Peertechz

CLINICAL GROUP

OPEN JOURNAL OF Parkinson's Disease and Treatment OPEN ACCESS JOURNAL

DOI: https://dx.doi.org/10.17352/ojpdt

Literature Review

Parkinson's disease dementia and dementia with lewy bodies differences and similarities

Joanna Krasowska[1] and Johan Lökk[1,2]

[1]Department of Neurobiology, Care Sciences, and Society, Karolinska Institutet, Stockholm, Sweden

[2]Geriatric Dept, Karolinska University Hospital, Stockholm, Sweden

Received: 27 March, 2023
Accepted: 13 April, 2023
Published: 14 April, 2023

***Corresponding author:** Johan Lökk, MD, PhD, Professor, Department of Neurobiology, Care Sciences, and Society, Karolinska Institutet, Stockholm, Sweden, Tel: +46736841233; E-mail: johan.lokk@regionstockholm.se

Copyright License: © 2023 Krasowska J, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

https://www.peertechzpublications.com

Check for updates

Abstract

The second most common neurodegenerative disease causing dementia in the population over 65 years is Parkinson´s Disease Dementia (PDD), sharing many clinical, genetic, pathophysiological, imaging, and morphological features with Dementia with Lewy Bodies (DLB). There is an ongoing debate whether these two diseases are separate diseases, just different phenotypes on the basis of the same Lewy Body pathology or the same disease. The differences are rather few and many authors tend to believe that PDD and DLB may be manifestations of the same neurodegenerative disorder.

Based on a single examination, without regard to the temporal sequence of events, it is difficult or impossible to differentiate a single patient with parkinsonism as PDD or DLB. The relative timing when cognitive and motor symptoms appear, applying the 1-year rule, could be helpful in clinical practice in distinguishing the diseases. The subtle differences are hard to observe with more executive problems in PDD and a tendency of more easily triggered psychotic problems in DLB. Eventually, PDD and DLB might be the same disease - as long as unquestionable biomarkers definitely distinguishing both entities are not found.

Introduction

Parkinson's Disease Dementia (PDD) is quite common in elderly patients in clinical practice and is the second next common dementia form after Alzheimer's Disease (AD). Another dementia form is Dementia with Lewy Bodies (DLB) which has been more and more recognized and diagnosed during the last decade [1]. Both diseases will first be described separately below, followed by a brief comparison of the two.

Dementia, despite its origin, is a devastating condition that brings suffering and burden not only to the patient but also to the carers as well as worsening the quality of life. There is no curable treatment available so far; the condition is responsible for a shortened life duration for an afflicted individual – in AD the average survival rate after diagnosis varies between 4 to 8 years [2] whereas PPD is associated with high morbidity and mortality, forerunning the death by approximately 4 years [3,4]. Mortality rates for PDD and DLB do not differ according to a study from Sweden published in 2018 (Larsson et al.) and are approximately three times higher than in the general population [5].

The cognitive decline is usually insidious. Memory impairment increases the risk of progression to dementia together with other risk factors like older age, early hallucination, cortical atrophy, and affected EEG changes [6].

AD is the main cause leading to dementia in modern times [7]. There is no doubt that the disease pathogenesis is complex and many molecular changes are involved. Mechanisms and interactions between changes are not fully explained [7,8]. Amongst existing hypotheses some regard the main proteins involved in pathogenesis - beta-amyloid (AB) and tau, normal proteins in the brain (not only there); the presence of pathological changes in these proteins is a sine qua non for the pathological process and diagnosis [7]. Metabolism of both – AB and tau - goes the wrong way for an unknown reason and leads for the first one to so-called amyloid plaques building outside neurons– AB aggregations which are insoluble oligomers and are supposed to be toxic. The tau protein

Citation: Krasowska J, Lökk J (2023) Parkinson's disease dementia and dementia with lewy bodies differences and similarities. Open J Parkinsons Dis Treatm 6(1): 001-013. DOI: https://dx.doi.org/10.17352/ojpdt.0000122

undergoes phosphorylation – and when hyperphosphorylated presents aberrant aggregations – neurofibrillary tangles which lead to destruction in the axons transportation system and eventually to cell death [8]. There is a hypothesis that AB and tau pathways can act parallel and enhance each other's toxic effects [9].

Synucleinopathies are the second most common process of neurodegenerative disorders after Alzheimer's disease that can lead to dementia [10]. They are characterized by the accumulation of aggregated protein alfa-synuclein (α -syn) in both neuronal and non-neuronal cells in the brain. Aggregations are called either Lewy Bodies (LB) - when accumulated in neurons, or Lewy neuritis (LN) - when found in neuronal processes. Most synucleinopathies are Lewy Body Diseases (LBDs), amongst them the most common is Parkinson's Disease (PD), PDD, and DLB. Multiple System Atrophy (MSA) is also considered synucleinopathy, but it neuropathologically differs from DLB:s as it builds a type of aggregated α-syn inclusions called GCIs in non-neuronal cells (in oligodendrocytes) [11].

Alfa-synuclein aggregates have a strong predilection to specific neurons – they are found in the Substantia Nigra (SN) in the midbrain, in the olfactory nerve, vagus nerve branches and nuclei, locus ceruleus, and other brainstems nuclei. When PD progresses and dementia symptoms occur, different cortical regions are also involved, the latest is very characteristic of DLB [12].

It is not completely known how α-syn spreads in the brain. The Braak hypothesis says that Lewy pathology primarily occurs in the lower brainstem, successively spreading up to the striatum and to the cortex. Later research localized primary changes in the nose and guts. These spreads are prion-like, transferring misfolded proteins from cell to cell [13].

However, the latest theories say that the propagation of the disease observed by Braak and colleagues is reflecting the vulnerability of specific cells that are first engaged in PD. These "vulnerable cells" are in SN, locus coeruleus, and pedunculopontine nucleus. A hypothesis trying to explain why and how these specific neurons are most affected describes some possible mechanisms disturbing cells' functioning. Which of those is the most critical is yet to be investigated and shown. What is common to these cells is the high demand for good mitochondrial and lysosome functions – and this can explain why mutations affecting mitochondrial functions are so common in PD [13]. Mitochondrial functions decrease with age [13] and many neurodegenerative diseases are age-dependent.

It is not clearly shown whether LB and LN have a neuroprotective or neurotoxic role. It is also unclear to what extent they contribute to the clinical picture of dementia - some individuals have had a severe α-syn pathology at autopsy but no clinical symptoms of DLB [5,11]. It is assumed that LB and LN in the neocortex are not associated with neuron loss or atrophy [12] but there is a correlation between total α-syn burden and neuronal loss [13]. Conversely, AD pathology (neurofibrillary tangles and amyloid β pathology) that often coexist in DLB and PDD, leads to cortical neuronal loss [12]. The prevalence of mixed α -syn and AD pathology is unknown; autopsy studies showed that more than 30% of clinically diagnosed AD patients had LB pathology to some extent as well – mostly located in the amygdala [11,14]. A mixed pathology can be assumed as a substrate of dementia and it differs slightly for PDD and DLB, which is described separately below.

Parkinson's Disease Dementia (PDD)

Diagnostic criteria: Cognitive impairments are common in PD and can be present as mild dysfunction in the prodromal and early stages, or as dementia in the advanced stages of the disease. Approximately 20% of patients with newly diagnosed PD have already Mild Cognitive Impairment (MCI). The concept of PD-MCI was introduced in 2012 (MDS Task Force) and is characterized by a cognitive decline that can be assessed by neuropsychological testing but does not impair activities of daily living or social functioning.

PDD is diagnosed with established PD which means that Parkinsonian signs always precede cognitive deficits [15]. There is a common agreement about the one-year rule – cognitive decline first appears one year after Parkinsonian motor signs onset. This is a completely arbitrary consensus that makes it possible to clinically distinguish PDD from DLB. The cognitive impairment is of such a level that it interferes with the activities of daily living.

Diagnostic criteria for PDD are shown in Movement Disorder Society Task Force which was designated to define and develop diagnostic guidelines for PDD and was published by Christopher G. Goetz, et al in 2008 [16]. The suggested clinical diagnostic criteria for PDD involve four domains and are anchored in core features, associated clinical features, features that make the diagnosis uncertain, and features that are not compatible with the diagnosis of PDD. When all four criteria are satisfactorily met, probable PDD is designated; when the first and last criteria are met, but clinical characteristics are atypical or uncertainty factors exist, possible PDD is designated. Diagnostic criteria are presented as followed [16]:

Features of dementia associated with Parkinson's Disease

I. Core features (Both 1 and 2 must be present)

1. Diagnosis of idiopathic Parkinson's disease
2. A dementia syndrome with insidious onset and slow progression with:

-Impairment in more than one cognitive domain (see later)

- Representing a decline from the premorbid level

- Deficits severe enough to impair daily life

II. Associated Clinical Features:

Cognitive features:

Impaired attention, which may fluctuate

Citation: Krasowska J, Lökk J (2023) Parkinson's disease dementia and dementia with lewy bodies differences and similarities. Open J Parkinsons Dis Treatm 6(1): 001-013. DOI: https://dx.doi.org/10.17352/ojpdt.0000122

Impaired executive functions and mental speed (bradyphrenia).

Impaired visuospatial functions

Impaired memory, which usually improves with cueing

Language is largely preserved.

Behavioral features:

Loss of motivation, interest, and effortful behavior.

Personality and mood changes.

Often hallucinations and delusions, mostly visual.

Excessive daytime sleepiness.

III. Features that do not exclude Parkinson's disease with dementia but make the diagnosis uncertain

Coexistence of any other abnormality that may by itself cause cognitive impairment.

The time interval between the development of motor and cognitive symptoms is not known.

