Revista Mexicana de Neurociencia

PERMANYER

Check for updates

ORIGINAL ARTICLE

Factors associated with psychotic symptoms in Parkinson's disease: a cross-sectional study

*Claudia N. Esparza-Hernández[1], David Garza-Brambila[1], Carlos D. Acevedo-Castillo[1], Pablo Ruiz-De las Fuentes[2], Elly M. Robles-Rodriguez[1], Ana M. Molina-Resendiz[1], Amin Cervantes-Arriaga[3], Karla Salinas-Barboza[4], Sara Isais-Millan[5], Antonio Anaya-Escamilla[6], Arnulfo Gonzalez-Cantú[7], Mayela Rodriguez-Violante[3], and Daniel Martinez-Ramirez[1]**

[1]Tecnológico de Monterrey, Escuela de Medicina y Ciencias de la Salud, Nuevo León, Monterrey; [2]Tecnológico de Monterrey, Escuela de Medicina y Ciencias de la Salud, Mexico City; [3]Laboratorio Clínico de Enfermedades Neurodegenerativas, Instituto Nacional de Neurología y Neurocirugía, Mexico City; [4]Servicio de Neurología, Hospital General de México, Mexico City; [5]Servicio de Neurología, Hospital Regional "General Ignacio Zaragoza" ISSSTE, Mexico City; [6]Servicio de Neurología, Christus Muguerza Hospital Sur, Nuevo León, Monterrey; [7]Servicio de Neurología, Christus Muguerza Alta Especialidad, Nuevo León, Monterrey. Mexico*

Abstract

Objective: *The study aimed to investigate the relationship between autonomic dysfunction, specifically orthostatic hypotension, and the presence of psychosis in Parkinson's disease (PD) patients. In addition, we aimed to identify other non-motor factors influencing the development of psychosis.* **Methods:** *We conducted a multicentric observational cross-sectional study to investigate the potential association between autonomic dysfunction and psychosis in PD patients. Approval was obtained from the institutional review board. Participants (n = 306) were recruited through non-probabilistic convenience sampling from the Mexican Parkinson Study Group cohort. Data collection occurred between July 2017 and June 2018. Demographic and clinical data were collected, including age, gender, disease duration, medication, and movement disorders society-unified Parkinson's disease rating scale (MDS-UPDRS) scores. Psychosis symptoms were assessed using MDS-UPDRS item 1.2, whereas autonomic dysfunction was assessed using items 1.10, 1.11, and 1.12. Descriptive statistics, Chi-square tests, Mann–Whitney U tests, and logistic regression were employed for analysis using IBM SPSS version 25.* **Results:** *In our multicenter cohort of 306 Mexican PD patients, 18% reported symptoms of psychosis. Among these patients, orthostatic hypotension on standing was significantly associated with symptoms of psychosis (p = 0.001, OR 2.82). Regression analysis identified apathy (p = 0.003), cognitive impairment (p = 0.012), and longer disease duration (p = 0.001) as predictors of symptoms of psychosis.* **Conclusions:** *While orthostatic hypotension is associated with symptoms of psychosis, cognitive impairment, apathy, and disease duration significantly contribute to its presence in our cohort. These findings underscore the complexity of factors contributing to psychosis in PD. Recognizing these non-motor factors is crucial for the comprehensive care and management of PD patients, especially those at risk of developing psychosis.*

Keywords: *Parkinson's disease. Psychosis. Apathy. Cognitive impairment. Autonomic dysfunction.*

***Correspondence:**
Daniel Martinez-Ramirez
E-mail: daniel.martinez-ramirez@tec.mx

Date of reception: 05-02-2024
Date of acceptance: 11-04-2024
DOI: 10.24875/RMN.24000012

Available online: 10-06-2024
Rev Mex Neuroci. 2024;25(5):125-130
www.revmexneurociencia.com

Factores asociados con síntomas psicóticos en la enfermedad de Parkinson: un estudio transversal

