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Original article

Visual misperceptions in favour of living beings in Parkinson's disease: A psychophysical study



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ABSTRACT

Background. – Parkinson's disease (PD) patients often report seeing persons or animals rather than objects but this phenomenon remains poorly understood. Here, we use three experimental tasks to confirm such observation and to explore its cognitive mechanisms. **Method.** – Fourteen PD patients with visual hallucinations (PD-VH), 14 PD patients without visual hallucinations (PD-NVH) and 14 controls with similar cognitive performance were tested using ambiguous stimuli. Ambiguous stimuli were morphs in which visual features from faces and flowers were melted together (Experiments 1 and 2) and a black and white picture where a Dalmatian dog was hidden (Experiment 3). In Experiment 1, participants categorised ambiguous stimuli either as face or flower. In Experiment 2, they were shown an ambiguous stimulus, then a mask, and finally two ambiguous stimuli, one of which was identical to the first stimulus. In this discrimination task, participants chose which of the two last stimuli had been presented before. In Experiment 3, participants guessed the items hidden in the picture. We assessed group differences for categorisation with logistic modelling and computed sensitivity index and criterion psychophysical measures in Experiments 1 and 2. The ratio of living beings identified in the Dalmatian dog task was compared across groups.

Results. – In the categorisation task, the PD-VH group tended to use a smaller proportion of visual features (point of subjective equality [PSE] = 41.5%) to label a stimulus as Face compared to PD-NVH (51%) and controls (56.2%). In the discrimination task, criterion *c* was lower in the PD-VH group compared to controls (*c*: -0.16 vs. 0.27; *P* = 0.005). In the Dalmatian dog task, the PD-VH group reported seeing living beings more frequently than

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controls ($P = 0.040$). A bias towards living beings was confirmed in the PD-VH group in the three tasks, and a bias toward non-living beings was measured in controls in the discrimination task.

Interpretation. – Observing that controls exhibited bias toward non-living beings in the discrimination task, we suggest that impaired top-down control over perception processes explains the bias toward living beings in PD-VH visual misperceptions.

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1. Abbreviations

BDI	Beck Depression Inventory
MDRS	Mattis Dementia Rating Scale
PD	Parkinson's disease
PD-NVH	Parkinson's disease patients without visual hallucinations
PD-VH	Parkinson's disease patients with visual hallucinations
UPDRS	Unified Parkinson's Disease Rating Scale

2. Introduction

Many patients with Parkinson's disease (PD) develop psychotic symptoms that are both difficult to treat and associated with more severe prognosis [1,2]. In longitudinal studies, more than half of patients with PD have been reported to have visual hallucinations [3]. Patients with PD also experience “minor” psychotic symptoms such as passage hallucinations (where a person or animal is briefly seen passing in the peripheral visual field), feelings of presence (the vivid sensation that somebody, distinct from oneself, is present nearby when no one is actually there), and illusions (the misinterpretation of a real stimulus) [4–7]. In cross-sectional studies, the prevalence of minor psychotic symptoms has ranged from 17 to 72% [3,7]. They may be present in the first years of PD [2,8], in drug-naïve de novo patients, and even in the prodromal phase of the disease [9]. Some data suggest that minor psychotic symptoms might predate visual hallucinations [7,9]. Psychotic symptoms similar to those of PD, including visual illusions, occur in the course of dementia with Lewy bodies (DLB) [10,11], these two conditions showing an important clinicopathological overlap [12].

In the course of visual misperceptions in people with PD and DLB, there is an overrepresentation of living beings (i.e., animals and humans; the term living beings designating in this context sentient animate beings, excluding plants) [10,13]. Under these conditions, visual illusions are commonly illusions of movement (kinetopsia) or misperceptions of an object or element of landscape, such as plants, trees or rocks, into a living being or part of a living being [1,14]. This latter type of illusions is also referred to as “pareidolia”.

The cognitive mechanisms of such bias towards living beings are unknown. According to the literature, the pathophysiology of visual hallucinations and illusions in PD is complex and multifactorial. Current explanatory models involve a dysfunction of bottom-up perceptive mechanisms,

i.e., visual pathway dysfunction (from the retina to visual cortex) and altered cognitive representations of visual stimuli, together with dysfunction of top-down visual mechanisms, such as impaired attentional focus [15–19]. However, none of these models has addressed the question of the content of hallucinations and illusions, and of the high prevalence of living beings among these misperceptions.

Here, we attempted to confirm experimentally a perception bias towards living beings in PD and to describe the cognitive mechanisms that account for this bias in visual misperceptions. To this end, we compared the behavioural and psychophysical performance of hallucinating PD patients, non-hallucinating PD patients, and healthy controls in three different experiments evaluating their perception of ambiguous images. During these three experimental tasks, we expected to measure bias towards living beings in PD patients with visual hallucinations. The use of different tasks requiring different cognitive processes would help to decipher the cognitive mechanisms accounting for such bias.

3. Materials and methods

3.1. Participants

Twenty-eight patients with PD, fulfilling the UK PD Society Brain Bank criteria for PD [20] and free of dementia according to current criteria [21], were enrolled between June 1st and December 31st, 2010 and divided into two groups. Fourteen PD patients with visual hallucinations had experienced visual hallucinations or visual illusions [5] in the preceding month and fulfilled criteria for PD-associated psychosis [22]; they were thereafter referred to as PD patients with visual hallucinations (PD-VH). Fourteen other patients with PD who had never experienced visual hallucinations or illusions nor any psychotic symptom, were also enrolled during the same time period and were referred to as PD patients without visual hallucinations (PD-NVH). The enrolled PD patients' motor severity was assessed using the Unified PD Rating Scale (UPDRS) part III (in the ON state) and the Hoehn and Yahr scale. The levodopa-equivalent daily dose (LEDD) was calculated [23,24]. All patients were under the effect of their usual treatment during the assessment. We also recruited fourteen healthy controls among patients' caregivers.

