Received: 2 November 2022 | Revised: 25 February 2023 | Accepted: 27 February 2023

DOI: 10.1111/jsr.13873

REVIEW ARTICLE

Neuropsychological evaluation of phenoconversion risk in REM sleep behaviour disorder: A scoping review

Giuseppe Fiamingo[1] | Cristina Capittini[2] | Annalisa De Silvestri[2] | Chiara Rebuffi[3] | Chiara Cerami[4,5] | Dario Arnaldi[6,7] | Michele Terzaghi[1,8]

[1]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy

[2]Clinical Epidemiology and Biometric Unit, Scientific Direction, IRCCS Policlinico S. Matteo Foundation, Pavia, Italy

[3]IRCCS Istituto Giannina Gaslini, Genoa, Italy

[4]Scuola Universitaria di Studi Superiori IUSS, Pavia, Italy

[5]Cognitive Computational Neuroscience Research Unit, IRCCS Mondino Foundation, Pavia, Italy

[6]Clinical Neurology, DINOGMI, University of Genoa, Genoa, Italy

[7]IRCSS Ospedale Policlinico San Martino, Genoa, Italy

[8]Unit of Sleep Medicine and Epilepsy, IRCSS Mondino Foundation, Pavia, Italy

Correspondence
Giuseppe Fiamingo, IRCCS Mondino Foundation, Via Mondino 2, 27100 Pavia, Italy.
Email: giuseppe.fiamingo01@universitadipavia.it

Summary

The objective of this study was to assess the role of cognitive evaluation in the prediction of phenoconversion in polysomnography-confirmed idiopathic or isolated rapid eye movement sleep behaviour disorder, through a scoping review focussing on a longitudinal comprehensive neuropsychological assessment of patients with idiopathic REM sleep behaviour disorder. A literature search (2006–2022) yielded 1034 records, and 20 were selected for analysis. The sample included 899 patients from eight different cohorts and five countries. We extracted data on clinical evolution, mild cognitive impairment diagnosis, neuropsychological tests used, and classification of cognitive domains. Tests, cognitive domains, and mild cognitive impairment definitions were heterogeneous across the studies, precluding a meta-analysis. Ten studies (50%) evaluated the presence of mild cognitive impairment; 14 studies (70%) grouped neuropsychological tests into between three (6 studies, 21.4%) and seven (1 study, 7.1%) cognitive domains. The most frequently used tests were semantic fluency, Stroop colour word test, trail making test A and B, digit span, Rey auditory verbal learning test, and Rey-Osterrieth figure. All except digit span showed a role in predicting phenoconversion. The authors did not consistently assign tests to specific cognitive domains. In conclusion, we discuss methodological differences between the studies and highlight the need for a standardised framework for neuropsychological data acquisition and presentation, based on a multilevel approach covering test selection, domain assignment, and mild cognitive impairment diagnostic criteria.

KEYWORDS
idiopathic REM sleep behaviour disorder (iRBD), longitudinal assessment, mild cognitive impairment (MCI), neuropsychology, PD-MCI diagnostic criteria, phenoconversion

1 | INTRODUCTION

Rapid eye movement (REM) sleep behaviour disorder (RBD) is a parasomnia characterised by dream enactment associated with loss of physiological muscle atonia during REM sleep. REM sleep without atonia, documented through video polysomnography (PSG), is a diagnostic criterion for RBD (Howell, 2020).

Longitudinal evidence that patients with idiopathic or isolated RBD (iRBD) often go on to develop a synucleinopathy has led to the view that iRBD represents a prodromal stage of a neurodegenerative

process. The risk of phenoconversion has been estimated to be 10.6% after 2 years, 17.9% after 3 years, 31.3% after 5 years, 51.4% after 8 years, 60.2% after 10 years, and 73.5% after 12 years (Postuma et al., 2019). In a recent meta-analysis, conversion was most frequently to Parkinson's disease (PD) (44%), followed by dementia with Lewy bodies (DLB) (25%), and other forms of dementia and/or a-synucleinopathies (Ferini-Strambi et al., 2019).

The existence of a close relationship between iRBD and neurodegeneration is supported by the identification of several biomarkers of neurodegeneration in iRBD, such as reduced dopamine transporter binding (Iranzo et al., 2017), cortical atrophy (Campabadal et al., 2020), impaired colour vision (Li et al., 2019), hyposmia (Iranzo et al., 2021), electroencephalographic changes (Roascio et al., 2022), autonomic instability (Rocchi et al., 2018; Terzaghi et al., 2022), and cognitive impairment (Arnaldi et al., 2021; Terzaghi et al., 2013).

Among these in vivo markers of neurodegeneration, assessment of cognitive function seems to be one of the most promising methods for identifying possible phenoconversion in iRBD patients: mild cognitive impairment (MCI) detected on neuropsychological evaluation showed a hazard ratio (HR) for phenoconversion of 2.37, with only abnormal quantitative motor testing, objective motor examination, and olfactory deficit showing a higher HR (Postuma et al., 2019). The presence of MCI in iRBD patients at baseline evaluation seems to predict a higher and faster rate of conversion to a dementia-first versus a parkinsonism-first phenotype (Marchand et al., 2017). In the same cohort, it was shown that 94% of iRBD patients who developed DLB had received a diagnosis of MCI on average 3.3 years before the onset of dementia, and had shown clear deficits in attention and executive functions even at their first assessment, up to 6 years before conversion (Marchand et al., 2018). In addition, cognitive deficits in the prodromal stages may evolve differently between DLB and PD convertors, with the former showing significant progressive impairment on verbal episodic learning and memory tests, and the latter predominantly attentive and executive deficits no earlier than 2 years before diagnosis (Marchand et al., 2018).

The aim of the present review was to evaluate whether phenoconversion of iRBD into neurodegenerative disease can be predicted on the basis of quantitative and qualitative neuropsychological assessment and, if so, whether neuropsychological profiles at baseline differ according to clinical evolution.

2 | METHODS

2.1 | Protocol

The study protocol was drawn up, formulating the review questions and establishing the eligibility criteria, primary outcome, search strategy, data extraction methods, and methods for assessing the study quality and risk of bias.

Longitudinal case–control studies and cohort studies on neuropsychological assessment in RBD were eligible for inclusion. Reviews and systematic reviews were excluded.

No study or participant was excluded on the basis of ethnicity.

Participants had to be adults (>18 years) with iRBD or RBD preceding a diagnosis of PD, DLB, or multiple system atrophy (MSA) (Population).

The iRBD diagnosis had to meet the diagnostic criteria for RBD according to the 2nd or 3rd edition of the International Classification of Sleep Disorders (American Academy of Sleep Medicine, 2005, 2014).

For PD, DLB, and MSA respectively, diagnoses had to meet:

- the UK PD Society Brain Bank criteria (Hughes et al., 1992);
- the DLB Consortium guidelines (McKeith et al., 2017);
- the second consensus statement on the diagnosis of MSA (Gilman et al., 2008).

Exclusion criteria were neurological diseases other than a-synucleinopathies and the presence of neurological comorbidities and/or sleep disorders other than RBD.

We extracted neuropsychological data, including MCI diagnosis and neuropsychological test scores (raw and *z*-scores), the presence of a quantitative and qualitative neuropsychological assessment and, if so, whether neuropsychological profiles at baseline differ according to clinical evolution (Intervention).

The primary outcome consisted of phenoconversion of iRBD into neurodegenerative disease (Outcome).

2.2 | Search strategy

We performed a systematic search on PubMed, EMBASE, Web of Science and Scopus databases, retrieving publications in English, French, Italian, and Spanish, published from inception to May 2022, on the neuropsychological profile in iRBD. Papers were selected in accordance with the PRISMA guidelines (PI(C)O model) (Page et al., 2021).

The search strategy was built using a free-text search and thesaurus descriptors search (MeSH and Emtree) (see appendix in Data S1), adapted by a librarian for all the selected databases and then we managed the retrieved results using a reference manager.

2.3 | Data extraction and analysis

After a critical reading of the articles, two investigators (G.F. and M.T.) independently verified the eligibility and performed data extraction according to the inclusion criteria listed above. A third participant (C.C.) was consulted to discuss and settle any disagreements.

The following items were extracted from each study: first author's last name, publication date, country of origin, title, abstract, neuropsychological test scores and *z*-scores, diagnosis of MCI, neuropsychological tests and cognitive domains assessed, number of subjects included and related clinical variables: age, gender distribution, RBD and follow-up duration, phenoconversion (number and types).

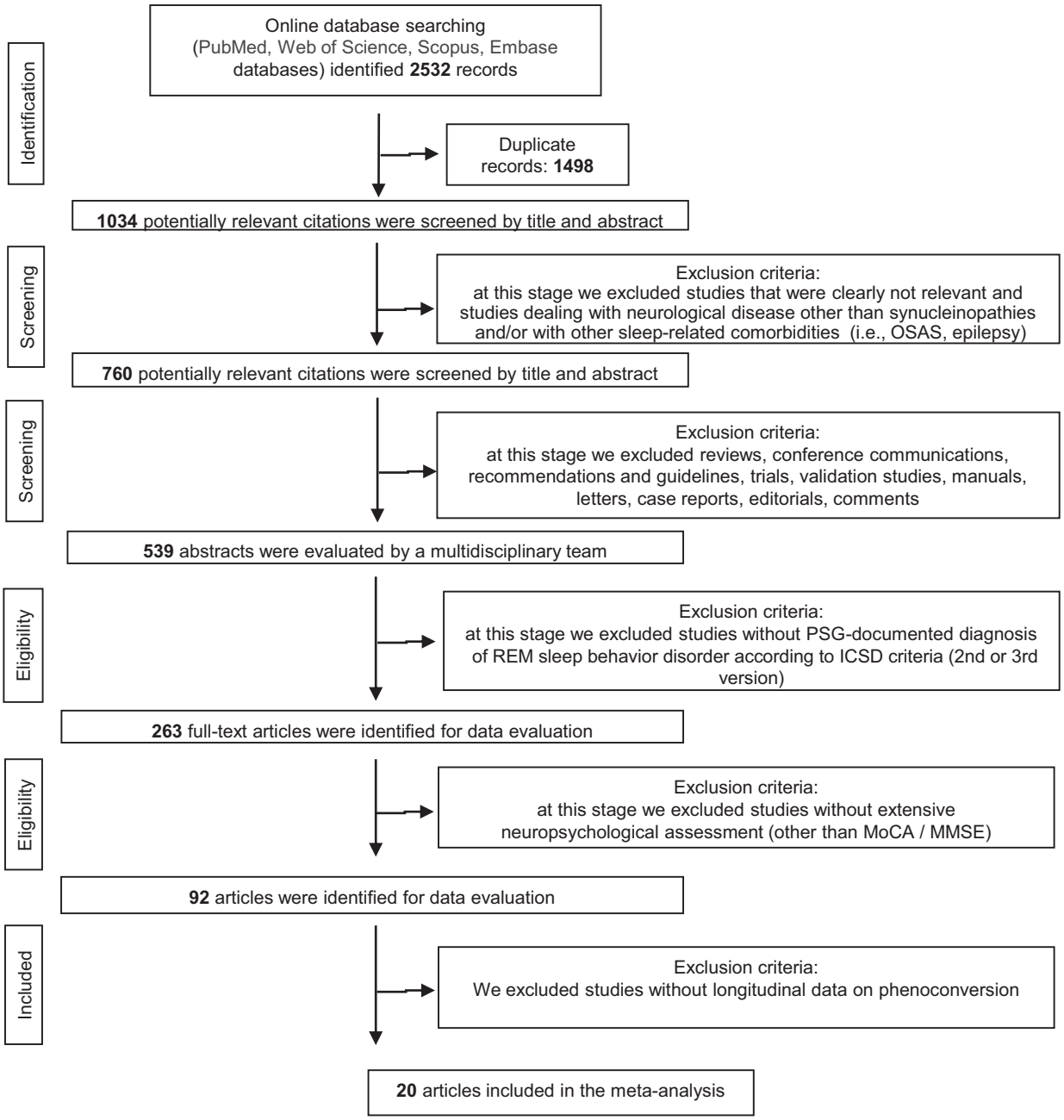


FIGURE 1 Flow chart for inclusion/exclusion of references. The flow diagram depicts the numbers of records identified, included and excluded according to the stated criteria. ICSD, International Classification of Sleep Disorders; MoCA, Montreal cognitive assessment; MMSE, mini-mental state examination; OSAS, obstructive sleep apnea syndrome; PSG, polysomnography

Figure 1 shows the complete flowchart of the search and selection process, conducted in accordance with the PRISMA statement (Page et al., 2021).

