessed with Version “A” of the ToM tasks and half with Version “B”. In the “off” condition, the former were assessed with Version “B” and latter with Version “A”. The same counterbalancing method was applied to the advanced PD group and the HC group: the advanced PD patient group and the HC group were both divided into two groups, half of each group were assessed with Version “A” and half with Version “B”.

The protocol was completed in a single 90-min session. The early PD patients in the unmedicated condition underwent a second 60-min session.

2.5. Statistical analysis

Given the small size of the three samples (<30), normality could not be assumed and we therefore performed non-parametric statistical analyses. The scores for the neuropsychological background and the sociodemographic data (except for age and education level) were compared using the non-parametric Mann–Whitney U test for two independent groups, i.e. the early PD group and the advanced PD group.

The scores for the remaining sociodemographic data (age and education level), the control tasks and the ToM tasks were first compared using the Kruskal–Wallis non-parametric one-way analysis by ranks for the three independent groups, i.e. the early PD group in the medicated condition, the advanced PD group and the HC group. If there was a significant group effect, pairwise comparisons were performed using the non-parametric Mann–Whitney U test for two independent groups. The same analyses were carried out with the early PD group in the unmedicated condition.

For the intragroup comparisons, Wilcoxon’s test for paired samples was used to assess the effect of the experimental condition (medicated vs. unmedicated) in the early PD group.

Correlations between (1) control tasks and ToM, and (2) neuropsychological background and ToM were assessed using Spearman’s rank correlation coefficient.

Table 2

Neuropsychological data (mean ± S.D.) for the two patient groups and the control group. Differential effects between the three groups are reported (Kruskal–Wallis and Mann–Whitney U test).

<table>
<thead>
<tr>
<th></th>
<th>Early PD (n = 17)</th>
<th>Advanced PD (n = 27)</th>
<th>HC (n = 26)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Medicated Mean</td>
<td>Unmedicated Mean</td>
<td>Mean</td>
</tr>
<tr>
<td></td>
<td>S.D.</td>
<td>S.D.</td>
<td>S.D.</td>
</tr>
<tr>
<td>M.M.S.E</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Depression</td>
<td>23.5 ± 4.4</td>
<td>23.6 ± 4.4</td>
<td>24.8 ± 5.0</td>
</tr>
<tr>
<td>Token Test</td>
<td>35.1 ± 1.3</td>
<td>35.2 ± 1.3</td>
<td>35.1 ± 1.3</td>
</tr>
</tbody>
</table>

...
Table 3
Performances of the two patient groups and the control group on ToM tasks (i.e. faux pas recognition test and “Reading the Mind in the Eyes” test). Differential effects between the three groups are reported (Kruskal–Wallis and Mann–Whitney U test).

