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RESEARCH ARTICLE

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Neuropsychological correlates of visual hallucinatory phenomena in Lewy body disease

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Abstract

Objectives: Visual hallucinations (VH) ranging from minor to complex, are the most common psychiatric feature of Lewy Body Disease (LBD). Despite their high prevalence and poor prognostic implications instigating extensive research, the precise mechanisms underlying VH remain unclear. Cognitive impairment (CI) is a risk factor and a consistent correlate of VH in LBD. To help shed light on their underlying mechanisms, this study investigates the pattern of CI across the spectrum of VH in LBD.

Methods: 30 LBD patients with minor VH (MVH), 13 with complex VH (CVH) and 32 without VH were retrospectively compared on the domains of higher-order visual processing, memory, language and executive functioning. The VH groups were further stratified to investigate whether phenomenological subtypes have distinct cognitive correlates.

Results: LBD patients with CVH were impaired on the visuo-spatial and executive functioning domains relative to controls. LBD patients with MVH were also impaired on the visuo-spatial domain. No differences emerged in cognitive domains affected between patient groups endorsing specific hallucinatory phenomena.

Conclusion: A pattern of CI indicating fronto-subcortical dysfunction in combination with posterior cortical involvement is implicated in the genesis of CVH. Moreover, this posterior cortical dysfunction may precede the occurrence of CVH as indicated by selective visuo-spatial deficits in LBD patients with MVH.

KEYWORDS
cognitive impairment, complex visual hallucinations, dementia with Lewy bodies, Lewy body disease, minor visual hallucinations, neuropsychology, Parkinson's disease, passage, presence, visual hallucinations

Key points

- VH, including CVH and MVH such as presence and passage phenomena, are a common feature of the LBD.
- VH are associated with a highly inconsistent profile of CI. Moreover, the cognitive profile of MVH is unknown.

- Patients with CVH performed poorly on tests of visuo-spatial ability and executive functioning, implicating a pattern of fronto-subcortical dysfunction with posterior cortical involvement.
- Patients with MVH also performed poorly on the test of visuospatial ability, suggesting that selective impairment in this domain precedes the development of complex hallucinations.

1 | INTRODUCTION

Lewy body disease (LBD) refers to a spectrum of disorders characterised by widespread cortical and subcortical intracellular deposits of alpha-synuclein, known as 'Lewy bodies' (LB). Clinical manifestations of LBD include Parkinson's disease (PD), Parkinson's disease dementia (PDD) and Dementia with Lewy Bodies (DLB).[1,2] In addition to shared alpha-synuclein pathology, the LBD spectrum has some common clinical features, one of which is hallucinations. Visual hallucinations (VH) are the most common, occurring in about 30%–70% of LBD patients,[3,4] and defined as involuntary experience of seeing something that is not veridically present, whilst awake.[5]

VH in LBD may be subdivided into complex or minor hallucinations. Complex VH (CVH) refer to well-structured perceptual experiences of clearly defined objects, animals and humans. Minor VH (MVH) include extracampine presence and passage phenomena.[6,7] Presence phenomena refer to the vivid sensation that someone distinct from oneself is present in close proximity. This 'presence' is usually unidentified, human, sometimes seen as an unformed visual shadow or a mist.[4,7] Passage phenomena describe the fleeting perception of an object, animal, human or shadow passing sideways through the peripheral visual field. Patients may experience MVH in isolation or in combination with CVH.[4] MVH are more common in PD, whereas CVH are usually the first visual symptom reported in DLB.[8] While the literature on the natural course of MVH is limited, they often precede the onset of CVH in PD and have important prognostic implications.[4,7]

VH in LBD are of grave importance. They have a significant impact on patients' and caregivers' quality of life,[9] predict the need for institutional care,[10] and are associated with increased risk of mortality.[11] However, despite the frequency and impact of VH in LBD, their underlying mechanisms are still not well understood. As a result, management can be extremely challenging; with some medications worsening hallucinations, and neuroleptic sensitivity in DLB limiting other options.[12,13] Therefore, it is vital to improve our understanding of the underlying mechanisms of VH in LBD, and particularly MVH, in order to develop more effective and earlier therapeutic interventions.[14,15]