IV. Features suggesting other conditions or diseases as the cause of mental impairment that when present makes it impossible to reliably diagnose Parkinson's disease with dementia:

Cognitive and behavioral symptoms appearing solely in the context of other conditions such as:

Acute confusion is caused by systemic diseases or abnormalities or by drug intoxication.

Major depression

Features compatible with "Probable Vascular dementia" e.g.onset of dementia within 3 months after a recognized stroke, abrupt deterioration in cognitive functions, and fluctuating, stepwise progression of cognitive deficits.

Criteria for the diagnosis of probable and possible Parkinson's Disease with Dementia (PDD)

Probable PDD

I must be met: Core features: both must be present.

II must be met: Associated clinical features:

The typical profile of cognitive deficits includes impairment in at least two of the four core cognitive domains (impaired attention that may fluctuate, impaired executive functions, impairment in visuospatial functions, and impaired free recall memory that usually improves with cueing). The presence of at least one behavioral symptom (apathy, depressed or anxious mood, hallucinations, delusions, excessive daytime sleepiness) supports the diagnosis of probable PDD; lack of behavioral symptoms, however, does not exclude the diagnosis.

III must be met: None of the uncertainty factors are present.

IV must be met: None of the factors suggesting other diagnoses are present.

Possible PDD

I must be met: Core features: both must be present.

II, III, or both not met

II not met: Atypical profile of cognitive impairment in one or more domains, such as prominent or receptive-type (fluent) aphasia, or pure storage failure–type amnesia (memory does not improve with cueing or in recognition tasks) with preserved attention. Behavioral symptoms may or may not be present OR

III did not meet: One or more of the uncertain items is present.

IV must be met: None of the factors suggesting other diagnoses is present.

Epidemiology of PDD

According to the literature prevalence numbers differ; up to 80% of patients with diagnosed PD will develop dementia [5]. The mean duration of PD symptoms prior to dementia in PDD is 10 years [14,17]. The incidence of dementia is approximately threefold higher than in the normal population [4].

Estimating the true occurrence of dementia in PD is not easy for the clinician [18]. In clinical practice, mild dementia may be missed because motor signs are dominating and problems requiring medication adjustments such as fluctuating motor symptoms, dyskinesias, sleep problems, or dysautonomia may overshadow cognitive problems or lead to their misinterpretation as the result of motor disability. The patient himself is often unaware of cognitive dysfunction whereas the relative is likely to relate all sorts of symptoms to the latter. It is most likely that patients with moderate or severe dementia are the first to be identified [19,20].

Age and PD duration are the leading risk factors for PDD [12]. Other clinical factors, such as male sex, low level of education, higher Hoehn & Yahr stage, axial impairment, akinetic-rigid or postural instability PD- type, excessive daytime sleepiness, cardiovascular autonomic dysfunction, REM sleep behavior disorder, hallucinations, and PD-MCI were found to be predictors of the development of PDD. Also specifically impairment of memory and language seems to be linked to a higher risk of PDD [21,22]. It is suggested, that some factors leading to earlier dementia development in PD may have some genetic underpinnings [13]. Dementia development leads to shortening lifetime expectancy and significantly worsens the quality of life both for the patient and the relatives, not to mention the huge economic care costs.

Genetics

The genetics of dementia with Lewy bodies (DLB), PDD, PD, and AD is overlapping. Most cases of DLBs seem to be sporadic. There is a rare autosomal dominant inheritance

Citation: Krasowska J, Lökk J (2023) Parkinson's disease dementia and dementia with lewy bodies differences and similarities. Open J Parkinsons Dis Treatm 6(1): 001-013. DOI: https://dx.doi.org/10.17352/ojpdt.0000122

involving mutations in the SNCA (gene for α-syn, a quite rare mutation) and LRRK2 (leucine-rich receptor kinase 2) genes. These mutations can manifest as PD, PDD, or DLB [5]. It is not known, though, if SNCA mutations add a risk to develop PDD [23]. Other genes identified by genome-wide association studies (GWAS) for late-life DLB or PDD that are also associated with the risk for both diseases are GBA (glucocerebrosidase A), MAPT (microtubule-associated protein tau), SCARB2 (scavenger receptor class B member 2) [12].

Heterozygous mutations in the GBA gene are a significant risk factor for both DLB and PDD. The homozygous mutations in GBA cause a lysosomal storage disorder called Gaucher disease [13]. The carriers of mutations in GBA may develop dementia at an earlier age than non-carriers, though the latest was not proven in all studies. There is an overrepresentation of the APOE ε 4 allele, which is a strong risk factor for late-onset AD, in sporadic LBDs [perhaps more in DLB than in PDD [23]], but it is less common than in patients with AD [5]. APOE ε 4, when present, brings an increased risk for more widespread synucleinopathy and dementia [23]. The APOE ε 2 allele (the least common allele) might reduce the risk of developing DLB [5]. According to Galasko, despite some genetic factors contributing to the understanding of both diseases' mechanisms, clinical genetic testing in DLB or PDD is not recommended at present [12].

Neuropathology

Lewy pathology (Lewy Bodies/LB and Lewy Neurites/LN) predominantly occurs in dopaminergic neurons in pure PD (nigrostriatal system); with the disease course, they are seen diffusely spread to different regions of the brain, including the neocortex (mainly parietal, temporal and frontal lobes). Limbic and neocortical α-synuclein lesions distinguish PDD from PD [12]. However, Lewy bodies also appear in most PD patients without dementia and, conversely, dementia may occur in patients without neocortical LB [24].

Alfa-synuclein, the main substrate in LB and LN, can induce tau hyperphosphorylation and in this way promote neurofibrillary tau tangle formation. This synergistic relationship between AD pathology and α-syn is bidirectional – the main modification in α-syn is that it becomes phosphorylated. Levels of phosphorylated α-syn correlate with the severity of the disease [13]. Cortical α-syn is assumed to be the strongest candidate substrate for PDD. The presence of cortical neurofibrillary tangles and beta-amyloid pathology leads to more advanced dementia, implying that the two pathologies work together [5,13]. Thus, the combination of Lewy pathology and AD pathology predicts dementia in PD better than the severity of any single pathology] [13]. There is little evidence that cerebrovascular pathology contributes substantially to cognitive impairment in PDD or DLB [5,25].

Clinical features of PDD

PD symptoms such as bradykinesia, rigidity, tremor, and postural instability are present in different combinations and with different intensities. Obviously, not all symptoms are present in every patient. These motor symptoms are most probably caused by impairment of the signaling from basal ganglia to various motor cortex areas via cortical- basal ganglia- thalamocortical loops [26]. In PDD impairment in signaling from other areas to the cortex, as well as within the cortex itself, is believed to play an important role [27]. Cognitive problems, as mentioned above, can be detected in about 20% of de novo diagnosed PD cases (defined as PD-MCI), but they do not interfere with daily activities in a significant way which is the case when dementia has been developing.

There is little known about the natural course of cognitive functions in PD patients --- studies that have cognition in PD in focus are few. There is a need for large cohort studies that use neuropsychological test battery covering all relevant domains with both base and longitudinal follow-up data [20]. Nevertheless, what seems to be characteristic is that changes in cognition over the disease course are not limited to one domain [20]. The cognitive profile in PDD typically shows impairments in executive and visuospatial functions. There is no consent between the authors which one of those can be predictive of dementia development. Some claim memory and language impairment predicts dementia as well [28,29]. Fluctuations in attention are often noticed, in the later stages of PD they can cycle as a peak-dose phenomenon related to dopaminergic medication [4]. The pure language deficit is not typical but naming and letter fluency may be impaired to a different degree [4,14]. Memory deficits are not due to encoding problems, as free recall can be improved with the cues, which suggests impairment in the retrieval (recall) function [4]. Bradyphrenia is often present and psychiatric symptoms are relatively common in PDD, mainly manifesting as visual hallucinations [4]. They should be differentiated from visual illusions, in which an object is visually misinterpreted. This is a relatively often described phenomenon in early disease and may occur at twilight or in poorly lit environments [4].

Hallucinations are very similar to those in DLB, often animated – patients can see humans, often children, persons who are known or already dead, or animals. Initially, there is no lack of insight when hallucinations occur. However, during the disease's progress insight may lack and patients may respond to hallucinations in various ways. When the symptoms lead to fear or dysphoria therapeutic interventions are often necessary [4,14]. Other modalities of hallucinations are seldom described. Delusions and psychosis may be very disabling and raise problems in mutual relations as the delusions can have a paranoid quality.

Diagnostic process

Neuropsychological assessment is necessary to assess cognitive functions. There are many tests that evaluate cognition. In clinical praxis screening for global cognition in suspected dementia is very useful. The most commonly used are MMSE (Mini-Mental State Examination) and MoCA (*The Montreal Cognitive Assessment)*. These were developed for AD assessment but they are widely used also for screening PD. The latest recommendations are preferable to MoCA, which was found superior to detect cognitive impairment in PD patients

Citation: Krasowska J, Lökk J (2023) Parkinson's disease dementia and dementia with lewy bodies differences and similarities. Open J Parkinsons Dis Treatm 6(1): 001-013. DOI: https://dx.doi.org/10.17352/ojpdt.0000122

[28,30]. Another test instrument found suitable is SCOPA-COG (SCales for Outcomes of Parkinson's Disease – Cognition) [31]. However, there is no strict regulation on what cognitive test battery to be used, but it is commonly agreed that cognitive scales must evaluate a broad range of cognitive domains - attention, language, visuospatial function, memory, and executive function [22,28].

