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PHOSPHORYLATION OF PERIPHERAL GLUCOCORTICOID RECEPTOR IN THE CONTINUUM FROM CURRENT DEPRESSIVE EPISODE TO VULNERABILITY TO DEPRESSION

N.P. Maric[1,2], *I. Simic*[3], *Z. Pavlovic*[1], *M. Mitic*[3], *I. Soldatovic*[2], *S. Andric*[1], *M. Mihaljevic*[1], *M. Radojcic*[3], *M. Adzic*[3]

[1]Clinic for Psychiatry, Clinical Centre of Serbia, [2]School of Medicine, University of Belgrade, [3]Laboratory of Molecular Biology and Endocrinology, VINCA Institute of Nuclear Sciences, Belgrade, Serbia

The impaired glucocorticoid receptor (GR) signaling has long been considered one of cornerstones in understanding the pathophysiology of depression. Phosphorylation of GR is very important for GR function, therefore we investigated: a) whether GR phosphorylation at serine 211 (pGR-S211) and serine 226 (pGR-S226) is altered in patients with episode of major depressive disorder (MDD); b) if neuroticism and negative affective states may be associated with altered GR phosphoisophorms of healthy adults. Phosphorylation at these sites is generally considered to be indicative of receptor activity. We studied leucocytes of :
a) 30 MDD patients and 35 controls, and
b) 37 healthy subjects, to assess the levels of nuclear total GR (tGR), pGR-S211 and pGR-S226 using Western blot technique.
Our results demonstrated increased phosphorylation of GR at S226 and, to a less extent, at S211 in MDD compared to controls. Also, pGR-S226 positively correlated with neuroticism and self report of stress in healthy. In MDD, the pGR-S211/pGR-S226 ratio was decreased ($p < 0.05$) implying reduced transcriptional activity of GR in patients. In healthy, pGR-S211/pGR-S226 was negatively correlated with self-repored subclinical depression. MDD had higher cortisol levels than others and cortisol concentrations positively correlated with S226 levels from the same blood samples.
We examined whether easily accessible peripheral markers of GR activity and disease status in depression exist. Although we examined leucocytes, we propose that reduced GR transcriptional activity could be one of mechanisms of impaired GR function in the brain, resulting in dysfunction of HPA axis observed as a risk for depression.

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