Cognitive impairment (CI) is the most consistent correlate of VH in LBD and therefore may shed light upon their underlying mechanisms.[16] However, the precise cognitive profile remains unclear. There are inconsistent reports of impairments across a broad range of cognitive domains, including visuo-perceptual[17–22] and visuo-spatial abilities,[19,20,22] executive functioning,[16,19,23,24] attention,[19,20,23,25,26] visual memory,[17,22,27,28] and less frequently visuo-constructional,[16,19,27,28] language[21] and verbal memory.[16,21,29,30] This variability reflects differences in clinico-demographic characteristics of participants, exclusion criteria, and neuropsychological test batteries. For instance, some studies used a Mini-Mental State Exam (MMSE)[31] cut-off score as an exclusionary criterion[16,18,19,26,27,29] whereas others did not.[17,21,22,24] Even among the studies that did, there was considerable variability in the cut-off score chosen, ranging from 18[26,27] to 25.[18]There was also considerable variability in the tests chosen to assess each cognitive domain. For instance, visuo-spatial functioning was assessed using the Visual Object and Space Perception Battery[17–20,26] Judgement of Line Orientation,[32,33] Benton Visual Form Discrimination test[22] and even Rey-Osterreith Complex Figure test.[16] Operational definitions of cognitive constructs also differ across studies, affecting choice of tests used. For instance, Judgement of Line Orientation was used as a visuo-perceptual test by Ozer et al., (2007),[33] but as a visuo-spatial test by Katzen et al. (2010).[32] These methodological differences make it challenging to reconcile findings across studies.

Moreover, the cognitive profile associated with VH subtypes remains unknown, as previous studies have mostly failed to distinguish between CVH and MVH. Among those that did make this distinction, many found comparable cognitive performance in patients with MVH and no VH,[34–36] leading to the suggestion that MVH may predate measurable cognitive decline.[37] However, other studies found impairments in attentional,[38] executive functioning,[38] memory[38] and higher-order visual processing[39] cognitive domains, as well as self-reports of CI.[34] Since MVH and CVH in LBD are understood to be on a spectrum,[7] it is reasonable to assume that CI in association with VH should follow a similar progressive pattern. However, the available data on CI associated with MVH are not enough to reliably support or refute this hypothesis.

It has also been proposed that phenomenologically distinct subtypes of VH may have distinct neural substrates.[34,40,41] Yet no study, that we are aware of, has investigated whether this translates into differences in cognitive profiles of patients experiencing different combinations of presence, passage and complex VH.

Therefore, the aim of the present study was to help shed light on the mechanisms underlying VH in LBD, by investigating the cognitive profile of VH subtypes, and exploring the cognitive correlates of presence and passage hallucinatory phenomena.

2 | METHODS

2.1 | Study design and participants

The present study is a retrospective cross-sectional analysis of neuropsychological data. Data were obtained from 60 LBD patients with VH (VH group) and 42 LBD patients without VH (control group) evaluated at the National Hospital of Neurology and Neurosurgery between 2019 and 2022. Information about diagnosis, age, disease duration, medical history, current medications, estimates of pre-morbid intelligence, cognitive and mood assessment were extracted from patient files and existing databases. The sample consisted of a combination of patients diagnosed with PD according to the Queen Square Brain Bank criteria[42] and patients with a probable diagnosis of DLB in accordance with the consortium criteria.[43] Patients were included on the basis of the following criteria:

Inclusion criteria:

1) A confirmed or probable diagnosis of PD or DLB.
2) For the VH group-reports of presence/passage/CVH in isolation or in combination with VI.
3) For the control group-absence of any visual hallucinatory phenomena.
4) Availability of test scores for at least visuo-perceptual and visuo-spatial domains.

Exclusion criteria:

1) Presence of a potentially confounding neurological or ophthalmic co-morbidity
2) Patients reporting isolated visual illusions (VI)

After application of the exclusion criteria, and further excluding 3 of the oldest patients in the VH group and 5 of the youngest patients in the control group in an attempt to age-match the groups, the final sample consisted of 43 patients in the VH group and 32 patients in the control group (refer Figure 1). The study was registered with and approved by the Queen Square Audit committee (registration reference number: 1120223-SE).