Brain imaging is necessary in diagnosing PD in order to exclude other similar conditions that can give rise to Parkinsonian signs. Structural brain imaging with CT or MRI can also be supportive in PDD mostly in order to exclude other diseases as there is no specificity in the findings of PDD. MRI is preferable as it better provides a measure of cerebral atrophy and gives specific tissue characterization. Studies investigating gray matter loss in order to compare PDD and DLB have shown it is more pronounced in DLB albeit no specific pattern could be found [32]. The finding of white matter hyperintensities (WMH) – a finding often observed in elderly – does not have a significant difference in PDD and DLB [33].

Molecular imaging has given the possibility to assess neurobiological functions in living objects. Functional imaging techniques are promising but more studies are necessary, given the variable results of existing investigations [26]. Single photon emission tomography (SPECT) can be used to trace presynaptic dopaminergic function in basal ganglia with a specific radiotracer [123I]FP-CIT and is useful to diagnose parkinsonian syndromes, however with no possibility to distinguish between PD or any atypical parkinsonian syndromes, including DLB) [32].

[123I]MIBG cardiac scintigraphy is another imaging technique that allows assessing cardiac postganglionic degeneration, which is specific for Lewy body pathology. Although its specificity and sensitivity are high for DLB, no data for PDD are available. Similarly, as for [123I]FP-CIT-SPECT, there is no possibility to distinguish between PDD and DLB [34].

[18F]FDG PET (positron emission imaging – PET)--- yet another imaging technique--- is used to detect cerebral glucose metabolism, which is pathological if neuronal degeneration or synaptic pathology is the case. Changes in frontal and temporoparietal association areas have been seen, similar for PDD and DLB, and more severe in non-demented PD [35]. Occipital hypometabolism has also been described but must be interpreted cautiously as it has been seen in other entities [4].

[11]C-PIB PET, technology targeting fibrillary amyloid in AD, tau imaging PET (using a specific tau binding substrate), as well α -syn imaging have a limited value in diagnosing PDD so far.

There is still insufficient evidence for using biomarkers in cerebrospinal fluid (CSF) that are specific for PDD. Both tau and beta-amyloid can be found and the possibility to assess α-syn is coming to the clinical practice, but the evidence is not sufficient to prove that it correlates to cognitive decline [26,34] The results of studies that assessed α-syn in CSF are conflicting. It seems that CSF α-syn levels may increase with the disease stage and this could be an explanation for high levels of α- syn and cognitive decline in more advanced disease stages [20]. In patients with newly diagnosed PD evidence for beta-amyloid pathology (e.g. low concentrations of Aβ1-42) in CSF is a significant predictor of subsequent cognitive impairment [13].

Therapy

PD symptoms with the disease progress are challenging for the clinician and good control of both motor and non-motor Parkinson's signs is seldom durable or fully satisfactory. It is important to remember that any Parkinsonian drug can be responsible for precipitating or exacerbating psychiatric symptoms and for cognitive impairment itself. Therapy modification is then necessary. Reducing dopaminergic replacement is recommended, but when the cognitive functions are improved, motor disabling problems can emerge. Usually, the nondopaminergic PD medications (MAO-B inhibitors, amantadin, anticholinergics) are discontinued at first, as they are believed to be less beneficial to motor symptoms [28]. Any other coexisting illness/condition that occurs must be evaluated if it is believed to contribute to cognitive impairment. Medications such as sedatives or psychoactive need to be assessed if they are necessary for the patient as they can exacerbate cognitive decline [28]. Currently, there is no curable treatment for any of the neurodegenerative disorders at present but studies targeting disease modification are currently being conducted [26,34]. As in all dementia syndromes, the treatment is complex and should focus on pharmacological and non-pharmacological approaches carried out by multi-professional teams together with caregivers, social workers, and municipalities as well as volunteer-driven organizations (day centers, and institutions). There is a range of pharmacological as well as non-pharmacological treatments and interventions, but very few of those are efficacious [36].

The goal is to decrease the disease burden for a patient and caregiver by slowing the progress of the illness; alleviating symptoms and postponing the worsening [37]. The pharmacological treatment of cognition in PDD takes advantage of studies on AD and is based on the knowledge that cholinergic projections to the cortex are disturbed in PD because of the affected nucleus basalis of Meynert (as in AD). Thus, acetylcholinesterase inhibitors (AChE-Is) are used, giving a modest but significant benefit to cognition in PD [23]. All three currently available AChE-I drugs - donepezil, rivastigmine, and galantamine - are in clinical use but only rivastigmine has been approved and donepezil is given a recommendation (lower evidence) in PDD [38]. They provide a benefit not only regarding global cognitive function and behavioral symptoms but also in specific cognitive domains [39]. AChE-Is are shown to reduce apathy and neuropsychiatric symptoms such as visual hallucinations and delusions [14]. Rivastigmine is available as a transdermal patch which can be preferable if gastrointestinal adverse effects or dysphagia are prominent. Moreover, it is possible to switch drugs within the group. Memantine is a glutamatergic NMDA receptor antagonist used for moderate

Citation: Krasowska J, Lökk J (2023) Parkinson's disease dementia and dementia with lewy bodies differences and similarities. Open J Parkinsons Dis Treatm 6(1): 001-013. DOI: https://dx.doi.org/10.17352/ojpdt.0000122

and severe AD, however, no substantial clinical evidence exists on the effects on PDD [14]. According to the latest meta-analysis [39], good results in certain cognitive domains have been shown as well as good safety outcomes. Stabilization or amelioration of cognitive outcomes is often the endpoint in many trials for novel treatments [1]. There is, however, a need for longitudinal further clinical studies in order to assess the efficacy and safety of AChE-Is and memantine in PDD better [39].

Hallucinations and psychosis may be very problematic, and if they do not respond to AChE-I other medications may need to be considered. Of neuroleptic drugs only clozapine and quetiapine are recommended, as they do not exacerbate parkinsonism or give rise to the neuroleptic malignant syndrome in a significant way [4]. The first one is more complicated in clinical use as it can produce an important adverse effect such as agranulocytosis implying that the white blood cells must be weekly monitored. Quetiapine is more sedative, which can be an advantage when sleep disorder coexists.

Other therapeutic pharmacological trials are ongoing in PD, having a potential for PDD. The focus is to modify the disease course. Studies regarding different approaches against α-syn are complicated by the fact that there is still an incomplete understanding of the precise role of α-syn in disease development, though, no doubts about its role in the pathogenesis of PD. The way to develop such a therapy seems to be complicated, costly, and takes a long time [40] as does the research on genetic interventions.

Dementia with Lewy Bodies (DLB)

Dementia with Lewy bodies is considered a diagnostic challenge because of the clinical and pathological overlap with other neurodegenerative diseases, such as AD, PDD, and frontotemporal lobar degeneration (FTLD) [41]. This is one of the reasons why DLB is not as frequently recognized as AD is; mis- or underdiagnoses are frequent [42]. Interestingly, DLB was described as a separate entity for the first time in 1984 as diffuse Lewy body disease (DLBD) and in 1995 at an international meeting the name" Dementia with Lewy bodies "was proposed [42]. This might be the reason why data on many aspects regarding DLB are still limited. DLB should be diagnosed when dementia occurs before, or concurrently with parkinsonism. Because of its clinical overlap with other forms of dementia, DLB is often underdiagnosed and misdiagnosed [41]. The term Parkinson's disease dementia should be used to describe dementia that occurs in the context of well-established Parkinson's disease. In research studies in which a distinction needs to be made between DLB and PDD the existing one-year rule between the onset of dementia and parkinsonism continues to be recommended [11].

Revised criteria for the clinical diagnosis of probable and possible DLB according to Outeiro, et al. [11]

Essential for a diagnosis of DLB is dementia, defined as a progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational functions, or with usual daily activities. Prominent or persistent memory impairment may not necessarily occur in the early stages but is usually evident with progression. Deficits on tests of attention, executive function, and visuoperceptual ability may be especially prominent and occur early [11].

Core clinical features (the first three typically occur early and may persist throughout the course)

1. Fluctuating cognition with pronounced variations in attention and alertness
2. Recurrent visual hallucinations that are typically well-formed and detailed
3. REM sleep behavior disorder (RBD) which may precede cognitive decline
4. One or more spontaneous cardinal features of parkinsonism – bradykinesia, rest tremor, or rigidity.

Supportive clinical features

- Severe sensitivity to antipsychotic agents
- Postural instability
- Repeated falls
- Syncope or other transient episodes of unresponsiveness
- Severe autonomic dysfunction e.g. constipation, orthostatic hypotension, urinary incontinence
- Hypersomnia
- Hyposmia
- Hallucinations in other modalities
- Systematized delusions
- Apathy, anxiety, and depression

Indicative biomarkers

Reduced dopamine transporter (DaT) uptake in basal ganglia demonstrated by SPECT or PET

Abnormal (low uptake) MIBG myocardial scintigraphy

Polysomnographic confirmation of REM sleep without atonia

Supportive biomarkers

- Relative preservation of medial temporal lobe structures on CT/MRI scan
- Generalised low uptake on SPECT/PET perfusion/ metabolism scan
- Prominent posterior slow wave activity on EEG with periodic fluctuations in the pre-alpha/theta range

Citation: Krasowska J, Lökk J (2023) Parkinson's disease dementia and dementia with lewy bodies differences and similarities. Open J Parkinsons Dis Treatm 6(1): 001-013. DOI: https://dx.doi.org/10.17352/ojpdt.0000122

Probable DLB if:

a) Two or more core clinical features of DLB are present, with or without the presence of indicative biomarkers or

b) Only one core clinical feature is present, but with one or more indicative biomarkers

Possible DLB if:

a) Only one core clinical feature of DLB is present, with no indicative biomarker evidence, or

b) One or more indicative biomarkers are present but there are no core clinical features

DLB is less likely:

a) In the presence of any other physical illness or brain disorder including cerebrovascular disease

b) If Parkinsonian features are the only core clinical feature and appear for the first time at a stage of severe dementia. DLB should be diagnosed when dementia occurs before, or concurrently with parkinsonism.