Participants (patients and controls) were French speakers, free of neurological disorders other than PD, and had a visual acuity for best eye $> 20/40$ on the Rosenbaum chart. The Rosenbaum chart assesses near visual acuity: it is a white panel with letters of different size held 14 inches (35 cm) away

from the patient's eyes. The patient covers one eye and reads aloud the smallest line of letters. Depression was assessed with the French revised version of the Beck Depression Inventory (BDI) [25]. Cognition was evaluated with the Mattis Dementia Rating Scale (MDRS) [26]. The exclusion criteria were as follow: best eye visual acuity $\leq 20/40$ on the Rosenbaum chart, MDRS total score ≤ 123 , existence of other brain disorders such as stroke or epilepsy, and being a non-native French-speaker. The medical ethics committee of Henri-Mondor Hospital approved the study and all participants signed an informed consent prior to study inclusion.

3.2. Experimental tasks

3.2.1. Computer-based tasks

The first two tasks were computer-based, derived from Newell and Bülthoff [27], and used ambiguous stimuli mixing faces and flowers features.

3.2.1.1. Stimuli. Stimuli consisted of morphs created from images of 20 flowers and 20 anonymous faces (8 women). Twenty continuums of images morphing from one face to one flower were obtained using Photoshop and Fantamorph software. Each continuum consisted of eleven 200×200 pixel black and white morphs controlled for contrast (total = 220 morphs; Fig. 1A) with one "pure" flower and one "pure" face morph at each end of the continuum and nine intermediate morphs mixing flower and face characteristics. Each morph was separated from the preceding and the following one by a 10% step in the morphing procedure, i.e. from 0% Face ("pure" Flower) to 100% Face ("pure" Face). Pure morphs constituted the unambiguous stimuli, and intermediate morphs (10–90% Face or Flower) the ambiguous stimuli. Twenty different squares composed of black and white points were used as masks. The experiments were run using E-Prime software. Stimuli were displayed on a 15.4-inch screen in a dark room. Morphs measured 2.5×2.5 cm on the monitor. Viewing distance was approximately 60 cm.

3.2.1.2. Experiment 1: categorisation task. Participants were shown consecutively morphs from the flower-face

continuums and were asked to categorise them as "Face" or "Flower". Each trial began with a 300-ms fixation cross. A stimulus then appeared for 100 ms, followed by a mask that remained on the screen until the participant responded (Fig. 1B). The participant had a 10-s period to respond. A 1-s inter-trial interval followed each response. After a training phase with 20 items not used in the testing phase, the 220 morphs from the 20 continuums were presented in two different blocks with a self-timed break between blocks. Morphs were randomized with the constraint of maximum four consecutive morphs on the same half of the continuum. Participants were instructed to respond "Face" or "Flower" by pressing on the right or left button of a button box (the location of the "Face" and "Flower" buttons were counterbalanced across subjects). This experiment lasted around 10 min. After discarding training data, we analysed data related to unambiguous (100% Face or 100% Flower) and to ambiguous stimuli separately.

3.2.1.2.1. Analysis of unambiguous stimuli. The unambiguous stimuli were expected to elicit close-to-perfect performance: seeing an item with 100% Face features, the participant was expected to answer Face. Altered performance for unambiguous stimuli would in turn suggest altered bottom-up visual processing (slow and altered transmission of visual input from retina to visual cortex).

For unambiguous stimuli, categorisation performance (perceiving an item as a "Face" when it looks like a face) was estimated thanks to the computation of the sensitivity index d' for each participant using the following formula (1) (psycho package, R software):

$$d' = Z(\text{Hit Rate}) - Z(\text{False Alarm Rate})(1)$$

The sensitivity index d' informs about the participant's capacity to form distinct representations for the two classes of stimuli, Faces and Flowers. The higher the sensitivity index d' , the better this capacity. The Hit Rate corresponds to the number of correct responses for one category of stimuli (e.g., Face) divided by the sum of both correct responses and missed responses (Flower response when Face is expected) for the same category. The False Alarm Rate corresponds to the number of wrong responses (false alarms) for the other category (Face response when Flower is expected) divided by

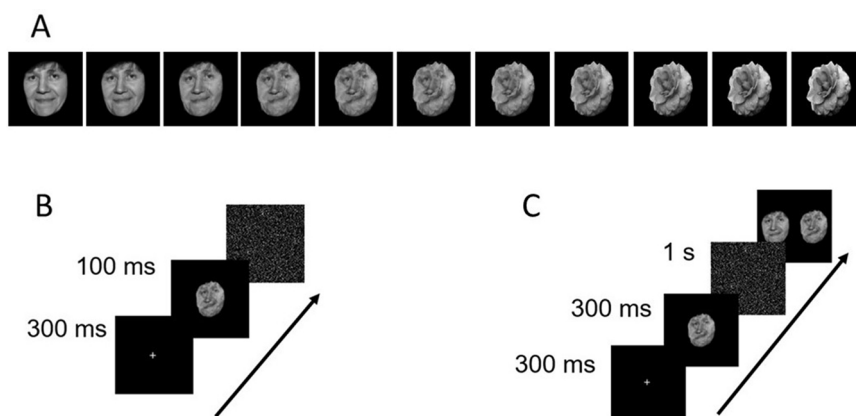


Fig. 1 – Visual stimuli and settings used in Experiments 1 and 2. A. Stimuli used in the categorisation (Experiment 1) and the discrimination (Experiment 2) tasks. The figure shows one of the continuums between 100% of face (first picture) to 100% of flower (last picture). B. Procedure for categorisation task. C. Procedure for discrimination task.

the sum of both false alarm responses and correct rejection responses (Flower response when Flower is expected). Z stands for Z value.

