



HAL
open science

Psycho-sensory modalities of visual hallucinations and illusions in Parkinson's disease

Anna Raquel Marques, S Beze, C Lambert, L Bonamy, Ingrid de Chazeron, Isabelle Rieu, F Chiambaretta, Franck Durif

► **To cite this version:**

Anna Raquel Marques, S Beze, C Lambert, L Bonamy, Ingrid de Chazeron, et al.. Psycho-sensory modalities of visual hallucinations and illusions in Parkinson's disease. *Revue Neurologique*, 2021, 177 (10), pp.1228. 10.1016/j.neurol.2021.04.007 . hal-03552255

HAL Id: hal-03552255

<https://uca.hal.science/hal-03552255v1>

Submitted on 5 Jan 2024

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

PSYCHO-SENSORY MODALITIES OF VISUAL HALLUCINATIONS AND ILLUSIONS IN PARKINSON'S DISEASE

Marques Ana, MD, PhD¹; Beze Steven, MD, MSc^{1,4}; Lambert Céline, MSc²; Bonamy Lea, MSc¹; de Chazeron Ingrid, PhD,³ Rieu Isabelle, PhD¹; Chiambaretta Frédéric, MD, PhD⁴; Durif Franck, MD, PhD¹.

1. *Université Clermont-Auvergne, EA7280, Neurology department, Clermont-Ferrand university Hospital, FRANCE*
2. *Biostatistics department, Clermont-Ferrand university Hospital, FRANCE*
3. *Université Clermont-Auvergne, EA7280, Psychiatry department, Clermont-Ferrand university Hospital, FRANCE*
4. *Ophthalmology department, Clermont-Ferrand university Hospital, FRANCE*

Corresponding author:

Ana Marques:

Service de Neurologie, Centre expert Parkinson

Hopital Gabriel Montpied, CHRU Clermont-Ferrand

Place Henri Dunant, 63000 Clermont-Ferrand, FRANCE

Phone: 0033 473 751600 - Fax: 003 473 751596

ar_marques@chu-clermontferrand.fr

Statistical analysis conducted by: LAMBERT Céline, Clermont-Ferrand University Hospital, Biostatistics Department, Clermont-Ferrand, FRANCE

Word Count:

Title Character count: 87

Number of references: 28

Number of tables: 1

Number of figures: 2

Supplemental data: 1 supplemental Table, STROBE checklist

Word count abstract: 247

Word count paper: 2995

Study funding: Funded by Fondation de France (n°76354)

Registration number: *clinicaltrials.gov* number NCT03454269

Key Words: Parkinson, Hallucinations, Illusions, phenomenology

Conflicts of interest/Competing interests:

Ana Marques reports grants from Fondation de France, during the conduct of the study;

Steven Beze has nothing to disclose;

Celine Lambert has nothing to disclose;

Lea Bonamy has nothing to disclose;

Ingrid de Chazeron has nothing to disclose;

Isabelle Rieu has nothing to disclose;

Frederic Chiambaretta has nothing to disclose;

Franck Durif has nothing to disclose.

ABSTRACT

Background: Visual illusions (VI) in Parkinson's disease (PD) are generally considered part of the prodrome towards fully formed visual hallucinations (VH), and classified as minor hallucinations. However, this sequential relationship has not been clearly demonstrated and very little is known about the specific phenomenology of VI in regards to VH. We aimed to describe and compare psycho-sensory modalities associated with VI and VH in PD patients.

Methods: PD patients with VI (PD-I, n=26) and VH (PD-H, n=28) were included in this case-controlled study. We compared qualitative and quantitative psycho-sensory modalities of VI and VH using the PsychoSensory hAllucinations Scale (PSAS), and demographical and clinical features of each group.

Results: PD-I perceptions were more often colored blots ($p=0.05$) or objects ($p=0.005$) compared to PD-H. Conversely, PD-H perceptions were more often described as animals ($p<0.001$), occurring at night ($p=0.03$) compared to PD-I. The experienced phenomena were more frequent in PD-H ($p=0.02$), and lasted longer ($p=0.02$) than for PD-I, but no between-group difference was observed for other repercussion factors including negative aspect, conviction, impact, controllable nature of the perception. Passage hallucinations and sense of presence were observed in both groups with similar frequencies (respectively $p=0.60$ and $p=0.70$). Multivariate analysis adjusting for disease severity or duration confirmed these results.

Conclusion: VI and VH in PD have different qualitative sensory modalities, with similar quantitative repercussion for patients, and similar association with modalities such as "sense of presence and passage hallucinations", in contrast to the generally accepted classification of VI as minor VH.

INTRODUCTION

A wide variety of visual perception impairments are reported in Parkinson's disease (PD), ranging from passage hallucinations and visual illusions (VI) to complex visual hallucinations (VH). VI and passage hallucinations are generally considered as prodromal symptoms of fully formed VH, although this sequential relationship has not been demonstrated in longitudinal studies [1–5]. Thus, whether VI (defined as a false perception of an existing stimuli) should be considered as part of VH (defined as a perception without existing stimuli), even minor, remains to be demonstrated. Indeed, while the phenomenology of sense of presence and passage hallucinations has been assessed in systematic studies, very little is known about the specific phenomenology of visual illusions in Parkinson's disease.[2] Recently, we demonstrated that PD patients with VH have greater retinal parafoveal thinning, as well as cortical and subcortical atrophy compared to PD patients with VI, independently of disease duration [6], in line with another study reporting decreased age-adjusted gray matter volume in PD with VH compared to PD patients with VI [7]. It has also been previously demonstrated that while sharing a substantial overlap in their neural correlates, visual illusions and hallucinations in PD were phenomenologically diverse [8], but thus far psycho-sensory modalities of VH and VI in PD have not been explored and compared using a specifically designed tool.

This study aimed to describe psycho-sensorial characteristics associated with VI and VH in PD patients, and to compare their specificities in those two groups. We also aimed to determine whether determinant demographical and clinical features associated with VI are distinct from those associated with VH in PD.

METHODS

Study design and settings

This study was nested in a previously published case-control study that included eighty-two PD patients who were recruited from the Parkinson expert center, Neurology Department, Clermont-Ferrand University Hospital, France, between March 2018 and April 2019 (clinicalTrials.gov n° NCT01114321).[6] PD patients were included in three groups: PD with VI (PD-I; n=26), PD with VH (PD-H; n=28), and PD without VI or VH (PD-C; n=28), matched for age and sex. In this ancillary study, we investigated the psycho-sensory characteristics of visual hallucinations and illusions in PD-I and PD-H patients. We also compared the demographic data, parkinsonian symptoms, cognitive, sleep and visual complaints associated with PD-I and PD-H.