Stata 17.0 (StataCorp, USA) was used for statistical analysis. Categorical variables were described as count and percentage, and quantitative variables as mean and standard deviation, or median and interquartile range. Violin plots (i.e., modified box plots that add plots of estimated kernel density to the summary statistics displayed by box plots) were used to represent the number of tests per domain.

3 | RESULTS

3.1 | Study selection and characteristics

Our database search strategy yielded, for consideration, 2532 records published between 2006 and 2022 (Figure 1).

Following elimination of 1498 duplicates, 1034 citations were potentially relevant and therefore screened by title and abstract: 495 were excluded on the basis of the selection/exclusion criteria, while 539 were reviewed by a multidisciplinary team, who, using an

TABLE 1 Summary table of the included studies, with demographic and clinical features of the subjects, available data on phenoconversion, and results on the role of biomarkers in predicting phenoconversion, including (last column) remarks on neuropsychological tests

Authors	Cohort origin	Study design	Subjects (no.)	Controls (no.)	Age (years)	Males, no. (%)	RBD duration (years)	Duration of FU (years)	Converted no. (%)	PD	DLB	MSA	Other	Predictive markers	Single predictive NPS tests
Iranzo et al. (2006)	Barcelona, Spain	R	44	-	74.1 (6.5)	39 (89)	11.5 (5.0)	5.1 (2.7)	16 (36.4)	9	6	1	-	-	-
Postuma et al. (2009)	Montreal, Canada	P	67	-	iRBD: 73.2 (2.0) converted: 74.5 (2.0)	iRBD: 73.2 (1.9) converted: 74.5 (2)	iRBD: NA. converted: 11.6 (1.5)	iRBD: NA. converted: 7.5 (1.2)	17 (25.4)	6	11	-	-	-	-
Fantini et al. (2011)	Milan, Italy	P	24	12	69.5 (7.3)	18 (75%)	7.6 (7.3)	2.19 (0.42)	3 (12.5)	3	-	-	-	-	-
Iranzo et al. (2013)	Barcelona, Spain	P	44	-	74.1 (6.5)	39 (89)	-	10.5. range 2–16	15 (34.1)	7	8	-	-	-	-
Terzaghi et al. (2013)	Pavia, Italy	P	20	20	66.1 (7.1)	19 (95)	7 (8.5)	43 (18.8)	5 (25.0)	2	-	1	2[a]	-	-
Sakurai et al. (2014)	Tokyo, Japan	P	9	-	71.1 (3.2)	7 (77.8)	6.5 (5.1)	1.9 (0.77)	0	-	-	-	-	-	-
Youn et al. (2016)	Seoul, South Korea	R	84	57	66 (4.88)	40 (70.2)	-	4.24 (2.11)	18 (21.4)	9	4	1	4 #	-	TMT-A ($p = 0.004$) word list recall ($p = 0.035$)
Marchand et al. (2017)	Montreal, Canada	P	76	30	67.36 (7.13)	56 (74%)	8.66 (9.20)	3.59 (2.36)	34 (45)	17	15	2	-	A trend ($p = 0.09$) for MCI. MCI diagnosis in 93% of dementia-first vs 42% of parkinsonism-first cases ($p = 0.002$).	SCWT, TMT-B, ROCF copy predictive of dementia-first compared with parkinsonism-first. On logistic regression analysis, the best tests predictive of dementia were TMT-B and ROCF copy
Marchand et al. (2018)	Montreal, Canada	P	109	36	70.74 (7.11)	79 (73)	12.36 (9.40)	6	38 (35)	20	18	-	-	-	DLB: TMT-B up to 6 years; SeF from year 2; RAVLT immediate recall from year 6; RAVLT sum of trials and delayed recall from year 2
Alotaibi et al. (2019)	Montreal, Canada	P	101	-	69.1 (7.8)	77 (76.3)	7.8 (8.0)	1.2 or 3	0	-	-	-	-	-	-
Shin et al. (2019)	Seoul, South Korea	P	25	13	69.6 (5.8)	13 (52)	4.2 (3.0)	2 (0)	0	-	-	-	-	Olfactory impairment predicts cognitive decline in iRBD	-

TABLE 1 (Continued)

Authors	Cohort origin	Study design	Subjects (no.)	Controls (no.)	Age (years)	Males, no. (%)	RBD duration (years)	Duration of FU (years)	Converted no. (%)	PD	DLB	MSA	Other	Predictive markers	Single predictive NPS tests
Terzaghi et al. (2019)	Pavia, Italy	P	67	-	66.46 (6.83)	55 (87.3)	14.54 (19.05)	6.7 (3.8)	30 (44.8)	19	7	4	-	MCI (12% in disease free vs. 50% in converters), no differences in MCI subtype. Executive functions were correlated with phenoconversion on multivariate analysis	No single test showed association with phenoconversion
Campabadal et al. (2020)	Barcelona, Spain	P	14	18	70.1 (6.9)	11 (78.6)	4.5 (3.4)	1.6 (0.3)	0	-	-	-	-	-	-
Arnaldi et al. (2021)	Genoa, Italy	P	44	-	68.5 (7.2)	38 (86.4)	iRBD-NC: 45.8 (37); iRBD-MCI: 30.9 (30.4)	2.55 (1.79)	10 (22.7)	5	5	-	-	The combination of OH, UPDRS-I, DaTSCAN + and VM/VA on a GLM logistic regression (HR 26.05) showed no power in discriminating phenoconversion types	-
Shin et al. (2021)	Seoul, South Korea	P	30	24	69.6 (5.5)	16 (53.3)	4.2 (2.9)	3.02 (NA)	12 (40.0)	7	4	1	-	FDG-PET dnPDRBD-RP predicted conversion, the same metabolic pattern correlated with ROCF	-
Sumi et al. (2022)	Shiga, Japan	R	36		75	32 (88.9)	Median 5.23 (range 3.11–8.86)	Median 2.5 (range 1.28–2.74)	5 (13.9)	2	3	-	-	Higher rate of conversion in subjects with minor hallucinations	-
Yoo et al. (2021)	Seoul, South Korea	P	44	13	iRBD-NC 70 (6); iRBD-MCI 71 (6)	iRBD-NC 11 (46); iRBD-MCI 12 (60)	iRBD-NC 5.3 (4.9); iRBD-MCI 5.1 (4.2)	iRBD-NC 4 (1.41); iRBD-MCI 3.75 (1.58)	12 (27.0)	-	12	-	-	FDG-PET dnPDRBD-RP predicted cognitive deterioration (HR = 5.98)	-
Arnaldi et al. (2022)	Genoa, Italy	P	47	40	68.53 (7.16)	40 (85.1)	3.1 (1.5)	0.5	17 (36.2)	8	9	-	-	On multivariate Cox-regression analysis, putamen SBR and NPS-AT/WM tests predicted conversion (HR = 6.2)	TMT-B, as the single most efficient stratification tool, made it possible to reduce the number of eligible subjects to 76.6% (sensitivity 1, specificity 0.37) at post-hoc analysis

(Continues)

TABLE 1 (Continued)

Authors	Cohort origin	Study design	Subjects (no.)	Controls (no.)	Age (years)	Males, no. (%)	RBD duration (years)	Duration of FU (years)	Converted no. (%)	PD	DLB	MSA	Other	Predictive markers	Single predictive NPS tests
Roascio et al. (2022)	Genoa, Italy	P	18	-	69.7 (7.5)	17 (94.4)	-	2 (0.49)	4 (22.2)	3	1	-	-	-	-
Yoon et al. (2022)	Seoul, South Korea	P	40	24	iRBD-NC 69.1 (5.2). iRBD-MCI 70.5 (5.8)	iRBD-NC 10 (52.6). iRBD-MCI 11 (52.4)	iRBD-NC 5.8 (4.9). iRBD-MCI 4.0 (2.6)	4.2 (2.6)	12	7	4	1	-	FDG-PET hypometabolism in the medial occipital cortex, occipital pole and precuneus predicted phenoconversion to PD/DLB; MCI did not predict phenoconversion	-

Note: # 3 Alzheimer's disease, 1 spinocerebellar ataxia.

Abbreviations: AT/WM, attention/working memory; DaTSCAN, dopamine transporter scan; nPDRBD-RP, de novo Parkinson's disease with RBD-related pattern; DLB, dementia with Lewy bodies; FDG-PET, fluorodeoxyglucose-positron emission tomography; GLM, generalised linear model; FU, follow up; HR, hazard ratio; iRBD, isolated or idiopathic REM sleep behaviour disorder; MCI, mild cognitive impairment; MSA, multisystem atrophy; NA, not available; NC, normal cognition; NPS, neuropsychological; OH, orthostatic hypotension; P, prospective; PD, Parkinson's disease; R, retrospective; RAVLT, Rey auditory verbal learning test; ROCF, Rey-Osterrieth complex figure; SBR, striatal binding ratio; SCWT, Stroop colour-word test; SeF, semantic fluency; TMT, trail making test (–A and –B); UPDRS, unified Parkinson's disease rating scale; VM/VA, verbal memory/visuoconstructional abilities.

[a]Parkinsonian features not fulfilling criteria for a diagnosis.

abstract-based selection process, selected 263 full-text articles for data evaluation. Of these, 20 were finally included in our review (Alotaibi et al., 2019; Arnaldi et al., 2021, 2022; Campabadal et al., 2020; Fantini et al., 2011; Iranzo et al., 2006, 2013; Marchand et al., 2017, 2018; Postuma et al., 2009; Roascio et al., 2022; Sakurai et al., 2014; C. Shin et al., 2019; J. H. Shin et al., 2021; Sumi et al., 2022; Terzaghi et al., 2013, 2019; Yoo et al., 2021; Yoon et al., 2022; Youn et al., 2016).