3.2.1.2.2. *Analysis of ambiguous stimuli.* Processing of ambiguous stimuli requires higher order cognitive capacities for categorical representation. For ambiguous stimuli, we expected participants to report more Faces when the ambiguous morphs contained more face content information. The probability of responding Face was expected to follow a logistic function. Thus, we fitted the responses of each participant with a logistic function formula (2): $PX = \frac{e^{\beta_0 + \beta X}}{1 + e^{\beta_0 + \beta X}}$ (2)

Within this formula, $P(X)$ is the probability of responding Face for an X percentage of face content in the stimuli. The intercept β_0 determines the probability P when $X = 0$, i.e., when the stimulus has 0% face content. The β coefficient determines the slope of the logistic function curve and is higher if categorisation is efficient.

In order to detect a bias in this categorisation task, we used the abovementioned logistic function and computed for each participant the point of subjective equality (PSE). The PSE corresponds to the X value for which the participant would choose randomly between the two categories face and flower, i.e., $P(\text{PSE}) = 0.5$. In this study, a small PSE suggests a bias toward faces. The PSE is given by (3): $\text{PSE} = \frac{\beta_0}{\beta}$ (3)

3.2.1.3. *Experiment 2: discrimination task.* This task followed an XAB design: a central morph (X) from a continuum was presented for 300 ms followed by a mask for one second and then by two lateralized morphs (A and B) presented simultaneously, on the left and the right of the screen respectively. Morphs A and B were always physically different from each other and morph X was identical to either morph A or B . The patient had to discriminate between A and B by selecting the morph identical to the previously shown X . Morphs A and B differed by steps of 20% of face (Fig. 1C). We used five pairs of morphs per continuum with different proportion of face content: 0–20%, 20–40%, 40–60%, 60–80%, and 80–100%. Each pair was used twice, one for $X = A$ and one for $X = B$. The pair of morphs (A and B) remained on the screen until the participant made a response on the button box, with a maximum 10-s period to answer. Each trial started with a central cross displayed for 300 ms for fixation and there was a 1-s inter-trial interval followed each participant's response. Five pairs for each of the 20 continuums were presented twice, up to 200 trials. We added 20 unambiguous trials with morphs A and B containing 0 and 100% of face to monitor the participant's attention level. Trials were randomized with the constraint of maximum four correct responses on the same button. After a training period (20 items not used in the testing phase), participants started the discrimination task that was divided into two blocks with a self-timed break between blocks. This second experiment lasted around 20 minutes. After discarding training data, we analysed data related to unambiguous and to ambiguous stimuli separately. For both unambiguous and ambiguous stimuli, we computed both the sensitivity index d' (see formula (1) above) and criterion c for each participant using formula (4) (psycho package, R software): $c = -\frac{1}{2} \times [Z(\text{Hit Rate}) + Z(\text{False Alarm Rate})]$ (4)

The sensitivity index d' estimates discrimination performance and a higher value of d' suggests better capacity to

distinguish between two categories. Criterion c informs about bias between two categories. The closer to zero the criterion, the less biased the participant's categorisation. In the discrimination task, a negative value for criterion c suggests bias towards living beings. A positive value of c would suggest bias towards non-living beings. Hit Rate, False Alarm Rate and Z are defined above in formula (1).

3.2.2. Experiment 3: Dalmatian dog task

We investigated propensity to identify living beings using a paper copy of a unique ambiguous picture. We used a 14.5×12 cm printed image taken from Gregory (1997) [28], composed of apparently random white and black spots, among which a Dalmatian dog can be distinguished (Fig. 2). The participant was shown the image and asked "What do you see in this picture?"; there was no time limit for the response. We categorised answers as "living beings" – including animals, human beings, parts of human beings or humanized objects (e.g., puppet) – or "non-living" items.

3.3. Statistical analyses

Data were analysed with R software (version 4.3.2). Kruskal-Wallis rank sum tests were performed for between-group analyses. Pairwise comparisons between the three groups were carried out using two-sided Wilcoxon tests. We used χ^2 tests for between-group comparisons in the Dalmatian dog test. In order to account for remaining confounding factors for between-group differences, we computed multivariate linear regression models with adjustment for depressive symptoms according to the BDI scale for the PD-VH group vs. controls and the PD-NVH group vs. controls comparisons. For comparisons between the PD-VH and PD-NVH groups, we also adjusted for disease duration and disease severity according to the Hoehn and Yahr scale. Spearman-rank correlation tests were used to assess the relationship between studied variables and



Fig. 2 – Stimulus for Experiment 3. In the Dalmatian dog picture (Gregory, 1997), a silhouette of a Dalmatian dog can be distinguished among the apparently random black stains.

demographic and clinical characteristics of the participants. The chosen threshold for statistical significance of P-values was set at 0.05. Bonferroni corrections were applied for correlations to account for multiple comparisons.

4. Results

4.1. Participants

The three groups of participants were matched for age, visual acuity of best eye, educational level (years of education since kindergarten) and cognitive performance using the MDRS (Table 1). The PD-VH group showed more depressive symptoms according to the BDI scale compared to both the PD-NVH and control groups ($P = 0.005$ and $P = 0.004$, respectively). The PD-VH group had a longer disease duration and a more advanced disease according to the Hoehn and Yahr scale compared to the PD-NVH group ($P < 0.001$ and $P = 0.008$, respectively). Motor performance was similar for the two PD groups but PD-VH patients tended to have a higher dosed dopaminergic treatment (Table 1).