Resumen

Objetivo: *Investigar la relación entre la disfunción autonómica, específicamente la hipotensión ortostática, y la presencia de psicosis en pacientes con enfermedad de Parkinson (EP). Además, identificar otros factores no motores que influyen en el desarrollo de la psicosis.* **Métodos:** *Realizamos un estudio multicéntrico observacional de corte transversal. Se obtuvo la aprobación del comité de ética institucional. Los participantes (n = 306) fueron reclutados mediante muestreo de conveniencia no probabilístico de la cohorte del Grupo Mexicano de Estudio de Parkinson. La recolección de datos ocurrió entre julio de 2017 y junio de 2018. Se recopilaron datos demográficos y clínicos, incluyendo edad, género, duración de la enfermedad, medicación y puntajes MDS-UPDRS. Los síntomas psicóticos se evaluaron utilizando el ítem 1.2, mientras que la disfunción autonómica se evaluó utilizando los ítems 1.10, 1.11 y 1.12 del MDS-UPDRS. Se emplearon estadísticas descriptivas, pruebas de chi-cuadrado, pruebas U de Mann-Whitney y regresión logística para el análisis.* **Resultados:** *El 18% reportó síntomas de psicosis. Entre estos pacientes, la hipotensión ortostática se asoció significativamente con síntomas de psicosis (p = 0.001, RM 2.82). El análisis de regresión identificó la apatía (p = 0.003), el deterioro cognitivo (p = 0.012) y una duración más larga de la enfermedad (p = 0.001) como predictores de síntomas de psicosis.* **Conclusiones:** *Aunque la hipotensión ortostática se asocia con síntomas de psicosis, el deterioro cognitivo, la apatía y la duración de la enfermedad contribuyen significativamente a su presencia en nuestra cohorte. Estos hallazgos subrayan la complejidad de los factores que contribuyen a la psicosis en la EP.*

Palabras clave: *Enfermedad de Parkinson. Psicosis. Apatía. Deterioro cognitivo. Disfunción autonómica.*

Introduction

Parkinson's disease (PD) stands as the second most prevalent neurodegenerative disorder, affecting millions globally[1]. Characterized by distinct motor symptoms encompassing bradykinesia, rigidity, and/or resting tremor, PD is accompanied by a wide array of non-motor manifestations[2]. These encompass cognitive decline, psychiatric conditions, autonomic irregularities, and sleep disturbances, among others[3]. It is of notable significance that the appearance of psychosis and autonomic dysfunction represents a critical moment in the trajectory of PD, exerting a profound impact on the quality of life for patients and heightening the risks associated with hospitalization, morbidity, and mortality[4-6].

Psychosis in PD is reported in approximately 40-60% of patients and may manifest early in the disease course[7], with potential triggers including intrinsic disease pathophysiology, PD medications, or as part of non-motor fluctuations[8]. Various risk factors for psychosis in PD patients have been identified, encompassing prior medical history, both dopaminergic and non-dopaminergic medications, disease duration, genetic predispositions, prior psychiatric symptoms, vivid dreams, and cognitive decline[9]. Autonomic dysfunction occurs in the majority of PD patients at some stage, potentially compromising one or several organ systems including gastrointestinal, cardiovascular, urinary, sexual, thermoregulatory, and pupillomotor functions[10]. When present, such dysfunction is associated with a more aggressive disease course and an accelerated progression[4,11].

It is worth noting that only a limited number of studies have reported a potential association between autonomic disturbances and psychosis in PD[12]. Despite the lack of consensus regarding the direct correlation between psychosis and autonomic dysfunction in PD, there is an accumulating body of evidence that may inform clinical understanding of their relationship. This observational study investigates the association between autonomic dysfunction and psychosis within a PD patient cohort, aiming to enrich the growing body of evidence on the subject.

Material and methods

We conducted a multicentric observational cross-sectional study to investigate the potential association between autonomic dysfunction and psychosis in PD patients. The study received approval from the appropriate institutional review board. A total of 306 participants were recruited through non-probabilistic convenience sampling from the Mexican Parkinson Study Group cohort, a national database comprising demographic and clinical data of PD patients from various neurological clinics across Mexico. Data collection took place between July 2017 and June 2018. The sample size was determined using convenience sampling, based on patients' attendance at their

scheduled appointments during the designated sampling period. All 306 selected subjects were included in the final analysis. The documented demographic data were current age, age at diagnosis, gender, and years of education. The clinical characteristics documented were disease duration, side of initial symptoms, PD motor subtype (based on previously reported classification)[13], PD and non-PD medications, and the movement disorders society-unified Parkinson's disease rating scale (MDS-UPDRS)[14].