<table>
<thead>
<tr>
<th></th>
<th>Early PD (n = 17)</th>
<th>Advanced PD (n = 27)</th>
<th>HC (n = 26)</th>
<th>Statistical value</th>
<th>p-Value</th>
<th>Statistical value</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Medicated</td>
<td>Unmedicated</td>
<td></td>
<td>Mean (%)</td>
<td>S.D.</td>
<td>Mean (%)</td>
<td>S.D.</td>
</tr>
<tr>
<td>Faux pas test</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Correct hits</td>
<td>82.7</td>
<td>16.7</td>
<td>91.3</td>
<td>8.8</td>
<td>77.3</td>
<td>22.8</td>
<td>88.8</td>
</tr>
<tr>
<td>Correct rejects</td>
<td>96.5</td>
<td>10.6</td>
<td>96.9</td>
<td>7.5</td>
<td>94.8</td>
<td>8.9</td>
<td>90.8</td>
</tr>
<tr>
<td>Faux pas story control questions</td>
<td>96.5</td>
<td>8.6</td>
<td>98.5</td>
<td>3.8</td>
<td>97.0</td>
<td>7.2</td>
<td>97.7</td>
</tr>
<tr>
<td>Neutral story control questions</td>
<td>98.8</td>
<td>3.3</td>
<td>98.5</td>
<td>5.5</td>
<td>98.1</td>
<td>5.6</td>
<td>98.1</td>
</tr>
<tr>
<td>Faux pas story detection</td>
<td>88.2</td>
<td>15.9</td>
<td>95.4</td>
<td>8.8</td>
<td>85.9</td>
<td>19.9</td>
<td>91.5</td>
</tr>
<tr>
<td>Explanation</td>
<td>84.3</td>
<td>16.8</td>
<td>92.8</td>
<td>9.6</td>
<td>79.3</td>
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<td>90.8</td>
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<tr>
<td>Intention attribution (ToM)</td>
<td>74.1</td>
<td>22.1</td>
<td>83.1</td>
<td>11.1</td>
<td>64.4</td>
<td>27.9</td>
<td>81.5</td>
</tr>
<tr>
<td>Emotion attribution (affective ToM)</td>
<td>81.1</td>
<td>18.0</td>
<td>90.8</td>
<td>17.5</td>
<td>75.6</td>
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<td>87.7</td>
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<tr>
<td>Total detection score</td>
<td>93.7</td>
<td>7.6</td>
<td>96.4</td>
<td>5.2</td>
<td>91.9</td>
<td>8.1</td>
<td>91.0</td>
</tr>
<tr>
<td>Total control questions</td>
<td>97.6</td>
<td>5.0</td>
<td>98.5</td>
<td>3.2</td>
<td>97.6</td>
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<td>Eyesh test</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender score</td>
<td>96.2</td>
<td>3.6</td>
<td>93.7</td>
<td>11.6</td>
<td>95.4</td>
<td>5.0</td>
<td>96.2</td>
</tr>
<tr>
<td>Emotion score</td>
<td>64.0</td>
<td>15.7</td>
<td>69.7</td>
<td>15.0</td>
<td>66.9</td>
<td>14.2</td>
<td>65.2</td>
</tr>
</tbody>
</table>

|                          |                   |                      |             |                   |         |                   |         |
| Emotion attribution (affective ToM) | 74.1      | 22.1                 | 83.1        | 11.1              | 64.4    | 27.9              | 81.5    |
| Total detection score    | 93.7              | 7.6                  | 96.4        | 5.2               | 91.9    | 8.1               | 91.0    |
| Total control questions  | 97.6              | 5.0                  | 98.5        | 3.2               | 97.6    | 4.2               | 97.9    |

Abbreviations: PD: Parkinson's disease; HC: healthy controls; ToM: theory of mind; S.D.: standard deviation.

a Comparisons (Kruskal–Wallis non-parametric one-way analysis) were performed between the three independent groups, i.e. the early PD group in the medicated condition, the advanced PD group and the HC group.

b Comparisons (Kruskal–Wallis non-parametric one-way analysis) were performed between the three independent groups, i.e. the early PD group in the unmedicated condition, the advanced PD group and the HC group.

* Significant (p < 0.05).

In order to compare the two parallel versions (A & B) of each of the ToM tasks, paired comparisons within the HC group (n = 26) were performed using the non-parametric Mann–Whitney U test for two independent groups.

In order to check whether gender influences ToM performances, as is the case with the recognition of facial expressions (Li, Yuan, & Lin, 2008), paired comparisons within the HC group (n = 26) were performed using the non-parametric Mann–Whitney U test for two independent groups. In addition, paired comparisons among all participants (n = 70) were performed using the parametric Student’s t-test for two independent groups. The p value was significant if less than 0.05.

Statistical analyses were performed using SPSS 15.0 software.

3. Results

3.1. Clinical, neuropsychological background and psychiatric assessment (Tables 1 and 2)

A significant difference was found between the early PD group and the advanced PD group for the H&Y and S&E scales in the “off” dopa condition. As far as the “on” dopa conditions were concerned, no difference was found between the early PD group and the advanced PD group for the H&Y and S&E scales (see Table 1).

No significant difference was found between either of the two early PD groups (medicated vs. unmedicated) and the advanced PD group for any of the neuropsychological and psychiatric tests, except the Stroop Test and the action (verb) fluency task (see Table 2).

No significant difference was found between the medicated and unmedicated conditions in the early PD group for the Mattis Dementia Rating Scale (Z = −0.3, p = .7).

3.2. Control tasks

No significant difference was found between the three groups, i.e. the advanced PD group and the two early PD groups (medicated vs. unmedicated) and the HC group for any of the inclusion tests (Benton Facial Recognition Test, Token Test and PPTT) (see Table 2).