4.1.1. Experiment 1: categorisation task

Missing data were scarce and due to late responses (over 10 s). We analysed 99.7% of responses from controls and PD-NVH groups, and 98.1% of responses from the PD-VH group.

4.1.2. Categorisation of unambiguous stimuli

Categorisation performance for unambiguous stimuli was lower in the PD-VH group, suggesting impaired bottom-up processing: the sensitivity index d' was lower in the PD-VH group compared to the control group ($P_{adjusted} = <0.001$). Reaction times for categorising unambiguous stimuli were longer in the PD-VH group compared to the other groups: PD-VH: 1352 ± 1371 ms; PD-NVH: 855 ± 575 ms; controls: 869 ± 856 ms ($P < 0.001$).

4.1.3. Individual psychometric curve fitting

We fitted each participant's responses using a logistic function (Fig. 3). Categorisation performance for ambiguous

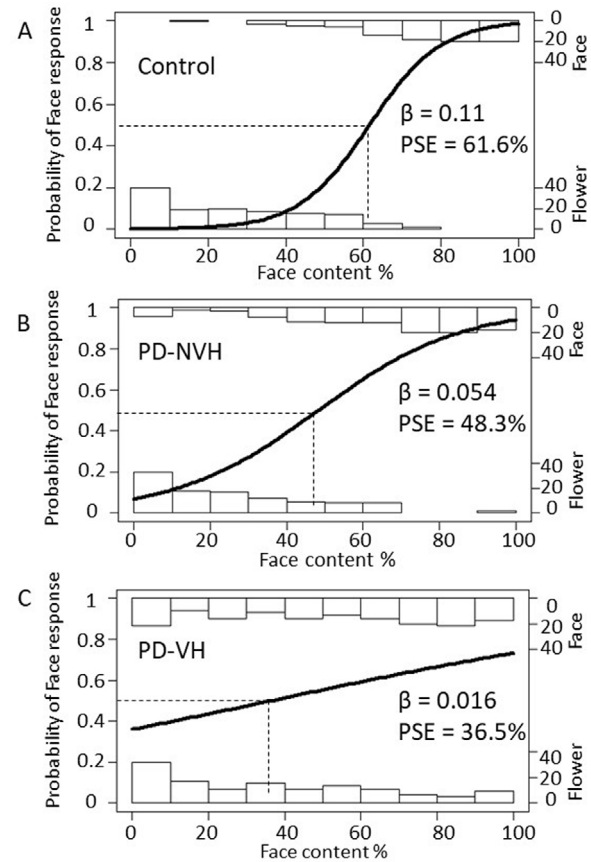


Fig. 3 – Fitted logistic curves of three individual subject's responses in the categorisation task Probability of face response according to percent face content in the stimulus. **A. Control subject. B. Non-hallucinating patient (from PD-NVH group). C. Hallucinating patient (from PD-VH group).** Higher coefficient β of the fitted logistic function denotes better categorisation performance. Lower point of subjective equality (PSE) (face content for which half of responses are flowers and half are faces) suggests bias towards faces.

Table 1 – Clinical characteristics (mean \pm SD) of participants.

Clinical characteristic	PD-VH (n = 14)	PD-NVH (n = 14)	Controls (n = 14)	P-value			
				Overall	PD-VH vs. PD-NVH	PD-VH vs. Controls	PD-NVH vs. Controls
Female/Male	5/9	5/9	9/5	–	–	–	–
Age (years)	69.2 (± 7.2)	69.8 (± 5.1)	67.2 (± 7.7)	0.405	0.746	0.433	0.279
Best eye visual acuity (/10)	6.5 (± 1.1)	6.6 (± 1.5)	7.0 (± 1.2)	0.358	0.962	0.115	0.232
Education (years)	12.5 (± 3.3)	11.7 (± 4.0)	10.7 (± 3.6)	0.341	0.610	0.115	0.318
Handedness (R/L)	13/1	13/1	13/1	–	–	–	–
MDRS total (/144)	134.1 (± 5.5)	136.3 (± 7.8)	136.5 (± 4.0)	0.246	0.112	0.258	0.548
BDI score (/39)	20.5 (± 9.6)	10.2 (± 6.5)	11.2 (± 6.1)	0.004	0.005	0.004	0.629
Disease duration (years)	12.6 (± 4.6)	6.3 (± 3.6)	–	–	< 0.001	–	–
Hoehn and Yahr score (/5)	2.8 (± 0.9)	2.0 (± 0.5)	–	–	0.008	–	–
UPDRS III score (/108)	18.2 (± 9.4)	13.4 (± 6.9)	–	–	0.189	–	–
LEDD (mg)	1053 (± 346)	824 (± 459)	–	–	0.077	–	–

MDRS: Mattis dementia rating scale; BDI: Beck depression inventory; UPDRS III: Unified Parkinson's disease rating scale, part III (motor); LEDD: levodopa-equivalent daily dose.

stimuli was also lower in the PD-VH group: coefficient β was lower in the PD-VH group compared to the control group ($P_{\text{adjusted}} = 0.002$). A tendency for bias towards faces was observed in the PD-VH group: PSE appeared smaller in the PD-VH group (41.5%) compared to the PD-NVH group (51.0%) and controls (56.2%), but without reaching statistical significance after adjustment (Fig. 3; Table 2). Reaction times for categorising ambiguous stimuli were longer for the PD-VH group compared to the other groups: PD-VH: 1542 ± 1546 ms; PD-NVH: 1011 ± 867 ms; controls: 1026 ± 981 ms ($P < 0.001$).