Epidemiology of DLB

The data regarding the epidemiology of DLB worldwide are limited [19]. Similar to PDD, the risk of DLB increases with age and is more frequent in men. The men-to-women difference in risk of DLB suggests different etiologic mechanisms - chromosomes X and Y depending, on endocrinological, environmental, social, and cultural factors [14,19]. The average age of disease onset is over 70 years [11]. The incidence is approximately 1 of 25 or 20% - 30% of new dementia diagnoses in the general population [14]. DLB patients survive from symptoms onset 5-8 years on average [43], whereas in cases with rapid progression, the average survival is 9 months [44].

Apart from the male gender and older age, there are some more factors modifying mortality rates - the presence of at least one APOE ε 4 allele and extrapyramidal signs are found to be strong predictors of mortality and long-term care placement [43]. In tremor-predominant forms of DLB, which are rare, better outcomes than in rigid-predominant forms of DLB were found [43,45].

Genetics

The genetic studies regarding distinctively DLB are few, as previous researchers focused on Lewy body disease (PD, PDD, and DLB) as a whole [46]. The GWAS (genome-wide association study) was conducted first in 2017, long after such studies were performed on other diseases [42]. Though most DLB cases are sporadic, there is strong evidence for genetic components and family occurrence has been reported [42]. Observations on familial DLB indicate a predominant PD- phenotype with parkinsonian signs at the onset--- very few families with suggested DLB present cognitive problems initially [11].

There are only three genes that have been convincingly established to be involved in DLB: APOE, GBA, and SNCA, meaning a strong risk for dementia with Lewy bodies [42]. These genes are also considered to increase the risk of either AD (APOE) or PD [GBA, SNCA] [42]. Even mutation in MAPT can give risk to DLB [34]. APOE ε 4 carries can often develop mixed DLB-AD pathology, but even pure DLB and PDD cases are seen; a greater severity of LB pathology and low AD pathology was also reported which implies that APOE is involved in the mechanism of LB pathology spread [11]. It does not seem that APOE ε 4 is an independent driver of synuclein pathology in DLB [46].

Some reports have shown that heterozygous carriers of mutations in GBA develop dementia at an earlier age than non-carriers but other large studies reported conflicting results [5]. GBA is likely the APOE gene involved in the mechanism of LB pathology in DLB, though there is more uncertainty about what the cause of this involvement is [11]. GWAS results indicate that DLB genetically resembles both AD and PD, probably in equal measure, whereas PD and AD genetically are different [23]. Some DLB patients have a family history of neurodegenerative disease, not necessarily of DLB, and family members were diagnosed with AD or PD [42].

According to the fourth consensus report of the DLB Consortium, it is not recommended to perform genetic testing in a clinical setting, neither for confirmation of diagnosis nor for prediction of disease, and genetic studies should be limited to research settings [47].

Neuropathology of DLB

Autopsy studies from research centers suggest that LB pathology (α-synuclein aggregations) occurs in about 20% to 25% of cases of dementia in the elderly [12]. Most DLB cases show loss of dopaminergic neurons in the substantia nigra in the midbrain, like PD cases, albeit the most characteristic sign is LB pathology [11,48],.

There are 3 variations of α-syn pathology in DLB: brainstem predominant, limbic (also called transitional), and neocortical. Brainstem lesions are found in the substantia nigra, nuclei of the vagus and glossopharyngeal nerves, reticular nuclei, and locus ceruleus. Limbic or transitional pathology occurs in the amygdala, transentorhinal cortex, and cingulate. Neocortical pathology is found in the temporal, frontal, and parietal cortex. Limbic and neocortical α-syn lesions are associated with clinical features characteristic of DLB [12]. As in PDD, concomitant AD pathology is often found and is believed to contribute to cognitive impairment [12]. Alfa-synuclein may induce tau hyperphosphorylation and in this way promote neurofibrillary tau tangle formation. This synergistic relationship between AD pathology and α-syn is bidirectional – the main modification in α-syn is that it becomes phosphorylated. Levels of phosphorylated α-syn correlate with the severity of the disease [13]. There are conflicting results considering which pathology plays a more important role in dementia: high cortical LB burden or AD-related pathology. However, it is agreed that there is a strong correlation between both cortical pathologies [34]. There is little evidence that cerebrovascular pathology, which is relatively mild, contributes substantially to cognitive

Citation: Krasowska J, Lökk J (2023) Parkinson's disease dementia and dementia with lewy bodies differences and similarities. Open J Parkinsons Dis Treatm 6(1): 001-013. DOI: https://dx.doi.org/10.17352/ojpdt.0000122

impairment in DLB [5,25,34]. Apart from the occurrence of AD pathology, findings of intracellular inclusions of TDP-43 (which is a hallmark of FTLD) have been recorded at different rates [11]. The presence of FTLD pathology is believed to worsen cognitive impairment [11]. LB pathology's role is not quite clear (toxic or protective) and no correlation between LB burden and clinical features of DLB has been shown [11].

Clinical features

Clinical features of DLB can be categorized into 3 groups: cognitive impairments, behavioral/ psychiatric phenomena, and physical symptoms [49].

Cognitive impairment

Cognitive deficit/dementia is characterized by both subcortical and cortical dementia. Disease often begins with dementia marked by fluctuating cognition and arousal [5,50]. Cognitive decline typically has a gradual onset and progression like in AD; sometimes DLB may, however, progress more rapidly [12]. Cognitive impairment usually affects attention, executive function, and visual processing leaving memory relatively preserved initially [5,11,14] unlike the cognitive profile in early AD. Memory impairment and naming problems appear later in the disease course [14], albeit patients with significant concomitant AD pathology show deficits on tests of memory and learning [12]. Moreover, short-term memory impairment reflects, as in PDD, disturbed retrieval of stored information, which can be improved with cues [4].

The presence of early, severe visuospatial deficits or delirium at disease onset predicts rapid decline [5,44]. Episodes of confusion occur otherwise during the course of the disease and may have confabulatory or delusional qualities [14]. Cognitive fluctuations can be described by caregivers as episodes of disengagement or "blank staring". Daytime somnolence is also frequently reported as a sign of fluctuating arousal [4,14].

Psychiatric/behavioral features

Visual hallucinations are prevalent in DLB in up to 80% of patients and are typically recurrent [14]. Early in the course of the illness hallucinations are usually unimodal, e.g. only visual. Typically they are well-formed and animate, patients can see adults or small children, deceased family members, or small animals [4]. They are usually emotionally neutral but can sometimes be scary or dysphoric [4]. Hallucinations must be differentiated from visual illusions, in which an object is visually misinterpreted; illusions are also common early in the illness, but are nonspecific for DLB [4]. Related phenomena, such as passage hallucinations, and a sense of presence, are reported [11].

It is observed that in the presence of severe vision loss, recurrent and vivid visual hallucinations suggest Charles Bonnet syndrome rather than DLB. When hallucinations are present only in a delirium state it is not sufficient for diagnosis of DLB [12]. A good indicator for the development of hallucinations is a severe visuospatial deficit early in the disease [14] although they may occur independently from visuospatial or perceptual impairment or dopaminergic medication [34,50]. Auditory and tactile hallucinations are seldom reported [14].

Delusions can arise typically later in the course and usually have a paranoid quality. Delusions about a partner's infidelity, house intruders, and theft are common. A phenomenon known as Capgras syndrome is described – as when a patient believes that a spouse or caregiver has been replaced by an imposter [4]. Delusions in some patients may relate to visual hallucinations and maybe systematized [12].

Depression and anxiety may be present but have no specific value as they are relatively common in the elderly (7, 43). Apathy without depression is often present, although not specific. With the progression of dementia, troublesome anxiety, and agitation may often develop [12].

Physical signs

Many patients with DLB have symmetric or axial predominant parkinsonism with bradykinesia and gait disturbance, while tremor is seen less frequently [51]. Tremor typically presents as a symmetric postural tremor, rather than an asymmetric rest tremor, though any variants are described. Gait impairment mimics that of PD with shuffling, slow turns, and decreased arm swing [4,52]. Stooped posture and postural instability are often present [12]. In up to 25% cases with autopsy verified DLB parkinsonian signs may be absent or very mild [11]. According to the Fourth consensus report of the DLB Consortium, 15% to 40% of DLB cases die without motor signs [47].

Rapid Eye Movement (REM) sleep Behavior Disorder (RBD), olfactory dysfunction, and constipation are common and may precede the illness over several years [53]. They are considered risk factors for all synucleinopathies [4]. RBD is a parasomnia in which normal paralysis of REM sleep is impaired. Dreams in RBD are acted out (e.g punching, kicking, shouting out), and often can result in injury – e.g. falling out of bed [4,49]. Other disturbances during sleep (common in DLB and PDD) are obstructive sleep apnea and periodic limb movements in sleep [12].

Autonomic impairments are very common in all LBDs. The most frequent are neurogenic urinary frequency or incontinence, orthostatic hypotension, constipation, siallorhea and seborrhea, altered sweating, and erectile dysfunction [4,12]. Orthostatic hypotension, more common later in the course of DLB, and its complications, particularly syncope and falls, can be exacerbated by medications [4]. It can be very problematic leading to inactivity and significantly worsening the quality of life. Falls are not only related to dysautonomia; they may be also due to cognitive impairment, motor symptoms, or a combination of these factors [52].