No significant difference was found in the early PD group between the medicated and unmedicated conditions for these inclusion tests (Benton Facial Recognition Test: Z = −0.7, p = .4; Token Test: Z = (0.1, p = .8, and PPTT: Z = (1.2, p = .1).

3.3. ToM tasks

Performances by the participants on the ToM tasks are shown in Table 3.

3.3.1. Comparisons between the two parallel versions (A&B) of each of the ToM tasks

No difference was found for any of the variables of the faux pas recognition task between versions A and B in the HC group (p > .1 for all the comparisons).

No difference was found for the emotion attribution score of the Reading the Mind in the Eyes test between versions A and B in the HC group (p > .1). Note that a significant difference was found for the control task score of the Reading the Mind in the Eyes test (gender score) between versions A and B in the HC group (p = .01).

3.3.2. Gender comparisons in each of the ToM tasks

No difference was found, and scores were totally comparable between men and women in the HC group and among all participants (p > .2 for all the comparisons).

3.3.3. Faux pas recognition test (“cognitive” and “affective” verbal ToM task)

A significant difference was found for the intention attribution score (“cognitive” ToM score) between the early PD patient group in the unmedicated condition, the advanced PD group and the HC group. Paired comparisons for the intention attribution score (“cognitive” ToM score) showed that the advanced PD group was impaired in comparison with the early PD group in the unmedicated condition (U = 105.5, p = .03) and the HC group (U = 224.5, p = .02). No significant difference, however, was found between the early PD group in the unmedicated condition and the HC group (U = 167.0, p = .9).
Note that a trend towards significance was observed for the intention attribution score ("cognitive" ToM score) between the early PD patient group in the medicated condition, the advanced PD group and the HC group. Paired comparisons for the intention attribution score ("cognitive" ToM score) showed that the advanced PD group was impaired in comparison with the HC group ($U = 224.5, p = 0.02$). No significant difference, however, was found between the advanced PD group and the early PD group in the medicated condition ($U = 186.5, p = 0.3$), nor between the early PD group in the medicated condition and the HC group ($U = 179.5, p = 0.3$).

Additionally, a trend towards significance was observed for the correct hits score ("cognitive" ToM score) between the early PD patient group in the unmedicated condition, the advanced PD group and the HC group. Paired comparisons for the correct hits score showed that the advanced PD group was impaired in comparison with the HC group ($U = 240.5, p = 0.045$). There was a trend towards a statistically significant difference between the advanced PD group and the early PD group in the unmedicated condition ($U = 111.0, p = 0.06$). No significant difference, however, was found between the early PD group in the unmedicated condition and HC group ($U = 165.0, p = 0.9$).

A trend towards significance was observed for the explanation score ("cognitive" ToM score) between the early PD patient group in the unmedicated condition, the advanced PD group and the HC group. Paired comparisons for the explanation score showed a trend towards significant difference between the advanced PD group and the HC group ($U = 262.0, p = 0.09$), and between the advanced PD group and the early PD group in the unmedicated condition ($U = 115.5, p = 0.07$). No significant difference, however, was found between the early PD group in the unmedicated condition and the HC group ($U = 150.0, p = 0.5$).

No significant difference was found between the three groups, i.e. the early PD group (medicated/unmedicated), the advanced PD group and the HC group, for any of the other variables of the faux pas recognition test, including the "affective" ToM score, i.e. the emotion attribution score.

Lastly, no significant difference was found between the medicated and unmedicated conditions in the early PD group for any of the variables of the faux pas recognition test (correct hits score: $Z = (1.5, p = 1$), correct rejects score: $Z = (0.5, p = 0.5$), correct faux pas story control score: $Z = (0.8, p = 0.4$), correct neutral story control score: $Z = (0.4, p = 0.6$), detection score: $Z = (1.1, p = 0.2$), explanation score: $Z = (1.5, p = 1$, intention attribution score: $Z = (0.9, p = 0.3$), emotion attribution score: $Z = (1.4, p = 1$), total detection score: $Z = (0.3, p = 0.7$), total control questions score: $Z = (0.5, p = 0.5$).

