***Al collegio docenti del Dottorato in Medicina Molecolare***

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***Introduction:*** Major Depression (MD) is a disorder with high prevalence worldwide. A critical risk factor for MD is psychosocial stress, while a protective factor is the ability to cope with adversity and stress (resilience). It is crucial to identify molecular targets that may help in MD prevention, diagnosis, and therapy, likely involved in neurobiological mechanisms that confer resilience or vulnerability to MD. Neurosteroids orchestrate stress responses and play a key role in MD pathophysiology. Neurosteroid synthesis requires the enzymes 5α-reductase type 1 (5αR1) and 2 (5αR2), characterized by distinct brain expression patterns. I studied 5αR expression in rat brain after acute stress exposure and in a model of MD induced by psychosocial stress (chronic social defeat, CSD).

***Methods:*** First, I analyzed 5αR1 and 5αR2 mRNA levels in male rats after acute stress exposure (20 min immobilization). Control and Stress groups were sacrificed, prefrontal cortex (PFC), hippocampus (HIP), amygdala (AMY) and hypothalamus (HYP) were excised, total RNA was extracted and retrotranscribed. 5αR1 and 5αR2 cDNAs were analyzed by real-time PCR. Primers for 5αR1 (Srd5a1 GenbankNM_017070.3) and 5αR2 (Srd5a2 Genbank NM_022711.4) were designed using Primer 3 Plus free software.
Next, I developed the CSD protocol adapting existing protocols. Male rats were exposed or not to social stress (CSD and Control groups). After a 10-day exposure, rats were sacrificed, brain regions excised and 5αR2 expression levels analyzed by western blotting.

***Results:*** 5αR1 mRNA levels were unmodified by acute stress exposure in the HIP, PFC, AMY, HYP regions. 5αR2 mRNA levels were increased in HIP and PFC, but not in AMY and HYP of the Stress group. In the CSD model, 5αR2 levels were selectively reduced in the nucleus accumbens, but not in PFC and HIP.
Further studies of transcriptional changes in the 5αR pathway after CSD exposure will test its role in stress sensitivity in both sexes. Information on these genes represents the “positive” internal control for the next RNA-Seq analysis of transcriptional patterns in the rat model of MD that aims to identify molecular targets that may help in MD prevention, diagnosis, and therapy.