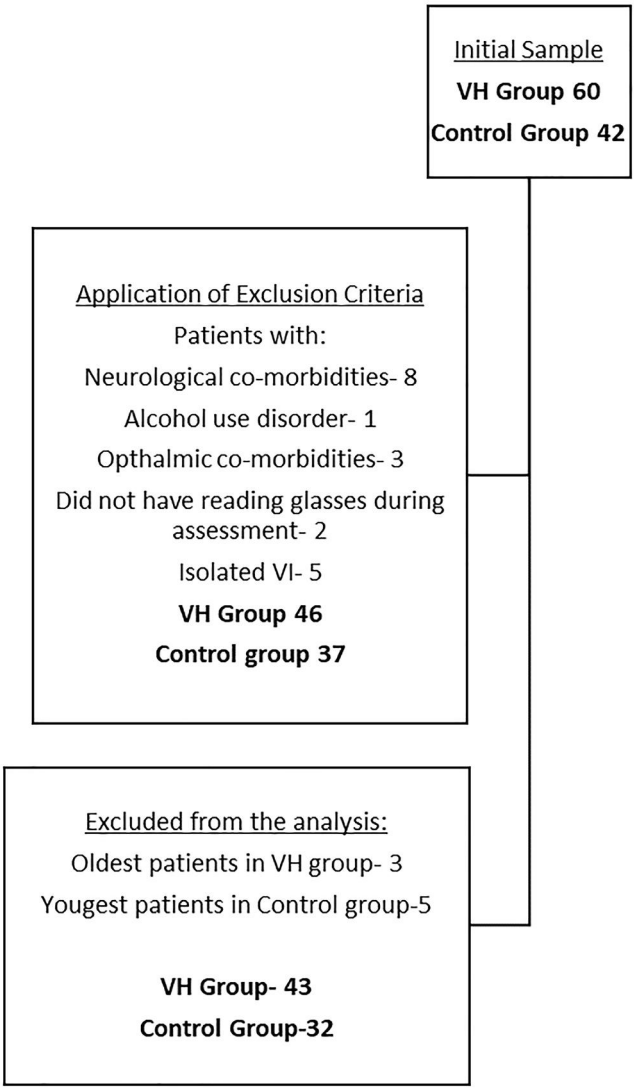

FIGURE 1 Flow-chart depicting sample selection.

2.2 | Assessment

All the patients underwent a routine clinical interview, during which they were asked about the presence and character of any recent VH, presence or passage phenomena, and VI. The patients had then completed a 2-h long battery of standardized neuropsychological assessments during which they were allowed to move their head freely. The battery included the National Adult Reading Test (NART)[44] as a measure of pre-morbid cognitive ability, and the Hospital Anxiety and Depression scale (HADS)[45] to assess the presence of anxiety and/or depression. The cognitive domains assessed included higher-order visual processing (visuo-perceptual, visuo-spatial and visuo-constructional abilities), recognition memory, language and executive functioning. Visuo-perceptual abilities were assessed using the Visual Object and Space Perception Battery (VOSP)[46] Incomplete Letters (IL) and Silhouettes (SIL) subtests. Visuo-spatial abilities were assessed using the Cube Analysis (CA) subtest.[46] Visuo-constructional abilities were assessed using Mini-Mental State Exam (MMSE)[31] interlocking pentagons copy or Adult Memory and Information Processing Battery (AMIPB)[47] complex figure copy. Recognition memory for verbal and visual material was assessed using Recognition Memory Test for Words (RMW)[48,49] and Faces (RMF) respectively.[48,49] Language was assessed using the Graded Naming Tests (GNT),[50,51] or the Oldfield Naming Test[52] for patients who did not have English as their first language. Executive functioning was assessed using phonemic fluency for the letter 'S'[52] and categorical fluency for the category 'animals,'[52] and the Stroop Colour-Word Test.[53] Test scores on visuo-perceptual, visuo-spatial, recognition memory, language and executive functioning domains were converted into z-scores for analysis, based upon normative

data. Visuo-constructional tests were given binary scores (0 = impaired; 1 = unimpaired).

2.3 | Statistical analysis

Patients were subdivided into three groups: isolated MVH (n = 30; MVH group), CVH ± MVH (n = 13; CVH group) and no VH (n = 33; Control group). After screening for normality and homogeneity of variance using Shapiro-Wilk and Levene's tests respectively, these groups were compared using one-way analyses of variance, Kruskal-Wallis, chi square, and Fisher's exact tests for normally and non-normally-distributed continuous variables and categorical variables, respectively. Variables with any missing data (12%, LEDD; 4%, NART; 9.3%, HADS; 20% Visuo-constructional test) were excluded pairwise from analyses.

Next, the VH group was further subdivided into presence (n = 13), passage (n = 14) and CVH ± MVH groups (n = 13), and compared using a similar approach as before. Three patients endorsing both presence and passage hallucinations, but not CVH, were excluded from this analysis, as we were interested in investigating the cognitive correlates of isolated presence and passage hallucinations.

