CSF LEVELS OF OREXIN AND A-SYNUCLEIN ARE LINKED IN DLB PATIENTS AND ELDERLY CONTROLS

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The hypothalamic neurotransmitter orexin regulates several important physiological functions including feeding behavior and wakefulness and is reduced in sleep disorders like narcolepsy. Patients with the α-synucleinopathies Parkinson's disease (PD) and dementia with Lewy bodies (DLB) often suffer from excessive daytime sleepiness and earlier studies have reported a dramatic loss of orexin-producing hypothalamic neurons in PD. Interestingly, a recent study reported that reduced brain-homogenate levels of orexin were correlated to α-synuclein accumulation in the DLB brain. The relationship between orexin and α-synuclein in CSF from DLB patients, compared to controls, remains however elusive. Here, we analyzed lumbar CSF levels of orexin (radioimmunoassay) and α-synuclein (ELISA) in a small cohort of clinically diagnosed DLB patients (n=18, MMSE 23±4, 74±7 years old) and elderly controls (n=24, MMSE 29±1, 72±8 years old). Both markers were significantly reduced in DLB versus controls (α-synuclein 378±166 vs 519±168 pg/mL p=0.01, orexin 493±108 vs 592±112 pg/mL p=0.01). We also observed a trend indicating that orexin and α-synuclein levels are higher in male DLB patients than female patients, interestingly however the reverse was observed in the control group. In both groups, orexin was strongly correlated to α-synuclein (controls r=0.674, p< 0.001, DLB r=0.471 p< 0.05) whereas none of the markers could be correlated to cognitive function (MMSE) or age. We conclude that α-synuclein and orexin levels are significantly decreased in CSF from DLB patients but not related to age or cognitive function. Levels of both markers appear to be linked in DLB but also in healthy elderly.