4.1.4. Correlations with clinical characteristics

Younger age and better cognitive performance were associated with better categorisation performance: coefficient β correlated negatively with age ($\rho_{\text{spearman}} = -0.47$, $P_{\text{Bonferroni}} = 0.015$) and positively with MDRS score ($\rho_{\text{spearman}} = 0.46$, $P_{\text{Bonferroni}} = 0.019$). No other significant correlations were found.

4.2. Experiment 2: discrimination task

Data from one PD-VH patient who did not complete the task were discarded. For the remaining participants, there were few missing data (due to late responses). We analysed 99.9% of responses from controls, and 99.6% of responses from the PD-NVH and PD-VH groups.

4.2.1. Discrimination of unambiguous stimuli

According to the sensitivity index d' , discrimination performance for unambiguous stimuli was lower in the PD-VH group than in controls ($P_{\text{adjusted}} = 0.011$). Criterion c exploring bias was not significantly different between groups (Table 2). Reaction times for discrimination of unambiguous stimuli (accurate responses) were longer in the PD-VH group compared to the PD-NVH and control groups: 1806 ± 1515 ms, 1310 ± 699 ms, and 1126 ± 442 ms, respectively ($P < 0.001$).

4.2.2. Discrimination of ambiguous stimuli

We computed the sensitivity index d' and criterion c for each participant and each stimulus pair (from 0–20% face content at

the flower end to 80–100% face content at the face end of the continuum). Discrimination performance according to the sensitivity index was lower in the PD-VH group compared to both the control and PD-NVH groups ($P_{\text{adjusted}} < 0.001$ and $P_{\text{adjusted}} = 0.004$, respectively). Discrimination performance differed according to stimulus pairs ($P < 0.001$). For the stimulus pair 60–80%, the sensitivity index was still lower in the PD-VH group compared to the control group ($P_{\text{adjusted}} < 0.001$) (Table 2; Fig. 4).

Criterion c informing about bias was overall lower in the PD-VH group compared to the control group ($P_{\text{adjusted}} = 0.001$). For the 60–80% pair, criterion c was negative in the PD-VH group indicating face bias (mean = -0.16), it was close to zero in the PD-NVH group indicating unbiased responses (mean = -0.01) and it was positive in the control group indicating flower bias (mean = 0.27) (Table 2; Fig. 5). After adjustment in multivariate analysis, criterion c was lower in the PD-VH group compared to the control group ($P_{\text{adjusted}} = 0.005$).

Reaction times were longer in the PD-VH group ($RT = 2275 \pm 1342$ ms) compared to the PD-NVH group ($RT = 1762 \pm 1024$ ms; $P < 0.001$) and to controls ($RT = 1636 \pm 750$ ms; $P < 0.001$).

4.2.3. Peak discrimination

The location of the peak in discrimination accuracy (highest sensitivity index indicating a perceptual boundary between two categories) was estimated on a participant-by-participant basis. The discrimination peak appeared for a smaller amount of face content (46.9%, yielding a broader face category) in PD-VH patients than in PD-NVH patients (63.6%), but was closer to the discrimination peak in controls (59.3%) (Table 2).

4.2.4. Correlations with clinical characteristics

For the whole cohort, better discrimination performance was associated with better cognitive performance: the sensitivity index d' for unambiguous stimuli correlated with the MDRS score ($\rho_{\text{spearman}} = 0.71$, $P_{\text{Bonferroni}} = 0.001$). We did not find any significant correlation between discrimination parameters and age, education, visual acuity, BDI score, duration of the disease, UPDRSIII motor score, Hoehn and Yahr stage, or LEDD.

Table 2 – Summary of group differences in the three experiments.

	Parameter	Controls	PD-NVH	PD-VH	P overall	P adjusted		
						PD-VH vs. PD-NVH	PD-VH vs. Controls	PD-NVH vs. Controls
Experiment 1: categorization task								
Unambiguous stimuli	d'	3.05	2.16	1.05	0.001	0.078	< 0.001	0.070
Individual curve fitting (all stimuli)	β	0.08	0.05	0.02	0.004	0.137	0.002	0.093
	PSE	56.2%	51.0%	41.5%	0.065	0.515	0.445	0.478
Experiment 2: discrimination task								
Unambiguous stimuli	d'	3.01	2.38	1.79	0.013	0.528	0.011	0.061
	c	-0.02	-0.06	-0.09	0.935	0.266	0.334	0.663
Ambiguous stimuli (60/80% pair)	d'	2.09	1.85	0.83	< 0.001	0.172	< 0.001	0.517
	C	0.27	-0.01	-0.16	0.018	0.230	0.005	0.075
Peak in discrimination		59.3%	63.6%	46.9%	0.032	0.330	0.639	0.382
Experiment 3: Dalmatian dog task								
Living responses ratio		18.4%	22.9%	39.8%	0.096	0.288	0.040	0.695

d' : sensitivity index; β : coefficient of the slope after individual curve fitting of Experiment 1 responses; c : criterion (bias); PSE: point of subjective equality. P adjusted: P-value in multivariate regression analyses adjusted for BDI scale for PD-VH vs. controls and PD-NVH vs. controls comparisons and adjusted for BDI score, disease duration, and Hoehn and Yahr score for PD-VH vs. PD-NVH comparisons.