All statistical analyses were carried out using SPSS.28.

3 | RESULTS

Clinico-demographic characteristics of the MVH, CVH and control groups can be found in Table 1.

As shown in Table 1, the MVH, CVH and control groups were matched in age, disease duration, gender, NART scores and depression ratings. There were no significant differences in levodopa equivalent daily dose (LEDD) or use of other medications. An ANOVA revealed a significant group difference of anxiety (F (2,65) = 8.25, $p < 0.001$). According to the pairwise between-group comparisons, both MVH ($p = 0.001$) and CVH ($p = 0.022$) groups had higher levels of anxiety compared to the control group.

Further analyses were undertaken to determine the relationship between anxiety and neuropsychological test performance. Spearman's Rho correlations, corrected for multiple comparisons, revealed that anxiety was negatively correlated with the performance on one test: VOSP CA. ($r = -0.451$, $p < 0.001$).

Neuropsychological test performance in MVH, CVH and control groups can be found in Table 2.

As shown in Table 2, there was a significant group difference on VOSP CA (H (2) = 14.63, $p < 0.001$). Post-hoc pairwise comparisons revealed that CVH ($p = 0.002$) and MVH ($p = 0.015$) groups performed significantly worse on VOSP CA compared to the control group. There was also a trend for higher frequency of impairment in visuo-constructional abilities in the VH groups, but this difference did not reach statistical significance ($p = 0.051$). Additionally, there was a significant group difference on one measure of executive functioning, the Stroop (H (2) = 8.41, $p = 0.015$). The CVH group, but not MVH group performed significantly worse relative to the control group ($p = 0.016$). MVH and CVH groups did not differ significantly in performance in any of the cognitive domains (Table 2, Figure 2). In a repeat analysis, this pattern of results was replicated in a sample exclusive to PD patients, to rule out any bias in the results by including DLB patients in the sample.

As both the MVH and CVH groups were characterised by impaired VOSP CA relative to the control group, a post-hoc binary logistic regression was used to reveal the predictive value of VOSP CA neuropsychological test performance upon presence of VH in LBD. For this, MVH and CVH groups were combined into a single VH group, which formed the outcome variable. A two-stage hierarchical approach was chosen because we were interested in whether VOSP CA predicted the occurrence of VH independent of anxiety. Therefore, anxiety was entered at stage 1 and VOSP CA, at stage 2. Prior to building the model, the assumptions of logistic regression were checked. The multicollinearity statistics of tolerance and VIF were found to be within acceptable limits, and a case-wise listing of residual values revealed that there were no outliers. The model is shown in Table 3.

At stage 1, anxiety contributed significantly to the regression model [X^2 (1, n = 68) = 15.381, $p < 0.001$] and explained 27.1% of the variance in likelihood of VH (Negelkerke R square). At stage 2, VOSP CA accounted for 10.8% of variance in the likelihood of VH, independent of anxiety. Moreover, the change in R2 with VOSP CA was significant [X^2 (2, n = 68) = 7.270, $p = 0.007$] and VOSP CA was a significant predictor ($\beta = -0.620$, $p = 0.023$). The logistic regression model was statistically significant [X^2 (2, N = 68) = 22.651, $p < 0.01$] and a good fit for the data (Hosmer and Lemeshow test, $p = 0.077$).

Next, the sample was further stratified into presence, passage and CVH groups. There were no significant differences in clinico-demographic variables. Neuropsychological test performance in the three groups can be found in Table 4.

As shown in Table 4, there were no significant group differences in neuropsychological test performance in any of the cognitive domains.

4 | DISCUSSION

The aim of this study was to help reveal the mechanisms underlying VH, a clinical feature shared between distinct clinical manifestations of the LBD spectrum including PD and DLB, by investigating their cognitive correlates. Firstly, we found that LBD patients with either MVH and/or CVH were impaired in visuo-spatial processing, and had weaker visuo-constructional abilities. Secondly, we found that those with CVH but not MVH demonstrated impairment in executive functioning. Importantly, these findings cannot be explained by group differences in age, disease duration, pre-morbid intelligence or medication burden.

TABLE 1 Clinico-demographic characteristics between MVH, CVH and control groups.