The protocol was approved by the South-West & Overseas II ethical committee, France (2017-A02605-48). All patients gave their written informed consent as per the Declaration of Helsinki. Registration number: clinicaltrials.gov number NCT03454269 (first registration 05/03/2018).

Participants

We included PD patients fulfilling the modified United Kingdom Parkinson Disease Society Brain Bank criteria [9], and defined the presence of VI or VH using the scale for outcomes in Parkinson's disease psychiatric complication (SCOPA-PC) [10] together with patient and caregiver interviews in order to distinguish VH from VI. VH was defined as a visual perception in the absence of an external stimuli, whereas VI was defined as a visual misperception of an identifiable external stimuli [7]. VI or VH had to occur at least once a week, within the past three months. When a patient had both VI and VH, they were classified according to their dominant manifestation (SCOPA-PC score item related to non-dominant manifestation not higher than 1). We excluded patients with neurological diseases other than PD or psychiatric conditions characterized by VH and patients with cognitive impairment (Montreal Cognitive Assessment (MoCA) score <21/30).[11] Treatment with antipsychotics represented a further

exclusion, as well as modifications of anti-parkinsonian treatments within the month before inclusion.

Main outcome

We assessed the characteristics and severity of VH or VI using the Psycho-Sensory Hallucinations Scale (PSAS),[12] which is a multimodal hetero-evaluation scale, validated in different populations of hallucinating patients suffering from schizophrenia and PD.[12, 13] This scale includes four domains (auditory, visual, olfactory/gustatory, cenesthetic modalities) and one specific item referring to sense of presence and defined as the “vivid sensation that somebody is present nearby, when no one is actually there, in the absence of sensory clues revealing a presence”. Each domain is declined in the same way: a qualitative part (moment of occurrence during the day: simple or complex; lights, geometric shapes, colored dots, flames; animal, faces, objects, people; animated or fixed scene; in relief, tiny, giant, colored) and a quantitative part (frequency, duration, unpleasant or negative aspects, conviction, impact, and control) assessing the repercussion on patient.

Secondary outcomes

We assessed duration and severity of PD (according to Movement Disorder Society - Unified Parkinson’s Disease Rating Scale (MDS-UPDRS)[14] and Hoehn & Yahr stage [15], and noted the dopaminergic treatment doses (expressed as total levodopa equivalent dose (LED) and dopamine agonists LED) [16], as well as psychotropic treatments users.

Cognitive functions were assessed with the Mattis dementia rating scale [17], and the copy of the complex figure of Rey-Osterrieth (ROCF) [18]. Sleep quality (Parkinson’s disease sleep scale (PDSS-2) [19], REM Sleep Behavior Disorder (REM Sleep Behavior Disorder Single-Question (RBD-1Q) [20], and excessive daytime sleepiness (Epworth scale) [21] were also

investigated. Visual complaints were recorded by an ophthalmologist using a semi-structured interview aiming to screen for the presence of various manifestations that could be experienced by patients: sensation of vision loss, visual field impairment, metamorphopsia, halos, diplopia, color vision impairment, epiphora, or eye pain. All clinical assessments were performed with participants on their regular antiparkinsonian treatment.

Statistical analysis

Statistical analyses were performed using Stata software (version 15, StataCorp, College Station, US) and R 3.5.1 (<http://cran.r-project.org/>). All tests were two-sided with type I error set at 0.05. Categorical variables were expressed as frequencies and associated percentages, and quantitative variables as mean \pm standard deviation or as median [interquartile range], according to statistical distribution and previously reported results in the literature. PD-I and PD-H patients were compared with the chi-squared test or the Fisher's exact test for categorical variables and with the Student's t test or the Mann-Whitney test for quantitative ones. The Gaussian distribution was verified by the Shapiro-Wilk test and homoscedasticity by the Fisher-Snedecor test. The results were then adjusted (separately) on MDS-UPDRS total, Hoehn and Yahr, and disease duration, using linear (for quantitative outcomes) or logistic (for binary outcomes) regressions. Finally, a factor analysis of mixed data was performed to study the similarities between individuals taking into account mixed variables (both continuous and categorical) and to study the relationships between all the variables. This analysis, which can be seen as a mixed between principal component and multiple component analysis, was performed with the `ade4` package (`dudi.mix` function) in R.[22] For this analysis, variables were chosen according to clinical relevance and statistical distribution (characteristics always present or always absent were not considered), and only individuals without missing data were used (n=49).

Data availability: The data that supports the findings of this study are available from the corresponding author, upon reasonable request.

RESULTS

Demographical and clinical characteristics

We included 54 PD patients in our analysis (n=26 PD-I; n=28 PD-H), matched for sex and age \pm 5 years. The total population was aged 69.9 ± 6.7 years, with a sex ratio 29/25 male to female and a mean PD disease duration of 10.2 ± 5.3 years. Among these patients, seven had coexisting VI and VH (n=3 had predominant VI; n=4 had predominant VH). Demographic and clinical characteristics of patients are resumed in **Table 1**.

Psycho-sensory modalities of VI and VH

The psycho-sensory modalities were assessed for VI and VH according to PSAS (ranging from 0 to 23) and compared between PD-I and PD-H groups. PSAS total score was higher in PD-H than in PD-I (respectively 11.04 ± 3.82 and 8.50 ± 2.55 ; $p=0.006$).

Qualitative modalities

Regarding the time of occurrence of phenomena during the day, PD-H reported more night experience compared to PD-I (54.2% vs. 21.1%; $p=0.03$), while no-between group difference was observed for occurrence during the day, or when waking up or falling asleep (**Figure 1**).

PD-I misperceptions (triggered by a real external stimuli) were more often colored blots (15.4% vs. 0.0%; $p=0.047$) or objects (50.0% vs. 14.3%; $p=0.005$) compared to PD-H perceptions (in the absence of an external stimuli). Conversely, PD-H perceptions were more often described

as animals (78.6% vs. 23.1%; $p < 0.001$) compared to PD-I misperceptions. No between-group difference was noted for perception of light, geometric shapes, flames, neither for faces, people, fixed or animated scenes. Groups did not differ for the experience of motionless or in motion, tiny or giant, in color or in three-dimension perceptions (Fig. 1).

Regarding associated modalities, 21.4% of PD-H had concomitant auditory hallucinations vs. 3.8% of PD-I ($p = 0.10$). Moreover, 17.9% of PD-H had associated olfactory hallucinations while no PD-I experienced that associated modality ($p = 0.052$). No other significant difference was observed for the associated hallucinations modalities, and the association with minor hallucinations (passage hallucinations and sense of presence) was observed in both groups with similar frequencies (respectively 7.7% (PD-I) vs. 3.6% (PD-H), $p = 0.60$); 21.4% (PD-I) vs. 29.4 (PD-H), $p = 0.70$).

