

## EPIGENETIC, RESILIENCE AND COMORBIDITY: DOES FOUR-DIMENSIONAL ULTRASOUND (4-D US) HELPS IN ANSWERING THE QUESTION DO PSYCHIATRIC DISEASES ORIGINATE IN FETAL LIFE

Milan Stanojević<sup>1</sup>, Asim Kurjak<sup>1</sup> & Miro Jakovljević<sup>2</sup>

<sup>1</sup>*Department of Obstetrics and Gynecology, Clinical Hospital "Sveti Duh",  
Medical School University of Zagreb, Zagreb, Croatia*

<sup>2</sup>*Department of Psychiatry and Psychological Medicine, University Hospital Centre Zagreb, Zagreb, Croatia*

The mankind from its beginnings is interested what the future brings, so predicting the future through the history was one of the most mysterious and intriguing questions. The medical professionals always dreamed to predict the future of the individual patient instead of being only historians speaking about the course of disease of their patients, or statisticians making the conclusions based on the population based statistical data of health indicators.

Development of sophisticated and precise scientific methods and their application in everyday clinical practice with the aim to timely predict the development of severe medical conditions affecting adversely the quality of life is now a reality, while only several decades ago it was considered as unrealistic assignment. There is a possibility of "Fetal Origin of Adult Disease", among which are mental and neurodevelopmental disorders. Epigenetic changes may produce the damage of the DNA which may be transgenerational. Prenatal noxious stimuli can modulate neurodevelopment which may be impaired due to the interaction of genetic, epigenetic and environmental factors influencing proliferation, migration and establishment of neuronal circuits of neuronal progenitor cells, resulting in damaged cognitive and intellectual function, and increased risk of neurodevelopmental and psychiatric disorders later in life.

The situation with the prediction of fetal outcome or prediction of postnatal health based on prenatal assessment is much more complicated than postnatal, because of at least two reasons: intrauterine environment is unpredictable and the role of the placenta is still poorly understood. Ultrasound, genetic testing of amniotic fluid, preimplantation genetic testing, detection of fetal cells in maternal blood, or even testing of fetal blood after cordocentesis, enabled the diagnosis of many congenital conditions based on the whole exome sequencing, while the problem with fetal origin of mental health problems is more complicated and demanding.

The aim of the paper is to present the risk factors in pregnancy for development of mental health problems later in life, role of four-dimensional ultrasound (4D US) in the assessment of fetal behavior and cognitive functions and to speculate about fetal and neonatal resilience to overcome possible threats affecting mental health.

**Key words:** prenatal psychiatry - comorbidity - resilience - epigenetics

\* \* \* \* \*

## ENDOMETRIOSIS, PAIN AND MENTAL HEALTH

Bernarda Škegro<sup>1</sup>, Sarah Bjedov<sup>2</sup>, Mislav Mikuš<sup>3,4</sup>, Filip Mustač<sup>2</sup>, Joško Lešin<sup>3,4</sup>,  
Valentina Matijević<sup>1,5</sup>, Mario Ćorić<sup>3,4</sup>, Vesna Elvedi Gašparović<sup>3,4</sup>,  
Filip Medić<sup>6</sup> & Vesna Sokol Karadjole<sup>3,4</sup>

<sup>1</sup>*Department of Rheumatology, Physical Medicine and Rehabilitation, University Hospital Center  
Sestre milosrdnice, Zagreb, Croatia*

<sup>2</sup>*Department of Psychiatry and Psychological Medicine, University Hospital Centre Zagreb, Zagreb, Croatia*

<sup>3</sup>*Department of Obstetrics and Gynecology, University Hospital Centre Zagreb, Zagreb, Croatia*

<sup>4</sup>*University of Zagreb, School of Medicine, Zagreb, Croatia*

<sup>5</sup>*Libertas International University, Zagreb, Croatia*

<sup>6</sup>*Ministry of Defence of the Republic of Croatia, Zagreb, Croatia*

**Background:** Endometriosis is a chronic and progressive disease which can significantly affect a woman's personal, as well as intimate and professional aspects of life. The aim of this study was to assess health-related quality of life and mental health status in patients with endometriosis, investigating also their relationship with endometriosis-related comorbid symptoms and conditions, such as pain and infertility.