Diagnostic process

As dementia is an essential feature of DLB neurocognitive assessment is necessary. Neurocognitive assessment is necessary to perform but there are no specific recommendations

Citation: Krasowska J, Lökk J (2023) Parkinson's disease dementia and dementia with lewy bodies differences and similarities. Open J Parkinsons Dis Treatm 6(1): 001-013. DOI: https://dx.doi.org/10.17352/ojpdt.0000122

on what neuropsychological tests should be performed [11,47]. However, as the cognitive profile is the same as that in PDD [12], the cognitive scales must evaluate a broad range of cognitive domains - attention, language, visuospatial function, memory, and executive function. It is useful to identify the first cognitive domains impaired, as these can point toward DLB [4,6]. The mixed pathology complicates the neuropsychological profile, making it difficult to distinguish mixed AD and DLB from pure AD [5]. The disease is a diagnostic challenge, especially at the early stages of the disease, and in patients with mixed neuropathology, which occur in over 50% of DLB patients [51].

Structural imaging of the brain can be performed by CT or MRI, the latter is superior because it offers better specific tissue characterization including gray matter atrophy [32]. MRI may show some overlap with atrophy patterns seen in AD [32] but generally shows a pattern of generalized cortical atrophy, with less marked atrophy in the hippocampus than in AD 25]. Medial temporal lobe atrophy on MRI has robust discriminatory power for distinguishing AD from DLB [32,47]. Vascular pathologies, which are often seen in the elderly, need still to be evaluated concerning the influence of dementia syndrome, clinical features of DLB, and its rate of progression [32]. The MRI is nondiagnostic in DLB as well as in PDD [25].

Molecular imaging

FDG-PET in DLB demonstrates decreased occipital glucose metabolism which is the most distinct finding that is helpful in distinguishing from other neurodegenerative diseases and healthy controls [5,52]. Both AD and DLB show hypometabolism in the temporal and parietal regions [5]. In some patients, only the AD pattern of hypometabolism may be present [4].

Dopamine transporter (DAT) imaging with [[123I] FP-CIT-SPECT, in order to assess dopaminergic function shows, decreased DAT uptake in basal ganglia which is, however, not characteristic just for DLB because it also occurs in other atypical Parkinsonian syndromes and PD/PDD. It has been useful to distinguish between AD and DLB and has high sensitivity (78% to 88%) and specificity (90% to 100%) [4]. Although [[123I] FP-CIT-SPECT has high accuracy, the absence of an abnormal scan cannot fully exclude the presence of DLB [32].

Reduced uptake of 123iodine-MIBG (123I-MIBG) on myocardial scintigraphy is a widely accepted biomarker for DLB [14]. A decreased uptake of 123I -MIBG is a sign of denervation of cardiac sympathetic ganglia [4], a characteristic of LBDs in general [32]. Patients with coexisting diabetes mellitus or cardiac disease might provide false positive results and should not be examined only for diagnostic purposes [5,32].

Imaging of amyloid, tau, cholinergic dysfunction, and neuroinflammation is not available in a routine assessment. Emerging knowledge relating to considering new as well as current biomarkers seems likely to give more information about the different pathologies and corresponding clinical picture, however, more research is needed [5,54].

Other diagnostic tools

There is still an area lacking sufficient evidence for using biomarkers in CSF that are specific to DLB. CSF may show decreased levels of Aβ1-42 or increased total and /or phospho tau (AD-related pathology) [12]. CSF levels of α-syn may be slightly decreased in DLB or PD (relative to AD and controls), but this cannot be used in the clinic yet [12]. Extracellular α-syn might be the pathological substrate of Lewy body disorders and is promising as a therapeutic target [5].

Polysomnography for RBD confirmation is a helpful diagnostic tool, especially in formal diagnosis but adequate information can be assessed by accurate questions/ questionnaires [5].

Analysis of electroencephalogram (EEG) is useful for differentiating DLB and AD [theta/delta waves in particularly posterior and anterior/temporal regions are more significant in DLB] [12,14] but measures and methods have not been validated for routine use [12].

Therapy

There is no curable treatment for any neurodegenerative disorder at present but studies targeting disease modification are being conducted [26,34]. The paucity of significant evidence for medications in the treatment of DLB for several agents alone or in combination with no medication approved either in Europa or in the US [55]. However, many medications known to be effective for PD or AD are found to be also beneficial for symptom management in DLB [12,47,52,56]. As in all dementia syndromes, the treatment is complex and should focus on pharmacological and non-pharmacological approaches carried by the multi-professional team together with caregivers, social workers, and municipality as well as volunteer-driven organizations (day centers, and institutions). Education both for the patients and caregivers is necessary for the satisfactory management of the disease's process--- the goal is to decrease the disease burden for a patient and caregiver by slowing the progress of the illness; alleviating symptoms and postponing the worsening [57].

The medication can be selected in groups targeting: cognitive impairment, neuropsychiatric/ behavioral symptoms, gait/balance problems, and other symptoms (e.g. due to autonomic failure). Dosing and medication must be selected and individualized taking into account the degree of the functional impact of symptoms being targeted and side-effect thresholds [52,58]. For cognition acetylcholinesterase inhibitors (AChE-Is) are used based on the loss of cholinergic neurons in the nucleus basalis of Meynert and decreased cortical choline acetyltransferase [52].

The results on cognition for the whole group of AChE-Is indicate beneficial effects on global impression and some specific cognitive domains (attention, processing speed, executive functions, memory, and language) but did not improve visuospatial cognition when compared to placebo [39]. Slightly different effects for separate AChE-I were noted as well as safety outcomes, which in general are very good. All

Citation: Krasowska J, Lökk J (2023) Parkinson's disease dementia and dementia with lewy bodies differences and similarities. Open J Parkinsons Dis Treatm 6(1): 001-013. DOI: https://dx.doi.org/10.17352/ojpdt.0000122

drugs- rivastigmine, donepezil, and galantamine - reduced visual hallucinations and delusions in mild to moderate states [39,55]. None of them has worsened Parkinsonian signs [55]. Memantine is a glutamatergic NMDA receptor antagonist and was proven to improve attention, processing speed and executive functions, and global impression [39,55]. It has been reported that memantine decreases the probable rapid eye movement sleep behavior disorder in patients with DLB and PDD [39] and improves behavior [55].

Hallucinations and psychosis may be very problematic if they don't respond to AChE-Is. Some patients may need low doses of an atypical antipsychotic drug such as quetiapine to manage their agitation and prevent cognitive fluctuations [55]. Clozapine has been established in PD psychosis, but efficacy and tolerability in DLB have not been proven [47]. Antipsychotic drugs are problematic as DLB patients are particularly sensitive to neuroleptics (specifically those with D2 receptor antagonism), e.g. typical antipsychotic agents such as haloperidol or high-potency atypical agents such as olanzapine [4,19,54]. Such drugs can trigger or exacerbate parkinsonism, as they can in PD, and this may be irreversible [4]. Neuroleptics have been associated with increased mortality, and patients with DLB are at increased risk for the neuroleptic malignant syndrome [4,19]. Neuroleptics can also negatively affect cognition and impair attention and alertness [4]. Some other drugs might be recommended in the future – such as low doses of valproic acid (or divalproex) as an adjunct to drugs like quetiapine in managing the agitation of DLB or pimavanserin [selective 5-hydroxytryptophan (5-HT) 2A receptor inverse agonist] which had been approved for psychosis in PD [55].

Treatment of parkinsonism may be challenging as patients with DLB often have a limited response to dopaminergic medications [4]. Levodopa is recommended - in low doses in order to avoid aggravating cognition or psychosis– but is generally less effective than in PD [4,55]. Dopamine agonists are usually not recommended as they are more likely to cause/worsen hallucinations and other side effects [12]. A phase 3 trial on zonisamide, an anticonvulsant that is approved in Japan for parkinsonism in PD, is ongoing in DLB patients [55].

In RBD, if treatment is required, a number of non-pharmacologic steps may be useful. These include removing sharp objects from the sleep environment, adding soft bedding to the floor next to the patient, or something alike. Several medications can be effective in REM sleep behavior disorder. Benzodiazepines (especially clonazepam) are particularly effective, but these carry the risk of exacerbating confusion. Melatonin can be effective as well and is usually well tolerated [4,55]. Some patients with REM sleep behavior disorder have concomitant obstructive sleep apnea, and the use of positive airway pressure may resolve both obstructive sleep apnea and REM sleep behavior disorder [4]. For insomnia, similar drugs used for agitation may be considered as well as low doses of benzodiazepines such as zolpidem [12]. There are newer sleep-promoting agents, e.g. extended-release zolpidem, which have a theoretic advantage of lower risk of tolerance but have not been formally studied in patients with DLB [12]. Selective serotonin reuptake inhibitors (SSRI) or serotonin-norepinephrine reuptake inhibitors (SNRI) for depression or apathy may be used [12].

There are some novel drugs in ongoing clinical trials with the potential for disease-modifying effects. Some immunotherapy interventions in animal models are tested (against α-syn) and the future will show what could be relevant in clinical practice [50].

Comparison of DLB *vs*. PDD

The similarity between DLB and PDD is striking [59]. However, there are some differences found between them, though not consistent in all researched papers [60]. First, patients with DLB may be younger at the onset of symptoms than patients with PDD [11]. A predominance of DLB incidence in men across all ages, more than in PDD, was found in the Olmsted County study [19]. PDD patients must have established Parkinsonian signs at the time of dementia onset, whereas not all DLB patients will develop them at all or only mild symptoms during the disease course. Parkinsonism may easily be foreseen by inexperienced movement disorders clinicians. Parkinsonian motor signs, if developed, are in DLB often symmetric, and bradykinesia and gait impairment is more common than the rest tremor [4]. Visual hallucinations are shown to be more frequent, as well as cognitive fluctuations at the disease onset in DLB [11,34]; hallucinations are more common during the course of DLB (62.5%) than in those of PDD (20%) [19]. Hallucinations in DLB may occur spontaneously, while in PDD they typically occur after dopaminergic therapy. However, they have been described even in drug-naïve PD patients [34].