Quantitative modalities

The experienced phenomena were more frequent in PD-H ($p = 0.02$), and lasted longer ($p = 0.02$) than for PD-I (Fig. 1). No between-group difference was observed for other repercussion factors including negative aspect, conviction, impact, controllable nature of the perception.

Factor analysis of mixed data

Factorial analysis was performed to analyze the relationships between clinical and PSAS variables. From this factorial analysis we have illustrated the two distinct profiles of patients based on the presence of VI or VH (Fig. 2). According to this approach, perceptions of animals or people, perceptions occurring at night, higher Epworth score, longer disease duration and worse MDS-UPDRS total score were associated with the PD-H group. Perceptions of objects and better Mattis total score are associated with the PD-I group.

Multivariate analysis of variables associated with VH and VI in PD

Multivariate analyses were applied to PD-H and PD-I groups, adjusting either for disease severity (UPDRS III or Hoehn and Yahr scale), for disease duration, or for age (Suppl. Table 1), and confirmed that independently of age, disease severity or duration, PD-H reported more abnormal perceptions of animals, occurring mostly at night, and had more probable RBD, whereas PD-I reported more abnormal perceptions of objects and tended to have more visual complaints such as epiphora.

DISCUSSION

VI and VH in PD are characterized by different psycho-sensorial characteristics as PD-H report more visual perceptions occurring at night and described as animals compared to PD-I, while PD-I report more visual perceptions described as color blots or objects compared to PD-H. The experienced phenomena are more frequent and last longer in PD-H than for PD-I, but no between-group difference was observed for other repercussion factors including negative aspect, conviction, impact, controllable nature of the perception. Associated olfactory and auditory hallucinations were greater in PD-H compared to PD-I, but associated minor hallucinations (passage hallucinations and sense of presence) did not differ between groups.

Phenomenology and repercussion

The clinical phenomenology of VH has been extensively investigated in previous studies [23, 24]? but very few assessed specifically clinical phenomenology of VI[8]. More importantly, to our knowledge, this is the first study to compare the psycho-sensorial phenomenology of VI versus VH.

Thus, one study evaluated the prevalence, phenomenology and risk factors for VH in 212 PD patients and reported that formed VH consisted in most cases of rather simple images of people or animals, and occurred mostly during the evening or night (46% of patients), in line with our results [23]. These authors reported VI in nine patients, consisting in transformation of an object into an animal (misidentification) [23]; they were not distinguished from minor hallucinations in the previous analysis, but they were described as static in 53% of patients, with no specific schedule in 66% of patients, and commonly very brief (a few seconds), similar to our findings. Another study assessed the phenomenology and neural substrates of VI in PD and revealed that illusions of motion (kinetopsia) was the most common type of visual illusion (26%), followed by object misidentification illusions, in which an individual misperceives an object as a different object (18%), and were associated in 10% of patients [8]. Moreover, VH coexisted in 50% of patients with VI [8].

We report low conviction and impact of VH, in line with previous results showing that VH were generally non-threatening, and lack of insight and associated delusions were only observed in a few patients with dementia [23]. Moreover, it has been demonstrated that the repercussion index summing characteristics of hallucinations (frequency, duration, negative aspects, conviction, impact, control) was lower in PD compared to schizophrenia [13]. Interestingly, we found no difference between VH and VI for the impact of experienced phenomena. While 31 patients with isolated minor hallucinations have been previously reported to be associated with less anxiety, less coexisting delusions, less need for a therapeutic change and more insight compared to complex VH [23], this could not be replicated in our study assessing specifically VI. Indeed, our results reveal that VH and VI have distinct qualitative psycho-sensory modalities but similar quantitative modalities in terms of impact on the patient, contrasting with the hypothesis of a continuum phenomenon with grading severity. In addition, two previous studies have demonstrated that VH and VI in Parkinson's disease are not

transitory or fluctuating phenomena and showed that their presence was stable over an 18-month to 5-year period, which would argue against the continuum hypothesis [25, 26]. From our cross sectional study it is not possible to further conclude as whether the former should be regarded or not as a prodromal stage of the latter. Longitudinal studies specifically addressing the question of the specific evolution of VI compared to VH in PD are needed.

Associated modalities

The association of other-sense hallucinatory modalities has not been specifically assessed with VI as of yet, but previous study reported the presence of coexisting auditory hallucinations in 33% to 36%, and coexisting olfactory hallucinations in 13% of PD-H patients [4, 13, 23, 27], in line with our results. Indeed, we observed more other-sense hallucinations associated with VH, and reported 21% of PD-H with concomitant auditory associated hallucinations and 18% with associated olfactory hallucinations. Conversely, passage hallucinations and sense of presence were reported similarly in both PD-I and PD-H, without any difference of prevalence, arguing against the generally proposed classification gathering illusions, presence and passage hallucinations as minor visual hallucinations, in opposition with formed visual hallucinations [23].

Clinical and imaging profile

One previous study, assessing minor and complex VH, identified three factors independently predictive of formed VH: severe cognitive disorders, daytime somnolence and a long duration of PD, while minor hallucination had higher scores of depression compared to non-hallucinators, but did not differ in other aspects [23]. More recently, the use of dopamine agonists, higher MDS-UPDRS Part II score, and presence of RBD (Odd Ratio=4.8, p=0.012) were reported to be independent predictors of VH and VI.[28] Yet, in those studies, illusions

were not assessed separately. As of yet, very few studies investigated specifically the clinical and imaging characteristics associated with VI and VH, and while a substantial clinical and imaging overlap was observed between VH and kinetopsia (a specific type of VI characterized by illusion of motion),[8] patients with object misidentification had distinct clinical and imaging features compared to those with VH.[6, 8] Indeed, unlike patients with VI, those with VH had cognitive impairment compared to those patients with no false perception. However these results were not corrected for disease severity and duration. More recently, it has been reported that PD patients with VH had significantly higher age, disease duration, rate of RBD and cognitive impairment compared to PD patients with other visual symptoms, and decreased age-adjusted grey matter volume compared to PD patients with VI [7]. We also previously reported a greater brain atrophy and retinal thinning associated with VH compared to VI, independently of disease duration [6]. In this study, we report a greater disease severity, more cognitive disorders and a higher prevalence of probable RBD in PD-H compared to PD-I, whereas PD-I had only more epiphora compared to PD-H. Multivariate analysis adjusting for disease severity or duration confirmed that PD-H presented more frequently probable RBD, whereas PD-I tended to have more visual complaints such as epiphora. Altogether, clinical and imaging data suggest that, while probably linked and driven by at least some similar mechanisms, specific distinct patterns could be associated with VI and VH regardless to disease duration and severity.

