**Lewy body diseases presenting with cognitive impairment and Parkinsonism**

**Introduction**

Neurodegenerative diseases often present with a great deal of overlap in clinical features and pathology, and lewy body diseases, specifically Dementia with Lewy Bodies (DLB) and Parkinson’s Disease Dementia (PDD), are no exception. Clinical features of these lewy body diseases include cognitive impairment and Parkinsonism, however the distinction between DLB and PDD is generally based on the timing of the onset of symptoms, as well as specific trends in the clinical presentation of the disease. The diagnosis of PDD applies when a patient presents with the signs/symptoms of Parkinson’s disease (tremor, muscle rigidity, slowed movement, and postural instability) for at least one year prior to the development of cognitive impairment 1,2. Conversely, DLB is the appropriate diagnosis when dementia and significant cognitive symptoms either precede or occur within the first year of Parkinsonism 2. The medical diagnostic criteria for DLB are dementia and two out of the three following core characteristics: fluctuations of cognition or alertness, visual hallucinations, and Parkinsonism 3,4. Parkinsonism is noted in up to 90% of patients with DLB, contributing to the similar physical appearance of DLB and PDD 4. A distinction in the Parkinsonism symptoms between PDD and DLB is that movement disturbances are often more symmetrical with DLB 4,5.

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|  | **Onset/Timing** | **Clinical Presentation** |
| **Dementia with Lewy Bodies** | Cognitive impairments/dementia precedes or occurs within one year of parkinsonism symptoms | Dementia  AND  2 of the 3 following features: fluctuations of cognition or alertness, visual hallucinations, Parkinsonism |
| **Parkinson’s Disease Dementia** | Diagnosis of Parkinson’s disease precedes onset of cognitive symptoms by at least one year. | Tremor, muscle rigidity, slowed movement, postural instability |

Despite the different diagnostic criteria for PDD and DLB, it appears that lewy body pathology occurs on a spectrum, with variable onset of the different clinical features. An additional complexity that has been introduced when considering PDD and DLB is the concept of mild cognitive impairment. Mild Cognitive Impairment (MCI) with Parkinson’s Disease is a description that has been used more recently to describe notable cognitive symptoms seen with PD that are below the threshold for diagnosing dementia. It is thought that over time this MCI may, but does not necessarily evolve into Parkinson’s Disease Dementia. This has been modeled after the progression of cognitive symptoms seen in Alzheimer’s disease (MCI to AD) 2. Prodromal Lewy body Dementia is another emerging concept that describes the onset of symptoms associated with Lewy Body Dementia prior to a full presentation 2. Prodromal symptoms are divided into three categories: cognitive impairment, behavioral/psychiatric phenomena, and physical symptoms. The most commonly reported prodromal symptoms include those in the behavioral and physical symptom categories, however cognitive fluctuations, primarily non-memory mild cognitive impairment has been noted to precede the development of Dementia with Lewy Bodies 2.

**Pathology**

The end result of PDD and DLB is actually quite similar, with both of these diseases presenting with diffuse lewy bodies, dopaminergic and cholinergic dysfunction, and accumulation of alpha-synuclein 2,6. Compared with PDD, DLB appears to have increased amyloid plaque accumulation in the striatum, more alpha-synuclein deposition in the hippocampus, and less cell loss in the substantia nigra 2. In both PDD and DLB there is significant wide spread neural damage. It has been suggested that lewy body pathology progresses from the medulla to the pons, midbrain and subcortical regions, and then finally to the neocortex 2. While less information is available to understand the process as compared to the end result of these diseases, some recent work suggests that there may be greater and earlier cortical involvement in DLB compared to PDD 7.

**Clinical presentation of DLB**

The focus of the remainder of this discussion will be the clinical presentation of DLB and the impact that the cognitive and physical impairments can have on the day to day functioning of the individual and their family/caregivers.

**APTA Practice Patterns**

Practice patterns that directly relate to DLB include 8:

5A: Primary Prevention/ Risk Reduction for Loss of Balance and Falling

5E: Impaired Motor Function and Sensory Integrity Associated with Progressive Disorders of the Central Nervous System

*Cognitive impairments (nervous system)*

Dementia is the key feature of DLB, however there are several other specific characteristics associated with the clinical presentation of DLB. Fluctuations in cognition are very common and often appear early with DLB 3. While this is associated with many types of dementia it is particularly common among individuals diagnosed with DLB and 60-80% of individuals display significant fluctuations in cognitive status or alertness 4. Fluctuations can be quite variable in terms of time and appearance; however generally there is a waxing/waning of cognition associated with periods of behavioral confusion, inattention, hyper somnolence, incoherent speech, or stupor 4,9. Other cognitive impairments associated with DLB include deficits in executive function (i.e., judgment, planning, organization), attention, and visuospatial skills 5,9. Memory deficits can occur as well, though they are not reported as commonly as with other dementias, and the memory deficits associated with DLB occur later in the disease progression and are often related to visual memory 4,10. Neuropsychiatric disturbances such as visual hallucinations and rapid eye movement behavior disorder (RBD) also occur in the majority of patients with DLB, and are often apparent in the earlier phases of disease 3-5. Depression, anxiety, and apathy are also frequently noted amongst individuals with DLB 3,5.