Table 1, which lists all the selected papers, shows demographic and clinical variables of the iRBD cohorts considered. Overall, the present study included 899 patients from eight different cohorts and five countries (Canada [Alotaibi et al., 2019; Marchand et al., 2017, 2018; Postuma et al., 2009], Italy [Arnaldi et al., 2022, 2021; Fantini et al., 2011; Roascio et al., 2022; Terzaghi et al., 2013, 2019], Japan [Sakurai et al., 2014; Sumi et al., 2022], Spain [Campabadal et al., 2020; Iranzo et al., 2006, 2013], South Korea [C. Shin et al., 2019; J. H. Shin et al., 2021; Yoo et al., 2021; Yoon et al., 2022; Youn et al., 2016]).

3.1.1 | MCI

We explored the methodological differences between studies regarding inclusion, definition, and subclassification of MCI, as these variables might interfere with sample substratification. Of the 20 selected papers, 10 (50%) stratified iRBD patients according to the presence/absence of a diagnosis of MCI, which was made using various criteria: (1) at least two impaired tests in one or more cognitive domains (Arnaldi et al., 2021; Campabadal et al., 2020; Terzaghi et al., 2019); (2) at least one impaired test in a given cognitive domain (Iranzo et al., 2006, 2013); (3) at least two impaired tests in the same cognitive domain (Marchand et al., 2017; Terzaghi et al., 2013); (4) at least two impaired tests on the neuropsychological battery used in the study, regardless of cognitive domain (Yoo et al., 2021; Yoon et al., 2022). Four studies considered single vs. multi-domain MCI, and amnestic versus non-amnestic MCI (Iranzo et al., 2013; Marchand et al., 2017; Terzaghi et al., 2013, 2019). Iranzo and colleagues (Iranzo et al., 2013) considered MCI a conversion phenotype rather than a prodromal stage of phenoconversion (Table 2). The presence and quality of subjective cognitive complaint was not reported by any authors.

Different thresholds were used to define tests as impaired: (1) performance ≥1 to 2 SD below the standardised mean for the test (Arnaldi et al., 2021; Campabadal et al., 2020; Iranzo et al., 2006, 2013; Marchand et al., 2017), or (2) a pathological equivalent score of 0 or 1 on a five-point scale (Terzaghi et al., 2013, 2019).

Overall, data on tests and domains were not homogeneous enough to be pooled for meta-analysis.

3.1.2 | Cognitive domains

Cognitive domains are a widespread method for pooling different cognitive tasks in the same category for research and clinical purposes.

TABLE 2 Mild cognitive impairment (MCI) criteria, thresholds, and subgroups included in the extracted studies

Authors	Arnaldi et al. (2021)	Arnaldi et al. (2022)	Campabadal et al. (2020)	Marchand et al. (2017)	Iranzo et al. (2006)	Iranzo et al. (2013)	Terzaghi et al. (2013)	Terzaghi et al. (2019)	Yoo et al. (2021)	Yoon et al. (2022)
MCI criteria	≥2 impaired tests in 1 domain **or** ≥1 impaired test in at least two domains	≥2 impaired tests in 1 domain **or** ≥1 impaired test in at least two domains	≥2 impaired tests in 1 domain **or** ≥1 impaired test in at least two domains	≥2 impaired tests in 1 cognitive domain	≥1 impaired test in ≥1 cognitive domain	≥1 impaired test in ≥1 cognitive domain	≥2 impaired tests in 1 cognitive domain	≥2 impaired tests in 1 domain **or** ≥1 impaired test in at least two domains	≥2 impaired tests of the NPS battery used (regardless of domain)	≥2 impaired tests of the NPS battery used (regardless of domain)
Cut-off	1 ≤ SD ≤ 2 below the standardised mean[a]	1 ≤ SD ≤ 2 below the standardised mean[a]	1 ≤ SD ≤ 2 below the standardised mean	1 ≤ SD ≤ 2 below the standardised mean	1 ≤ SD ≤ 2 below the standardised mean	1 ≤ SD ≤ 2 below the standardised mean	ES 0 **or** 1 (5-point scale)	ES 0 **or** 1 (5-point scale)	1 ≤ SD ≤ 2 below the standardised mean	1 ≤ SD ≤ 2 below the standardised mean
aMCI versus na-MCI	No	No	No	Yes	No	Yes	Yes	Yes	N/A	N/A
sd-MCI versus md-MCI	No	No	No	Yes	No	Yes	Yes	Yes	N/A	N/A

Abbreviations: aMCI, amnestic MCI; ES, equivalent score; md-MCI, multiple-domain MCI; N/A, not applicable; na-MCI, non-amnestic MCI; SD, standard deviation; sd-MCI, single-domain MCI.
[a]These authors used factor analysis with varimax rotation to minimise multicollinearity and to reduce the number of neuropsychological variables for further statistical analysis, applied to the baseline native neuropsychological measures. A conventional threshold of 0.4 or 0.5 was applied to factor loadings, to identify the group of variables mainly represented by each factor.

In 6 of the 20 studies analysed, the neuropsychological tests performed were not grouped into cognitive domains (Alotaibi et al., 2019; Sakurai et al., 2014; C. Shin et al., 2019; J. H. Shin et al., 2021; Sumi et al., 2022; Yoo et al., 2021). In the remaining 14, between three (six studies, 21.4%) (Arnaldi et al., 2021; Fantini et al., 2011; Marchand et al., 2018, 2017; Postuma et al., 2009; Youn et al., 2016) and seven (one study, 7.1%) (Terzaghi et al., 2013) cognitive domains were assessed.

A total of 15 author-defined cognitive domains were found to be assessed by only one neuropsychological test, 15 by 2, 13 by 3, 4 by 4, 7 by 5, 2 by 6, and 7 by 4. Domains evaluated using at least two neuropsychological tests numbered two in three studies (Arnaldi et al., 2021; Fantini et al., 2011; Postuma et al., 2009), three in four studies (Campabadal et al., 2020; Marchand et al., 2018, 2017; Youn et al., 2016), four in three studies (Iranzo et al., 2006, 2013; Terzaghi et al., 2013), and five in one (Terzaghi et al., 2019). Overall, 21 different terms were used to refer to the cognitive domains considered; nine of them were used only once (Figure 2). Among these author-defined domains, the most frequently used nomenclature across studies was "executive functions" (11/14 studies, 78.6%), followed by "visuospatial abilities" (8/14, 57.1%), "memory" (7/14, 50.0%), and "language" (5/14, 35.7%) and "attention and working memory" (5/14, 35.7%) (Figure 3).

3.1.3 | Clustering

The authors' cognitive domains were compared with those identified in the diagnostic criteria proposed by the Movement Disorder Society (MDS) for MCI in Parkinson's disease (PD-MCI) (Litvan et al., 2012), which were regarded as the gold standard for the neuropsychological assessment and test clustering into cognitive domains in Parkinson's disease. In three cases, two different cognitive domains were merged (i.e., "attention and executive functions" or "verbal memory/visuoconstructional abilities") (Arnaldi et al., 2021; Marchand et al., 2018, 2017); on the other hand, two author-defined domains from three studies (Iranzo et al., 2013, 2006; Terzaghi et al., 2013) did not correspond to any domain proposed (namely, "praxis", and "verbal fluency").

We then reclassified the authors' stated cognitive domains according to the five domains proposed by the PD-MCI criteria (Litvan et al., 2012). Those not referring to a single domain (Marchand et al., 2017, 2018; Terzaghi et al., 2019) were counted twice, that is, for each domain referred to. In the case of overlapping domains (Terzaghi et al., 2013), we decided to retain the domain that was qualitatively better evaluated in terms of number and appropriateness of tests and to exclude the other one (namely, "long-term verbal memory" was retained instead of "short-term verbal and spatial memory" for memory domain; "executive functions and non-verbal logic" instead of "verbal fluency" for executive function domain; "visuospatial abilities" instead of "visuoconstructional learning skills" and "visual search abilities" for visuospatial function domain).

In this way, we found that the most frequently assessed domains were "memory", "executive function", and "visuospatial function" (14/14, 100%), followed by "attention and working memory" (10/14, 71.4%) and "language" (5/14, 35.7%) (Figure 3).

3.1.4 | Cognitive testing

Finally, we focussed on single cognitive tests used across studies, in order to clarify which ones are more frequently used in this research field, and which have shown some potential in phenoconversion prediction.

Some tests were used widely across multiple studies. Semantic fluency (SeF) evaluation (free word naming by given category in a determined time span, usually 1 min) was used in every study considered except one (19/20, 95.0%). Other frequently used tests, all belonging to the "attention and working memory" domain, were the Stroop colour word test (SCWT) and its variants (16/20, 80.0%), the trail making test (TMT) part A and/or B (15/20, 75.0% and 16/20, 80.0%, respectively), and digit span (DS, 15/20, 75.0%). In the "memory" domain, the Rey auditory verbal learning test (RAVLT) was the most frequently used test (11/20, 55.0%) (Table 3). With the exception of DS, all the aforementioned frequently used tests may play a role either in predicting phenoconversion of iRBD generally (Arnaldi et al., 2022; Youn et al., 2016), or in distinguishing prodromal DLB from prodromal PD (Marchand et al., 2017, 2018) (see Table 1).

With regard to neuropsychological tests not proposed in the PD-MCI criteria, the Rey-Osterrieth complex figure test (ROCF) copy was the one most frequently used (10/20, 50%) (Table 4). This test is the only one of those listed in Table 4 that may predict conversion of iRBD into a dementia-first phenotype (Marchand et al., 2017). In studies providing information on clustering of tests, the ROCF copy was invariably assigned to the "visuospatial domain", although in three cases (30%), it was not assigned to any domain. The variant ROCF recall (5/20, 25%) was assigned to the "memory" domain in 80% of cases. Compared with the tests considered for PD-MCI assessment (Litvan et al., 2012), these tests appeared to be more consistently classified across studies. However, their use is much less frequent, meaning that this agreement is likely overestimated.