Limitations

A number of limitations of this study must be identified. First, VI and VH coexisted in a subset of PD patients, which could be a confounding factor even if we considered the clinically predominant phenomenon. Also, precise clinical criteria allowing to clearly distinguish VI from minor hallucinations such as passage hallucinations and sense of presence are lacking. In this

study, the patient and caregiver interview allowed us to distinguish sense of presence hallucinations, which are closer to a delusional idea or a social hallucination, since the belief that a person is present behind oneself is not associated with any sensory clue. Yet, distinguishing VI from passage hallucination appears more challenging since it relies on the patient's ability to determine whether there was or not a real visual external stimulation. Finally, this study is cross sectional, and does not allow to draw any conclusions on the longitudinal evolution of VI and VH in PD or their relations. It should also be recognized that our population was selected since PD patients with cognitive impairment were excluded, thus our results, and particularly the lack of difference regarding the impact of VI and VH, may not apply to PD patients with more severe cognitive impairment. Another limitation of this study is the small sample size in this study precluding a multivariable analysis with several covariables. We therefore adjusted univariate results for only one covariate at a time.

Conclusion

VI and VH in PD have different qualitative sensory modalities, but a similar repercussion for patients, and similar association with modalities such as “sense of presence and passage hallucinations”. To our knowledge, this work is the first to explore and compare psycho-sensory modalities of visual hallucinations and illusions in PD using a specifically designed tool. The description of VH and VI phenomenological specificities in PD contribute significantly towards their comprehension, but prospective studies addressing the question of the evolution and prognosis of these phenomena will be needed in order to clearly determine whether VI should be distinguished from minor VH.

REFERENCES

1. Ffytche DH, Creese B, Politis M, et al (2017) The psychosis spectrum in Parkinson disease. *Nat Rev Neurol* 13:81–95. <https://doi.org/10.1038/nrneurol.2016.200>
2. Nishio Y, Yokoi K, Uchiyama M, et al (2017) Deconstructing psychosis and misperception symptoms in Parkinson's disease. *J Neurol Neurosurg Psychiatry* 88:722–729. <https://doi.org/10.1136/jnnp-2017-315741>
3. O'Brien J, Taylor JP, Ballard C, et al (2020) Visual hallucinations in neurological and ophthalmological disease: pathophysiology and management. *J Neurol Neurosurg Psychiatry* 91:512–519. <https://doi.org/10.1136/jnnp-2019-322702>
4. Goetz CG, Leurgans S, Pappert EJ, et al (2001) Prospective longitudinal assessment of hallucinations in Parkinson's disease. *Neurology* 57:2078–2082. <https://doi.org/10.1212/wnl.57.11.2078>
5. de Maindreville AD, Fénelon G, Mahieux F (2005) Hallucinations in Parkinson's disease: a follow-up study. *Mov Disord Off J Mov Disord Soc* 20:212–217. <https://doi.org/10.1002/mds.20263>
6. Marques A, Beze S, Pereira B, et al (2020) Visual hallucinations and illusions in Parkinson's disease: the role of ocular pathology. *J Neurol*. <https://doi.org/10.1007/s00415-020-09925-x>
7. Barrell K, Bureau B, Turcano P, et al (2018) High-Order Visual Processing, Visual Symptoms, and Visual Hallucinations: A Possible Symptomatic Progression of Parkinson's Disease. *Front Neurol* 9:999. <https://doi.org/10.3389/fneur.2018.00999>
8. Nishio Y, Yokoi K, Hirayama K, et al (2018) Defining visual illusions in Parkinson's disease: Kinetopsia and object misidentification illusions. *Parkinsonism Relat Disord* 55:111–116. <https://doi.org/10.1016/j.parkreldis.2018.05.023>
9. Hughes AJ, Daniel SE, Kilford L, Lees AJ (1992) Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. *J Neurol Neurosurg Psychiatry* 55:181–184
10. Visser M, Verbaan D, van Rooden SM, et al (2007) Assessment of psychiatric complications in Parkinson's disease: The SCOPA-PC. *Mov Disord Off J Mov Disord Soc* 22:2221–2228. <https://doi.org/10.1002/mds.21696>
11. Nasreddine ZS, Phillips NA, Bédirian V, et al (2005) The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc* 53:695–699. <https://doi.org/10.1111/j.1532-5415.2005.53221.x>
12. de Chazeron I, Pereira B, Chereau-Boudet I, et al (2015) Validation of a Psycho-Sensory hAllucinations Scale (PSAS) in schizophrenia and Parkinson's disease. *Schizophr Res* 161:269–276. <https://doi.org/10.1016/j.schres.2014.11.010>
13. Llorca PM, Pereira B, Jardri R, et al (2016) Hallucinations in schizophrenia and Parkinson's disease: an analysis of sensory modalities involved and the repercussion on patients. *Sci Rep* 6:38152. <https://doi.org/10.1038/srep38152>
14. Movement Disorder Society Task Force on Rating Scales for Parkinson's Disease (2003) The Unified Parkinson's Disease Rating Scale (UPDRS): status and recommendations. *Mov Disord Off J Mov Disord Soc* 18:738–750. <https://doi.org/10.1002/mds.10473>
15. Hoehn MM, Yahr MD (1967) Parkinsonism: onset, progression and mortality. *Neurology* 17:427–442
16. Tomlinson CL, Stowe R, Patel S, et al (2010) Systematic review of levodopa dose equivalency reporting in Parkinson's disease. *Mov Disord Off J Mov Disord Soc* 25:2649–2653. <https://doi.org/10.1002/mds.23429>
17. Mattis (1988) *Dementia Rating Scale Professional Manual*. Odessa, FL
18. Shin M-S, Park S-Y, Park S-R, et al (2006) Clinical and empirical applications of the

Rey-Osterrieth Complex Figure Test. *Nat Protoc* 1:892–899.