3.3.4. Reading the Mind in the Eyes test ("affective" visual ToM task)

No significant difference was found between the three groups, i.e. the early PD group, the advanced PD group and the HC group, for the "affective" ToM task (Reading the Mind in the Eyes test) (see Table 3). No significant difference was found between the medicated and unmedicated conditions in the early PD group for any of the variables of the Reading the Mind in the Eyes test (gender score: $Z = (0.7, p = 0.4$), emotion score: $Z = (0.1, p = 0.5$).

3.4. Correlations

3.4.1. Correlations between the control tasks and the ToM task

In the advanced PD group, there was a significant correlation between the PPTT score and the correct hits score ($r = 0.540, p = 0.004$), the explanation score ($r = 0.504, p = 0.007$), and the intention attribution score ($r = 0.466, p = 0.001$) of the faux pas recognition test.

There was no significant correlation in the advanced PD group, however, between the Token Test score and the correct hits score ($r = 0.104, p = 0.6$), the explanation score ($r = 0.190, p = 0.3$), and the intention attribution score ($r = 0.972, p = 0.007$) of the faux pas recognition test.

3.4.2. Correlations between the neuropsychological background and the ToM task

In the advanced PD group, there was no significant correlation between the interference score of the Stroop test and either the intention attribution score ($r = 0.295, p = 0.13$) or the correct hits score of the faux pas test ($r = 0.368, p = 0.59$). Nevertheless, analysis revealed that there was a significant correlation between the interference score of the Stroop test and the explanation score of the faux pas test ($r = 0.424, p = 0.02$). There was no significant correlation between the action verb fluency test and either the intention attribution score ($r = 0.114, p = 0.57$), the correct hits score ($r = 0.261, p = 0.18$) or the explanation score of the faux pas test ($r = 0.298, p = 0.13$).

4. Discussion

The aim of the present study was to clarify the possible role of the nigrostriatal and mesolimbic dopaminergic pathways in ToM. We compared the performances of patients with PD in the early and advanced stages of the disease with those of HC on two ToM tasks: a verbal one (faux pas recognition test), which is thought to reflect both the cognitive and affective subcomponents of ToM, and a visual one (Reading the Mind in the Eyes test), which is thought to reflect the affective subcomponent of ToM. In addition, we compared the performances of the early PD patients with and without DRT on the same tasks. Both the patient and the HC groups were randomly selected and matched for age and education level in order to avoid non-specific biases. Similarly, all participants performed normally on the tasks assessing the early processing stages of the cognitive abilities required for each experimental task.

Results showed that the performances by the early PD patients on the ToM tasks were no different from those of the HC participants. Furthermore, there was no significant difference between the medicated and unmedicated conditions in the early PD patients. The advanced PD patients, however, displayed specific impairment on the intention attribution score ("cognitive" ToM score) of the faux pas recognition task and a trend towards impairment on the explanation and correct hits scores ("cognitive" ToM scores) of the faux pas test. The advanced PD patients did not present any impairment in the ToM tasks sustained by affective ToM components (emotion attribution score of the Reading the Mind in the Eyes test and emotion attribution score of the faux pas recognition test).

Our results could therefore suggest an absence of ToM impairment in the early stages of PD, regardless of the presence or absence of DRT, unlike the more advanced PD patients, who did present ToM impairment. A ToM deficit may therefore be present in PD patients whose degenerative process has spread beyond the dopaminergic pathways, in particular to the limbic system, unlike the early PD patients, whose neuronal loss is thought to be restricted to the nigrostriatal and mesolimbic dopaminergic systems (Braak et al., 2003). In addition, our results appear to indicate that the errors made by the advanced PD patients in the faux pas recognition task can be ascribed to an inability to construct mental representations (i.e. impaired "cognitive" ToM), rather than to general ToM impairment (i.e. impaired "cognitive" and "affective" ToM). Our results seem to be in line with previous findings suggesting that cognitive...
and affective mentalizing abilities are partly dissociable (Brothers and Ring, 1992; Coricelli, 2005).

There were several limitations to the present study that need to be acknowledged and addressed.

First, the notion of ToM refers not only to the ability to represent other people’s mental states but also to the ability to build a representation of one’s own mental states. In the present study, however, we did not investigate all the facets of ToM because we did not test the ability of PD patients to construct representations of their own behaviour.