The pattern of initial cognitive dysfunction was found in some studies slightly different between DLB and PDD with greater deficiencies of attention, executive function, and constructive abilities, as well as significantly lower ratings in episodic verbal memory tasks in DLB. The rate of cognitive decline can be faster in DLB than in PDD [34]. A visuospatial function may be disproportionally affected in DLB compared to PDD, possibly related to the higher degree of parietal atrophy seen in DLB compared to PDD [5].

Nonmotor features develop typically early in DLB, many of which may be subtle, including olfactory dysfunction, sleep disorders, autonomic dysfunction, constipation, and sialorrhea, although not specific to DLB [52]. RBD (REM sleep behavior disorder) shows a high prevalence in DLB. It may precede cognitive decline by decades and is now included as a core clinical feature, though it is not specific to DLB [34]. Generalized myoclonus can occur in some patients with DLB [4], which is not typical for PDD.

Genetically, there is a significant genetic overlap between PDD and DLB, as well as AD [42,61] but GWAS suggests that DLB may also have genetic risk factors that are distinct from those in AD and PD [42]. The genetic differences between PDD and DLB have, so far, not been studied in detail [13].

Neuropathologically, PDD and DLB are difficult to differentiate, apart from a higher prevalence of Alzheimer's-like pathology (found in the limbic and striatum) that occurs

Citation: Krasowska J, Lökk J (2023) Parkinson's disease dementia and dementia with lewy bodies differences and similarities. Open J Parkinsons Dis Treatm 6(1): 001-013. DOI: https://dx.doi.org/10.17352/ojpdt.0000122

in DLB [11,13,32]. The presence of severe AD pathology is rather a result of pathological aging, not necessarily determining the severity of cognitive impairment. Many research studies have shown that overwhelming AD pathology may mask PDD or DLB symptoms, thus resulting in AD diagnosis rather than PDD or DLB [61]. Brainstem may show minimal LB pathology in DLB and cortical distribution occur earlier than in PDD. However, in later stages, PDD and DLB show similar LB patterns [62]. Some studies have shown higher cortical LB load in the temporal and parietal regions, which seems to be a distinguishing feature of DLB [34]. Moreover, a lesser degree of dopaminergic cell loss is found in DLB compared to PDD [11,61].

On brain imaging a higher degree of parietal atrophy is seen in DLB compared to PDD, as well as temporal and occipital atrophy is more pronounced in DLB [23]. Normal FP-CIT scan excludes a diagnosis of PDD, but it does not exclude a diagnosis of DLB [5]. Some authors claim that dopamine uptake in the striatum is significantly lower in PDD compared to DLB [63]. A reduced occipital metabolism on FDG-PET is the most distinguishable finding for DLB, but patients with PDD may show hypometabolism in frontal, parietal, and occipital regions as well [5,52]. The same pattern without a significant difference in PDD and DLB is found when white matter hyperintensities (WMH) are investigated, however also often observed in elderly persons [33].

Patients with DLB are generally very sensitive to medications, especially neuroleptics. An almost pathognomic adverse worsening of symptoms is found when DLB patients are having neuroleptics in order to cope with psychotic problems. They often have a limited response to dopaminergic medications or show a lower threshold for adverse effects on them [4]. Despite the lack of specific studies on medication for symptoms of DLB, the pharmacological treatments do not differ from that approved for symptoms of PDD [36]. Symptom treatments are often managed by different specialist and in isolation, which make care more difficult to achieve [37].

Summary

DLB and PDD together are the second most common neurodegenerative disease causing dementia in the population over 65 years [5], sharing many clinical, genetic, pathophysiological, imaging, and morphological features [34]. There is a continuous debate among scientists whether these two are separate diseases, just different phenotypes on the basis of the same LB pathology (within the LBD spectrum), or the same disease [12,13,19,34,64]. Many authors tend to believe that PDD and DLB may be manifestations of the same neurodegenerative disorder [13,19]. The differences shown above are rather few and had not been reproduced in all studies [54,59].

It is difficult or impossible to differentiate a single patient with parkinsonism as PDD or DLB based on a single examination, without regard to the temporal sequence of events [5]. The 1-year rule, distinguishing both entities by the relative timing of when cognitive and motor symptoms appear, is helpful in clinical practice [59]. However, recent studies question this 1-year rule, because emerging new evidence has shown that cognition may be severely impaired in PD several years before the onset of motor symptoms [34].

The research regarding these issues is in progress, but many questions are still unanswered. With more information given, new questions and doubts arise, which make science a challenge but also an attractive field to deal with despite the huge efforts and economic costs needed. One of the questions is why dopaminergic neurons in substantia nigra are more vulnerable to PDD despite the same underlying LB pathology [61]. What is the role of AD pathology in the occurrence of LB pathology? What is driving the processes that can give rise to different phenotypes [61]? Why are there different phenotypes despite the same gene mutations? Is it due to other loci for mutations, or are other factors cooperating? And, if so, which are those? Another issue is the clinical similarity between AD and DLB, especially at the beginning of the disease courses [64-66]. It might be, at the end of the day that "DLB and PDD are the same diseases - as long as unquestionable biomarkers definitely distinguishing both entities are not found [64-66].

References

1. Koros C, Stefanis L, Scarmeas N. Parkinsonism and dementia. J Neurol Sci. 2022 Feb 15;433:120015. doi: 10.1016/j.jns.2021.120015. Epub 2021 Oct 2. PMID: 34642023.

2. Rabinovici GD. Late-onset Alzheimer Disease. Continuum (Minneap Minn). 2019 Feb;25(1):14-33. doi: 10.1212/CON.0000000000000700. PMID: 30707185; PMCID: PMC6548536.

3. Kempster PA, O'Sullivan SS, Holton JL, Revesz T, Lees AJ. Relationships between age and late progression of Parkinson's disease: a clinico-pathological study. Brain. 2010 Jun;133(Pt 6):1755-62. doi: 10.1093/brain/awq059. Epub 2010 Apr 5. PMID: 20371510.

4. Gomperts SN. Lewy Body Dementias: Dementia With Lewy Bodies and Parkinson Disease Dementia. Continuum (Minneap Minn). 2016 Apr;22(2 Dementia):435-63. doi: 10.1212/CON.0000000000000309. PMID: 27042903; PMCID: PMC5390937.

5. Walker Z, Possin KL, Boeve BF, Aarsland D. Lewy body dementias. Lancet. 2015 Oct 24;386(10004):1683-97. doi: 10.1016/S0140-6736(15)00462-6. PMID: 26595642; PMCID: PMC5792067.

6. Aarsland D, Batzu L, Halliday GM, Geurtsen GJ, Ballard C, Ray Chaudhuri K, Weintraub D. Parkinson disease-associated cognitive impairment. Nat Rev Dis Primers. 2021 Jul 1;7(1):47. doi: 10.1038/s41572-021-00280-3. Erratum in: Nat Rev Dis Primers. 2021 Jul 13;7(1):53. PMID: 34210995.

7. Scheltens P, Blennow K, Breteler MM, de Strooper B, Frisoni GB, Salloway S, Van der Flier WM. Alzheimer's disease. Lancet. 2016 Jul 30;388(10043):505-17. doi: 10.1016/S0140-6736(15)01124-1. Epub 2016 Feb 24. PMID: 26921134.

8. Sanabria-Castro A, Alvarado-Echeverría I, Monge-Bonilla C. Molecular Pathogenesis of Alzheimer's Disease: An Update. Ann Neurosci. 2017 May;24(1):46-54. doi: 10.1159/000464422. Epub 2017 Apr 21. PMID: 28588356; PMCID: PMC5448443.

9. Small SA, Duff K. Linking Abeta and tau in late-onset Alzheimer's disease: a dual pathway hypothesis. Neuron. 2008 Nov 26;60(4):534-42. doi: 10.1016/j.neuron.2008.11.007. PMID: 19038212; PMCID: PMC2692134.

10. Boström F, Jönsson L, Minthon L, Londos E. Patients with Lewy body dementia use more resources than those with Alzheimer's disease. Int J Geriatr Psychiatry. 2007 Aug;22(8):713-9. doi: 10.1002/gps.1738. PMID: 17195278.

Citation: Krasowska J, Lökk J (2023) Parkinson's disease dementia and dementia with lewy bodies differences and similarities. Open J Parkinsons Dis Treatm 6(1): 001-013. DOI: https://dx.doi.org/10.17352/ojpdt.0000122

11. Outeiro TF, Koss DJ, Erskine D, Walker L, Kurzawa-Akanbi M, Burn D, Donaghy P, Morris C, Taylor JP, Thomas A, Attems J, McKeith I. Dementia with Lewy bodies: an update and outlook. Mol Neurodegener. 2019 Jan 21;14(1):5. doi: 10.1186/s13024-019-0306-8. PMID: 30665447; PMCID: PMC6341685.

12. Galasko D. Lewy Body Disorders. Neurol Clin. 2017 May;35(2):325-338. doi: 10.1016/j.ncl.2017.01.004. PMID: 28410662; PMCID: PMC5912679.

13. Weil RS. Current concepts and controversies in the pathogenesis of Parkinson's disease dementia and Dementia with Lewy Bodies[version 1; peer review: 2 approved] F1000Res 2017; 6:1604 F1000Res.doi: 10.12688/f1000research.11725.1

14. Capouch SD, Farlow MR, Brosch JR. A Review of Dementia with Lewy Bodies' Impact, Diagnostic Criteria and Treatment. Neurol Ther. 2018 Dec;7(2):249-263. doi: 10.1007/s40120-018-0104-1. Epub 2018 Jul 9. PMID: 29987534; PMCID: PMC6283803.