<https://doi.org/10.1038/nprot.2006.115>

19. Chaudhuri KR, Pal S, DiMarco A, et al (2002) The Parkinson's disease sleep scale: a new instrument for assessing sleep and nocturnal disability in Parkinson's disease. *J Neurol Neurosurg Psychiatry* 73:629–635

20. Postuma RB, Arnulf I, Hogl B, et al (2012) A single-question screen for rapid eye movement sleep behavior disorder: a multicenter validation study. *Mov Disord Off J Mov Disord Soc* 27:913–916. <https://doi.org/10.1002/mds.25037>

21. Johns MW (1991) A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep* 14:540–545

22. Dray S, Dufour A-B (2007) The **ade4** Package: Implementing the Duality Diagram for Ecologists. *J Stat Softw* 22:. <https://doi.org/10.18637/jss.v022.i04>

23. Fenelon G (2000) Hallucinations in Parkinson's disease: Prevalence, phenomenology and risk factors. *Brain* 123:733–745. <https://doi.org/10.1093/brain/123.4.733>

24. Barnes J, David A (2001) Visual hallucinations in Parkinson's disease: a review and phenomenological survey. *J Neurol Neurosurg Psychiatry* 70:727–733. <https://doi.org/10.1136/jnnp.70.6.727>

25. Goetz CG, Stebbins GT (1995) Mortality and hallucinations in nursing home patients with advanced Parkinson's disease. *Neurology* 45:669–671. <https://doi.org/10.1212/wnl.45.4.669>

26. Peyser C, Naimark D, Pappert EJ, et al (1998) Stability of hallucinations and illusions in Parkinson's disease: 18 month prospective study. *Mov Disord* 90

27. Bannier S, Berdagué J, Rieu I, et al (2012) Prevalence and phenomenology of olfactory hallucinations in Parkinson's disease. *J Neurol Neurosurg Psychiatry* 83:1019–21. <https://doi.org/10.1136/jnnp-2012-302414>

28. Barrett MJ, Smolkin ME, Flanigan JL, et al (2017) Characteristics, correlates, and assessment of psychosis in Parkinson disease without dementia. *Parkinsonism Relat Disord* 43:56–60. <https://doi.org/10.1016/j.parkreldis.2017.07.011>

FIGURE CAPTIONS

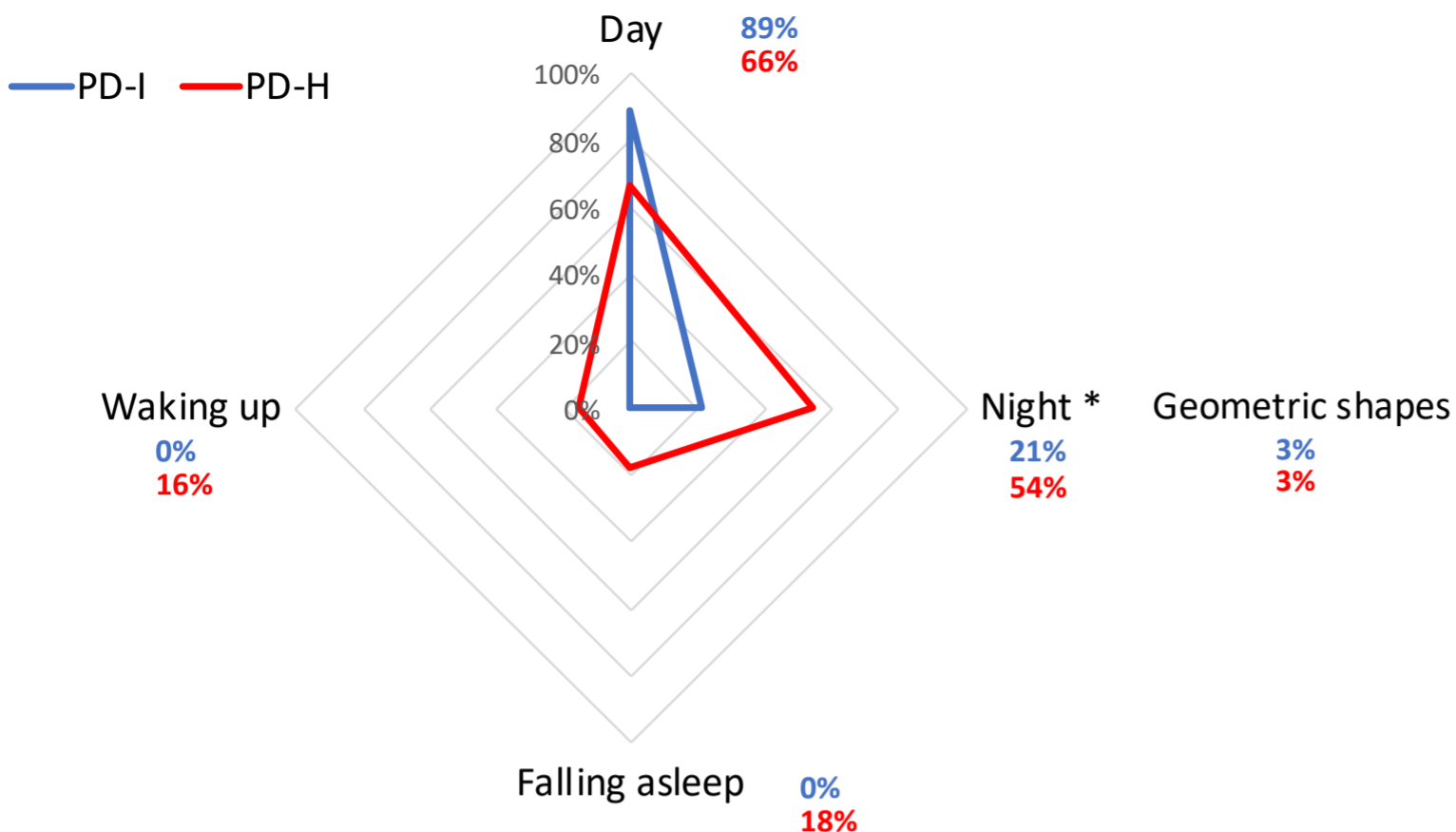
Figure 1: Spider diagram representation of qualitative and quantitative modalities of visual hallucinations or illusions in Parkinson's disease. C: conviction; Du: duration; Fq: frequency; I: impact; NA: negative aspects; PD-I: Parkinson's disease patients with visual illusions; PD-H: Parkinson's disease patients with visual hallucinations; SD: standard deviation. For qualitative modalities (Time of occurrence, simple and complex kind, characteristics), data are expressed as percentages. For quantitative modalities, data are expressed as means (standard deviations in the box). Control subitem is not presented as no subject experienced any sensation of control on their perception. * $p < 0.05$.

Figure 2: Distinct profiles of Parkinson's disease patients based on the presence of visual hallucinations or illusions illustrated by the factor analysis of mixed data.