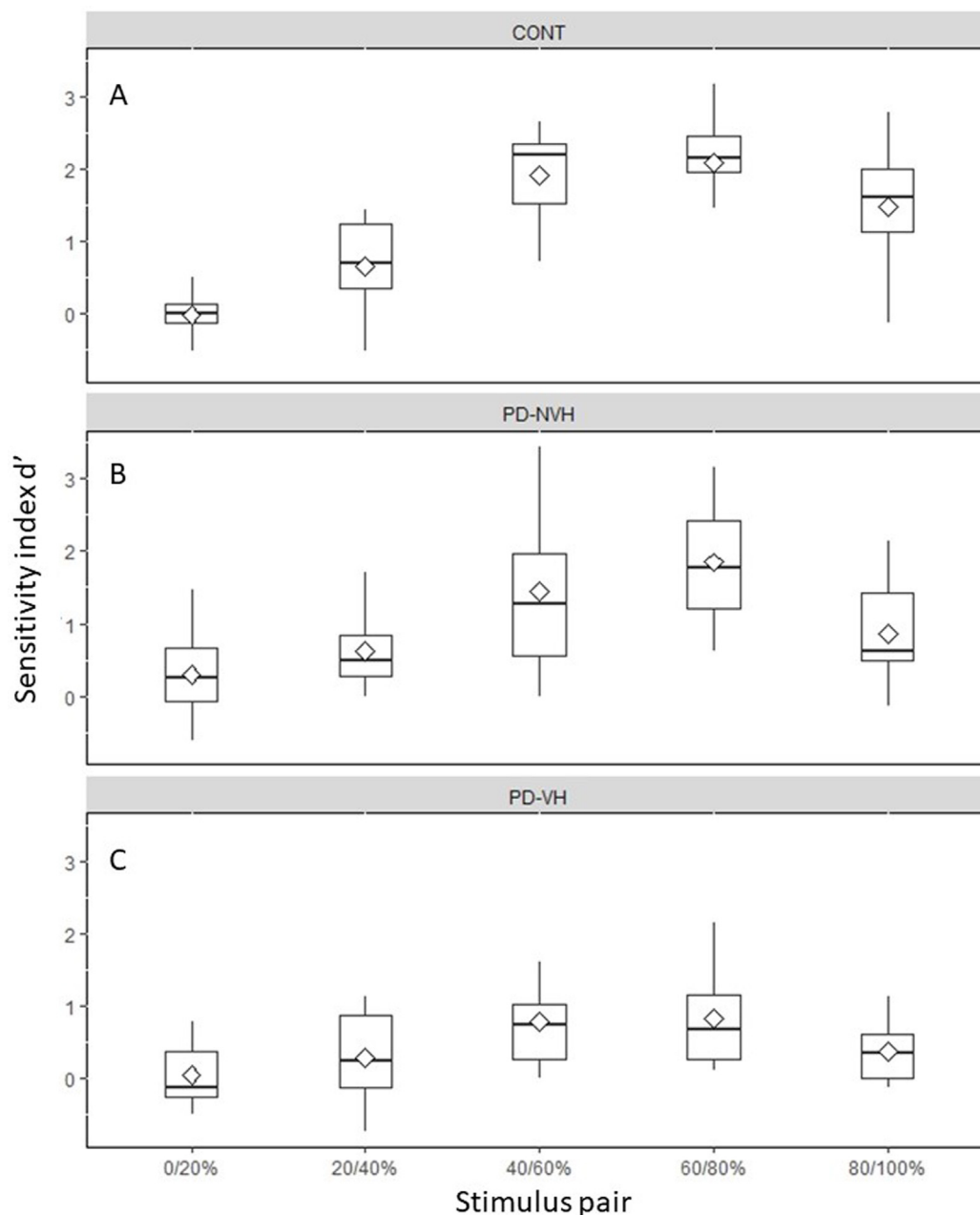


Fig. 4 – Discrimination performance according to stimulus pairs. A. Discrimination performance according to sensitivity index in controls. B. Discrimination performance in PD-NVH group. C. Discrimination performance in PD-VH group. Higher sensitivity index d' denotes better discrimination performance. A peak of discrimination performance is observed for the 60%/80% pair in the control and PD-NVH groups.

4.3. Experiment 3: Dalmatian dog task

We collected 29 living-being responses and 29 non-living item responses in the PD-VH group, six living-being responses and 27 non-living item responses in the PD-NVH group, 17 living-being responses and 36 non-living item responses in the control group (between-group comparison: $\chi^2 = 9.82$, $P = 0.007$). We computed the ratio of living-being responses to the total responses for each participant. This ratio tended to be higher in the PD-VH group ($R = 39.8\%$) compared to the PD-NVH group ($R = 22.9\%$) and to the control group ($R = 18.4\%$). In

multivariate analyses, the living-being ratio was higher in the PD-VH group compared to the control group ($P_{\text{adjusted}} = 0.040$). None of the participants identified the Dalmatian dog. The ratio of living-being responses to the total responses was not correlated with any of the clinical measures studied.