Outcome variables

To determine the presence of symptoms of psychosis as our dependent variable, we used item 1.2 from the MDS-UPDRS. Item 1.2 asks the patient if, over the past week, they have seen, heard, smelled, or felt things that were not really there. For this study, we registered the presence of symptoms if the score was from 1 (slight) to 4 (severe). If the score was 0 (normal), we registered symptoms as not present. To determine the presence of autonomic dysfunction as our independent variable, we used items 1.10 (urinary problems), 1.11 (constipation problems), and 1.12 (orthostatic hypotension) from the MDS-UPDRS. Item 1.10 asks the patient if, over the past week, they have had trouble with urine control; item 1.11 asks the patient if, over the past week, they have had constipation troubles that cause them difficulty moving their bowels; and item 1.12 asks the patient if, over the past week, they have felt faint, dizzy, or foggy when standing up after sitting or lying down. For this study, we registered the presence of symptoms if the score in either item was from 1 (slight) to 4 (severe). If the score was 0 (normal), we registered symptoms as not present.

Statistical analysis

Descriptive statistics were used to report central tendency measures, frequencies, and percentages as required. A Kolmogorov–Smirnov test was used to verify the assumptions of the distribution of continuous variables. A Chi-square test was used to determine associations between independent categorical variables and dependent categorical variables. We employed a Mann–Whitney U test to assess associations between independent continuous variables and dependent categorical variables. A multiple logistic regression model was constructed to identify variables that independently explained the presence of the items exploring psychosis in our cohort. The significantly associated variables ($p \leq 0.05$) from the univariate analysis were included in the model. The model with less deviance was selected. The IBM Statistical Package for the Social Sciences version 25 was used in the analysis.

Results

Table 1 provides an overview of the sociodemographic and clinical characteristics of our study cohort. In relation to symptoms of psychosis, among the 306 patients analyzed, 55 (18%) reported experiencing symptoms. Within this group, 32 (58.2%) reported slight symptoms, 13 (23.6%) reported mild symptoms, 8 (15.0%) reported moderate symptoms, and 2 (0.04%) reported severe symptoms. Concerning dysautonomic symptoms, a significant number of 229 (74.8%) patients reported experiencing one or a combination of these symptoms, which included orthostatic hypotension, urinary issues, and constipation problems.

The bivariate analysis revealed that the presence of urinary and constipation problems was not significantly associated with the presence of symptoms of psychosis ($p = 0.076$ and $p = 0.361$, respectively). The presence of orthostatic hypotension on standing was significantly associated with the presence of symptoms of psychosis ($p = 0.001$, OR 2.82, 95% CI 1.53-5.21). These results suggest that symptoms of orthostatic hypotension on standing but not urinary or constipation problems may affect the presence of symptoms of psychosis.

Other variables in the bivariate analysis found to be significantly associated with the presence of symptoms of psychosis were postural instability and gait difficulty motor subtype ($p = 0.048$, OR = 2.14, 95% CI 1.15-3.96), Hoehn and Yahr (HY) IV-V stage ($p < 0.001$, OR = 4.23, 95% CI 1.80-9.92), presence of symptoms of cognitive impairment ($p < 0.001$, OR 3.26, 95% CI 1.76-6.05), depression ($p = 0.030$, OR 1.99, 95% CI 1.06-3.76), anxiety ($p = 0.003$, OR 2.45, 95% CI 1.35-4.43), apathy ($p < 0.001$, OR 4.23, 95% CI 2.19-8.17), freezing of gait ($p = 0.006$, OR 2.51, 95% CI 1.29-4.89), disease duration ($p < 0.001$, $d = 0.67$), MDS-UPDRS part I ($p < 0.001$, $d = 0.99$), part II ($p = 0.037$, $d = 0.27$), part III ($p = 0.003$, $d = 0.40$), part IV ($p = 0.002$, $d = 0.43$), and the total score ($p < 0.001$, $d = 0.70$). These results suggest that other non-motor symptoms, such as cognitive impairment, depression, anxiety, and apathy, as well as PD motor subtype, HY stage, disease duration, and motor severity, may affect the presence of symptoms of psychosis.

