P1872

## IMMUNOPROTEOMIC PROFILING OF BRAIN STEROID 5 ALPHA REDUCTASES IN SLEEP-DEPRIVATED RATS

A. Soggiu [1,*], M. Bortolato [2], G. Piras [3], P. Devoto [4], L. Bonizzi [5], P. Roncada [6]
[1]Dipartimento di Neuroscienze "Bernard B. Brodie", Università di Cagliari, Monserrato, Italy, [2]Department of Pharmacology and Pharmaceutical Sciences, University of Southern California, Los Angeles, United States, [3]Dipartimento di Scienze Zootecniche, Università of Sassari, Sassari, [4]Dipartimento di Neuroscienze "Bernard B. Brodie, Università di Cagliari, Monserrato, [5]Dipartimento di Patologia Animale, Igiene e Sanità Pubblica Veterinaria, Università Statale di Milano, [6]Istituto Sperimentale L.Spallanzani, Milano, Italy

**Background:** Steroid 5α reductase (S5αR) is rate-limiting enzyme of one of two major metabolic pathways in brain steroidogenesis. Recent evidence indicates that neuroactive steroids may involved in pathogenesis of schizophrenia spectrum disorders. Moreover, 5αR inhibition has been shown to induce therapeutic effects in animal models of schizophrenia and in several disorders associated to dopaminergic hyperreactivity (1). In rodents, sleep deprivation (SD) is known to induce a series of behavioural patterns, including sensory-motor gating deficit, which might be reflective of psychosis and mania and are countered by antipsychotics (2). The aim of this study was to evaluate, by using proteomics approaches, the impact of SD on expression levels of 5αR isozymes in rat brain
**Methods:** After 72 h of SD, rats were sacrificed and brain areas dissected. Quantitative 1D and 2D western blotting (WB) with antibodies were performed on four brain areas of both control group and SD group (n = 8 each): medial prefrontal cortex (mPFC), nucleus accumbens (nACC), ippocampus (IC) and amigdala (AM). Statistical significance for the differences in the optical density of the protein bands/spots were calculated using Student's t-tests
**Results:** 1D WB revealed that the expression of 5αR-1 and 5αR-2 was significantly augmented in SD animals in comparison to controls ($p < 0.05$) in mPFC and nACC area. These effects were confirmed by the analysis of 2D WB. In IP and AM expression of 5αR-1 and 5αR-2 was unchanged in SD animals in comparison to controls
**Conclusion:** Present study shows that SD induce significant increases in the expression of 5αR-1 and 2 in the dopaminergic areas NAcc and mPFC, while no increase is noted in other two areas. Regarding therapeutic effect of 5αR inhibition on gating deficit, our data suggest that 5αR increase might cause altered balancing in neurosteroid levels, and it could be responsible of behavioral disruption observed in SD animals.
**References:** 1) Paba S, Frau R, Godar SC, Devoto P, Marrosu F, Bortolato M (2011) Curr Pharm Des. 17:151. 2) Frau R, Orrù M, Puligheddu M, Gessa GL, Mereu G, Marrosu F, Bortolato M (2008) Int J Neuropsychopharmacol. 11:947.

**Disclosure of Interest:** None Declared

P1873

## MRM QUANTITATION OF JC VIRUS IN BRAIN TISSUE FOR A CASE OF PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML) CAUSED BY SELECTIVE IMMUNE DEFICIENCY

A. Buko [1,*], J. Wei [1], K. Wharton, Jr. [2], C. Quigley [2], M. Themeles [2], C. Reid [3], C. Sun [3], J. Carulli [3], S. Goelz [4], S. M. Staugaitis [5], R. J. Fox [5]
[1]translational medicine, [2]Comparative Pathology, [3]Genetics, [4]Neurology, BIOGENIDEC, Cambridge, [5]Mellen Center for Multiple Sclerosis, Cleveland Clinic, Cleveland, United States

**Background:** Over half of humanity is seropositive for the human JC polyomavirus (JCV), but only a tiny fraction of individuals develop PML, a destructive JCV infection of CNS white matter. PML is receiving increased attention due to its occurrence in a rare subset of patients on a variety of selective immunomodulatory agents, including natalizumab (Tysabri®, Biogen Idec / Elan) used as a therapy for multiple sclerosis (MS) and Crohn's disease. Fundamental aspects of JCV biology and PML pathology remain mysterious, including the cell type(s) infected, the mechanism of viral spread throughout the CNS, and the abundance and distribution of virus throughout affected brain.
**Methods:** To investigate PML without the potential confounding demyelination of MS, we analyzed a case of histologically-confirmed PML that was acquired by a 70-year-old man treated for psoriasis with efalizumab (Raptiva®, Genentech) for four years. Examination of postmortem brain revealed gross and microscopic pathology characteristic of PML, and virions were identified by electron microscopy. We further sampled the center, edge, and adjacent grossly normal-appearing white matter of three different lesions. For each sample, we correlated immunohistochemical findings with the abundance of selected viral and non-viral proteins measured by multiple reaction monitoring (MRM) mass