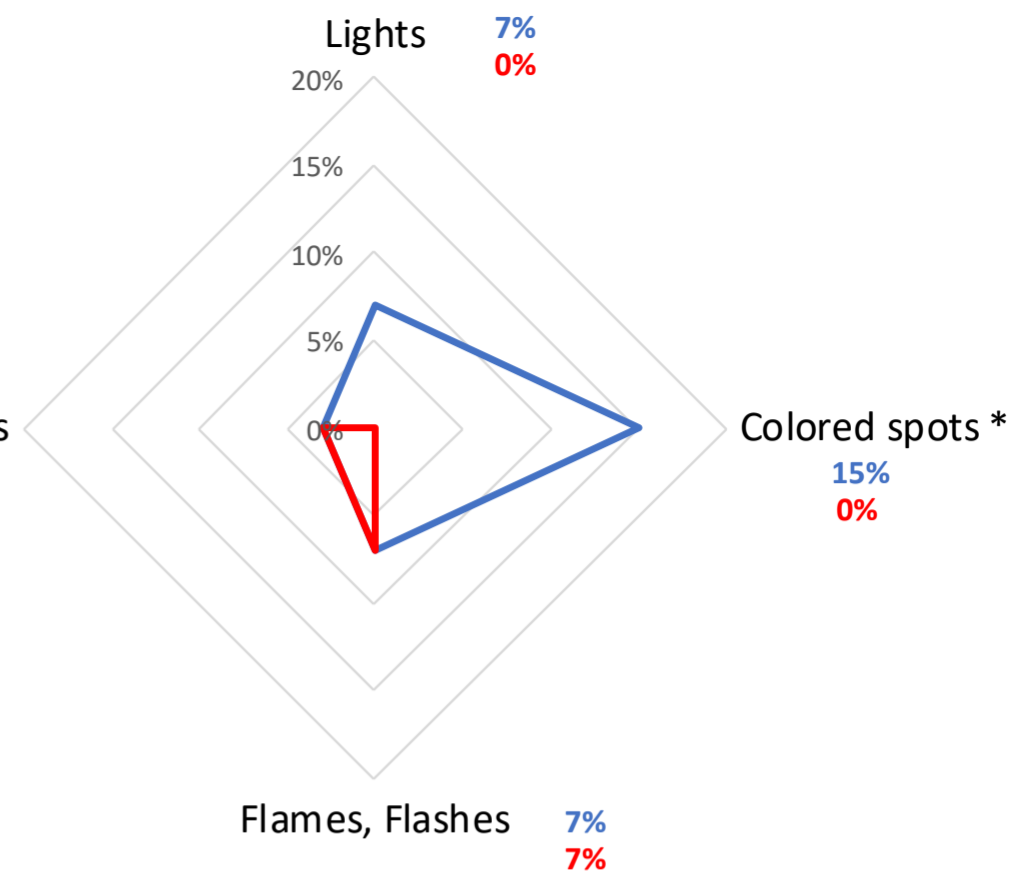
This figure presents the first two dimensions obtained from the factor analysis of mixed data. This analysis is a variant of factor analysis which can account for both categorical and continuous variables, and which aims to reduce the number of factors in the dataset while retaining as much of the variation as possible from the original dataset. Projections of variables/variable categories are illustrated by black frames and projections of patients are illustrated by colored dots (PD-I in blue and PD-H in red). Variables that are close to each other on the figure are correlated, negatively correlated variables are plotted on opposite sides of the origin, and patients with similar profiles are close to each other on the plot. Besides, variables closed to the origin of the plot have low discriminatory power, i.e. do not divide observations in distinct groups. As we can see in this figure, the two groups of patients (PD-I and PD-H) are opposed on the first axis (the horizontal one) but not on the second axis (the vertical one). It means that PD-I patients are characterized by the variables projected on the left of the figure (e.g. Mattis total or Animals-) and that PD-H are characterized by the variables projected on the right (e.g. Disease duration or Animals+).

Animals +: perceptions described as animals; Animals -: perceptions not described as animals; Epworth: Epworth score measuring excessive diurnal somnolence; Night +: perception occurring at night; Night -: not occurring at night; Night Ø: missing data regarding occurrence at night; Objects +: perceptions described as objects; Objects -: perceptions not described as objects; Other sense hallu +: other sense hallucinations are reported; Other sense hallu -: other sense hallucinations are not reported; PD-I: Parkinson's disease patients with visual illusions; PD-H: Parkinson's disease patients with visual hallucinations; PDSS total: Parkinson's disease sleep scale total score; People +: perceptions described as people; People -: perceptions not described as people; PSAS: repercussion score of psycho-sensory hallucinations scale; RBD +: association with REM sleep behavior disorder; RBD -: not associated with REM sleep behavior disorder; Sex F: female; Sex M: male; Vis comp +: visual complaints reported; Vis comp -: no visual complaints reported.

