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Protective effects of phycobiliprotein on streptozotocin induced behaviour and biochemical deficits in experimental model of Alzheimers disease

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The present study was designed to explore the neuroprotective efficacy of a promising antioxidant and anti-inflammatory, phycobiliprotein (PB) against intracerebroventricular (ICV) streptozotocin (STZ) induced cognitive impairment in rats. STZ (3 mg/kg) was introduced in rats??? brains on 1st and 3rd day bilaterally, followed by treatment with PB or rivastigmine for 28 days. Estimation of alteration in the behaviour of treated and untreated group of rats were done by Morris water maze, elevated plus maze and open field test. Afterwards, rats were sacrificed, and brains were harvested for the evaluation of various biochemical parameters in post mitochondrial supernatant fractions of cerebral cortex and hippocampus. The levels of several oxidative stress (SOD, CAT, LPO) and inflammatory (TNF-?, NF-?B) biomarkers activity were analyzed towards acetylchoinesterase and was also investigated by ChAT assay. The amelioration of ICV-STZ induced spatial learning and memory impairment by PB could be associated partially to the down regulation of NF-?B activity and the mitigation of expression of neuroinflammatory cytokines, along with modulation of cholinesterase, suggesting that PB may be explored further as a potent candidate for Alzheimer???s disease therapy.

The synucleinopathies comprise several neurodegenerative disorders characterised by the accumulation of aggregated forms of the protein α-synuclein (α-syn) in both neuronal and non-neuronal cells in the brain. Most idiopathic synucleinopathies are age-associated and, therefore, their prevalence is increasing in parallel with the world wide increase in life expectancy. Synucleinopathies are second to Alzheimer's disease (AD) amongst the most common neurodegenerative disorders known to cause dementia. As with most neurodegenerative disorders, there are still no disease-modifying drugs, limiting treatment options to symptomatic relief and palliative measures. Therefore, synucleinopathies pose a growing socio-economic burden to modern societies, and demand urgent attention.

Most synucleinopathies are Lewy body diseases (LBD), as they are characterised by the accumulation of aggregated a α-syn into Lewy bodies (LBs) within vulnerable neurons and Lewy neurites (LN) in neuronal processes. The LBD comprise Parkinson's disease (PD), Parkinson's disease dementia (PDD), and dementia with Lewy bodies (DLB), among other less common disorders. The central role of α-syn in LBD originated from almost simultaneous findings of mutations in the gene encoding for α-syn (SNCA) in familial forms of PD, and of α-syn comprising the major protein component of Lewy bodies.

Multiple system atrophy (MSA) is neuropathologically characterised by accumulation of aggregated α-syn in oligodendrocytes, inclusions known as glial cytoplasmic inclusions (GCIs), while LB pathology is absent and, therefore, MSA is not an LBD.

The initial clinical and neuropathological studies which established the distinct clinical and neuropathological phenotype of the disorder now known as DLB, preceded immunohistochemical methods to detect α-syn in human brain tissue, but later revisions of international consensus for diagnostic guidelines now recommend the use of immunohistochemistry.

Clinical under-diagnosis of DLB, and over-diagnosis of PD, have led to most studies of LBD focusing on PD and PDD, leaving DLB historically under-researched relative to its population prevalence. Increasing recognition of DLB as a distinct and prevalent age-associated neurodegenerative dementia has stimulated increasing numbers of high-quality studies on its aetiology and pathogenesis. Here, we summarise contemporary findings from this rapidly expanding field, focusing on genetics, diagnostic biomarkers and molecular mechanisms.

DLB is now the preferred term for a variety of previously used clinical diagnoses including diffuse LB disease (DLBD, LB dementia, dementia associated with cortical Lewy bodies (DCLB), the LB variant of Alzheimer's disease (LBVAD), and senile dementia of LB type (SDLT).

Recognition and definition of the DLB syndrome originally occurred through post-mortem neuropathological observations, of a particular distribution of LB and LN in the brains of elderly subjects with dementia, followed by a retrospective review of their clinical histories. This revealed two major findings – the first was that a significant number of LB pathology cases had a clinical presentation that was discernibly different from other dementia subtypes, even at an early stage in the disease. Fluctuating levels of cognitive impairment, recurrent visual hallucinations, spontaneous extrapyramidal motor features and a history of rapid eye movement (REM) sleep behavior disorder (RBD) were the most prominent symptoms, and the presence of two or more of these symptoms in an individual with dementia is now considered sufficient for a clinical diagnosis of probable DLB.

The other major observation was that approximately 50% of subjects showing full blown DLB pathology at neuropathological post-mortem examination did not show the characteristic clinical picture of DLB during life but typically presented with global cognitive decline reminiscent of AD. Unsurprisingly, such cases usually show additional high levels of AD neuropathological change.