To evaluate whether authors assigned single neuropsychological tests to the appropriate cognitive domains, we again considered the classification (PD-MCI criteria) proposed by Litvan et al (Litvan et al., 2012) as reference: many differences were found between studies, especially when considering the "attention and working memory" domain (Table 3). Some of the aforementioned tests, namely SCWT, TMT-A, and TMT-B, were more frequently assigned to the "executive function" than to the "attention and working memory" domain (53.3% vs. 13.3%, 40% vs. 13.3%, and 50% vs. 12.5%, respectively). Overall, no single test was consistently assigned to the "attention and working memory" domain. Much broader agreement across studies was found

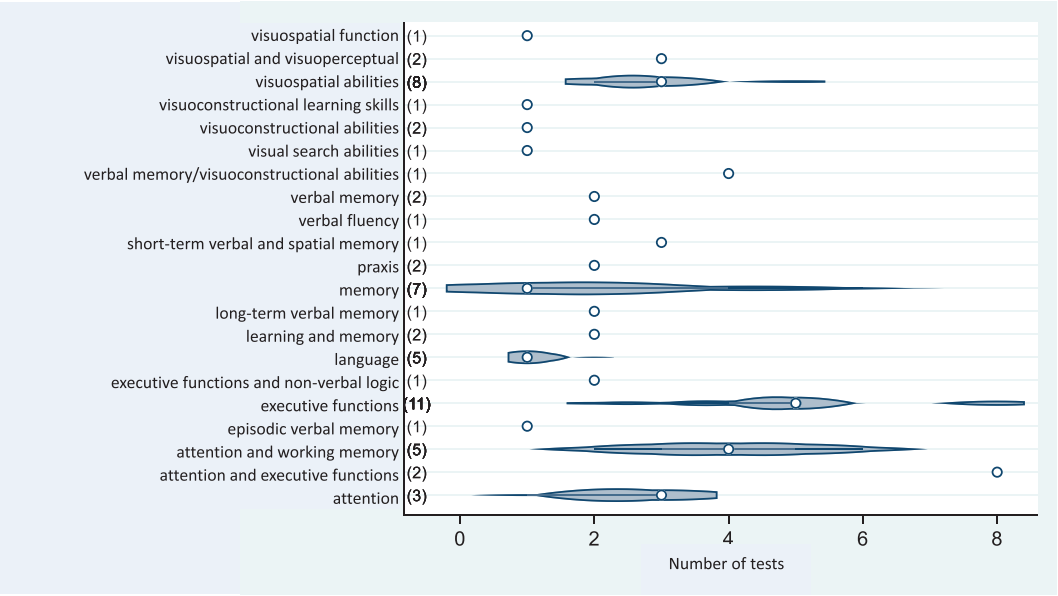
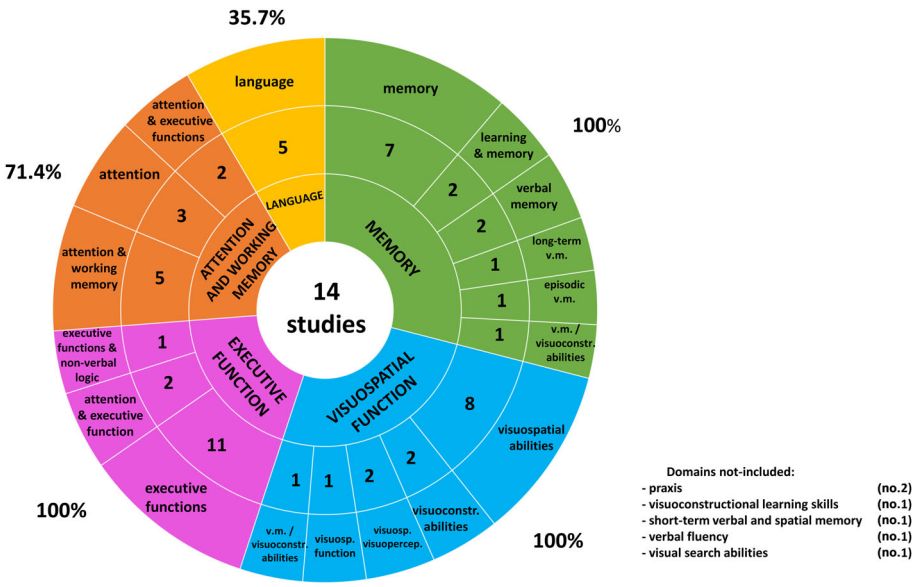


FIGURE 2 Graphic representation through violin plots of the different terms used by the authors to define cognitive domains (*y*-axis) and distribution of number of tests per domain (*x*-axis). A violin plot is a cross between a box plot and a kernel density plot that displays data peaks and it is used to show distribution and density of data; the values in the region of the thicker part have greater frequency. The small circle represents the median. The number in brackets is the number of studies in which a given term is used

FIGURE 3 Schematic view of the cognitive domains assessed by the authors. The inner circle shows the cognitive domains proposed in the PD-MCI criteria. The outer circle the domain names used by the authors, with the frequency (middle circle). Percentages show the overall frequency of each domain assessed in the extracted studies. Some domains (shown in the lower right corner) were not clustered as they were superfluous within the study in question or lacked unequivocal attribution (see main text). v.m., verbal memory; visuoconstr., visuoconstructional; visuosp., visuospatial; visuopercep., visuoperceptual



for "memory" and "visuospatial function". The "language" domain was mainly evaluated using the Boston naming test, which was correctly classified every time the authors clustered the tests in domains. Accuracy of assignment to the "executive function" domain, mainly evaluated through phonemic fluency (PhF) and SeF tests in our sample, was intermediate: PhF and SeF were correctly classified in 46.7% and 42.1% of studies, respectively.

Compared with the tests considered for the assessment of PD-MCI (Litvan et al., 2012), those not considered were classified more consistently across studies. However, their use is much less frequent, meaning that this agreement is likely overestimated.

3.1.5 | Current knowledge in iRBD phenoconversion prediction by cognitive assessment

As shown in Table 1, cognitive tests as predictive markers of iRBD phenoconversion, are reported in five out of the 20 selected studies. Namely, possible predictive tests pertaining to memory domain are the word list recall (Youn et al., 2016) and the RAVLT (Marchand et al., 2018). Regarding the RAVLT subscores, the immediate recall seems to be more sensitive than RAVLT sum of trials or the delayed recall, as it predicted DLB phenoconversion up to 6 years before diagnosis versus 2 years (Marchand et al., 2018). The study by Marchand

TABLE 3 Cognitive test domain assignment in the reviewed literature compared with the PD-MCI criteria (Litvan et al., 2012)

			Test domain according to authors							
Cognitive domain (PD-MCI criteria)	**Test**	**No. studies**	**Attention/working memory (%)**	**Executive function (%)**	**Language (%)**	**Memory (%)**	**Visuospatial function (%)**	**Merged domain (%)**	**NA (%)**	**Author-defined domain name (n°)**
Attention and working memory	SDMT	7	**57.1**	28.6	-	-	-	-	14.3	Executive functions (2) Attention and working memory (2) Attention (2) -NA (1)
	DS	14	**50**	7.1	-	14.3	-	14.3	14.3	Attention (3) Attention and working memory (4) Attention and executive functions[b] (2) Executive functions (1) Memory (2) Short-term verbal and spatial memory[a] (1) NA (2)
	SCWT/SCT	15	**13.3**	53.3	-	-	-	13.3	20	NA (3) Attention and working memory (2) Executive functions (8) Attention and executive functions[b] (2)
	TMT-A	15	**13.3**	40	-	-	6.7	20	20	NA (3) Executive functions (6) Attention and working memory (2) Attention and executive functions[b] (3) Visuospatial abilities (1)
	TMT-B	16	**12.5**	50	-	-	-	12.5	25	NA (4) Executive functions (8) Attention and working memory (2) Attention and executive functions[b] (2)
Executive function	WCST	1	-	**100**	-	-	-	-	-	Executive functions and non-verbal logic (1)
	PhF	15	6.7	**46.7**	-	-	-	13.3	26.7	NA (4) Executive functions (7) Attention and executive functions[b] (2) Attention and working memory (1) Verbal fluency[a] (1)
	SeF	19	10.5	**42.1**	-	-	5.3	10.5	26.3	NA (5) Attention and working memory (2) Executive functions (8) Attention and executive functions[b] (2) Verbal fluency[a] (1) Visuospatial abilities (1)
	Tower of London	1		**0**					100	NA (1)
Language	BNT	6	-	-	**66.7**	-	-	-	33.3	Language (4) NA (2)
	Similarities (WAIS-III)	2	-	100	-	-	-	-	-	Executive functions (2)
Memory	Story recall	3	-	-	-	**100**	-	-	-	Memory (1) Verbal memory (2)
	FCSRT	2	-	-	-	**100**	-	-	-	Memory (2)
	Word list recall	1	-	-	-	**100**	-	-	-	Memory (1)

TABLE 3 (Continued)

Cognitive domain (PD-MCI criteria)	Test	No. studies	Test domain according to authors: Attention/working memory (%)	Executive function (%)	Language (%)	Memory (%)	Visuospatial function (%)	Merged domain (%)	NA (%)	Author-defined domain name (n°)
	RAVLT	11	-	-	-	**72.7**	-	9.1	18.2	NA (2) Memory (2) Learning and memory (2) Episodic verbal memory (1) Long-term verbal memory (1) Verbal memory/ visuoconstructional abilities (1)[b] Verbal memory (2)
	Logical memory	3	-	-	-	**66.6**	-	-	33.3	NA (1) Memory (1) Long-term verbal memory (1)
Visuospatial function	BJLO	3	-	-	-	-	**100**	-	-	Visuospatial abilities (2) Visuospatial and visuoperceptual (1)
	Clock test	6	-	-	-	-	**83.3**	16.7	-	Verbal memory/visuoconstructional abilities[b] (1) Visuospatial abilities (5)

Note: The grey area shows rates of agreement between authors' assignments and proposed criteria. When a test was assigned to a merged domain, it was considered separately as it was not possible to assess the intentions of the authors. When the test was not assigned to a domain, it was counted in the "not available" (NA) category.

Abbreviations: BJLO, Benton judgement of line orientation; BNT, Boston naming test; DS, digit span; FCSRT, free and cued selective reminding test; PhF, phonemic fluency; RAVLT, Rey auditory verbal learning test; SCT, Stroop colour test; SCWT, Stroop colour word test; SDMT, symbol digit modalities test; SeF, semantic fluency; TMT-A, trail making test, A; TMT-B, trail making test, B; WAIS-III Wechsler adult intelligence scale-III; WCST, Wisconsin card sorting test.

[a]Domain not included in PD-MCI criteria.

[b]Merged domain.

