Altered Theory of Mind in Parkinson's Disease and Impact on Caregivers: A Pilot Study

Ariane Giguère-Rancourt [ORCID], Marika Plourde, Eva Racine, Marianne Couture, Mélanie Langlois, Nicolas Dupré [ORCID], Martine Simard

ABSTRACT: Mild cognitive impairment (MCI) in Parkinson's disease (PD) includes deficits in theory of mind (ToM). However, associations between ToM and caregiver burden and distress are still unclear. The objective of this pilot study was to preliminarily explore the relation between ToM and caregiver burden and distress in a sample of PD-MCI patients. Twelve PD-MCI patients were evaluated on a ToM task (*Faux Pas*), whereas their caregivers were assessed on caregiver burden (*Zarit Burden Interview-12 items*) and distress (*Neuropsychiatric Inventory*–Distress). Cognitive ToM was significantly associated with caregiver distress, but caregiver burden was associated with the severity of patient psychiatric symptoms.

RÉSUMÉ : **Altération de la théorie de l'esprit dans des cas de maladie de Parkinson et impact sur les personnes soignantes : une étude pilote.** Les troubles cognitifs légers (TCL) qui affectent les patients atteints de la maladie de Parkinson (MP) peuvent aussi inclure des déficits à ce qu'on appelle la « théorie de l'esprit » (TE ou *theory of mind*). Cela dit, les associations qui peuvent exister entre, d'une part, la TE et, d'autre part, le fardeau et la détresse psychologique des personnes soignantes demeurent encore méconnues. L'objectif de cette étude pilote a donc consisté à explorer ces associations dans le cas d'un groupe de patients atteint de la MP et de TCL. Au total, douze d'entre eux ont été évalués en fonction d'une tâche relevant de la TE et d'un test dit de « faux pas » tandis que les personnes soignantes, elles, ont été évaluées en ce qui regarde leur fardeau (*Short Form Zarit Burden Interview* ou ZBI-12) et leur détresse psychologique (*Neuropsychiatric Inventory*, détresse psychologique). Ainsi, la TE de nature cognitive s'est révélée significativement associée à la détresse psychologique des personnes soignantes alors que leur fardeau a été plutôt associé à la gravité des symptômes psychiatriques des patients.

Because of motor symptoms, Parkinson's disease (PD) patients need a caregiver to assist them with their daily activities. Although research on PD caregivers is limited, data show that taking care of someone with a chronic condition is considered a chronic life stressor.[1,2] As for mental health, depression and anxiety are approximately two and three times more frequent in PD caregivers, respectively, than in general population.[1,2,3]

A study showed that, together with disease stage, behavioural problems associated with cognitive dysfunction in PD patients explained 66% of caregiver burden variance.[3] Cognitive symptoms alone are also associated with caregiver burden.[1,2]

Among cognitive functions, theory of mind (ToM) can be defined as 'the ability to attribute mental states (beliefs, intentions) to others as well as to understand and predict others' behaviour based on mental states'.[4] ToM is part of social cognition.[4,5] Affective ToM, referring to empathy (i.e., attribution of feelings different from oneself), and cognitive ToM, referring to attribution of beliefs and intentions, are two components of ToM.[5] In PD, both affective and cognitive ToM deteriorate overtime.[4]

Impaired ToM has an impact on the relationship PD patients have with their social environment, especially their caregivers.[5,6] To our knowledge, few studies have investigated the association between social cognition, such as impairments in ToM, and caregiver well-being in PD. So far only a study[6] reported some link between patient empathy (affective ToM) and caregiver burden. However, this study has neither investigated cognitive ToM nor its association with caregiver burden or distress. Thus, the association between impairment of both components of patient's ToM and caregiver burden and distress needs further investigation.

In a previous study (submitted for publication) conducted by our team,[7] additional data were gathered about caregiver burden and distress, as well as data of patients' cognitive and affective ToM. The present pilot study thus performed secondary analyses

Table 1: Descriptive statistics at screening of participants with PD-MCI total sample (_n_ = 12)

	Mean (SD)
Age	70.50 (5.35)
Sex (_n_ men/12)	10/12
Education (years)	16.50 (4.02)
Time since diagnosis (years)	8.67 (5.43)
Hoehn and Yahr stage	1.97 (0.59)
LED (mg/day)	681.13 (376.81)
Faux Pas test	
Hits, correct detection of _Faux Pas_ (Z score)	0.66 (0.83)
Intentions, correct explication of intentions (Z score)	−0.97 (1.64)
Empathy, correct explication of emotions (Z score)	0.35 (0.37)
Age of caregivers	64.91 (6.87)
Sex of caregivers (% women)	100.00
Education of caregivers (years)	15.42
Caregiver burden	
ZBI-12 total score (max. 48)	8.00 (7.00)
Neuropsychiatric Inventory, 12 items	
NPI-12 emotional distress (of caregivers) subscale score (max. 60)	4.00 (3.61)
NPI-12 severity (patients) subscale score (max. 36)	6.00 (5.18)
NPI-12 symptoms	
Depression (_n_ patients/12)	10/12
Anxiety (_n_)	7/12
Sleep disorders (_n_)	7/12
Apathy (_n_)	3/12
Irritability (_n_)	2/12
Global cognition (patients)	
MoCA (raw score/30)	23.92 (2.15)
MoCA (Z score)	−1.26 (0.56)

LED = levodopa equivalent dose; ZBI-12 = Zarit Burden Interview, 12 items; AES = apathy evaluation scale; MoCA = Montreal cognitive assessment; PDQ-39 = Parkinson disease questionnaire, 39 items.

on these data to verify if caregiver burden and distress are associated with patient's cognitive and affective ToM. It was hypothesised that caregiver burden and distress would be associated with both components of patients' ToM, that is, affective and cognitive ToM.