Second, the fact that early PD patients did not display any impairment at the behavioural level does not mean that these patients used exactly the same resources to perform the task as the HC participants. It is possible to put forward the hypothesis that these early PD patients used more resources and put more effort into this task than their HC counterparts. This alternative explanation of our results could be linked to reduced sensitivity to the ToM tasks we used in the present study. The faux pas recognition task and the Reading the Mind in the Eyes test were not developed in the context of PD, but rather to test ToM abilities in psychiatric pathologies characterised by major social maladjustment (e.g. autism) (Baron-Cohen et al., 1997). If ToM deficits do indeed occur in PD, even in the early stages of the disease, they may be less pronounced than in autism and require extremely sensitive tasks to be detected. These two ToM tasks also present other limitations, notably the fact that they are not ecological. The faux pas recognition task features verbal material, and the different subprocesses required for attributing other people’s mental states in everyday life may differ from those required for verbal material. In futures studies, it might be interesting to include a multimodal task, as this would make it possible to take all the sensory modalities into consideration. As far as the Reading the Mind in the Eyes test is concerned, the main problem arises from the poorness of the categories used in such a context. Moreover, the recognition of mental states based on the alternatives suggested (four in this experiment) does not necessarily correspond to the inferences we are called upon to make (without explicitly listed alternatives) in everyday life.

Third, even though we counterbalanced the “on” and “off” conditions in the early PD patients, and even though analysis failed to show a significant difference between the two parallel versions of the ToM tasks we used, the double testing may have induced a learning effect, which may in turn have influenced our results.

Lastly, we need to bear in mind that we did not directly test the involvement of the dopaminergic system in ToM. In humans, it is possible to study the dopaminergic system in two ways. The first direct way consists in reducing the dopamine level by administering neuroleptics to healthy volunteers. To our knowledge, no published studies have investigated the impact of neuroleptics on ToM in healthy volunteers. The second way of studying the dopaminergic system consists in using the dopaminergic denervation model of PD. However, this model presents several methodological limitations. First, as we have already pointed out, it does not allow for the directly testing of the dopaminergic pathways. Second, even if the hallmark of PD is dopamine depletion in the striatum and the mesolimbic area, thereafter other areas (including cortical ones) gradually become affected by the disease. At these more advanced stages of the disease, the deficits that are observed (e.g. in ToM) can no longer be as attributed specifically to dopaminergic depletion.

The hypothesis of an absence of ToM impairment in patients in the early stages of PD, as opposed to more advanced PD patients, who do present ToM impairment, would appear to be confirmed by the results reported in the handbook of studies (Mengelberg & Siegert, 2003; Mimura et al., 2006; Saltzman et al., 2000) that have already explored ToM in PD patients. Although the patients included in these studies were not accurately described, making it difficult to identify the stages of the disease with any degree of accuracy, all three studies reported ToM deficits in PD, accompanied by a major dysexecutive syndrome. This proves that these patients were in the advanced stages of the pathology, and the presence of a dysexecutive syndrome strongly suggests that the degenerative process had spread beyond the dopaminergic pathways.

The first study exploring ToM in PD was published by Saltzman et al. (2000). The authors examined ToM and its relationship to executive functioning by administering four ToM tests and three executive tasks to 11 non-demented patients with idiopathic PD, 8 elderly HC and 9 university-age HC. The ToM battery consisted of two false belief stories (one first- and one second-order belief attribution task), a Drodle task (a type of perspective task), a “spy” model task and a deception task called the Knower/Guesser task. The executive battery consisted of the 5-point fluency test, the California card-sorting task and the verbal fluency task. Compared with both HC groups, PD patients displayed deficits on both the five-point fluency task and the verbal fluency task. Moreover, significant relationships between the ToM measures and the executive tasks were also found. Mengelberg and Siegert (2003) replicated these results, adding a control condition of sequencing abilities in order to avoid a specific bias. The relationship between ToM, decision-making and executive functioning has also been examined by Mimura et al. (2006) in 18 PD patients and 40 HC. These authors used the Iowa Gambling Task (ICT), which assesses the ability to take profitable decisions, the Reading the Mind in the Eyes test and a battery of executive tests assessing set-shifting, planning and inhibition abilities, as well as lexical availability. This study showed that PD patients performed significantly more poorly than matched HC on the whole set of tasks.