TABLE 4 Frequency of cognitive tests included in the studies and not proposed in the PD-MCI criteria, together with most frequent domain assignment and authors' terms for the relevant cognitive domains

Test	No. papers	Most frequent assignment domain	% of cases in which the test is not included in any defined domain	Authors' nomenclature
ROCF copy	10	Visuospatial function (70%)	30	Visuoconstructional abilities (20%) Visuospatial abilities (30%) Visuospatial and visuoperceptual (10%) Visuospatial function (10%)
Corsi test	7	-	-	Executive functions (28.6%) Memory (28.6%) Attention and working memory (28.6%) Short-term verbal and spatial memory (14.3%)
Constructional praxia	6	Visuospatial function (66.7%)	-	Visuospatial abilities (66.7%) Praxis (33.3%)
ROCF recall	5	Memory (80%)	-	Memory (40%) Learning and memory (40%) Visuoconstructional learning skills (20%)
Block design (WAIS-IV)	5	Visuospatial function (60%)	-	Visuospatial abilities (40%) Praxis (40%) Visuospatial and visuoperceptual (20%)
SVLT	4	Memory (25%%)	75	Memory (25%)
Raven matrices	3	Executive function (100%)	-	Executive functions (66.6%) Executive functions and non-verbal logic (33.3%)
Bells test	3	Visuospatial function (100%)	-	Visuospatial abilities (66.6%) Visuospatial and visuoperceptual (33.3%)
Attentional matrices	3	-	-	Executive functions (33.3%) Attention and working memory (33%) Visual search abilities (33%)
Visual span (From WMSr)	2	Attention and working memory (100%)	-	Attention (100%)
Word span	2	-	-	Attention and working memory (50%) Short-term verbal and spatial memory (50%)
VOSP	2	Visuospatial function (100%)	-	Visuospatial abilities (100%)
WST	1	Executive Function	-	Executive functions
Sartori	1	Language	-	Language
VFD	1	Visuospatial function	-	Visuospatial and visuoperceptual
FRT	1	Visuospatial function	-	Visuospatial and visuoperceptual
Figure copy (no ROCF)	1	merged domain ("Verbal memory/ visuoconstructional abilities")	-	Verbal memory/visuoconstructional abilities
VPTA	1	-	100	-
ADAS-Jcog	1	-	100	-
Token	1	-	100	-

Abbreviations: ADAS-Jcog, Alzheimer's disease assessment scale – cognitive subscale Japanese version; FRT, facial recognition test; ROCF, Rey-Osterrieth complex figure; SVLT, Seoul verbal learning test; VFD, visual form discrimination; VOSP, visual object and space perception battery; VPTA, visual perception test for agnosia;WAIS-III Wechsler adult intelligence scale-III; WCST, Wisconsin card sorting test; WMSr, Wechsler memory scale-revised; WST, Weigl's sorting test.

and colleagues (Marchand et al., 2018) also showed a predictive role for TMT-B, as also reported by Arnaldi et al. (2022), and the same authors in a previous paper (Marchand et al., 2017), along with the SCWT and ROCF copy task. Youn et al. (2016) reported a possible predictive role for TMT-A variant. In the study by Arnaldi et al. (2022), the pooled score for the "attention and working memory" domain (assessed with TMT-A and B, Symbol digit, Corsi span, and SeF) could predict iRBD phenoconversion. Overall, deficits in the "attention and

working memory" domain are the most accounted across the studies as predictive of iRBD phenoconversion.

The only paper that explored the differences in the prediction of PD versus DLB phenoconversion by means of specific cognitive tests is by Marchand et al. (2018), in which DLB was preceded by more deficit in TMT-B, SeF, and RAVLT immediate recall compared with Parkinson's disease subjects, who showed an impairment in attention and executive function no sooner than 2 years before diagnosis.

Two of the 20 selected studies reported higher rates of MCI diagnosis at baseline in converters, and highlighted its utility in predicting later phenoconversion (Marchand et al., 2017; Terzaghi et al., 2019).

DLB and PD converters differed also for baseline MCI rates (93% for dementia-first vs. 42% for parkinsonism-first) (Marchand et al., 2018).

4 | DISCUSSION

Cognitive impairment is well known to be a marker of state, of progression of underlying neurodegeneration, and of impending phenoconversion to a defined neurodegenerative disease (Natale et al., 2022). The aim of this study was to clarify, through a review of the literature, the role of cognitive deficits as predictive markers of iRBD phenoconversion to synucleinopathies, namely to evaluate whether phenoconversion of iRBD into neurodegenerative disease can be predicted on the basis of quantitative/qualitative neuropsychological assessment and whether neuropsychological profiles differ according to clinical evolution.

In the light of our extensive literature selection process, which resulted in the extraction of 20 longitudinal studies, both research aims remain unsolved due to the huge heterogeneity of the current literature on cognitive assessment as a marker of iRBD conversion We compared the various methods of neuropsychological data collection and categorisation used, and discuss here the differences found between them and why they prevent further statistical comparison.

4.1 | Mild cognitive impairment

The term MCI is used by clinicians to indicate the intermediate phase between normal cognition and dementing diseases (Winblad et al., 2004). It was introduced nearly 30 years ago (Flicker et al., 1991), in reference to the prodromal phase of Alzheimer's disease (AD). The definition of MCI has been revised several times. Initially considered a pure memory complaint, MCI is now understood to be into a much broader cognitive complaint (Albert et al., 2011; American Psychiatric Association, 2013) that deserves attention and proper neuropsychological evaluation, not least because it has been observed that not all affected patients developed Alzheimer's disease, but rather that different dementias could arise (Payne et al., 2022). Comprehensive age- and education-adjusted neuropsychological test batteries meet the need for objective assessment of cognitive deficits in this setting.

The DSM-V classification (American Psychiatric Association, 2013) includes six cognitive domains: learning and memory, attention, language, executive function, perceptual-motor function, and social cognition. While social cognition is seldom investigated outside specific research settings, it is generally recommended that the other five domains be included in an extensive neuropsychological evaluation (Boccardi et al., 2021). However, to date, no gold standard neuropsychological assessment battery has been established.

Through clustering of neuropsychological tests into cognitive domains, MCI can be evaluated and classified into subtypes: amnestic versus non-amnestic, and single-domain versus multiple-domain MCI (Petersen, 2004). Identification of a patient's MCI subtype provides insights into the likely underlying substrate. Indeed, although the evidence is limited, significant differences in cognitive deficits and related MCI subtypes exist between the prodromal stages of AD versus DLB or PD-MCI, which primarily affect memory and attention/executive/visual performance, respectively (Boeve, 2012; Molano et al., 2010).

However, further classification of MCI raises diagnostic challenges (Jak, Urban, et al., 2009), and to date, we lack a universally accepted approach to MCI subclassification (Jak, Bondi, et al., 2009). The main differences between existing approaches concern cut-offs (ranging from 1 SD to 2 SD) or the use of percentiles (pathological scores), the definition of MCI (i.e., the number of tests within given domains that need to be impaired), and the minimum number of cognitive domains that need to be affected in order to diagnose MCI.

We found that only 10 (50%) studies used established diagnostic criteria to determine the presence of MCI, and that these criteria varied from study to study.

Further MCI subtype assessment was carried out in 4/10 studies (40%, 20% of the overall sample). PD-MCI criteria were used in three of these, of which only one reached the recommended level II of assessment (at least two tests per domain) (Terzaghi et al., 2019). It is worth mentioning that Terzaghi et al. identified a role for MCI diagnosis in predicting phenoconversion based on the PD-MCI criteria (Terzaghi et al., 2019). However, a possible drawback of the neuropsychological battery they used is the uneven distribution of tests per domains, with the number ranging from two to five (Terzaghi et al., 2019).

Jak and colleagues (Jak, Bondi, et al., 2009) compared five different MCI classifications, finding a lack of agreement between the criteria in up to 59% of the individuals assessed and diagnostic instability in a substantial minority of them over time. Since use of the one-test-one-domain approach to define impaired domains leads to a higher proportion of false-positive diagnoses, the authors suggested that the use of either comprehensive (cut-off 1 SD, ≥2 impaired tests in a given domain, up to two impaired domains) or conservative criteria (1.5 SD, ≥2 tests in a given domain, up to two impaired domains) might be a much more valid strategy than other approaches. In another study, the comprehensive approach demonstrated a better balance of sensitivity and reliability (Jak, Urban, et al. 2009). Furthermore, compared with the approach of Petersen and Morris (Petersen, 2004), comprehensive criteria showed a better ability to

distinguish between non-amnestic and amnestic presentations (Petersen & Morris, 2005). Overall, Jak/Bondi's neuropsychological assessment criteria for MCI seemed to be preferable, especially when forms of neurodegeneration other than Alzheimer's disease are suspected (Bondi, 2014).

The problem of different levels of certainty between MCI diagnostic criteria has also been highlighted by the MDS, which proposed a two-level assessment for PD-MCI diagnosis (Litvan et al., 2012). According to this proposal, level I (*abbreviated*) assessment for possible PD-MCI does not allow complete subtyping of PD-MCI, whereas a *comprehensive* or level II assessment must involve the evaluation of five cognitive domains, with at least two tests per domain (i.e., the use of an at least 10-test neuropsychological battery), to allow adequate MCI subclassification. They also stressed the importance of balanced evaluation across domains, that is, of evaluating each domain with the same number of tests. However, a recognised limitation of the PD-MCI criteria is the lack of definite cut-offs, which means that their sensitivity in the definition of MCI might still vary across studies.

Overall, with the rationale that iRBD belongs to the spectrum of synucleinopathies, and considering that the cognitive deficits seen in iRBD subjects reflect those seen in full-blown DLB, PD-MCI, or PD dementia (Biundo et al., 2016; Ferini-Strambi et al., 2019; Martini et al., 2020), it seems more appropriate that MCI be defined according to PD-MCI criteria, despite the presence of margins of uncertainty in the definition of cut-offs and of evolutivity (Biundo et al., 2016).

In our discussion, we have taken into consideration only objective and quantitative measures for MCI definition. However, MCI is generally defined also by the presence of subjective cognitive complaints. In the included studies there are no published data about presence, details and quality of subjective cognitive complaint in the iRBD population, In our opinion, this datum should be included in the longitudinal cognitive assessment of any neurodegenerative condition, since subjective complaints frequently precede objective fails on cognitive tests and might allow earlier categorisation of iRBD subtypes and help to predict later phenoconversion,

4.2 | Cognitive domains

In clinical neuropsychology, cognitive domains are important in test clustering and in the classification of MCI or of subclinical deficits detected within the range of normal cognition. In this setting, cognitive performance is characterised and classified by domains. Cognitive domains are defined mainly on the basis of regional brain functions (i.e., data derived from lesion studies) or hierarchical criteria, that is, complexity of operations (Harvey, 2019). As mentioned above, a comprehensive neuropsychological assessment requires evaluation of five cognitive domains, which Boccardi et al. identify as: learning and memory, attention, language, executive function, and perceptual-motor function (Boccardi et al., 2021). Indeed, although there is a generally broad consensus on the nature of most of these domains, there are also clear inconsistences (Harvey, 2019), as reflected in the considerable variability, both across studies and in the studies herein reviewed, in the names given to them.

In view of the observed evolution of iRBD toward a-synucleinopathies, we deemed the PD-MCI criteria (Litvan et al., 2012) to be the most appropriate to use in seeking to achieve a common language for the assessment of cognitive domains in RBD. When we tried to cluster the authors' stated cognitive domains into the five considered in the PD-MCI criteria (language, memory, visuospatial function, executive function, attention, and working memory), we found that at least three different author-defined domains corresponded to each of them, except for "language", which was assessed in only 35.7% of the studies. In some cases, domains proposed by authors could not be included in the clustering procedure as they were overlapping.

This inconsistency was greatest in the authors' various definitions of "executive function" and "attention and working memory", which are broad cognitive domains referring to complex tasks that depend on the association of simpler functions and/or sensory modalities, whose brain networks are not well defined. In this framework, some functional overlap does exist and could lead to ambiguous definition of domains. Notably, Marchand et al. (2017, 2018) merged the above two domains in a single category ("attention/executive functions"), a choice that highlights the difficulty of interpreting and differentiating between the relevant cognitive functions. In this case, it is difficult to ascertain whether and to what extent "attention" and "executive functions", respectively, contribute to deficits in this domain, and thus how important they are in defining MCI in iRBD.