5. Discussion

This experimental study confirmed that PD patients with visual hallucinations more often interpret ambiguous visual

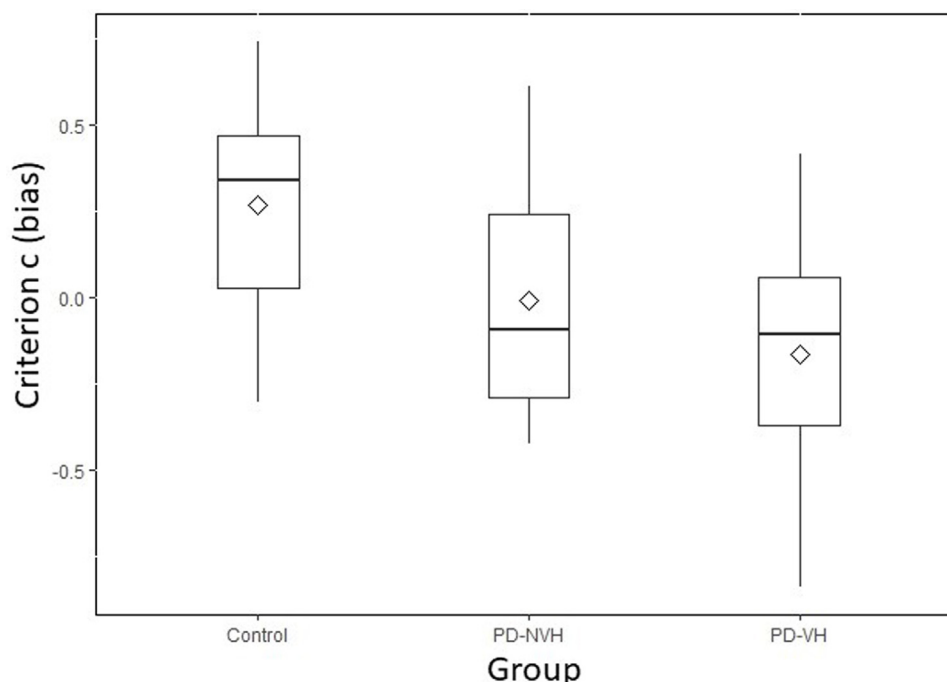


Fig. 5 – Criterion value at peak discrimination for ambiguous stimuli. Peak discrimination was observed for ambiguous stimuli between 60 and 80% of face content. The criterion value at peak of discrimination was positive in controls (flower bias) and negative in PD-VH patients (face bias).

stimuli as human faces and living beings compared to PD patients without hallucinations or control subjects. The analysis of participants' behavioural performance confirmed that PD patients and especially those with visual hallucinations suffer from bottom-up impaired visual perception processing and lower categorisation performance. Yet, the results from the discrimination task suggest that the bias towards living beings might arise because of impaired top-down processes in hallucinating PD patients.

5.1. A bias towards seeing faces or living beings

Our three experimental tasks bring new evidence for a bias towards faces or living beings in PD-VH patients. In the categorisation task, the point of subjective equality (PSE) was smaller in the PD-VH patients compared to the controls, which means that PD-VH participants interpreted as faces ambiguous stimuli with a smaller amount of face content compared to controls. In the discrimination task, the PD-VH patients showed a negative criterion value, suggesting a bias towards faces, which was not the case for the PD-NVH patients and the control subjects. In the Dalmatian dog task, the ratio of responses referring to living beings tended to be higher in the PD-VH group compared to controls, pointing again to a tendency for hallucinating PD patients to interpret neutral, inanimate stimuli, as living beings. Our study confirms the existence of a bias towards living beings previously described in PD [1,7,29]. Recently, "pareidolia tasks" have also been used to elicit visual illusions in patients with DLB. The stimuli consisted either of scenes (animals, plants, artefacts) filtered by Gaussian blurring [11], meaningless noise stimuli [30], or both [31]. DLB patients with visual hallucinations had more induced illusions than

patients without hallucinations or controls [32]. In 70 to 90% of the cases, elicited pareidolia consisted in seeing people or animals [30,32]. Thus, patients with Lewy body diseases (either PD or DLB) have a tendency, either spontaneously in everyday life or when experimentally tested with specific tasks, to interpret inanimate objects as living beings.

5.2. Impaired visual perception

Our PD-VH patients exhibited lower performance and thus impaired visual perception of unambiguous stimuli (100% flower and 100% face) due to altered bottom-up visual processing compared to controls in Experiments 1 and 2, but also compared to PD-NVH patients in Experiment 1. Low performance for discriminating ambiguous stimuli in Experiment 2 further confirms visual perception impairment at higher cognitive levels. This lower visual perception performance did not correlate with visual acuity, but was associated with lower cognitive performance in Experiment 2. Accordingly, patients with PD have shown visual dysfunctions at each stage of visual processing, from the retina to higher cortical visual processing [33]. Structural, metabolic and functional imaging studies comparing PD patients with and without hallucinations suggest that patients with hallucinations have atrophy, hypometabolism and hypoactivity in occipito-temporal and occipito-parietal regions involved in visual processing [2,34,35]. Taken together, both experimental and neuroimaging data suggest that PD patients with visual hallucinations exhibit bottom-up impairment in visual perception processing [2,34,35]. Yet, such visual perception impairment still cannot explain the observed bias towards living beings in PD.

5.3. Impaired visual categorisation

Our PD-VH patients also exhibited impaired categorisation processing, a higher order cognitive capacity allowing interpretation of visual stimuli. Indeed, statistical modelling of their performance in Experiment 1 shows that the PD-VH group had a lower β coefficient for their slope responses (Fig. 3). Older age and impaired cognition are associated with lower categorisation performance. Confronted with the uncertainty of ambiguous stimuli, patients with PD, especially those with visual hallucinations, have difficulties in making a categorisation decision. Their impaired perception abilities may explain these results, because it is difficult to make an efficient categorisation of misperceived stimuli, thus altering the perceptual decision-making process itself [36]. In line with this view, a study fitting a hierarchical drift diffusion model to an attentional task suggested that PD patients with hallucinations have alterations in the dynamic process of sensory evidence accumulation needed to reach a minimal threshold for perceptual decision-making [37]. Thus, impairments in both visual perception and categorisation processes may be linked in PD-VH patients suggesting that bottom-up processes could be necessary for visual misperceptions to occur. However, the bias towards living beings remains unexplained.