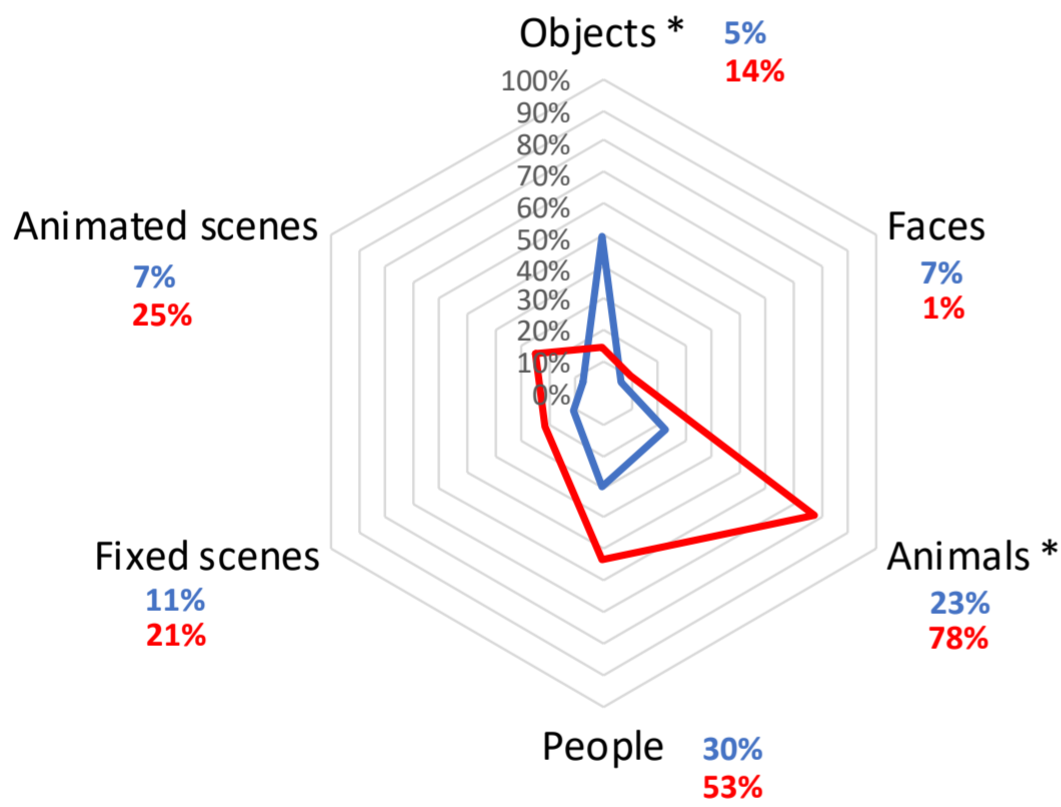
Time of occurrence



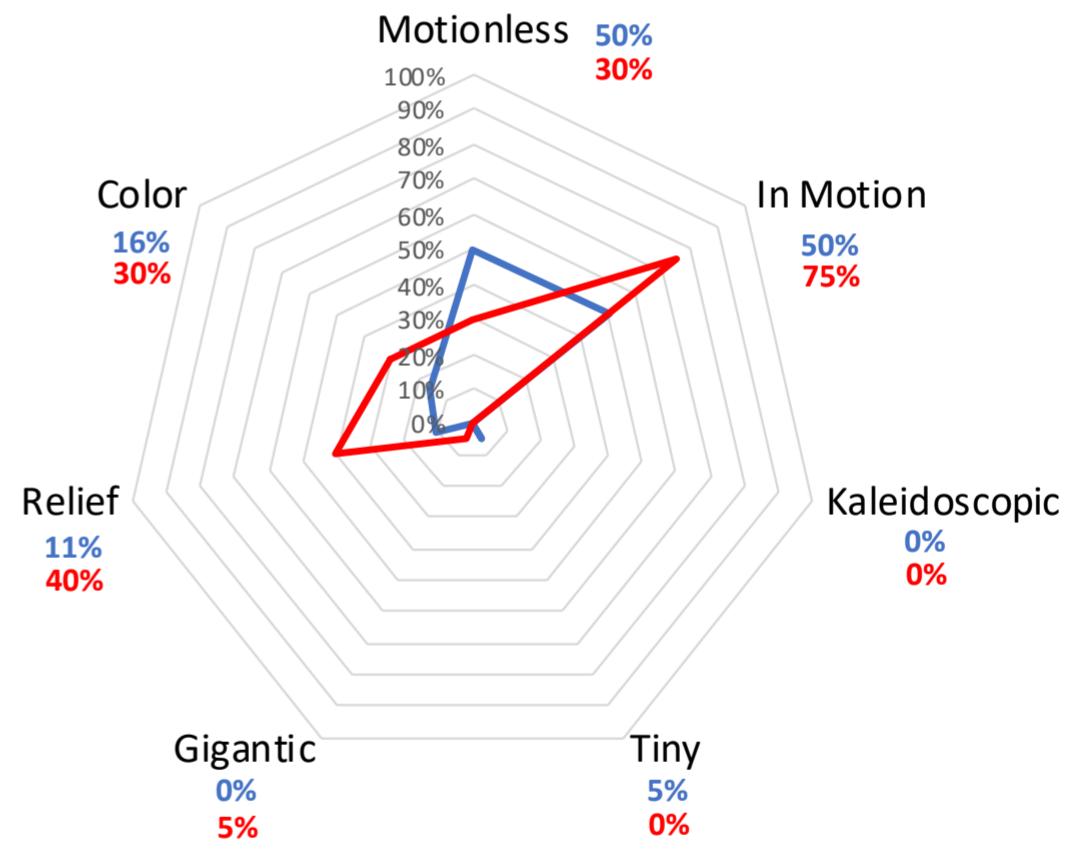
Simple kind



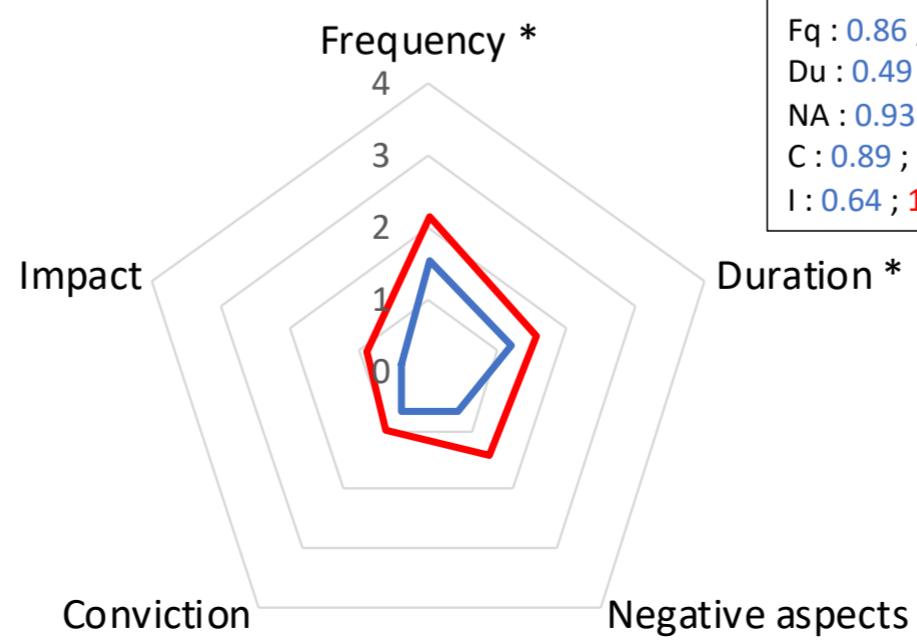
Complex kind



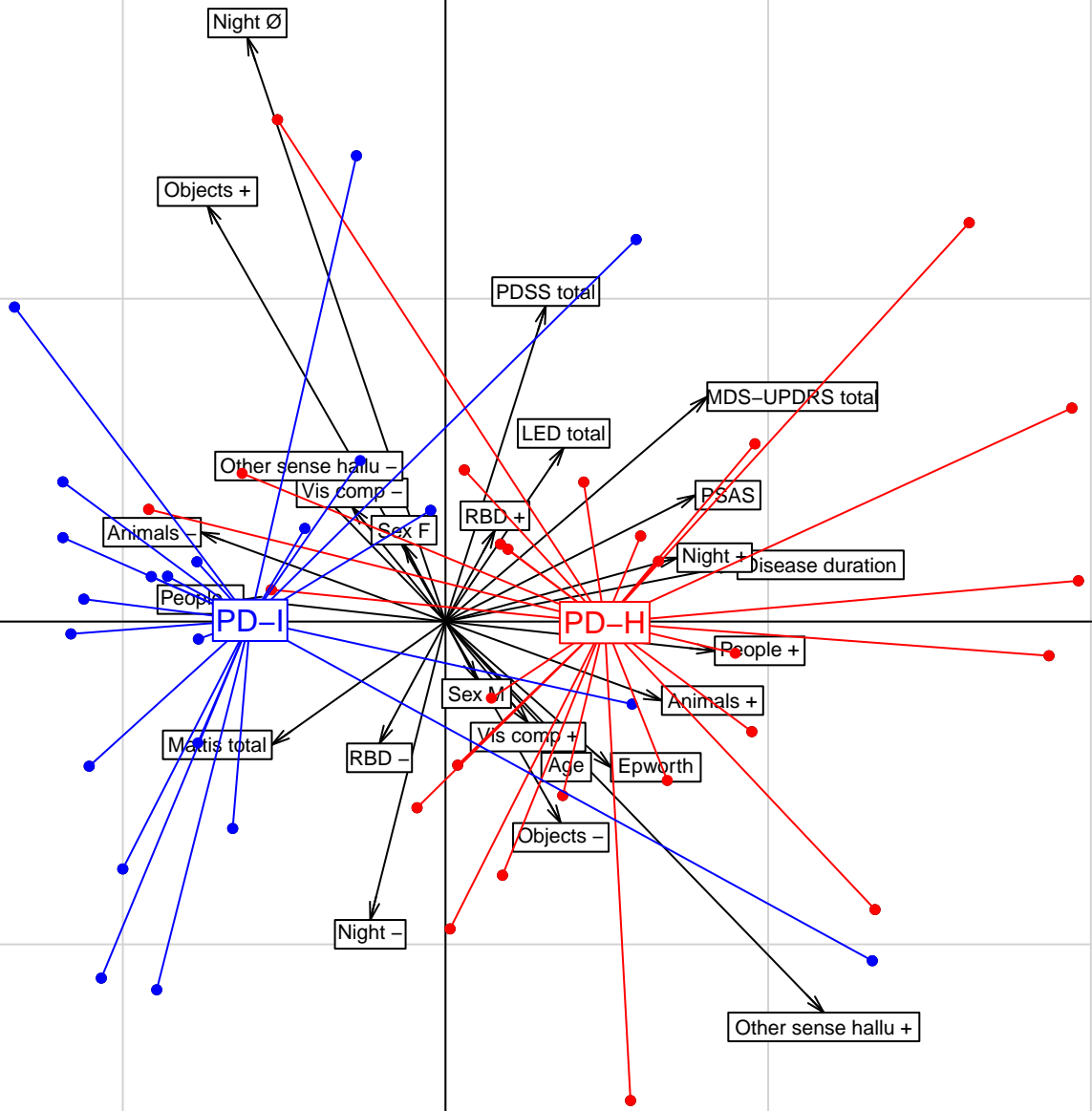
Characteristics



Quantitative Modalities



SD	
Fq :	0.86 ; 1.04
Du :	0.49 ; 0.74
NA :	0.93 ; 1.57
C :	0.89 ; 1.05
I :	0.64 ; 1.18



	PD-I n=26	PD-H n=28	p
Age (years)	68.3 ± 6.4	71.3 ± 6.8	0.11
Male sex	15 (57.7)	14 (50.0)	0.57
Education level (years)	18.3 ± 4.1	17.8 ± 3.8	0.63
Disease duration (years)	9.1 ± 5.3	11.1 ± 5.1	0.11
Hoehn and Yahr (score 0-21)	2.52 ± 0.79	3.00 ± 0.83	0.02
MDS-UPDRS			
Total (score 0-260)	53.1 ± 22.3	78.9 ± 30.1	0.001
I (score 0-52)	12.2 ± 5.5	19.5 ± 6.1	<0.001
II (score 0-52)	12.6 ± 4.7	18.9 ± 9.0	0.002
III (score 0-132)	27.0 ± 13.5	35.5 ± 18.2	0.07
IV (score 0-24)	2.5 ± 3.1	5.0 ± 5.0	0.13
SCOPA-PC (score 0-21)	3.19 ± 1.83	4.71 ± 2.99	0.046
PDSS (score 0-60)	12.8 ± 5.9	15.4 ± 6.9	0.15
Epworth (score 0-24)	8.2 ± 6.0	9.2 ± 5.7	0.44
Probable RBD	11 (42.3)	20 (71.4)	0.03
LED total (mg/day)	963 [700; 1,210]	965 [525; 1,216]	0.94
LED DA (mg/day)	121 [18; 210]	53 [0; 273]	0.43
Rivastigmine users	0 (0.0)	3 (10.7)	0.24
Antiepileptic users	4 (15.4)	7 (25.0)	0.38
Antidepressant users	10 (38.5)	11 (39.3)	0.95
Benzodiazepine users	6 (23.1)	8 (28.6)	0.65
Opioid users	1 (3.8)	0 (0.0)	0.48
MoCA (score 0-30)	26.6 ± 2.5	24.8 ± 2.5	0.04
Mattis			
Total (score 0-144)	131.8 ± 8.9	124.9 ± 13.8	0.04