Similarly, the memory domain was not clearly named in the studies analysed, in which six different definitions were used; although, memory function as a whole was found to be well-characterised, many subfunctions were considered and described, which seems to explain the domain name variations observed (episodic or declarative memory, encoding, retrieval, etc.) (Gliebus, 2018).

Different definitions were also used to indicate visuospatial function, although in this case the different terms adopted clearly referred to subfunctions generally acknowledged to be part of visuospatial function (i.e., visual search abilities, visuoconstructional learning skills) (Possin, 2010).

The only domain univocally defined was language; this may be because there is a standardised definition in the literature, which includes consistent definitions of the functions, subdomains and brain areas involved (Richardson & Dalton, 2022). However, this domain was assessed in only five studies.

It is important to achieve clear definitions of specific domains, but it is equally important to define pathological performance within them: as already mentioned, sensitivity is increased when at least two tests are assessed for a given domain (Jak, Bondi, et al., 2009). In our review, 15 author-defined cognitive domains were found to be assessed by only one neuropsychological test, and therefore lack reliability.

Overall, the approach considered optimal for comprehensive neuropsychological assessment (Jak, Bondi, et al. 2009; Litvan et al., 2012), namely evaluation of the five cognitive domains as

proposed by the MDS in the PD-MCI criteria, each one assessed by no less than two cognitive tests, was adopted in only one of the analysed studies (Terzaghi et al., 2019). It therefore seems that, even though there is growing attention to cognition in iRBD, most of the works in the literature, failing to refer to these criteria, lacked reliability in terms of sensitivity and accuracy.

4.3 | Tests

Cognitive tests are essential tools for the evaluation of neuropsychological deficits in different settings. The decision on which tests to include in the neuropsychological battery depends on many factors, such the aim of the evaluation, the raters' experience and confidence with specific tests, the target population and the time available for the assessment. Each neuropsychological laboratory chooses the most suitable neuropsychological battery according to its needs and aims. No standardised neuropsychological evaluation protocols are available for RBD specifically, making it difficult for research groups to share and compare data. The practice of clustering tests into cognitive domains could make it possible to overcome single test differences between studies, provided the clustering is standardised.

To assess agreement with regard to the cognitive tests used and their assignment to cognitive domains, we extracted all the tests used in the studies, and verified whether they were among those suggested in the PD-MCI reference criteria (Litvan et al., 2012); we also evaluated whether the authors assigned them to the same domains indicated in the PD-MCI criteria.

We found that some widely used tests, especially those that could play a significant role in predicting phenoconversion, were not unequivocally clustered into the different cognitive domains (Table 3).

The most divergent results concerned the SCWT and the TMT; both these tests were more frequently categorised in the "executive function" rather than the "attention and working memory" domain as proposed by the criteria.

The SCWT is considered one of the gold standards for measuring attention (Carone et al., 2007), although many studies highlight the complexity of its multifactorial structure; it evaluates several cognitive mechanisms, including verbal fluency, processing speed, reading skills, interference control, and cognitive flexibility (Periáñez et al., 2021). The exact contribution of each test subdomain to the overall SCWT score is an open question, making it difficult to choose which cognitive domain it should belong to and to interpret such choices. As for the TMT, there is evidence of involvement of multiple cognitive functions and activation of multiple brain regions during its execution. Graphomotor speed, visual scanning, but also executive function components, such as inhibition control and set-shifting, are involved (Llinàs-Reglà et al., 2017). Both the SCWT and the TMT have been shown to be reliable tools in predicting later conversion. In the cohort from Montreal, iRBD subjects who converted to a dementia-first phenotype recorded lower SCWT scores at baseline (Marchand et al., 2017). Similarly, TMT part B alone has been shown to be a good early predictive marker of DLB phenoconversion (Marchand et al., 2018), and it is the only test (either part A or B) shown to able to predict any kind of phenoconversion across multiple cohorts (Arnaldi et al., 2022; Marchand et al., 2017, 2018; Youn et al., 2016). However, the variable assignment of these tests to different cognitive domains across studies leads to different interpretations of the cognitive functions affected by the neurodegeneration process, that is, whether they reflect impairment of attentional or executive functions.

Other tests whose assignment to domains was not clear-cut across the studies were those evaluating SeF and PhF. The mechanisms that drive performance in these tasks are argued to rely on language (semantic level, phonological output lexicon, and assembly) and executive functions (set shifting, information updating and monitoring, inhibition of responses) (Rofes et al., 2020). Functional imaging studies of verbal fluency have demonstrated the involvement of a distributed brain network (Wagner et al., 2014). Hence, verbal fluency tests combine many sources of cognitive differences, and it is argued that their use as a cognitive measure may not be particularly useful as a research tool for the purpose of isolating specific mechanisms (Rofes et al., 2020).

Overall, although SCWT, TMT, and fluency tests are widely employed in neuropsychological batteries, it is currently far from possible, on the basis of current knowledge, to assign them unequivocally to a specific domain. We therefore suggest that they should not be used in cognitive domain classification until there is the necessary consensus. On the other hand, since preliminary results on the predictive power of these tests warrant further exploration, it is justified to include them in the longitudinal assessment of iRBD subjects.

Analysis of cognitive tests not proposed in the PD-MCI criteria (Table 3) showed that many were used widely across studies, with overall strong agreement on their domain assignment. Most of the tests were assigned to the "visuospatial function" domain. The most frequently used test was the ROCF (Rey, 1941), a longstanding test that is used widely in neuropsychology on account of its multidomain structure. The functions it explores, depending on the subtask considered, are attention and concentration, motor coordination, visuospatial perception, nonverbal memory, and executive skills (M. S. Shin et al., 2006). The test is widely employed in iRBD, and in one study a poor performance on ROCF copy was subsequently associated with a dementia-first phenoconversion (Marchand et al., 2017), confirming the utility of the test in prodromal cognitive evaluation in iRBD. Even though it is not included in the MDS criteria, the widespread use of the ROCF and the observation of a clear correspondence between ROCF subtasks and MDS domains (namely, ROCF copy and "visuospatial function"; immediate recall and "attention and working memory"; delayed recall and "memory") make it a reliable test for assessment of multiple domains and comparison between studies (M. S. Shin et al., 2006).

A large, comprehensive and standardised NPS battery for cognitive assessment of iRBD is lacking and needs to be created. The existing level II assessment for PD-MCI, is the natural reference approach, as it provides for subdivision of the assessment into definite cognitive domains and allows MCI subtype diagnosis (Litvan et al., 2012). In our selected studies, PD-MCI criteria were found to be used by many authors investigating the longitudinal course of iRBD, and are already

TABLE 5 Proposed neuropsychological battery with cognitive tests and their cognitive domain assignment for baseline and longitudinal assessment in iRBD, modified from the PD-MCI criteria and the results of the current review

Cognitive domain	Neuropsychological tests
Attention and working memory	Trail making test (A and B)
	Stroop colour-word test (SCWT)
	Digit span backward
Executive function	Raven matrices
	Wisconsin card sorting test (WCST)
	Verbal fluency (either letter fluency, or category fluency, or both)
Language	Boston naming test
	WAIS-IV (or previous versions) similarities
Memory	Rey's auditory verbal learning test (RAVLT)
	Free and cued selective reminding test (FCSRT)
	Prose recall test with delayed recall conditions (i.e., "Logical Memory" part of the Wechsler memory scale)
Visuospatial function	Rey-Osterrieth complex figure copy (ROCF)
	Visual object and space perception battery (VOSP)
	Clock test (copy)

Note: For a level II assessment (comprehensive), there must be included at least two tests for each domain, hence the battery is composed of at least 10 tests.

the most frequent choice for MCI assessment and categorisation. Moreover, although the criteria propose various tests for each domain, investigators can freely select the ones they wish to use, providing the number of tests used in each domain is the same. To allow multicentre and between-study comparisons of the data presented, the assignment of the chosen tests needs to be implemented in a standardised way across centres and studies.

Some tests more than others (namely TMT part A and/or B, RAVLT and its subitems, ROCF copy, SCWT, SeF) have shown a predictive role of cognitive impairment in iRBD, even though the data need further confirmation (Arnaldi et al., 2022; Marchand et al., 2017, 2018; Youn et al., 2016). To better understand their role in this setting, these tests should, in our opinion, be included in neuropsychological evaluation, even though their domain clustering is, in some cases, still questionable and needs to be clarified by consensus.

On the basis of these affirmations, the already established PD-MCI criteria, and the results of the current review, we propose a neuropsychological battery that may fulfill the scope of providing a comprehensive cognitive assessment through tests already widely used by researchers in the field of RBD and cognition (Table 5).

5 | LIMITATIONS

We are aware that some studies used overlapped samples as directly stated by the authors (Iranzo et al., 2006, 2013). Furthermore, the subjects from the 20 included studies come from eight different cohorts in five countries only. Therefore, we believe that the overlap entity might be more frequent, despite not being stated in all the studies by the same research group. This fact could have biased the reported results.

Secondly, as a direct consequence of the stated inclusion criteria for the primary aim of this review, we selected only longitudinal studies. Hence, our results and statements about using and/or rejecting specific tests for iRBD cognitive assessment lack an evidence-based revision on cross-sectional studies.

6 | CONCLUSIONS

Cognitive impairment is recognised as a promising candidate marker of state, of evolution and of type of phenoconversion in iRBD (parkinsonism- versus dementia-first pattern) (Natale et al., 2022). Cognitive assessment should be included as a standard evaluation, because MCI and even subtle cognitive deficits seem to indicate a higher risk of neurodegeneration and their identification could help clinicians in the risk stratification of subjects for inclusion in research protocols and clinical trials.

Research on neuropsychological deficits in iRBD is still far from standardised. However, the findings of our scoping review show that efforts to improve neuropsychological data acquisition in iRBD should focus on the following: choosing tests, assigning them to cognitive domains, establishing the minimum number of tests per domain, setting thresholds for defining objective deficits, and identifying criteria for defining MCI.

Given the considerable heterogeneity of current literature on cognitive assessment as a marker of iRBD evolution, a consensus among researchers is needed, probably within the framework of the International RBD Study Group.

AUTHOR CONTRIBUTIONS

Giuseppe Fiamingo and Michele Terzaghi selected the significant scientific literature for this review and gave the major contribution in the writing of this manuscript. Chiara Cerami and Dario Arnaldi reviewed the manuscript and provided major corrections and insights. Cristina Capittini, Annalisa De Silvestri, and Chiara Rebuffi conducted the database investigation and organised data presentation by means of tables and images. All authors read and approved the final manuscript.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interest.

ACKNOWLEDGEMENT

Open access funding provided by BIBLIOSAN.