	MVH group (n = 30)	CVH group (n = 13)	Control group (n = 32)	Significance	Post-hoc tests
Diagnosis (n, %)	PD = 25 (83.33) DLB = 5 (16.66)	PD = 12 (92.31) DLB = 1 (7.69)	PD = 28 (87.50) DLB = 4 (12.50)		
Age (median, IQR)	71 (10)	66 (14)	65 (15)	p = 0.198	-
Sex (male: female)	21:9	8:5	23:9	p = 0.789	-
Disease duration (median, IQR)	7.5 (10) PD = 10 (9) DLB = 1 (2)	10 (12) PD = 11 (12) -	5 (7) PD = 5.50 (7) DLB = 2.50 (3)	p = 0.159	-
NART (mean, SD)	110.40 (10.74)	105.42 (12.77)	108.30 (10.32)	p = 0.401	-
Presence hallucinations (n, %)	13 (30.23)	0	0		
Passage hallucinations (n, %)	14 (32.56)	0	0		
Presence and passage hallucinations (n, %)	3 (6.98)	0	0		
LEDD (mg: mean, SD)	639.25 (484.00)	663.62 (391.55)	656.72 (437.89)	p = 0.984	-
Current use of amantadine (n, %)	7 (23.33)	7 (53.85)	8 (25)	p = 0.182	-
Current use of dopamine agonists (n, %)	8 (26.66)	1 (7.69)	9 (28.13)	p = 0.303	-
Current use of anticholinergics (n, %)	3 (10)	3 (23.08)	2 (6.25)	p = 0.295	-
Current use of cholinesterase inhibitors (n, %)	4 (13.33)	3 (23.08)	1 (0.03)	p = 0.104	-
Current use of anti-psychotics (n, %)	0	1 (7.69)	0	p = 0.186	-
Current use of anti-depressants (n, %)	13 (43.33)	5 (38.46)	9 (28.13)	p = 0.364	-
Current use of benzodiazepines (n, %)	4 (13.33)	3 (23.08)	5 (15.63)	p = 0.839	-
HADS- anxiety (mean, SD)	10.15 (3.92)	10 (3.80)	6.42 (3.33)	p < 0.001*	MVH > controls (p = 0.001)** CVH > controls (p = 0.022)**
HADS- depression (median, IQR)	8 (6)	8 (4)	7 (3)	p = 0.225	-
Anxiety/Visuo-construction[a]				p = 0.644	-
Depression/Visuo-construction[b]				p = 0.177	-

[ab]The relationship of mood variables with the categorical variable of visuo-constructional ability was assessed using a Fisher's exact test by converting the former into binary categorical variables. The raw scores on HADS anxiety and depression scales were classified as normal, mild, moderate and severe based on normative data. Normal and mild classes were coded as 0 = not anxious/depressed while moderate and severe classes were coded as 1 = anxious/depressed.

Abbreviations: HADS- Hospital Anxiety and Depression Scale; IQR- Interquartile Range, LEDD- Levodopa Equivalent Daily Dose; NART- National Adult Reading Test; SD- Standard Deviation.

*significant at 0.05. **significance adjusted by Bonferroni correction for multiple comparison.

4.1 | Impairment in higher-order visual processing

Our results are in line with previous studies reporting visuo-spatial impairments in LBD patients with VH[19,20,22,32] as well as in LBD patients with isolated MVH.[38,39] While previous studies have found visuo-spatial impairments on other VOSP subtests (Dot Counting[20] and Position Discrimination[19]), only one other recent study reported finding similar impairments specifically on the VOSP CA in LBD patients with VH.[54] CA requires three-dimensional mental reconstruction of two-dimensional line drawings in order to infer the number of cubes, including those hidden from view. The test relies on intact stereoscopic processing and three-dimensional perception,

TABLE 2 Comparison of neuropsychological measures between MVH, CVH and control groups.

	MVH group (n = 30)	CVH group (n = 13)	Control group (n = 32)	Significance	Post-hoc tests
Higher-order visual processing					
VOSP IL/SIL	−0.55 (1.50)	−0.55 (3.14)	−0.18 (1.87)	p = 0.386	-
VOSP CA	−0.59 (2.50)	−1.00 (5.00)	0.67 (1.46)	p < 0.001*	CVH < controls (p = 0.002)**
					MVH < controls (p = 0.015)**
Figure Copy (% impaired)	23.07	33.33	0.04	p = 0.051	-
Memory					
RMW	0.17 (1.94)	0.67 (2.31)	0.58 (1.45)	p = 0.237	-
RMF	−1.34 (2.38)	−0.42 (2.04)	−0.24 (2.34)	p = 0.216	-
Language					
GNT	−0.60 (1.16)	−0.88 (1.46)	−0.52 (1.03)	p = 0.650	-
Executive functioning					
Phonemic fluency	−0.43 (1.27)	−0.64 (2.87)	0.11 (1.86)	p = 0.197	-
Categorical fluency	−0.55 (1.37)	−0.56 (1.49)	0.09 (1.23)	p = 0.130	-
Stroop	−1.63 (2.14)	−2.50 (1.71)	−0.81 (2.26)	p = 0.015*	CVH < controls (p = 0.016)**