Attention (score 0-37)	35.8 ± 0.9	35.3 ± 2.0	0.75
Initiation (score 0-37)	31.4 ± 4.7	28.4 ± 6.3	0.04
Construction (score 0-6)	5.6 ± 0.6	5.4 ± 1.0	0.65
Conception (score 0-39)	36.9 ± 2.7	35.3 ± 4.4	0.12
Memory (score 0-25)	21.9 ± 2.4	20.5 ± 3.4	0.12
ROCF (score 0-36)	26.8 ± 11.3	22.1 ± 12.0	0.04

	PD-I n=26	PD-H n=28	p
Visual complaints	16 (61.5)	14 (50.0)	0.39
Vision loss	11 (42.3)	7 (25.0)	0.18
Visual field impairment	3 (11.5)	2 (7.1)	0.66
Metamorphopsia	1 (3.8)	2 (7.1)	1.00
Halos	4 (15.4)	1 (3.6)	0.18
Diplopia	4 (15.4)	3 (10.7)	0.70
Color vision complaint	4 (15.4)	1 (3.6)	0.18
Epiphora	12 (46.2)	6 (21.4)	0.054
Eye pains	3 (11.5)	0 (0.0)	0.11

Table 1: Clinical and demographical characteristics of Parkinson's disease patients with visual hallucinations and illusions. Data are presented as frequencies (associated percentages), mean \pm standard deviation, or median [interquartile range]. p: unadjusted p-value. DA: Dopamine agonists; LED: Levodopa equivalent dose; MDS-UPDRS: movement disorder society - unified Parkinson's disease rating scale; MoCA: Montreal cognitive assessment; PD-H: Parkinson's disease patients with visual hallucinations; PD-I: Parkinson's disease patients with illusions; PDSS: Parkinson's disease sleep scale; RBD: REM sleep behavior disorder; ROCF: Rey-Osterrieth complex figure; SCOPA-PC: scales for outcomes in Parkinson's disease - psychiatric complications.