15. Goldman JG, Sieg E. Cognitive Impairment and Dementia in Parkinson Disease. Clin Geriatr Med. 2020 May;36(2):365-377. doi: 10.1016/j.cger.2020.01.001. Epub 2020 Jan 23. PMID: 32222308.

16. Goetz CG, Emre M, Dubois B. Parkinson's disease dementia: definitions, guidelines, and research perspectives in diagnosis. Ann Neurol. 2008 Dec;64 Suppl 2:S81-92. doi: 10.1002/ana.21455. PMID: 19127578.

17. Aarsland D, Kurz MW. The epidemiology of dementia associated with Parkinson disease. J Neurol Sci. 2010 Feb 15;289(1-2):18-22. doi: 10.1016/j.jns.2009.08.034. Epub 2009 Sep 4. PMID: 19733364.

18. Severiano E Sousa C, Alarcão J, Pavão Martins I, Ferreira JJ. Frequency of dementia in Parkinson's disease: A systematic review and meta-analysis. J Neurol Sci. 2022 Jan 15;432:120077. doi: 10.1016/j.jns.2021.120077. Epub 2021 Dec 3. PMID: 34896923.

19. Savica R, Grossardt BR, Bower JH, Boeve BF, Ahlskog JE, Rocca WA. Incidence of dementia with Lewy bodies and Parkinson disease dementia. JAMA Neurol. 2013 Nov;70(11):1396-402. doi: 10.1001/jamaneurol.2013.3579. PMID: 24042491; PMCID: PMC4181848.

20. Roheger M, Kalbe E, Liepelt-Scarfone I. Progression of Cognitive Decline in Parkinson's Disease. J Parkinsons Dis. 2018;8(2):183-193. doi: 10.3233/JPD-181306. PMID: 29914040; PMCID: PMC6004891.

21. Prell T, Witte OW, Grosskreutz J. Biomarkers for Dementia, Fatigue, and Depression in Parkinson's Disease. Front Neurol. 2019 Mar 8;10:195. doi: 10.3389/fneur.2019.00195. PMID: 30906277; PMCID: PMC6418014.

22. Vasconcellos LF, Pereira JS. Parkinson's disease dementia: Diagnostic criteria and risk factor review. J Clin Exp Neuropsychol. 2015;37(9):988-93. doi: 10.1080/13803395.2015.1073227. PMID: 26332178.

23. Walker L, Stefanis L, Attems J. Clinical and neuropathological differences between Parkinson's disease, Parkinson's disease dementia and dementia with Lewy bodies - current issues and future directions. J Neurochem. 2019 Sep;150(5):467-474. doi: 10.1111/jnc.14698. Epub 2019 Apr 23. PMID: 30892688.

24. Martin WRW, Younce JR, Campbell MC, Racette BA, Norris SA, Ushe M, Criswell S, Davis AA, Alfradique-Dunham I, Maiti B, Cairns NJ, Perrin RJ, Kotzbauer PT, Perlmutter JS. Neocortical Lewy Body Pathology Parallels Parkinson's Dementia, but Not Always. Ann Neurol. 2023 Jan;93(1):184-195. doi: 10.1002/ana.26542. Epub 2022 Nov 22. PMID: 36331161.

25. Parkkinen L, Pirttilä T, Alafuzoff I. Applicability of current staging/categorization of alpha-synuclein pathology and their clinical relevance. Acta Neuropathol. 2008 Apr;115(4):399-407. doi: 10.1007/s00401-008-0346-6. Epub 2008 Feb 23. PMID: 18297293; PMCID: PMC2270355.

26. Caviness JN, Lue L, Adler CH, Walker DG. Parkinson's disease dementia and potential therapeutic strategies. CNS Neurosci Ther. 2011 Feb;17(1):32-44. doi: 10.1111/j.1755-5949.2010.00216.x. Epub 2010 Dec 28. PMID: 21199444; PMCID: PMC6493795.

27. Braak H, Rüb U, Jansen Steur EN, Del Tredici K, de Vos RA. Cognitive status correlates with neuropathologic stage in Parkinson disease. Neurology. 2005 Apr 26;64(8):1404-10. doi: 10.1212/01.WNL.0000158422.41380.82. PMID: 15851731.

28. Caviness JN, Driver-Dunckley E, Connor DJ, Sabbagh MN, Hentz JG, Noble B, Evidente VG, Shill HA, Adler CH. Defining mild cognitive impairment in Parkinson's disease. Mov Disord. 2007 Jul 15;22(9):1272-7. doi: 10.1002/mds.21453. PMID: 17415797.

29. Kehagia AA, Barker RA, Robbins TW. Cognitive impairment in Parkinson's disease: the dual syndrome hypothesis. Neurodegener Dis. 2013;11(2):79-92. doi: 10.1159/000341998. Epub 2012 Oct 3. PMID: 23038420; PMCID: PMC5079071.

30. Hoops S, Nazem S, Siderowf AD, Duda JE, Xie SX, Stern MB, Weintraub D. Validity of the MoCA and MMSE in the detection of MCI and dementia in Parkinson disease. Neurology. 2009 Nov 24;73(21):1738-45. doi: 10.1212/WNL.0b013e3181c34b47. PMID: 19933974; PMCID: PMC2788810.

31. Kulisevsky J, Pagonabarraga J. Cognitive impairment in Parkinson's disease: tools for diagnosis and assessment. Mov Disord. 2009 Jun 15;24(8):1103-10. doi: 10.1002/mds.22506. PMID: 19353727.

32. Yousaf T, Dervenoulas G, Valkimadi PE, Politis M. Neuroimaging in Lewy body dementia. J Neurol. 2019 Jan;266(1):1-26. doi: 10.1007/s00415-018-8892-x. Epub 2018 May 14. PMID: 29761296; PMCID: PMC6342883.

33. Burton EJ, McKeith IG, Burn DJ, Firbank MJ, O'Brien JT. Progression of white matter hyperintensities in Alzheimer disease, dementia with lewy bodies, and Parkinson disease dementia: a comparison with normal aging. Am J Geriatr Psychiatry. 2006 Oct;14(10):842-9. doi: 10.1097/01.JGP.0000236596.56982.1c. PMID: 17001024.

34. Jellinger KA, Korczyn AD. Are dementia with Lewy bodies and Parkinson's disease dementia the same disease? BMC Med. 2018 Mar 6;16(1):34. doi: 10.1186/s12916-018-1016-8. PMID: 29510692; PMCID: PMC5840831.

35. Brooks DJ. The role of structural and functional imaging in parkinsonian states with a description of PET technology. Semin Neurol. 2008 Sep;28(4):435-45. doi: 10.1055/s-0028-1083690. Epub 2008 Oct 8. PMID: 18843572.

36. Weintraub D, Aarsland D, Chaudhuri KR, Dobkin RD, Leentjens AF, Rodriguez-Violante M, Schrag A. The neuropsychiatry of Parkinson's disease: advances and challenges. Lancet Neurol. 2022 Jan;21(1):89-102. doi: 10.1016/S1474-4422(21)00330-6. PMID: 34942142; PMCID: PMC8800169.

37. Taylor JP, McKeith IG, Burn DJ, Boeve BF, Weintraub D, Bamford C, Allan LM, Thomas AJ, O'Brien JT. New evidence on the management of Lewy body dementia. Lancet Neurol. 2020 Feb;19(2):157-169. doi: 10.1016/S1474-4422(19)30153-X. Epub 2019 Sep 10. PMID: 31519472; PMCID: PMC7017451.

38. Poewe W, Gauthier S, Aarsland D, Leverenz JB, Barone P, Weintraub D, Tolosa E, Dubois B. Diagnosis and management of Parkinson's disease dementia. Int J Clin Pract. 2008 Oct;62(10):1581-7. doi: 10.1111/j.1742-1241.2008.01869.x. PMID: 18822028; PMCID: PMC2658001.

39. Meng YH, Wang PP, Song YX, Wang JH. Cholinesterase inhibitors and memantine for Parkinson's disease dementia and Lewy body dementia: A meta-analysis. Exp Ther Med. 2019 Mar;17(3):1611-1624. doi: 10.3892/etm.2018.7129. Epub 2018 Dec 24. PMID: 30783428; PMCID: PMC6364145.

40. Brundin P, Dave KD, Kordower JH. Therapeutic approaches to target alpha-synuclein pathology. Exp Neurol. 2017 Dec;298(Pt B):225-235. doi: 10.1016/j.expneurol.2017.10.003. Epub 2017 Oct 4. PMID: 28987463; PMCID: PMC6541231.

41. Sanford AM. Lewy Body Dementia. Clin Geriatr Med. 2018 Nov;34(4):603-615. doi: 10.1016/j.cger.2018.06.007. Epub 2018 Aug 21. PMID: 30336990.

42. Orme T, Guerreiro R, Bras J. The Genetics of Dementia with Lewy Bodies: Current Understanding and Future Directions. Curr Neurol Neurosci Rep. 2018

Citation: Krasowska J, Lökk J (2023) Parkinson's disease dementia and dementia with lewy bodies differences and similarities. Open J Parkinsons Dis Treatm 6(1): 001-013. DOI: https://dx.doi.org/10.17352/ojpdt.0000122

Aug 10;18(10):67. doi: 10.1007/s11910-018-0874-y. PMID: 30097731; PMCID: PMC6097049.

43. Williams MM, Xiong C, Morris JC, Galvin JE. Survival and mortality differences between dementia with Lewy bodies vs Alzheimer disease. Neurology. 2006 Dec 12;67(11):1935-41. doi: 10.1212/01.wnl.0000247041.63081.98. PMID: 17159097.

