ROLE OF NF-KAPPAB/C-REL IN PARKINSON'S DISEASE

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Introduction: To date, the primary cause of the progressive loss of dopaminergic neurons in Parkinson's Disease (PD) endures elusive. NF-kappaB transcription factors exhibit a key role in the progression of neurodegeneration. In particular, the neuroprotective NF-kappaB/c-Rel subunit contribute to brain resilience to stress. Mice lacking c-Rel subunit expression develop a late-onset, progressive parkinsonian pathology characterized by neuronal loss in the substantia nigra (SN), a Braak-like pattern of brain ascending α-synuclein deposition, non-motor symptoms and L-DOPA- responsive motor deficits. The peculiar phenotype of c-rel$^{-/-}$ mice envisages a potential contribution of c-Rel dysregulation to the pathogenesis of PD. The present study was aimed at verifying whether a c-Rel deficit occurs in brain and in peripheral blood mononuclear cells (PBMCs) of PD patients.

Materials and methods: Frozen brain tissue from PD patients and age-matched control subjects were kindly supplied by the Parkinson's UK Brain Bank. PBMCs were isolated from the venous blood of PD and healthy subjects in different cohorts from Venice San Camillo Hospital and from Neurology Division of University of Brescia. The c-Rel activity was evaluated in protein extracts by DNA-based ELISA.

Results: The c-Rel DNA-binding activity was reduced in protein extracts from SN of post-mortem PD brains when compared to SN from control brains. DNA-based ELISA analysis of PBMCs extracts unveiled a significant decrease of c-Rel function in PD patients, when compared to age-matched controls, in both cohorts of subjects.

Discussion and conclusions: The deficit of c-Rel activity in human SN of PD patients and the development of a parkinsonian phenotype in c-rel$^{-/-}$ mice suggest a possible role of c-Rel dysfunction in the pathogenesis of PD. The detection of decreased c-Rel activity also in patients' PBMCs infers the potential worth of this parameter as a peripheral biomarker of PD.