Participants and methods were described in another paper from our team.[7] Table 1 presents demographics and clinical characteristics of PD patients with mild cognitive impairment (PD-MCI) and their caregivers.

As for this study and the present analyses, all participants and caregivers signed an informed consent before entering in the study. All nominative data were kept confidential by coding of all documents. The present analyses were approved by the Ethics and Research Committee of _CHU de Québec – Université Laval_.

Faux Pas recognition test (social mistaking) is a classical test of ToM and was administered to patients. In this test, participants

are asked to read a story that may or may not contain a social _Faux pas_. After each story, participants were asked the following questions:

'Did anyone say something s/he should not have said or something awkward?' (_Faux Pas_ detection, referred as 'Hits' in Table 1). If participants answered 'yes', they were asked the following questions:
'Who said something s/he should not have said or something awkward?' (_Faux Pas_ comprehension).
'Why shouldn't s/he have said it or why was it awkward?' (_Faux Pas_ comprehension).
'Why do you think s/he said it?' (_Faux Pas_ comprehension).
'Did X know that Y (. . .)?' (test for realising that the _Faux pas_ was unintentional, referred as 'Intentions' in Table 1).
'How did X feel?' (test for attributing emotions to the protagonists, referred as 'Empathy' in Table 1).

Questions 7 and 8 were control questions to check that participants understood the details of the story: scores are adjusted if the person does not understand the story. Three composite scores were calculated for the present study, as follows:

'Hits', correct detection of _Faux Pas_ (max/10, converted to %);
'Intentions', correct explanation of characters intentions (max/10, converted to %);
'Empathy', correct explanation of emotions (max/10, converted to %).

'Intentions' is considered a cognitive ToM measure, whereas 'Empathy' is considered an affective ToM measure. All the scores were analysed using normative data adjusted for sex and education that were developed for French-speaking elderly. The analysis provides Z-score for each composite score of the _Faux Pas_ test. This task has validity to assess ToM.[4]

The Zarit Burden Interview-12 items or ZBI-12 was administered to measure the caregiver burden. Items are rated on a five-point Likert scale from 0 (never) to 4 (very often), with higher scores indicating more burden.

The Neuropsychiatric Inventory-12 items or NPI-12 was conducted with the caregiver who had to answer questions about psychiatric symptoms of PD patients and about their own distress. For each symptom, frequency is rated on a three-point scale (max. 3), impact is rated on a four-point scale (max. 4) and distress of the caregiver is rated on a six-point scale (max. 5). Impact scores of 12 items are multiplied by frequency scores, resulting in a severity score (possible maximum score = 144). A total distress score can be obtained with a possible maximum score of 60.

Because of small sample size, Spearman's _rho_ was applied to calculate non-parametric correlations between different variables at baseline. To add corrections for multiple comparisons, _p_ values were adjusted with false discovery rate correction.[8]

All statistical analyses were performed with SAS software (version 9.4 for Windows) at the $\alpha = 0.1$ level of significance.

Table 1 shows descriptive statistics of the total sample. The Schapiro–Wilks test confirmed that most variables were not normally distributed. Thereafter, non-parametric tests were conducted.

Table 2 shows non-parametric correlations between variables. There is a significant correlation between Hits and Empathy scores ($r = 0.96$, $p < 0.0001$). This means that Empathy and Hits scores measure a related construct, that is, ToM. Patient symptom

Table 2: Spearman correlations between variables in a PD-MCI sample

Variables	1	2	3	4	5	6	7
1	1	0.56	0.96**	0.26	0.31	0.08	−0.69
2		1	0.59	0.13	−0.76*	0.46	−0.52
3			1	0.27	0.45	0.19	−0.67
4				1	0.49	0.75*	−0.15
5					1	0.87**	−0.42
6						1	−0.20
7							1

Numbers in the table are interpreted as follows: (1) Hits (number of Faux Pas detected correctly); (2) Intentions (correct explication of intentions in the Faux Pas stories); (3) Empathy (correct explication of character's feeling in the Faux Pas stories); (4) Caregiver burden (ZBI-12); (5) caregiver distress (distress subscale of NPI-12); (6) Severity of neuropsychiatric symptoms (severity subscale of NPI-12); and (7) Disease stage (Hoehn and Yahr).
$p < 0.1$.
$^{*}p < 0.05$.
$^{**}p < 0.01$.

severity and caregiver distress scores of the NPI-12 are correlated ($r = 0.86$, $p = 0.011$), meaning that the more patients present with psychological and behavioural problems, the more the caregivers are in distress. There is a significant correlation between Faux Pas Intentions and distress score of NPI-12 ($r = -0.76$, $p = 0.008$). The less skillful patients are at sensing another person's intentions, the more distressed the caregivers are. There is also a significant correlation between ZBI-12 and severity score of NPI ($r = 0.75$, $p = 0.0853$). The more patients present with psychological and behavioural problems, greater the burden on caregivers (Table 2).

