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PSYCHOSOCIAL STRESS AND PSYCHIATRIC PHENOTYPES: ENDOCANNABINOIDS AND CANNABINOID RECEPTOR (CBR) EXPRESSION IN CORTICO-STRIATAL CONNECTIVITY

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INTRODUCTION:

Aim of study: to investigate the consequences of chronic psychosocial stress on behavior, endocannabinoids and CBR expression in prefrontal cortex (PFC) and striatum of mice.

MATERIALS AND METHODS: Psychosocial stress was induced in adult C57Bl/6 mice by resident-intruder paradigm (Brzózka et al. 2011). After 3 weeks daily exposure to psychosocial stress for 1 hour, animals were studied during the rodent active phase (night) by behavioral tests such as Functional Observational Battery (FOB), Rota-Rod (R-R), Open Field (OF), Prepulse Inhibition test (PPI). After behavioral testing, mice were sacrificed. 4 mice brains (prefrontal cortex, dorsal striatum) were studied by LC-MS to estimate the concentration of anandamide (AEA), 2-arachidonoylglycerol (2-AG), N-oleoylethanolamine (OEA), palmitoylethanolamide (PEA) (coll. di Marzo). In Situ Hybridization (ISH)and Immunohistochemistry (IHCH) against CB1 receptor were performed on free floating brain coronal sections fixed by 4% paraformaldehyde (coll del Río).

RESULTS 1.After psychosocial stress, mice displayed lower body weight ($p<0.01$), higher scratching and miccions activity compared to controls ($p<0.05$), decreased number of falls ($p<0.01$) and increased latency ($p<0.05$) in Rotarod. No effects in PPI were found. 2. In the same mice psychosocial stress reduced AEA levels in dorsal striatum and PFC ($p<0.05$). Endocannabinoids significantly showed an inverse relationship in PFC compared to striatum in control mice (AEA, $p<0.001$; 2-AG, $p<0.001$; OEA, $p<0.001$) and in psychosocially stressed mice (PEA, $p<0.001$; OEA, $p<0.001$). 3. Psychosocial stress increased the protein CBR1 expression in striatum ($p<0.05$) but not in prefrontal cortex.

CONCLUSION: Chronic psychosocial stress significantly changes behavior, endocannabinoids, CB receptor function and the striatal-cortical connectivity. These changes may contribute to vulnerability for psychosis and addiction.

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