DATA AVAILABILITY STATEMENT

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

ORCID

Giuseppe Fiamingo https://orcid.org/0000-0002-5030-6425

REFERENCES

Albert, M. S., DeKosky, S. T., Dickson, D., Dubois, B., Feldman, H. H., Fox, N. C., Gamst, A., Holtzman, D. M., Jagust, W. J., Petersen, R. C., Snyder, P. J., Carrillo, M. C., Thies, B., & Phelps, C. H. (2011). The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimer's & Dementia*, *7*(3), 270–279. https://doi.org/10.1016/j.jalz.2011.03.008

Alotaibi, F., Pelletier, A., Gagnon, J. F., Montplaisir, J. Y., & Postuma, R. B. (2019). Prodromal marker progression in idiopathic rapid eye movement sleep behavior disorder: Sample size for clinical trials. *Movement Disorders*, *34*(12), 1914–1919. https://doi.org/10.1002/mds.27869

American Academy of Sleep Medicine. (2005). *International classification of sleep disorders. Diagnostic and Coding Manual* (pp. 148–152). Author.

American Academy of Sleep Medicine. (2014). *International classification of sleep disorders* (3rd ed.). Author.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed., Vol. 21, pp. 591–643). Author.

Arnaldi, D., Chincarini, A., De Carli, F., Famà, F., Girtler, N., Brugnolo, A., Pardini, M., Massa, F., Meli, R., Schenone, C., Bauckneht, M., Morbelli, S., & Nobili, F. (2021). The fate of patients with REM sleep behavior disorder and mild cognitive impairment. *Sleep Medicine*, *79*, 205–210. https://doi.org/10.1016/j.sleep.2020.02.011

Arnaldi, D., Mattioli, P., Famà, F., Girtler, N., Brugnolo, A., Pardini, M., Donniaquio, A., Massa, F., Orso, B., Raffa, S., Bauckneht, M., Morbelli, S., & Nobili, F. (2022). Stratification tools for disease-modifying trials in prodromal synucleinopathy. *Movement Disorders*, *37*(1), 52–61. https://doi.org/10.1002/mds.28785

Biundo, R., Weis, L., & Antonini, A. (2016). Cognitive decline in Parkinson's disease: The complex picture. *Npj Parkinson's Disease*, *2*(1), 16018. https://doi.org/10.1038/npjparkd.2016.18

Boccardi, M., Monsch, A. U., Ferrari, C., Altomare, D., Berres, M., Bos, I., Buchmann, A., Cerami, C., Didic, M., Festari, C., Nicolosi, V., Sacco, L., Aerts, L., Albanese, E., Annoni, J.-M., Ballhausen, N., Chicherio, C., Démonet, J.-F., Descloux, V., … Consortium for the Harmonization of Neuropsychological Assessment for Neurocognitive Disorders. (2021). Harmonizing neuropsychological assessment for mild neurocognitive disorders in Europe. *Alzheimer's & Dementia*, *18*, 29–42. https://doi.org/10.1002/alz.12365

Boeve, B. F. (2012). Mild cognitive impairment associated with underlying Alzheimer's disease versus Lewy body disease. *Parkinsonism & Related Disorders*, *18*(Suppl 1), S41–S44. https://doi.org/10.1016/S1353-8020(11)70015-3

Bondi, M. (2014). Neuropsychological criteria for MCI improves diagnostic accuracy. *Journal of the Alzheimer's Association*, *42*(1), 275–289. https://doi.org/10.3233/JAD-140276.Neuropsychological

Campabadal, A., Inguanzo, A., Segura, B., Serradell, M., Abos, A., Uribe, C., Gaig, C., Santamaria, J., Compta, Y., Bargallo, N., Junque, C., & Iranzo, A. (2020). Cortical gray matter progression in idiopathic REM sleep behavior disorder and its relation to cognitive decline. *NeuroImage: Clinical*, *28*, 102421. https://doi.org/10.1016/j.nicl.2020.102421

Carone, D. A., Strauss, E., Sherman, E. M. S., & Spreen, O. (2007). A compendium of neuropsychological tests: Administration, norms, and commentary. *Applied Neuropsychology*, *14*(1), 62–63. https://doi.org/10.1080/09084280701280502

Fantini, M. L., Farini, E., Ortelli, P., Zucconi, M., Manconi, M., Cappa, S., & Ferini-Strambi, L. (2011). Longitudinal study of cognitive function in idiopathic REM sleep behavior disorder. *Sleep*, *34*(5), 619–625. https://doi.org/10.1093/sleep/34.5.619

Ferini-Strambi, L., Fasiello, E., Sforza, M., Salsone, M., & Galbiati, A. (2019). Neuropsychological, electrophysiological, and neuroimaging biomarkers for REM behavior disorder. *Expert Review of Neurotherapeutics*, *19*(11), 1069–1087. https://doi.org/10.1080/14737175.2019.1640603

Flicker, C., Ferris, S. H., & Reisberg, B. (1991). Mild cognitive impairment in the elderly: Predictors of dementia. *Neurology*, *41*(7), 1006–1009. https://doi.org/10.1212/wnl.41.7.1006

Gilman, S., Wenning, G. K., Low, P. A., Brooks, D. J., Mathias, C. J., Trojanowski, J. Q., Wood, N. W., Colosimo, C., Dürr, A., Fowler, C. J., Kaufmann, H., Klockgether, T., Lees, A., Poewe, W., Quinn, N., Revesz, T., Robertson, D., Sandroni, P., Seppi, K., & Vidailhet, M. (2008). Second consensus statement on the diagnosis of multiple system atrophy. *Neurology*, *71*(9), 670–676. https://doi.org/10.1212/01.wnl.0000324625.00404.15

Gliebus, G. P. (2018). Memory dysfunction. *CONTINUUM Lifelong Learning in Neurology*, *24* (3, BEHAVIORAL NEUROLOGY AND PSYCHIATRY), 727–744. https://doi.org/10.1212/CON.0000000000000619

Harvey, P. D. (2019). Domains of cognition and their assessment. *Dialogues in Clinical Neuroscience*, *21*(3), 227–237. https://doi.org/10.31887/DCNS.2019.21.3/pharvey

Howell, M. J. (2020). Rapid eye movement sleep behavior disorder and other rapid eye movement parasomnias. *Continuum (Minneapolis, Minn.)*, *26*(4), 929–945. https://doi.org/10.1212/CON.0000000000000896

Hughes, A. J., Daniel, S. E., Kilford, L., & Lees, A. J. (1992). Accuracy of clinical diagnosis of idiopathic Parkinson's disease: A Clinico-pathological study of 100 cases. *Journal of Neurology, Neurosurgery, and Psychiatry*, *55*(3), 181–184. https://doi.org/10.1136/jnnp.55.3.181

Iranzo, A., Marrero-González, P., Serradell, M., Gaig, C., Santamaria, J., & Vilaseca, I. (2021). Significance of hyposmia in isolated REM sleep behavior disorder. *Journal of Neurology*, *268*(3), 963–966. https://doi.org/10.1007/s00415-020-10229-3

Iranzo, A., Molinuevo, J. L., Santamaría, J., Serradell, M., Martí, M. J., Valldeoriola, F., & Tolosa, E. (2006). Rapid-eye-movement sleep behaviour disorder as an early marker for a neurodegenerative disorder: A descriptive study. *Lancet Neurology*, *5*(7), 572–577. https://doi.org/10.1016/S1474-4422(06)70476-8

Iranzo, A., Santamaría, J., Valldeoriola, F., Serradell, M., Salamero, M., Gaig, C., Niñerola-Baizán, A., Sánchez-Valle, R., Lladó, A., De Marzi, R., Stefani, A., Seppi, K., Pavia, J., Högl, B., Poewe, W., Tolosa, E., & Lomeña, F. (2017). Dopamine transporter imaging deficit predicts early transition to synucleinopathy in idiopathic rapid eye movement sleep behavior disorder. *Annals of Neurology*, *82*(3), 419–428. https://doi.org/10.1002/ana.25026

Iranzo, A., Tolosa, E., Gelpi, E., Molinuevo, J. L., Valldeoriola, F., Serradell, M., Sanchez-Valle, R., Vilaseca, I., Lomeña, F., Vilas, D., Lladó, A., Gaig, C., & Santamaria, J. (2013). Neurodegenerative disease status and post-mortem pathology in idiopathic rapid-eye-movement sleep behaviour disorder: An observational cohort study. *The Lancet Neurology*, *12*(5), 443–453. https://doi.org/10.1016/S1474-4422(13)70056-5

Jak, A. J., Bondi, M. W., Delano-Wood, L., Wierenga, C., Corey-Bloom, J., Salmon, D. P., & Delis, D. C. (2009). Quantification of five neuropsychological approaches to defining mild cognitive impairment. *The American Journal of Geriatric Psychiatry: Official Journal of the American Association for Geriatric Psychiatry*, *17*(5), 368–375. https://doi.org/10.1097/JGP.0b013e31819431d5

Jak, A. J., Urban, S., McCauley, A., Bangen, K. J., Delano-Wood, L., Corey-Bloom, J., & Bondi, M. W. (2009). Profile of hippocampal volumes and stroke risk varies by neuropsychological definition of mild cognitive impairment. *Journal of the International Neuropsychological Society*, *15*(6), 890–897. https://doi.org/10.1017/S1355617709090638

Li, Y., Zhang, H., Mao, W., Liu, X., Hao, S., Zhou, Y., Ma, J., Zhuqin, G., & Chan, P. (2019). Visual dysfunction in patients with idiopathic rapid

eye movement sleep behavior disorder. *Neuroscience Letters*, *709*-(June), 134360. https://doi.org/10.1016/j.neulet.2019.134360

Litvan, I., Goldman, J. G., Tröster, A. I., Schmand, B. A., Weintraub, D., Petersen, R. C., Mollenhauer, B., Adler, C. H., Marder, K., Williams-Gray, C. H., Aarsland, D., Kulisevsky, J., Rodriguez-Oroz, M. C., Burn, D. J., Barker, R. A., & Emre, M. (2012). Diagnostic criteria for mild cognitive impairment in Parkinson's disease: Movement Disorder Society Task Force guidelines. *Movement Disorders*, *27*(3), 349–356. https://doi.org/10.1002/mds.24893

Llinàs-Reglà, J., Vilalta-Franch, J., López-Pousa, S., Calvó-Perxas, L., Rodas, D. T., & Garre-Olmo, J. (2017). The trail making test: Association with other neuropsychological measures and normative values for adults aged 55 years and older from a Spanish-speaking population-based sample. *Assessment*, *24*(2), 183–196. https://doi.org/10.1177/1073191115602552

Marchand, D. G., Montplaisir, J., Postuma, R. B., Rahayel, S., & Gagnon, J. F. (2017). Detecting the cognitive prodrome of dementia with Lewy bodies: A prospective study of REM sleep behavior disorder. *Sleep*, *40*(1), zsw014. https://doi.org/10.1093/sleep/zsw014

Marchand, G., Daphné, R. B., Postuma, F. E., De Roy, J., Pelletier, A., Montplaisir, J., & Gagnon, J. F. (2018). How does dementia with Lewy bodies start? Prodromal cognitive changes in REM sleep behavior disorder. *Annals of Neurology*, *83*(5), 1016–1026. https://doi.org/10.1002/ana.25239