In our study, although the advanced PD patients did not present a major dysexecutive syndrome, their performances on the action (verb) fluency task, which were poorer than those of the early PD group, would appear to confirm the impairment of executive abilities. Whereas the tests used to assess neuropsychological background may not be sufficiently sensitive to detect early impairment, the hypothesis of a broad cognitive deficit stemming from diffuse brain damage (Borod, 1992; Mandal et al., 1991) can be excluded in the case of our early PD patient group, and the absence of marked neuropsychological dysfunction in this patient group is in favour of neuronal loss being restricted to the dopaminergic systems.

In the three studies described above, the fact that the PD patients displayed a dysexecutive syndrome could explain their mental state inference deficit. In our own advanced PD patients group, we found a significant correlation between the Stroop Interference score and one subscore of the faux pas recognition test (explanation score). Some authors have demonstrated double dissociations between ToM and executive functioning by controlling for executive functions in their results (Fine et al., 2001; Gregory et al., 2002; Lough et al., 2001; Rowe et al., 2001). Others have claimed that ToM is dependent upon executive functioning (Carlson, Moses, & Breton, 2002; Channon & Crawford, 2000; Stuss et al., 2001). Even though the relationship between executive functioning and ToM remains subject to debate, the ToM impairments reported in both the previous studies and our group of advanced PD patients could be the consequence of general cognitive deterioration in the advanced stages of the disease, rather than of a more specific dopaminergic deficit.

The discrepancy between our results and the results reported in previous studies could be explained by the greater homogene-
ity of our patient groups in terms of age, duration, and severity of the disease, and mood as measured by the Montgomery–Asberg Depression Rating Scale (MADRS, Montgomery & Asberg, 1979). In the present study, PD patients were divided into two distinct and homogeneous groups on the basis of disease duration and severity, age at the time of the interviews and dopa sensitivity. The results obtained on the H&Y and S&E scales in the "off" conditions attest to the fact that the two groups differed in terms of disease severity. In addition, the fact that there was no difference in the "on" dopa conditions attests to the fact that the advanced PD patients still had dopa sensitivity. In addition, we explored ToM in early PD patients who either were or were not receiving DRT. It is the homogeneity of our patient groups that allows us to infer the specific involvement of the dopaminergic pathways in ToM. In contrast, the patients in previous studies were not accurately described. Mimura et al. (2006) examined PD patients from a broad age range (49–76 years) and for whom neither the duration nor the severity of the disease were clearly reported. Mengelberg and Siegert (2003) and Saltzmann et al. (2000) studied similarly heterogeneous PD patient groups. In Mengelberg and Siegert’s study, out of a total of 13 PD patients, 2 were in Stage 4, 6 were in Stage 3 and 4 were in Stage 2 on the H&Y disability scale (note that the H&Y stage of the 13 patient was not reported); their ages ranged from 50 to 84 years and their ages at the onset of the first Parkinsonian symptoms ranged from 48 to 82 years. In Saltzmann et al.’s study, ages ranged from 48 to 84 years and disease duration was not reported. Moreover, dopa sensitivity remained unknown in all three studies because disability scales, such as the H&Y scale, were not scored in “off” periods. The homogeneity of our patient groups was also controlled in terms of mood as measured by the Montgomery–Asberg Depression Rating Scale (Montgomery & Asberg, 1979). In addition, the fact that the two groups differed in terms of disease severity. It is now well documented that patients with depression, may have given rise to confounding factors, which may have influenced the results.

In conclusion, our results do not allow us to conclude that ToM abilities are impaired in the early stages of PD, when neuronal loss is mainly restricted to the dopaminergic systems. Rather, like previous studies, our results seem to indicate impairment of ToM abilities at the stage in the disease where the degenerative process has spread beyond the dopaminergic pathways. In addition, they seem to suggest that advanced PD patients display deterioration in the “cognitive” ToM component, rather than a general ToM impairment (“cognitive” and “affective” ToM), thus supporting the idea that cognitive and affective mentalizing abilities are partly dissociable. Moreover, the fact that DRT did not influence the results of this study suggests that the nigrostriatal and mesolimbic dopaminergic pathways do not contribute to ToM abilities.

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References


