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### Correlations between synaptic proteins expression and clinico-pathological features in dementia with Lewy bodies and Parkinson's disease dementia

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**Background:** dementia with lewy bodies (dlb) and Parkinson's disease Dementia (PDD) represent together the second most common cause of dementia after Alzheimer's disease (AD). The synaptic dysfunctions underlying the cognitive decline and psychiatric symptoms observed throughout the development of PDD and DLB are still under investigation. In this study we target the SNARE complexes and key proteins of exocytosis and endocytosis as potential markers of molecular processes specifically deregulated with DLB and/or PDD.

**Material & methods:** We examined protein levels (western blot and ELISA) and distribution (Immunohistochemistry) of Munc18 (vesicle docking regulator), Syntaxin1 and SNAP25 (transmembrane SNARE proteins), VAMP2 (vesicular SNARE protein) and Dynamin1 (vesicle endocytosis regulator) in post-mortem prefrontal cortex area (BA 9) and anterior cingulate gyrus (BA 24) from DLB and PDD patients in comparison to age-matched controls and a group of AD cases. Clinical and pathological data available included MMSE score, Neuropsychiatric history, and semi-quantitative scores for AD pathology (plaques - tangles) and for  $\alpha$ -synuclein.

**Results:** Striking changes of the SNARE markers were observed in the prefrontal cortex. Both Munc18 and Syntaxin1 protein expression were significantly higher in DLB group than PDD and controls, and negatively correlated with the duration of Parkinson symptoms. In addition, Syntaxin1 expression was strongly increased in AD cases whereas VAMP2 expression was specifically decreased in this group. Moreover Syntaxin1 and VAMP2 were respectively positively and negatively correlated with tangle scores. On the other hand, Dynamin1 level in BA9 while unaltered between diagnostic groups was negatively correlated to the rate of cognitive decline observed in our cohort of DLB and PDD cases. We observed less change in expression of these proteins in BA 24. However, Munc18 expression in both BA 9 and BA 24 was negatively correlated with severity of depression.

**Conclusions:** There are striking changes of the SNARE markers in the prefrontal cortex in Lewy body dementias. Deregulations in expression of these proteins may underlay specific psychiatric symptoms and pathological patterns reported in these cases of dementia. These results highlight key SNARE proteins as potential new targets for the development of treatments for both cognitive and behavioural symptoms of DLB/PDD.

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