Table 1. Sociodemographic and clinical characteristics of our PD cohort

Study variables	Total	Presence of symptoms of psychosis (n = 55)	Absence of symptoms of psychosis (n = 251)	p-value
Male, n (%)	171 (55.9)	29 (52.7)	142 (56.6)	0.603
Age, years. mean (SD)	65.29 (11.7)	67.73 (11.3)	64.76 (11.8)	0.110
Education, years. mean (SD)	10.55 (5.3)	10.31 (5.0)	10.61 (5.4)	0.719
Disease duration, years. mean (SD)	6.69 (4.8)	9.31 (5.0)	6.12 (4.6)	< 0.001
PIGD motor subtype, n (%)	160 (52.3)	37 (67.3)	123 (49.0)	0.048
Cognitive impairment, n (%)	134 (43.8)	37 (67.3)	97 (38.6)	< 0.001
Depression, n (%)	177 (57.8)	39 (70.9)	138 (55.0)	0.030
Anxiety, n (%)	123 (40.2)	32 (58.2)	91 (36.3)	0.003
Apathy, n (%)	53 (17.3)	21 (38.2)	32 (12.7)	< 0.001
Sleep problems, n (%)	166 (54.2)	33 (60.0)	133 (53.0)	0.344
Daytime sleepiness, n (%)	150 (49.0)	31 (56.4)	119 (47.4)	0.229
Pain, n (%)	151 (49.3)	30 (54.5)	121 (48.2)	0.394
Urinary problems, n (%)	173 (56.5)	37 (67.3)	136 (54.2)	0.076
Constipation, n (%)	161 (52.6)	32 (19.9)	129 (51.4)	0.361
Orthostatic symptoms, n (%)	78 (25.5)	24 (43.6)	54 (21.5)	0.001
Fatigue, n (%)	178 (58.2)	30 (54.5)	148 (59.0)	0.547
Freezing of gait, n (%)	55 (18.0)	17 (30.9)	38 (15.1)	0.006
MDS-UPDRS part I, mean (SD)	8.13 (6.2)	13.65 (8.3)	6.92 (4.9)	< 0.001
MDS-UPDRS part II, mean (SD)	5.32 (5.7)	6.78 (7.6)	5.0 (5.2)	0.037
MDS-UPDRS part III, mean (SD)	35.92 (15.7)	41.64 (19.8)	34.67 (14.4)	0.003
MDS-UPDRS part VI, mean (SD)	2.74 (4.0)	4.25 (4.7)	2.4 (3.8)	0.002
Hoehn and Yahr stage I-II, n (%)	281 (91.8)	44 (80.0)	237 (94.4)	< 0.001
LEED, mean (SD)	741.45 (479.9)	809.25 (484.8)	726.59 (478.6)	0.216

PIGD: postural instability with gait difficulty; MDS-UPDRS: movement disorders society-unified Parkinson's disease rating scale; LEED: levodopa equivalent daily dosage.

A regression model was constructed to identify variables that independently predict the presence of symptoms of psychosis. Those patients with the presence of apathy (p = 0.003, ß 2.99), cognitive impairment (p = 0.012, ß 2.33), and longer disease duration (p = 0.001, ß 1.10) were more likely to present symptoms of psychosis, as shown in table 2. The presence of orthostatic hypotension was not a significant independent predictor of symptoms of psychosis in our regression model (p = 0.052, ß 1.95). The results of the model suggest that non-motor symptoms of cognitive impairment and apathy, and disease duration best predicted the presence of symptoms of psychosis in our cohort.

Discussion

We conducted an observational cross-sectional study with the aim of investigating the association between autonomic dysfunction and the presence of symptoms of psychosis among a multicenter cohort of Mexican PD patients. The key findings of this study were as follows: (1) the reported frequency of dysautonomias (74.8%) was higher than that of symptoms of psychosis (18%); (2) patients who reported symptoms of orthostatic hypotension upon standing were 2.82 times more likely to exhibit symptoms of psychosis; and (3) patients presenting symptoms of apathy,

Table 2. Logistic regression model identifying predictors of symptoms of psychosis

Parameters	ß	SE	Wald	p	Exp (ß)	95% CI
Constant	–3.17	0.37	-	-	-	-
Presence of apathy	1.09	0.37	8.78	0.003	2.99	1.45-6.16
Presence of cognitive impairment	0.85	0.34	6.36	0.012	2.33	1.21-4.51
Disease duration	0.10	0.03	10.38	0.001	1.10	1.04-1.17
Presence of orthostatic hypotension	0.67	0.34	3.78	0.052	1.95	1.00-3.83

cognitive impairment, and longer disease duration were more likely to manifest symptoms of psychosis.

The reported frequency of symptoms of psychosis and dysautonomic symptoms in our study population is consistent with the literature, where the prevalence of psychosis varies from 16% to 75%[8], and that of dysautonomia varies from 27% to 87%[15], depending on the specific manifestations studied and the criteria or scales utilized. In our study, we employed Part I of the MDS-UPDRS scale, which assesses the presence of certain non-motor symptoms over the past week, potentially influencing the reported frequency.