*Physical impairments (musculoskeletal, cardiovascular, genitourinary, GI)*

Parkinsonism is a core physical feature associated with DLB, with rigidity and bradykinesia being the most frequently noted motor symptoms 3,4. Motor symptoms tend to be bilateral and more symmetrical than with traditional Parkinson’s disease presentation 4. Tremors are less frequent with DLB as compared to typical Parkinson’s disease presentation, however when present, tremors are often postural rather than resting. 3-5 Autonomic dysfunction is another clinical feature associated with DLB; orthostatic hypotension and urinary/gastrointestinal changes are frequently observed with individuals with DLB. 3-5

**Impact of physical and cognitive impairments: Activity limitations, participation restrictions and quality of life**

Both the cognitive and physical impairments associated with DLB can contribute to a reduction in functional mobility and decreased participation in daily life. Bradykinesia (or akinesia), gait/postural instability, and increased tone/rigidity can all contribute to slow and inefficient movement, which may result in a decreased ability to perform ADLs independently, an increased risk of falls, a decreased ability to ambulate in community or household settings, and a limited ability to engage in social or recreational activities. 3 Executive dysfunction may lead to additional safety issues and lead to further restrictions in activity and independence. For example, poor judgment, planning and attention may increase the risk of falling or sustaining an injury during seemingly simple tasks. Additionally, fluctuations in cognitive status may mean that an individual’s safety risks are somewhat unpredictable necessitating a global restriction in independence. Furthermore, orthostatic hypotension can significantly increase the risk of falls and sustaining a fall related injury 9,11. Other autonomic dysfunction such as incontinence and GI dysfunction, even in the early stages, can limit an individual’s participation in social and community based activities and when combined with mobility impairments can severely limit ADLs and quality of life. As physical and/or cognitive impairments become more severe, and an individual with DLB is likely to become increasingly dependent on caregivers; this may create a shift in family dynamics or necessitate changing living arrangements (i.e., assisted living, SNF,etc). 12

**Personal and environmental factors**

The individual onset or presentation of symptoms can provide some insight or suggestion about disease progression for individuals with DLB. For example, visual hallucinations are associated with more severe cognitive impairments 4. It has also been suggested that as compared to other dementias (i.e., Alzheimer’s), DLB is associated with an increased risk and rate of functional decline. 13 Additionally, certain autonomic, cognitive, or neuropsychiatric symptoms may initially be more disruptive, and more difficult to treat 12. Significant neuroleptic/antipsychotic sensitivity is a fairly common problem occurring in up to 50% of individuals with DLB, which can interfere with medical management of DLB symptoms and lead to an increase in motor symptoms. 4,9 The recent discussion surrounding prodromal DLB also suggests that certain features of the disease may present early on and signal potential development of DLB. While there is currently a lack of disease modifying agents, in the future there may be a benefit to early identification and intervention for DLB. 2

Caregivers also play a significant role in the course of DLB. Based on the significant cognitive and functional decline and the eventual decrease in independence associated with DLB, the individual’s family or caregiver is likely to experience a growing burden as the disease progresses. While the support of family or a caregiver may improve the patient’s quality of life and participation in daily life, such care can be taxing on the caregiver. Caregiver distress is frequently noted when the DLB presents with greater neuropsychiatric symptoms. 12 Placement in a nursing home or utilization of support services has the potential to affect both the caregiver and patient’s experience throughout the disease process.

**Treatment/Interventions**

Currently, there are not any disease modifying drugs or FDA approved treatments for DLB, and the treatment of DLB is primarily based on symptom management 14. Medical management is often quite challenging because medications that address a subset of symptoms often exacerbate other symptoms associated with DLB. For example, dopaminergic agents that can be used for Parkinsonism may increase neuropsychiatric symptoms 5. Neuroleptic sensitivity, as mentioned above, is a significant issue for patients with DLB, and while certain antipsychotic drugs could potentially alleviate some neuropsychiatric symptoms, the side effects or risk of neuroleptic sensitivity may outweigh the benefits. Generally, traditional antipsychotics are avoided; however, atypical antipsychotics and acetylcholinesterase inhibitors may help to address neuropsychiatric and cognitive impairments. Additionally, an improvement in cognitive symptoms is frequently accompanied by a decline in motor symptoms 14. Interventions may struggle to find a balance between the unique concerns (i.e., motor vs cognitive symptoms) of the patient/family/caregiver and the safety/potential harm of certain interventions 14.

Addressing the autonomic dysfunction associated with DLB is an important aspect of intervention. Orthostatic hypotension is one of the most common autonomic dysfunction symptoms, and there are several interventions such as appropriate hydration, salt tablets, utilization of compression stockings, and medications, that can assist in managing this impairment 9. Incontinence is another aspect of autonomic dysfunction that if addressed appropriately, may alter quality of life. Improving functional mobility may reduce the frequency of incontinent episodes, however utilization of diapers/GI medications/supportive care may also be necessary to manage the impact of incontinence 5.

Patient and family education regarding the expected prognosis and possible types of interventions is a necessary component of managing a patient DLB 14. A key area of intervention for physical therapists working with individuals with DLB is addressing safety and fall prevention with the patient, as well as family/caregivers, when appropriate. Home/environmental safety, prescription of assistive devices and review of medications can all help to minimize the risk of falls and improve functional, safe mobility 5. Additionally, addressing postural, gait, and tone impairments through therapeutic exercise may also help to reduce the risk of falls in patients with DLB 5.

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