Journal of
Alzheimer's Disease & Parkinsonism

Tousi, J Alzheimers Dis Parkinsonism 2016, 6:1
DOI: 10.4172/2161-0460.1000206

Short Communication Open Access

New Perspectives in the Search for Reliable Prediction of Dementia with Lewy Bodies

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During the 2015 International Dementia with Lewy Bodies (DLB) Conference, the world's leading DLB researchers, caregivers and practitioners convened to share and learn the latest in DLB research over past decade. The field of dementia is already moving to earlier clinical trials at the prodromal stage of dementia. Different study groups sought to examine the prodromal factors that best predict the risk of progression from "normal cognition" to DLB, specifically focused on sleep disorders in DLB.

It has long been known that detection of rapid eye movement sleep behavior disorder (RBD) in patients with neurodegenerative dementia may suggest Lewy body pathology [1]. RBD occurs in up to 70% of DLB patients.

Alex Iranzo reviewed the results from his large cohort study of 174 patients with idiopathic RBD. The risk of developing a neurodegenerative syndrome from the time of idiopathic RBD diagnosis was 90.9% at 14 years [2]. In a 4 year follow up, 37% (n=65) converted to a neurodegenerative disorder. While 51 out of 65 converted to DLB or Parkinson's disease (PD)2. It was also noted that in subjects with idiopathic RBD, abnormal striatal dopamine transporter brain imaging (DAT scan), hyposmia and color vision impairment are indicative of short term conversion, within 2 years, to DLB and PD [3,4].

Dr. Iranzo also explained that most DLB patients recall having an unpleasant dream but less than third of patients have self-awareness of acting their dreams while sleeping [5]. He emphasized that RBD should be differentiated from confusional arousal in the middle of the night, nocturnal visual hallucinations and obstructive sleep apnea by Polysomnogram.

This opinion was also supported by Dr. Postuma. He strongly supported the belief that RBD, when diagnosed by Polysomnogram, might be the strongest risk factor for DLB when compared with other signs [6,7]. In a study of patients with non-amnestic mild cognitive impairment (MCI) who progressed to DLB a year later, about half of the patients had RBD which was more common than two other features of DLB, Visual Hallucinations and Parkinsonism [8].

Dr. McKeith noted that the third report of DLB consortium added REM sleep behavior disorder to the suggestive features of DLB diagnosis in 2005. During the workshop sessions, there was strong support among the experts to revisit the criteria and to consider RBD as one of the core features of DLB. Basically, RBD in the presence of dementia represents DLB.

There is a high level of interest to identify Prodromal DLB (MCI with symptoms of Lewy Body disease). Prodromal Alzheimer's disease has been studied extensively over past decades but limited studies are available for prodromal DLB.

Dr. Donaghy discussed the New Castle LewyPro study. Patients with mild cognitive impairment and symptoms suggestive of DLB were recruited. His group classified them to two groups of "probable Lewy Body MCI"(LB-MCI) and other MCI. LB-MCI group was more likely to report Parkinsonian symptoms such as change in handwriting, postural change and falls. They also showed more problems with anosmia, drooling and misjudging objects [9]. Cognitive phenotype of DLB may emerge at this time with decreased attention and relatively preserved delayed recall and cognitive function. They plan to follow these patients longitudinally.

Dr. Postuma reviewed autonomic issues in DLB. He cited two studies in which the patients with orthostatic hypotension were followed over a few year periods. Autonomic failure has been studied by Gibbon in a prospective study [10]. They followed patients with orthostatic hypotension over a 10-year period. 52% of those developed a neurodegenerative synucleopathy [10].

Anang and colleagues followed Parkinson's disease patients in 4.5 year follow up [11]. Those who had OH developed dementia more significant than the ones who did not have more than 10 mm Hg drop in systolic blood pressure upon standing on baseline [11].

Metaiodobenzylguanidine or MIBG cardiac scintigraphy is already in use to identify dysfunction in neuronal system by using a noradrenaline analogue to identify presynaptic sympathetic nerve terminals in the heart. MIBG has been a supportive feature for diagnosis of DLB. When results of different studies combined in a Meta-analysis. Pooled sensitivity was 94% with specificity of 98% [12].

Dr. Orimo from Japan presented cardiac tissue pathology data from patients who underwent MIBG cardiac scintigraphy. He suggested reduced cardiac MIBG uptake, corresponding to sympathetic denervation, can be another potential biomarker for the presence of Lewy Body disease. The author would like to note that MIBG uptake can be abnormal in congestive heart failure or diabetic autonomic neuropathy which may limit its usefulness in the geriatric population [13].

In early stage or atypical presentation lacking hallucinations or Parkinsonism, MCI or AD are commonly made diagnosis for patients with DLB. Cognitive testing at office may show relatively preserved delayed recall in DLB compared to Alzheimer's Disease patients and worse performance in drawing clock in DLB [14]. Systematic questioning about the prodromal symptoms such as REM behavior disorder is most helpful in making diagnosis. Idiopathic RBD maybe a target to identify these prodromal DLB group for neuroprotective trials.

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Received December 21, 2015; **Accepted** January 18, 2016; **Published** January 25, 2016

Citation: Tousi B (2016) New Perspectives in the Search for Reliable Prediction of Dementia with Lewy Bodies. J Alzheimers Dis Parkinsonism 6: 206. doi: 10.4172/2161-0460.1000206

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