We observed that PD patients reporting symptoms of orthostatic hypotension on standing were more likely to manifest symptoms of psychosis. This observation is consistent with findings from both a longitudinal study, which noted an increased risk of developing psychosis in the presence of orthostatic hypotension[16], and a cross-sectional study that reported a higher risk of psychosis associated with a greater burden of autonomic symptoms[17]. The association between dysautonomia and psychosis in PD may be explained by the higher density of Lewy bodies found in the brainstem nuclei, such as the dorsal vagal nucleus, of patients with PD who experience visual hallucinations[18]. Furthermore, the correlation between symptoms of psychosis and autonomic symptoms in PD may not merely be based on their presence but rather on the overall disease burden.

Our study population demonstrated that the symptoms most strongly associated with the presence of symptoms of psychosis were apathy, cognitive impairment, and a longer disease duration. These findings are consistent with prior literature reports. A cross-sectional study found that patients with lower scores on the Frontal Assessment Battery were more likely to develop psychosis at an earlier stage of the disease[19]. In addition, it has been documented that cognitive impairment or dementia are significant factors related to the presence of psychosis symptoms[20]. Apathetic symptoms, along with other affective neuropsychiatric disorders, are commonly reported in PD patients with psychosis[21]. Moreover, patients displaying symptoms of apathy have been linked to lower cognitive levels[22]. Apathy in PD is associated with not only executive dysfunction but also a decline in overall cognitive function, particularly in tasks related to the temporal lobes, which may contribute to its role as an early indicator of dementia in the disease[23]. It has also been previously reported that the duration of the disease is associated with the presence of visual hallucinations, typically occurring in the later stages of the disease[20]. These findings indicate that although there is an association between orthostatic hypotension and psychosis in PD, other non-motor symptoms such as cognitive impairment and apathy, along with disease duration, significantly contribute to the presence of symptoms of psychosis in the cohort. Furthermore, it is important to consider unexplored factors in our study, such as pharmacological treatments, disease severity, and genetics, among others.

Our study has several limitations that should be taken into consideration when interpreting our results. First, it was conducted within a specific cohort of Mexican PD patients, which prompts consideration of the generalizability of our findings to broader populations. Second, certain influential factors, such as pharmacological treatments, and lack of objective evaluation of other non-motor aspects such as sleep, disease severity, and genetic influences, were not included in our study, limiting the comprehensiveness of our results. We should also take into account that some patients may have an alternative cause of synucleinopathy. In addition, our reliance on Part I of the MDS-UPDRS scale, which assesses symptoms over the past week, might have influenced the reported frequency of certain symptoms and could be a limitation. We would like to emphasize the constraints posed by available resources and study design in utilizing more objective measures to assess dysautonomic symptoms, while also highlighting the potential for future investigations to

explore the incorporation of specific scales for psychotic symptoms to further enhance the comprehensiveness of our findings. The cross-sectional design of our study restricts our ability to establish causal relationships between variables. There may also be unmeasured confounding factors not accounted for in our analysis. Finally, the use of a specific language and cultural context in our study may introduce biases or limitations related to linguistic and cultural variations in symptom reporting.

Conclusion

Our findings suggest that while orthostatic hypotension is associated with symptoms of psychosis, other non-motor symptoms such as cognitive impairment and apathy, along with disease duration, significantly contribute to the presence of symptoms of psychosis in the cohort. These findings contribute to the body of literature on the complex interplay between non-motor symptoms and psychosis in PD.

Acknowledgments

The authors wish to acknowledge the contributions of medical students Edna Sophia Velazquez-Avila and Alejandro Banegas-Lagos, who diligently supported and participated in the data collection process.

Funding

The authors declare that this work was carried out with the authors' own resources.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that no patient data appear in this article. Furthermore, they have acknowledged and followed the recommendations as per the SAGER guidelines depending on the type and nature of the study.

Right to privacy and informed consent. Right to privacy and informed consent. The authors have obtained approval from the Ethics Committee for analysis and publication of routinely acquired clinical data and informed consent was not required for this retrospective observational study.

Use of artificial intelligence for generating text. The authors declare that they have used generative artificial intelligence, specifically Chat GPT-3.5 in the writing of this manuscript. The authors declare that generative artificial intelligence was not used in the creation of images, graphics, tables, or their corresponding captions.