Martini, A., Weis, L., Schifano, R., Pistonesi, F., Fiorenzato, E., Antonini, A., & Biundo, R. (2020). Differences in cognitive profiles between Lewy body and Parkinson's disease dementia. *Journal of Neural Transmission*, *127*(3), 323–330. https://doi.org/10.1007/s00702-019-02129-2

McKeith, I. G., Boeve, B. F., Dickson, D. W., Halliday, G., Taylor, J.-P., Weintraub, D., Aarsland, D., Galvin, J., Attems, J., Ballard, C. G., Bayston, A., Beach, T. G., Blanc, F., Bohnen, N., Bonanni, L., Bras, J., Brundin, P., Burn, D., Chen-Plotkin, A., … Kosaka, K. (2017). Diagnosis and management of dementia with Lewy bodies: Fourth consensus report of the DLB Consortium. *Neurology*, *89*(1), 88–100. https://doi.org/10.1212/WNL.0000000000004058

Molano, J., Boeve, B., Ferman, T., Smith, G., Parisi, J., Dickson, D., Knopman, D., Graff-Radford, N., Geda, Y., Lucas, J., Kantarci, K., Shiung, M., Jack, C., Silber, M., Pankratz, V. S., & Petersen, R. (2010). Mild cognitive impairment associated with limbic and neocortical Lewy body disease: A clinicopathological study. *Brain*, *133*(2), 540–556. https://doi.org/10.1093/brain/awp280

Natale, E. R. d., Wilson, H., & Politis, M. (2022). Predictors of RBD progression and conversion to synucleinopathies. *Current Neurology and Neuroscience Reports*, *22*(2), 93–104. https://doi.org/10.1007/s11910-022-01171-0

Page, M. J., McKenzie, J. E., Bossuyt, P. M., Boutron, I., Hoffmann, T. C., Mulrow, C. D., Shamseer, L., Tetzlaff, J. M., Akl, E. A., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J. M., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E. W., Mayo-Wilson, E., McDonald, S., … Moher, D. (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ*, *29*(372), n71. https://doi.org/10.1136/bmj.n71

Payne, S., Shofer, J. B., Shutes-David, A., Li, G., Jankowski, A., Dean, P., & Tsuang, D. (2022). Correlates of conversion from mild cognitive impairment to dementia with Lewy bodies: Data from the National Alzheimer's coordinating center. *Journal of Alzheimer's Disease*, *86*(4), 1643–1654. https://doi.org/10.3233/JAD-215428

Periáñez, J. A., Lubrini, G., García-Gutiérrez, A., & Ríos-Lago, M. (2021). Construct validity of the sroop color-word test: Influence of speed of visual search, verbal fluency, working memory, cognitive flexibility, and conflict monitoring. *Archives of Clinical Neuropsychology*, *36*(1), 99–111. https://doi.org/10.1093/arclin/acaa034

Petersen, R. C. (2004). Mild cognitive impairment as a diagnostic entity. *Journal of Internal Medicine*, *256*(3), 183–194. https://doi.org/10.1111/j.1365-2796.2004.01388.x

Petersen, R. C., & Morris, J. C. (2005). Mild cognitive impairment as a clinical entity and treatment target. *Archives of Neurology*, *62*(7), 1160–1163. https://doi.org/10.1001/archneur.62.7.1160

Possin, K. L. (2010). Visual spatial cognition in neurodegenerative disease. *Neurocase*, *16*(6), 466–487. https://doi.org/10.1080/13554791003730600

Postuma, R. B., Gagnon, J. F., Vendette, M., & Montplaisir, J. Y. (2009). Idiopathic REM sleep behavior disorder in the transition to degenerative disease. *Movement Disorders*, *24*(15), 2225–2232. https://doi.org/10.1002/mds.22757

Postuma, R. B., Iranzo, A., Michele, H., Högl, B., Boeve, B. F., Manni, R., Oertel, W. H., Arnulf, I., Ferini-Strambi, L., Puligheddu, M., Antelmi, E., De Cock, V. C., Arnaldi, D., Mollenhauer, B., Videnovic, A., Sonka, K., Jung, K.-Y., Kunz, D., Dauvilliers, Y., … Pelletier, A. (2019). Risk and predictors of dementia and parkinsonism in idiopathic REM sleep behaviour disorder: A multicentre study. *Brain*, *142*(3), 744–759. https://doi.org/10.1093/brain/awz030

Rey, A. (1941). L'examen Psychologique Dans Les Cas d'encéphalopathie Traumatique.(Les Problems.). *Archives de Psychologie*, *28*, 215–285.

Richardson, J. D., & Dalton, S. G. (2022). Assessment of language impairment and function. *Handbook of Clinical Neurology*, *185*, 175–193. https://doi.org/10.1016/B978-0-12-823384-9.00009-8

Roascio, M., Canessa, A., Trò, R., Mattioli, P., Famà, F., Giorgetti, L., Girtler, N., Orso, B., Morbelli, S., Nobili, F., Arnaldi, D., & Arnulfo, G. (2022). Phase and amplitude electroencephalography correlations change with disease progression in people with idiopathic rapid eye-movement sleep behavior disorder. *Sleep*, *45*(1), 1–9. https://doi.org/10.1093/sleep/zsab232

Rocchi, C., Placidi, F., Liguori, C., Del Bianco, C., Lauretti, B., Diomedi, M., Pisani, A., Mercuri, N. B., & Izzi, F. (2018). Daytime autonomic activity in idiopathic rapid eye movement sleep behavior disorder: A preliminary study. *Sleep Medicine*, *52*, 163–167. https://doi.org/10.1016/j.sleep.2018.08.023

Rofes, A., de Aguiar, V., Jonkers, R., Se Jin, O., DeDe, G., & Sung, J. E. (2020). What drives task performance during animal fluency in people with Alzheimer's disease? *Frontiers in Psychology*, *11*(July), 1–11. https://doi.org/10.3389/fpsyg.2020.01485

Sakurai, H., Hanyu, H., Inoue, Y., Kanetaka, H., Nakamura, M., Miyamoto, T., Sasai, T., & Iwamoto, T. (2014). Longitudinal study of regional cerebral blood flow in elderly patients with idiopathic rapid eye movement sleep behavior disorder. *Geriatrics and Gerontology International*, *14*(1), 115–120. https://doi.org/10.1111/ggi.12068

Shin, C., Lee, J. Y., Kim, Y. K., Nam, H., Yoon, E. J., Shin, S. A., Kim, H. J., & Jeon, B. (2019). Cognitive decline in association with hyposmia in idiopathic rapid eye movement sleep behavior disorder: A prospective 2-year follow-up study. *European Journal of Neurology*, *26*(11), 1417–1420. https://doi.org/10.1111/ene.14025

Shin, J. H., Lee, J. Y., Kim, Y. K., Yoon, E. J., Kim, H., Nam, H., & Jeon, B. (2021). Parkinson disease-related brain metabolic patterns and neurodegeneration in isolated REM sleep behavior disorder. *Neurology*, *97*(4), e378–e388. https://doi.org/10.1212/WNL.0000000000012228

Shin, M. S., Park, S. Y., Park, S. R., Seol, S. H., & Kwon, J. S. (2006). Clinical and empirical applications of the Rey-Osterrieth complex figure test. *Nature Protocols*, *1*(2), 892–899. https://doi.org/10.1038/nprot.2006.115

Sumi, Y., Ubara, A., Ozeki, Y., & Kadotani, H. (2022). Minor hallucinations in isolated rapid eye movement sleep behavior disorder indicative of early phenoconversion: A preliminary study. *Acta Neurologica Scandinavica*, *145*(3), 348–359. https://doi.org/10.1111/ane.13555

Terzaghi, M., Pilati, L., Ghiotto, N., Arnaldi, D., Versino, M., Rustioni, V., Rustioni, G., Sartori, I., & Manni, R. (2022). Twenty-four-hour blood pressure profile in idiopathic REM sleep behavior disorder. *Sleep*, *45*(2), zsab239. https://doi.org/10.1093/sleep/zsab239

Terzaghi, M., Toscano, G., Casoni, F., Picascia, M., Arnaldi, D., Rustioni, V., Versino, M., Sinforiani, E., & Manni, R. (2019). Assessment of cognitive profile as a prodromal marker of the evolution of rapid eye movement sleep behavior disorder. *Sleep*, *42*(8), 1–8. https://doi.org/10.1093/sleep/zsz103

Terzaghi, M., Zucchella, C., Rustioni, V., Sinforiani, E., & Manni, R. (2013). Cognitive performances and mild cognitive impairment in idiopathic rapid eye movement sleep behavior disorder: Results of a longitudinal follow-up study. *Sleep*, *36*(10), 1527–1532. https://doi.org/10.5665/sleep.3050

Wagner, S., Sebastian, A., Lieb, K., Tüscher, O., & Tadić, A. (2014). A coordinate-based ALE functional MRI meta-analysis of brain activation during verbal fluency tasks in healthy control subjects. *BMC Neuroscience*, *15*(1), 1–13. https://doi.org/10.1186/1471-2202-15-19

Winblad, B., Palmer, K., Kivipelto, M., Jelic, V., Fratiglioni, L., Wahlund, L. O., Nordberg, A., Bäckman, L., Albert, M., Almkvist, O., Arai, H., Basun, H., Blennow, K., de Leon, M., DeCarli, C., Erkinjuntti, T., Giacobini, E., Graff, C., Hardy, J., … Petersen, R. C. (2004). Mild cognitive impairment - beyond controversies, towards a consensus: Report of the international working group on mild cognitive impairment. *Journal of Internal Medicine*, *256*(3), 240–246. https://doi.org/10.1111/j.1365-2796.2004.01380.x

Yoo, D., Lee, J. Y., Kim, Y. K., Yoon, E. J., Kim, H., Kim, R., Nam, H., & Jeon, B. (2021). Mild cognitive impairment and abnormal brain metabolic expression in idiopathic REM sleep behavior disorder. *Parkinsonism and Related Disorders*, *90*, 1–7. https://doi.org/10.1016/j.parkreldis.2021.07.022

Yoon, E. J., Lee, J.-Y., Kim, H., Yoo, D., Shin, J. H., Nam, H., Jeon, B., & Kim, Y. K. (2022). Brain metabolism related to mild cognitive impairment and Phenoconversion in patients with isolated REM sleep behavior disorder. *Neurology*, *98*(24), e2413–e2424 https://doi.org/10.1212/wnl.0000000000200326

Youn, S., Kim, T., Yoon, I. Y., Jeong, J., Kim, H. Y., Han, J. W., Kim, J. M., & Kim, K. W. (2016). Progression of cognitive impairments in idiopathic REM sleep behaviour disorder. *Journal of Neurology, Neurosurgery and Psychiatry*, *87*(8), 890–896. https://doi.org/10.1136/jnnp-2015-311437

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Fiamingo, G., Capittini, C., De Silvestri, A., Rebuffi, C., Cerami, C., Arnaldi, D., & Terzaghi, M. (2023). Neuropsychological evaluation of phenoconversion risk in REM sleep behaviour disorder: A scoping review. *Journal of Sleep Research*, e13873. https://doi.org/10.1111/jsr.13873