44. Gaig C, Valldeoriola F, Gelpi E, Ezquerra M, Llufriu S, Buongiorno M, Rey MJ, Martí MJ, Graus F, Tolosa E. Rapidly progressive diffuse Lewy body disease. Mov Disord. 2011 Jun;26(7):1316-23. doi: 10.1002/mds.23506. Epub 2011 Apr 11. PMID: 21484863.

45. Louis ED, Marder K, Cote L, Tang M, Mayeux R. Mortality from Parkinson disease. Arch Neurol. 1997 Mar;54(3):260-4. doi: 10.1001/archneur.1997.00550150024011. PMID: 9074394.

46. Kaivola K, Shah Z, Chia R; International LBD Genomics Consortium; Scholz SW. Genetic evaluation of dementia with Lewy bodies implicates distinct disease subgroups. Brain. 2022 Jun 3;145(5):1757-1762. doi: 10.1093/brain/awab402. Erratum in: Brain. 2023 Apr 06;: PMID: 35381062; PMCID: PMC9423712.

47. McKeith IG, Boeve BF, Dickson DW, Halliday G, Taylor JP, Weintraub D, Aarsland D, Galvin J, Attems J, Ballard CG, Bayston A, Beach TG, Blanc F, Bohnen N, Bonanni L, Bras J, Brundin P, Burn D, Chen-Plotkin A, Duda JE, El-Agnaf O, Feldman H, Ferman TJ, Ffytche D, Fujishiro H, Galasko D, Goldman JG, Gomperts SN, Graff-Radford NR, Honig LS, Iranzo A, Kantarci K, Kaufer D, Kukull W, Lee VMY, Leverenz JB, Lewis S, Lippa C, Lunde A, Masellis M, Masliah E, McLean P, Mollenhauer B, Montine TJ, Moreno E, Mori E, Murray M, O'Brien JT, Orimo S, Postuma RB, Ramaswamy S, Ross OA, Salmon DP, Singleton A, Taylor A, Thomas A, Tiraboschi P, Toledo JB, Trojanowski JQ, Tsuang D, Walker Z, Yamada M, Kosaka K. Diagnosis and management of dementia with Lewy bodies: Fourth consensus report of the DLB Consortium. Neurology. 2017 Jul 4;89(1):88-100. doi: 10.1212/WNL.0000000000004058. Epub 2017 Jun 7. PMID: 28592453; PMCID: PMC5496518.

48. Toledo JB, Abdelnour C, Weil RS, Ferreira D, Rodriguez-Porcel F, Pilotto A, Wyman-Chick KA, Grothe MJ, Kane JPM, Taylor A, Rongve A, Scholz S, Leverenz JB, Boeve BF, Aarsland D, McKeith IG, Lewis S, Leroi I, Taylor JP; ISTAART Lewy body dementias Trial Methods Working Group. Dementia with Lewy bodies: Impact of co-pathologies and implications for clinical trial design. Alzheimers Dement. 2023 Jan;19(1):318-332. doi: 10.1002/alz.12814. Epub 2022 Oct 14. PMID: 36239924; PMCID: PMC9881193.

49. Donaghy PC, McKeith IG. The clinical characteristics of dementia with Lewy bodies and a consideration of prodromal diagnosis. Alzheimers Res Ther. 2014 Jul 21;6(4):46. doi: 10.1186/alzrt274. PMID: 25484925; PMCID: PMC4255387.

50. Cagnin A, Gnoato F, Jelcic N, Favaretto S, Zarantonello G, Ermani M, Dam M. Clinical and cognitive correlates of visual hallucinations in dementia with Lewy bodies. J Neurol Neurosurg Psychiatry. 2013 May;84(5):505-10. doi: 10.1136/jnnp-2012-304095. Epub 2012 Dec 21. PMID: 23264688.

51. Chin KS, Teodorczuk A, Watson R. Dementia with Lewy bodies: Challenges in the diagnosis and management. Aust N Z J Psychiatry. 2019 Apr;53(4):291-303. doi: 10.1177/0004867419835029. Epub 2019 Mar 8. PMID: 30848660.

52. Mayo MC, Bordelon Y. Dementia with Lewy bodies. Semin Neurol. 2014 Apr;34(2):182-8. doi: 10.1055/s-0034-1381741. Epub 2014 Jun 25. PMID: 24963677.

53. Donaghy PC, O'Brien JT, Thomas AJ. Prodromal dementia with Lewy bodies. Psychol Med. 2015 Jan;45(2):259-68. doi: 10.1017/S0033291714000816. Epub 2014 Apr 3. PMID: 25066469.

54. Walker L, Stefanis L, Attems J. Clinical and neuropathological differences between Parkinson's disease, Parkinson's disease dementia and dementia with Lewy bodies - current issues and future directions. J Neurochem. 2019 Sep;150(5):467-474. doi: 10.1111/jnc.14698. Epub 2019 Apr 23. PMID: 30892688.

55. Hershey LA, Coleman-Jackson R. Pharmacological Management of Dementia with Lewy Bodies. Drugs Aging. 2019 Apr;36(4):309-319. doi: 10.1007/s40266-018-00636-7. PMID: 30680679; PMCID: PMC6435621.

56. Rektorova I. Current treatment of behavioral and cognitive symptoms of Parkinson's disease. Parkinsonism Relat Disord. 2019 Feb;59:65-73. doi: 10.1016/j.parkreldis.2019.02.042. Epub 2019 Feb 28. PMID: 30852149.

57. Frazer M, Rashid N, Bunner S, Skoog B, Abler V. Burden of Illness Among Patients with Psychosis due to Dementia with Lewy Bodies and Other Dementias. Am J Alzheimers Dis Other Demen. 2023 Jan-Dec;38:15333175231163521. doi: 10.1177/15333175231163521. PMID: 36893766.

58. Kyle K, Bronstein JM. Treatment of psychosis in Parkinson's disease and dementia with Lewy Bodies: A review. Parkinsonism Relat Disord. 2020 Jun;75:55-62. doi: 10.1016/j.parkreldis.2020.05.026. Epub 2020 May 25. PMID: 32480308.

59. Sezgin M, Bilgic B, Tinaz S, Emre M. Parkinson's Disease Dementia and Lewy Body Disease. Semin Neurol. 2019 Apr;39(2):274-282. doi: 10.1055/s-0039-1678579. Epub 2019 Mar 29. PMID: 30925619.

60. Pennington C, Duncan G, Ritchie C. Altered awareness of cognitive and neuropsychiatric symptoms in Parkinson's disease and Dementia with Lewy Bodies: A systematic review. Int J Geriatr Psychiatry. 2021 Jan;36(1):15-30. doi: 10.1002/gps.5415. Epub 2020 Sep 14. PMID: 32869379.

61. Tsuboi Y, Dickson DW. Dementia with Lewy bodies and Parkinson's disease with dementia: are they different? Parkinsonism Relat Disord. 2005 Jun;11 Suppl 1:S47-51. doi: 10.1016/j.parkreldis.2004.10.014. PMID: 15885629.

62. Beach TG, Adler CH, Lue L, Sue LI, Bachalakuri J, Henry-Watson J, Sasse J, Boyer S, Shirohi S, Brooks R, Eschbacher J, White CL 3rd, Akiyama H, Caviness J, Shill HA, Connor DJ, Sabbagh MN, Walker DG; Arizona Parkinson's Disease Consortium. Unified staging system for Lewy body disorders: correlation with nigrostriatal degeneration, cognitive impairment and motor dysfunction. Acta Neuropathol. 2009 Jun;117(6):613-34. doi: 10.1007/s00401-009-0538-8. Epub 2009 Apr 28. PMID: 19399512; PMCID: PMC2757320.

63. Colloby SJ, McParland S, O'Brien JT, Attems J. Neuropathological correlates of dopaminergic imaging in Alzheimer's disease and Lewy body dementias. Brain. 2012 Sep;135(Pt 9):2798-808. doi: 10.1093/brain/aws211. PMID: 22961551.

64. Friedman JH. Dementia with Lewy Bodies and Parkinson Disease Dementia: It is the Same Disease! Parkinsonism Relat Disord. 2018 Jan;46 Suppl 1:S6-S9. doi: 10.1016/j.parkreldis.2017.07.013. Epub 2017 Jul 18. PMID: 28756177.

65. Litvan I, Goldman JG, Tröster AI, Schmand BA, Weintraub D, Petersen RC, Mollenhauer B, Adler CH, Marder K, Williams-Gray CH, Aarsland D, Kulisevsky J, Rodriguez-Oroz MC, Burn DJ, Barker RA, Emre M. Diagnostic criteria for mild cognitive impairment in Parkinson's disease: Movement Disorder Society Task Force guidelines. Mov Disord. 2012 Mar;27(3):349-56. doi: 10.1002/mds.24893. Epub 2012 Jan 24. PMID: 22275317; PMCID: PMC3641655.

66. Emre M, Aarsland D, Brown R, Burn DJ, Duyckaerts C, Mizuno Y, Broe GA, Cummings J, Dickson DW, Gauthier S, Goldman J, Goetz C, Korczyn A, Lees A, Levy R, Litvan I, McKeith I, Olanow W, Poewe W, Quinn N, Sampaio C, Tolosa E, Dubois B. Clinical diagnostic criteria for dementia associated with Parkinson's disease. Mov Disord. 2007 Sep 15;22(12):1689-707; quiz 1837. doi: 10.1002/mds.21507. PMID: 17542011.

Citation: Krasowska J, Lökk J (2023) Parkinson's disease dementia and dementia with lewy bodies differences and similarities. Open J Parkinsons Dis Treatm 6(1): 001-013. DOI: https://dx.doi.org/10.17352/ojpdt.0000122