References

1. Bloem BR, Okun MS, Klein C. Parkinson's disease. Lancet. 2021;397: 2284-303.
2. Kalia LV, Lang AE. Parkinson's disease. Lancet. 2015;386:896-912.
3. Sauerbier A, Rosa-Grilo M, Qamar MA, Chaudhuri KR. Nonmotor subtyping in Parkinson's disease. Int Rev Neurobiol. 2017;133:447-78.
4. Merola A, Romagnolo A, Rosso M, Suri R, Berndt Z, Maule S, et al. Autonomic dysfunction in Parkinson's disease: a prospective cohort study. Mov Disord. 2018;33:391-7.
5. Wetmore JB, Li S, Yan H, Irfan M, Rashid N, Peng Y, et al. Increases in institutionalization, healthcare resource utilization, and mortality risk associated with Parkinson disease psychosis: retrospective cohort study. Parkinsonism Relat Disord. 2019;68:95-101.
6. Akbar U, McQueen RB, Bemski J, Carter J, Goy ER, Kutner J, et al. Prognostic predictors relevant to end-of-life palliative care in Parkinson's disease and related disorders: a systematic review. J Neurol Neurosurg Psychiatry. 2021;92629-36.
7. Ffytche DH, Creese B, Politis M, Chaudhuri KR, Weintraub D, Ballard C, et al. The psychosis spectrum in Parkinson disease. Nat Rev Neurol. 2017;13:81-95.
8. Chang A, Fox SH. Psychosis in Parkinson's disease: epidemiology, pathophysiology, and management. Drugs. 2016;76:1093-18.
9. Ffytche DH, Aarsland D. Psychosis in Parkinson's disease. Int Rev Neurobiol. 2017;133:585-622.
10. Pfeiffer RF. Autonomic dysfunction in Parkinson's disease. Neurotherapeutics. 2020;17:1464-79.
11. Fereshtehnejad SM, Romenets SR, Anang JB, Latreille V, Gagnon JF, Postuma RB. New clinical subtypes of parkinson disease and their longitudinal progression: a prospective cohort comparison with other phenotypes. JAMA Neurol. 2015;72:863-73.
12. Zhu K, van Hilten JJ, Putter H, Marinus J. Risk factors for hallucinations in Parkinson's disease: results from a large prospective cohort study. Mov Disord. 2013;28:755-62.
13. Eisinger RS, Hess CW, Martinez-Ramirez D, Almeida L, Foote KD, Okun MS, et al. Motor subtype changes in early Parkinson's disease. Parkinsonism Relat Disord. 2017;43:67-72.
14. Goetz CG, Tilley BC, Shaftman SR, Stebbins GT, Fahn S, Martinez-Martin P, et al. Movement disorder society-sponsored revision of the unified Parkinson's disease rating scale (MDS-UPDRS): scale presentation and clinimetric testing results. Mov Disord. 2008;23:2129-70.
15. Zhang Z, Chen SD. Autonomic dysfunctions in Parkinson's disease: prevalence, clinical characteristics, potential diagnostic markers, and treatment. Parkinsons Dis. 2020;2020:8740732.
16. Yoritaka A, Shimo Y, Hatano T, Hattori N. Motor/nonmotor symptoms and progression in patients with Parkinson's disease: prevalence and risks in a longitudinal study. Parkinsons Dis. 2020;2020:2735361.
17. Barrett MJ, Smolkin ME, Flanigan JL, Shah BB, Harrison MB, Sperling SA. Characteristics, correlates, and assessment of psychosis in Parkinson disease without dementia. Parkinsonism Relat Disord. 2017;43:56-60.
18. Gallagher DA, Parkkinen L, O'Sullivan SS, Spratt A, Shah A, Davey CC, et al. Testing an aetiological model of visual hallucinations in Parkinson's disease. Brain. 2011;134:3299-309.
19. Lenka A, George L, Arumugham SS, Hegde S, Reddy V, Kamble N, et al. Predictors of onset of psychosis in patients with Parkinson's disease: who gets it early? Parkinsonism Relat Disord. 2017;44:91-4.
20. Fenelon G, Alves G. Epidemiology of psychosis in Parkinson's disease. J Neurol Sci. 2010;289:12-7.
21. Marsh L, Williams JR, Rocco M, Grill S, Munro C, Dawson TM. Psychiatric comorbidities in patients with Parkinson disease and psychosis. Neurology. 2004;63:293-300.
22. Dujardin K, Langlois C, Plomhause L, Carette AS, Delliaux M, Duhamel A, et al. Apathy in untreated early-stage Parkinson disease: relationship with other non-motor symptoms. Mov Disord. 2014;29:1796-801.
23. Pagonabarraga J, Kulisevsky J, Strafella AP, Krack P. Apathy in Parkinson's disease: clinical features, neural substrates, diagnosis, and treatment. Lancet Neurol. 2015;14:518-31.