5.4. Explaining the bias towards living beings

Humans are fast and efficient at detecting animals and faces in natural scenes, an ability that might have been selected during evolution for survival and social purposes [38–41]. Such advantage for detecting and reaching animals and faces can be demonstrated experimentally [42,43]. Presumably, the ability to rapidly detect faces derives from a network of interactive

brain regions, in particular the fusiform face area (FFA) [44,45]. Interestingly, in healthy subjects, neuronal FFA activity before ambiguous stimulus presentation can bias subsequent categorisation toward faces [46], and this FFA activity itself can be controlled by a predictive top-down signal from frontal and parietal areas [47,48].

In our Experiment 2, we observed that when forced to discriminate between two ambiguous stimuli, healthy controls had a bias towards flowers (positive criterion c) while the opposite was seen in the PD-VH patients who had a bias towards faces (Fig. 5). In this experimental setting, we suggest that healthy controls inhibit their natural advantage to detect rapidly living beings by exerting a top-down control over face perception processes. In PD-VH patients, impaired top-down control would suppress the inhibition of face perception processes, yielding a face bias (Fig. 6). Presumably, such top-down control would be linked to attentional or executive capacities, but we lack precise neuropsychological data in this study to confirm this hypothesis. This interpretation could apply to the Charles Bonnet syndrome in which subjects with visual loss experience visual illusions or hallucinations involving disembodied faces and people, especially when cognitive impairment is associated [49,50]. Accordingly, a functional magnetic resonance imaging study in PD-VH patients showed that visual misperceptions correlated with reduced functional connectivity between dorsal attention and salience networks necessary for selecting and controlling the stimuli deserving attention [51]. As a whole, visual misperceptions in PD might arise because of a combination of impaired bottom-up and top-down processes, but our study suggests that the bias toward living beings relies on impaired top-down executive control over living being perception processes.

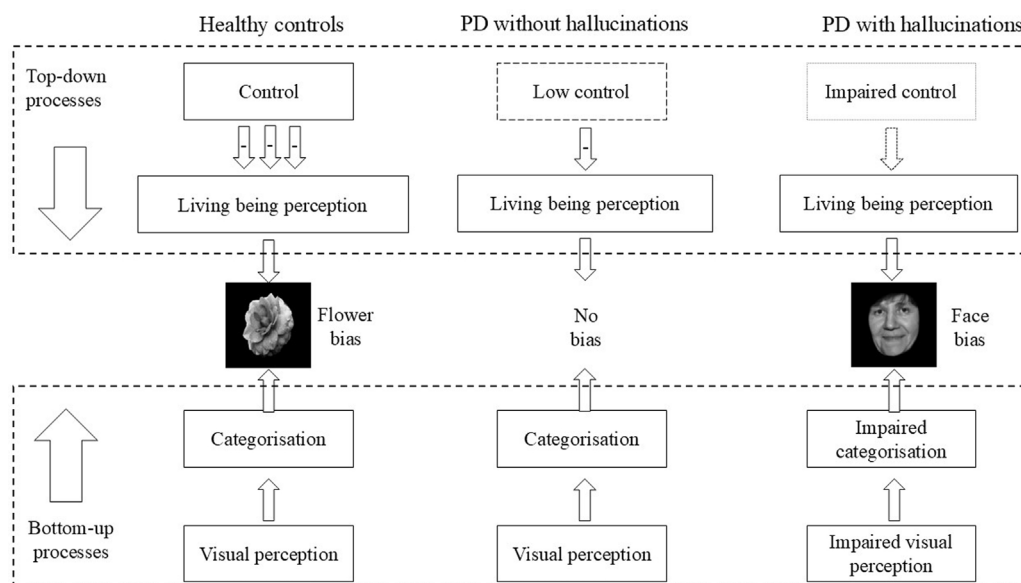


Fig. 6 – Interpretation of bias towards living beings. Brain processes allowing the recognition of living beings might be preferentially activated, due to the evolutionary advantage of detecting friends, foes, mates, and preys or predators in our environment. We hypothesize that efficient top-down control and inhibition upon living being perception processes results in a flower bias in healthy controls in the discrimination task. Conversely, impaired top-down control would release living being perception processes yielding a face bias in PD patients with hallucinations.

5.5. Potential limitations

This study was based on a limited numbers of participants for each group to ensure matching for cognitive performance, age, visual acuity, and educational level. Multivariate analyses might have been underpowered. Further studies in larger groups of individuals would be needed to replicate these results. Data were collected in 2010, thus explaining the use of UK PD Society Brain Bank criteria for PD and of the UPDRS scale. The reaction times recorded in both computerized tasks were slower in the PD-VH group compared to the PD-NVH and control groups. Reaction times depend upon a number of cognitive and motor processes [52]. Accordingly, our PD-VH group had a more severe motor state than our PD-NVH group. However, performance in the different tasks was not associated with UPDRS motor score or LEDD. The PD groups also differed according to depression score, disease duration, and disease severity. Yet, multivariate analyses demonstrated that such differences did not impact critically our results.

6. Conclusion

The bias towards living beings in visual misperceptions of PD patients might be the consequence of impaired top-down control over cognitive processes for perception of living being entities. Yet, PD patients also experience hallucinations resembling living beings in other sensory modalities (not only visual but also auditory or tactile modalities). This holds true also for feelings of presence, where the presence of a person is vividly felt in the absence of any sensory clue for such presence [6]. Further studies are needed to explore whether the interpretation of our results also applies in other sensory modalities.

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Disclosure of interest

The authors declare that they have no competing interest.

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