**Subjects and methods:** An observational cross-sectional study involved 79 women with endometriosis. All patients filled the Endometriosis Health Profile (EHP-5), the Depression Anxiety Stress Scales (DASS-21)

and the Visual Analogue Scale (VAS). Their medical data were retrieved from medical records. Data was analyzed using the SPSS 23.0 (IBM Corp., Armonk, NY).

**Results:** Of all the patients evaluated in our study, 44.3% presented depressive symptoms and 25.3% presented anxiety, while 31.7% reported stress symptoms. Moderate correlations were found between results on EHP-5 and depression ( $r=0.515$ ), stress ( $r=0.558$ ) and VAS score ( $r=0.565$ ). Furthermore, weak positive relationship was observed between EHP-5 and anxiety ( $r=0.295$ ) and infertility ( $r=0.267$ ). Additionally, moderate correlation was found between depression and infertility ( $r=0.519$ ), while there was weak association between VAS score and stress ( $r=0.236$ ).

**Conclusions:** This study showed complex relationships between symptoms and conditions manifesting in patients with endometriosis. Due to diversity of symptoms, potentially including mental health issues, it is important to emphasize the need for combined personalized treatment for these patients, taking into account both physical and psychological aspect of the disease.

**Key words:** endometriosis - pain - mental health

\* \* \* \* \*

## BIOMARKERS OF DEPRESSION ASSOCIATED WITH COMORBID SOMATIC DISEASES: A MINI-REVIEW

Sandra Uzun<sup>1</sup>, Marina Sagud<sup>2,3</sup> & Nela Pivac<sup>4</sup>

<sup>1</sup>*Department for Anesthesiology, Reanimatology, and Intensive Care, University Hospital Center Zagreb, Zagreb, Croatia*

<sup>2</sup>*School of Medicine, University of Zagreb, Zagreb, Croatia*

<sup>3</sup>*Department of Psychiatry and Psychological Medicine, University Hospital Center Zagreb, Zagreb, Croatia*

<sup>4</sup>*Division of Molecular Medicine, Rudjer Boskovic Institute, Zagreb, Croatia*

Depression is heterogeneous clinical entity with different clinical symptoms, that imply diverse biological underpinning, different molecular substrates and pathways. Besides different psychiatric comorbidities, depression is frequently interrelated with somatic diseases. Multi-morbidities, i.e. somatic diseases associated with depression, reduce quality of life, worsen clinical picture and increase mortality. The most frequent somatic diseases co-occurring with depression are cardiovascular and metabolic diseases. Vulnerable individuals will develop depression, and the goal in modern research and in precision/personalized medicine is to determine vulnerability factors associated with development of depression and to find easy available biomarkers of depression, especially comorbid with somatic diseases. This mini-review aimed to describe the latest published data (from 2015-2012) considering biomarkers of depression related to somatic diseases. Biomarkers related to inflammatory processes, atherosclerosis, imbalance of the hypothalamic-pituitary-adrenal axis, autonomic nerve system, sympathetic and parasympathetic nervous system, heart rate variability and endothelial dysfunction could improve the understanding of the underlying biological mechanisms of the common pathways of depression comorbid with somatic diseases. These targeted biomarkers might be used to reduce the symptoms, improve the treatment of these interrelated diseases, and decrease the morbidity and mortality.

**Key words:** biomarkers - depression - comorbid somatic disorders - HPA axis - inflammatory response - endothelial dysfunction

\* \* \* \* \*

## MICRORNAS AS CANDIDATES FOR BIPOLAR DISORDER BIOMARKERS

Ivana Delalle

*Lifespan Academic Center, Department of Pathology and Laboratory Medicine,  
The Warren Alpert Medical School of Brown University, Providence, US*

Bipolar disorder (BD) is a common, recurring psychiatric illness with unknown pathogenesis. Much like other psychiatric diseases, BD suffers from the chronic lack of reliable biomarkers and innovative pharmacological interventions. Better characterization of clinical profiles, experimental medicine, genomic data mining, and the utilization of experimental models, including stem cell and genetically modified mice, are suggested