Abbreviations: CA, Cube Analysis; GNT, Graded Naming Test; IL, Incomplete Letters; RMF, Recognition Memory for Faces; RMW, Recognition Memory for Words; SIL, Silhouettes; VOSP, Visual Object and Space Perception Battery.

*significant at 0.05. **significance adjusted by Bonferroni correction for multiple comparison.

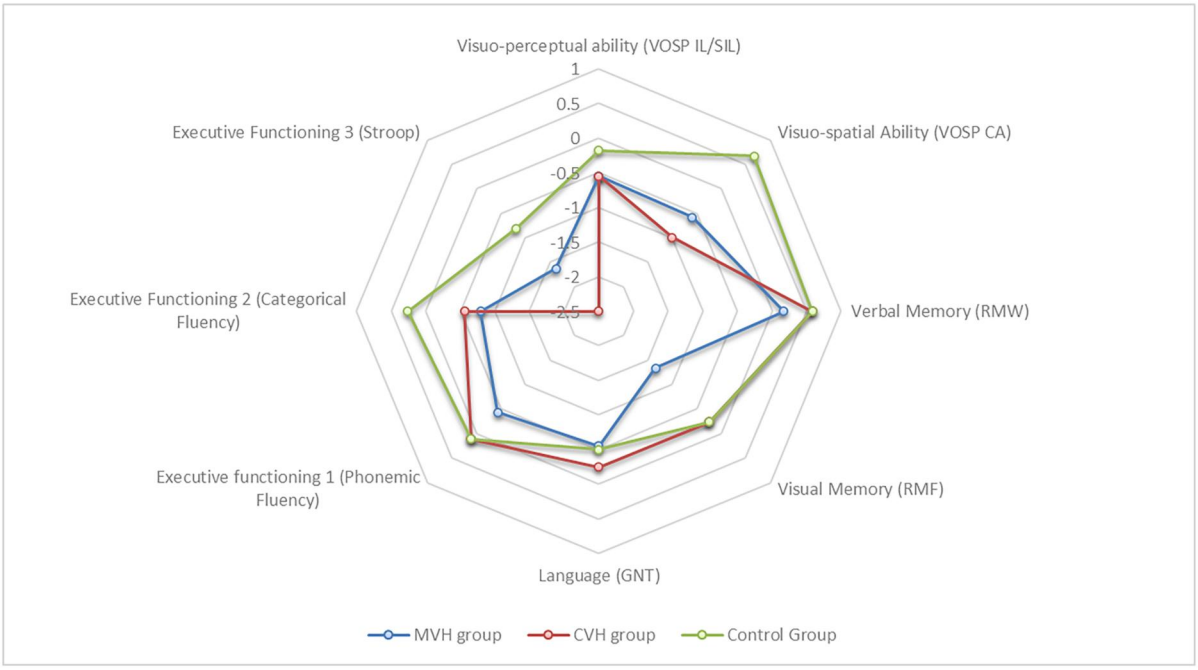

FIGURE 2 A Radar Chart illustrating the performance of LBD patients with MVH, CVH and without VH on neuropsychological domains. Median z scores were used for this illustration as some of the variables did not have a normal distribution.

along with an element of executive functioning apparent in the strategies used by examinees to meet the task demands. This makes it the most challenging spatial subtest of the VOSP.[55]

It is also worth noting that there is evidence to suggest that visuo-spatial problem-solving deficits in LBD patients reflect a genuine visuo-spatial deficit, not accounted for by executive dysfunction or cognitive slowing.[56,57] Poorer performance on the VOSP CA was associated with higher levels of anxiety. Anxiety is unlikely to cause poorer VOSP CA performance; rather, it is more likely that the increased anxiety reflects disequilibrium caused by

TABLE 3 Binary logistic regression model.