Interestingly, the more difficult it is for patients to understand and guess the intentions (cognitive ToM) of their interlocutor, the greater the distress (NPI-12) experienced by caregivers. In mental health disorder literature, ToM is generally linked to social and occupational functioning of patients,[5,6] but to date, no study has investigated the impact of ToM on the mental health of their caregivers. In PD, the relationship with the caregiver might be considered as a social functioning outcome. Caregiver distress is therefore an important variable to consider, especially because it is directly related to institutionalisation of PD patients.[9,10] Given the frequency of caregivers' psychological symptoms, a future target of PD-MCI cognitive training might be ToM in order to help caregivers in their daily tasks and prevent caregiver distress.

Contrary to our hypotheses, the caregiver burden (ZBI-12) was not associated with the ToM in this PD-MCI sample. The small range of ZBI scores in this sample might have decreased correlations. However, to our knowledge, no study investigated the link between caregiver burden and both components (cognitive and affective) of ToM; therefore, this result cannot be compared with previous findings.

There was a positive correlation between ZBI-12 score and NPI-12 severity of neuropsychiatric symptoms subscale, supporting the results of previous studies indicating that psychological symptoms of PD are associated with caregiver burden.[2,3,9,10] For the majority of PD patients included in this sample, depression or anxiety symptoms were identified by the caregiver, but there was also apathy, irritability and sleep problems identified for some patients. Those symptoms may also have contributed to the caregiver burden.

The caregiver burden and distress reported by the caregivers were not associated. Since there was no caregiver that scored higher than moderate burden on the ZBI-12, it is possible that caregivers in this sample might not have reported enough burden to find a correlation between the ZBI score and the NPI distress subscale score.

The small number of participants is the biggest limit of this study; it prevents generalisation to all PD-MCI. Another limitation is inherent to Spearman *rho* correlations, which have a tendency to inflate the effect sizes of the associations. Indeed, the *rho* in the present study was elevated for a small sample. Therefore, these effect sizes, although significant, must be interpreted with caution. This type of correlation, with the FDR correction, is frequently used in exploratory studies with small samples not distributed normally.

In conclusion, PD-MCI's cognitive ToM difficulties seem to be linked to caregiver feelings of distress. However, PD-MCI's ToM and caregiver burden must be investigated in larger samples in the future.

DISCLOSURES

The authors have no conflicts of interest to declare.

STATEMENT OF AUTHORSHIP

AGR designed experiments, wrote the first version of the article, performed evaluations and interventions with participants.

She executed statistical analyses. MP, MC and ER were blind assessors at FU and entered data in the database. ML and ND were neurologists in charge of recruitment. MS co-designed experiments, contributed to data analysis and writing of the manuscript. All authors reviewed the manuscript.

DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author, AGR, upon reasonable request.

REFERENCES

1. Bevan M, Sternberg E. Caregiving burden, stress, and health effects among family caregivers of adult cancer patients. J Am Med Assoc. 2012;307:398.
2. Kudlicka A, Clare L, Hindle JV. Quality of life, health status and caregiver burden in Parkinson's disease: relationship to executive functioning. Int J Geriatric Psych. 2014;29: 68–76.
3. Grün D, Pieri V, Vaillant M, Diederich NJ. Contributory factors to caregiver burden in Parkinson disease. J Am Med Direct Assoc. 2016;17:626–32.
4. Bora E, Walterfang M, Velakoulis D. Theory of mind in Parkinson's disease: a meta-analysis. Behav Brain Res. 2015; 292:515–20.
5. Dvash J, Shamay-Tsoory SG. Theory of mind and empathy as multidimensional constructs: neurological foundations. Topics Lang Dis. 2014;34:282–95.
6. Pomponi M, Ricciardi L, La Torre G, et al. Patient's loss of empathy is associated with caregiver burden. J Nervous Ment Dis. 2016; 204:717–22.
7. Giguère-Rancourt A, Plourde M, Couture M, et al. Goal management training and psychoeducation for treatment of executive dysfunction in Parkinson's disease: a feasibility pilot trial. PLOS One 2021 [in press].
8. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. J Royal Stat Soc B. 1995;57:289–300.
9. Goldman JG, Vernaleo BA, Camicioli R, et al. Cognitive impairment in Parkinson's disease: a report from a multidisciplinary symposium on unmet needs and future directions to maintain cognitive health. NJP Parkinson's Dis. 2018;4:19.
10. Carrilho PEM, Rodrigues MA, Oliveira BCRD, et al. Profile of caregivers of Parkinson's disease patients and burden measured by Zarit scale analysis of potential burden-generating factors and their correlation with disease severity. Dement Neuropsychol. 2018;12:299–305.