	Stage 1				Stage 2			
	Coefficient β	SE	Sig.	Exp(B)	Coefficient β	SE	Sig.	Exp(B)
Constant	−2.082	0.705	0.003	0.125	−1.834	0.722	0.011	0.160
Anxiety	0.277	0.082	<0.001	1.320	0.223	0.085	0.009	1.250
VOSP CA	-	-		-	−0.620	0.274	0.023	0.538
Model fit								
Log likelihood	78.357				71.087			
Omnibus model X^2	15.381		<0.001		22.651		<0.001	

Abbreviations: CA, Cube Analysis; VOSP, Visual Object and Space Perception Battery.

TABLE 4 Comparison of neuropsychological parameters between presence, passage and CVH groups.

	Presence group (n = 13)	Passage group (n = 14)	CVH group (n = 13)	Significance
Higher-order visual processing				
VOSP IL/SIL	−0.80 (1.60)	−0.43 (1.31)	−0.55 (3.14)	$p = 0.955$
VOSP CA	−1.00 (2.50)	−0.17 (1.88)	−1.00 (5.00)	$p = 0.351$
Figure Copy (Impaired: Unimpaired)	18.18	33.33	33.33	$p = 0.693$
Memory				
RMW	0.17 (2.06)	0.03 (1.73)	0.67 (2.31)	$p = 0.610$
RMF	−1.44 (2.95)	−1.00 (2.97)	−0.42 (2.04)	$p = 0.469$
Language				
GNT	−0.61 (1.11)	−0.66 (1.34)	−0.88 (1.46)	$p = 0.856$
Executive functioning				
Phonemic fluency	−0.85 (1.39)	−0.43 (1.27)	−0.64 (2.87)	$p = 0.814$
Categorical fluency	−0.67 (1.30)	−0.63 (1.47)	−0.56 (1.49)	$p = 0.979$
Stroop	−2.06 (1.54)	−1.61 (1.48)	−2.56 (1.54)	$p = 0.282$

Abbreviations: CA, Cube Analysis; GNT, Graded Naming Test; IL, Incomplete Letters; RMF, Recognition Memory for Faces; RMW, Recognition Memory for Words; SIL, Silhouettes; VOSP, Visual Object and Space Perception Battery.

retained insight into changes in cognitive performance. Indeed, even when the effects of anxiety were statistically controlled for, performance on VOSP CA remained a significant predictor of VH, accounting for 10.8% of the variance.

Visuo-spatial impairment in association with both MVH and CVH may reflect an early pathophysiological alteration in the regions corresponding to the dorsal visual stream.[26,40,58] The dorsal visual stream extends from the occipito-parietal cortex to posterior inferior parietal lobule and gives rise to distinct processing pathways extending all the way to the dorsolateral prefrontal cortex.[59] The nodes and tracts of the dorsal visual stream subserve distinct visuo-spatial functions such as spatially guided actions, spatial working memory and integration of spatial imagery.[40,59] Impairment in these functions is also evident in the phenomenological aspects of VH subtypes. For instance, it may explain the spatial nature of presence and passage hallucinations.

Higher frequency of visuo-constructional impairment observed in patient groups with VH implicates the parietal cortex, further supporting involvement of the dorsal visual stream in the development of VH. Accurate figure copying relies on several abilities including basic visual perception, visuo-spatial organization, motor co-ordination and executive functioning. These abilities map onto a widespread neural network involving the parietal cortex.[60] Grey matter (GM) atrophic changes in the parietal lobe have been previously reported in association with VH in LBD,[26,61,62] which may account for this relative weakness.

4.2 | Impairment in executive functioning

The present study also found evidence of executive dysfunction associated with VH; LBD patients with CVH but not MVH were impaired on the Stroop test, relative to controls. There is considerable previous evidence of impaired performance of LBD patients with VH on the Stroop test.[24,25,30,63,64] Consistent with our findings, LBD patients with isolated MVH have not been found to be impaired on the Stroop test.[38]

Executive dysfunction in LBD can be attributed to disruption of fronto-striatal circuitry, secondary to the striatal dopaminergic deficits characteristic of this disorder,[64] as well as the GM atrophy in these regions.[25] The non-motor divisions of the frontostriatal circuits form connections between the anterior cingulate, dorsolateral prefrontal, orbitofrontal cortices and the striatum. These circuits are thought to subserve distinct executive functions including inhibitory control that is of particular relevance here.[64,65]

The Stroop Colour-Word test requires the examinee to suppress a habitual response of reading the Colour-Word in favour of a novel response of naming the ink colour by selectively attending to it.[66] The functions of conflict monitoring, attentional biasing and top-down inhibitory control of responses necessary to perform well on this task, are subserved by the anterior cingulate cortex and related regions also within the fronto-striatal circuitry.[64] Impairments in inhibitory control have also been linked to reality-monitoring deficits implicated in the genesis of VH in LBD.[17,24]

Additionally, functional neuroimaging studies have uncovered a pattern of increased frontal activation coupled with a decreased activation of the visual cortices in response to visual stimuli in LBD patients with chronic VH.[67] This pattern may be indicative of an aberrant interaction of top-down and bottom-up systems,[38,67] thereby providing a contextual framework to interpret the current findings of executive dysfunction in combination with higher-order visual processing impairments in association with CVH.

4.3 | Cognitive correlates of presence, passage and complex hallucinations

It has been suggested that presence, passage and CVH may have distinct underlying mechanisms and anatomical substrates reflecting their phenomenological manifestations.[34,40,41] The praecuneus, which plays a role in multisensory integration of egocentric mental representations and extra-personal spatial information, has been implicated in presence hallucinations.[34,40,68] Similarly, passage hallucinations have been linked to areas associated with processing objects in the peripheral visual field, such as the superior parietal lobe and the parahippocampus.[35,40] Finally, CVH are thought to be a function of bottom-up changes in visual acuity and top-down changes in cognition reflected in more extensive cortical and subcortical involvement.[37] Building on this reasoning, it is plausible to speculate that these distinct subtypes of VH may have distinct cognitive correlates. However, our current findings do not support this theory; our study found no significant differences in cognitive domains affected between presence, passage and CVH (CVH ± MVH) groups of LBD patients. The frequent co-existence of presence and passage hallucinations[69] may be suggestive of an overlap in their neural substrates, possibly corresponding to the dorsal visual stream. Our findings regarding visuo-spatial impairment in patients with MVH support this notion.

Our study has provided a systematic and thorough investigation of discrete domains of cognitive function associated with both MVH and CVH, while controlling for pre-geniculate visual abnormalities, making it an important addition to the neuropsychological literature on VH in LBD in general, and on isolated MVH in particular. To the best of our knowledge, this is the first study investigating the neuropsychological correlates of isolated presence and passage hallucinations. However, there were also important limitations. Firstly, the modest sample sizes, which make it possible that the present study was underpowered to detect any subtle group differences. Secondly, hallucinations were assessed using a routine clinical interview as opposed to a standardized questionnaire, which may have introduced some heterogeneity in terms of duration and frequency of VH experience in the VH groups. Thirdly, compared to the control group, the VH groups had longer disease durations. Although not statistically significant, this may have led to some heterogeneity in the sample with respect to disease stage. Fourthly, VI, a subtype of MVH that is commonly observed in LBD patients, were not analysed in the current study. A small sample size of patients with isolated VI (n = 5), impeded any meaningful comparison between VI and other VH subtypes. Finally, because of the study's retrospective design, there was some variability in neuropsychological tests used to assess the same cognitive domain (eg. IL and SIL subtests for visuo-perceptual ability) or between versions of the same test (eg. RMT words and faces-long and short). Care was taken to keep this variability to a minimum and ensure that the different versions of the tests used were comparable as far as possible.

5 | CONCLUSION

Our study found evidence of visuo-spatial and executive functioning impairment in association with CVH in LBD, suggesting that CVH occur on the background of fronto-subcortical dysfunction in combination with some posterior cortical involvement. Our findings also suggest that a selective but measurable decline in visuo-spatial domain precedes the occurrence of CVH, implicating early posterior cortical dysfunction in LBD patients with MVH. Moreover, our measure of visuo-spatial function was a significant predictor of VH in LBD. Therefore, tests that discretely measure visuo-spatial ability may be a useful addition to routine neuropsychological batteries to monitor LBD patients over time. Future studies should longitudinally investigate the cognitive correlates of the full spectrum of psychosis in LBD, ranging from illusions, to VH without insight, with secondary delusions and multimodal involvement. It would also be worth comparing the neuropsychological correlates of VH between different clinical manifestations of the LBD spectrum in future studies.

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CONFLICT OF INTEREST STATEMENT

The authors declare that there is no conflict of interest to disclose regarding this paper.

DATA AVAILABILITY STATEMENT

Due to patient confidentiality, the data supporting the findings of this study are not freely available.

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