

Univerzita Karlova

Přírodovědecká fakulta

Errata k bakalářské práci

Posttraumatická stresová porucha a její biomarkery

Post-traumatic stress disorder and its biomarkers

Autor: Ilia Shalkin

Vedoucí práce: Mgr. Petr Telenský, Ph.D.

Replace original English abstract with:

Post-traumatic stress disorder (PTSD) has a wide range of symptoms (intrusion, avoidance, hyperarousal, negative cognition and mood) that disrupt everyday life. For the treatment and development of drugs, it is necessary to understand the aetiology of the development of PTSD, which is currently not clear. For this reason, it is necessary to study the biomarkers of PTSD. Therefore, this article studies the most investigated biomarkers of PTSD and the main preclinical and clinical methods of searching for biomarkers to understand the processes and risk factors behind the development of PTSD.

The literature review shows that PTSD has a complex aetiology and affects systems associated with regulating stress hormones (decreased cortisol level). Impaired memory consolidation (amygdala hyperactivity, reduced volumes of the hippocampus and prefrontal cortex). PTSD has genetic and hereditary predisposition (BDNF5, SLC18A2, NR1F1 polymorphisms; SLC6A4 methylation; alteration in GABAergic neurotransmission). Increased sympathetic nervous system reactivity and increased inflammatory cytokines (IL-6, IL-1 β , IL-8).

Modeling PTSD in animals has difficulties interpreting the results of studies, and the caused symptoms overlap with other disorders. Further development of the methodology of experiments and methods of biomarker research will allow us to discover new aspects of the development of PTSD.

Keywords: Post-traumatic Stress Disorder, Biomarker, Preclinical Method, Clinical Method, Stress, “Two-hit” hypothesis, Allostatic Load

Replace original Czech abstract with:

Posttraumatická stresová porucha (PTSD) má širokou škálu příznaků (kognitivní intruze, únikům, zvýšené vzrušení, negativní vnímání a snížená nálada), které narušují každodenní život. Pro léčbu a vývoj léků je třeba pochopit etiologii vývoje PTSD, která v současné době není jasná. Z tohoto důvodu biomarkery PTSD jsou předmětem badatelského zájmu. Tato práce poskytuje souhrn nejvíce prozkoumaných biomarkerů PTSD a základních preklinických a klinických technik vyhledávání biomarkerů pro pochopení procesů a rizikových faktorů, které jsou základem pro rozvoj PTSD.

Literární rešerše ukazuje, že PTSD má složitou etiologii a ovlivňuje systémy spojené s regulací stresových hormonů (snížení hladiny kortizolu). Porucha konsolidace paměti (hyperaktivita amygdaly, snížení objemu hipokampu a prefrontální kůry). PTSD má genetickou a dědičnou predispozici (například polymorfismus BDNF5, SLC18A2, NR1F1; metilace SLC6A4; změna gamkerické neurotransmise). U pacientů s PTSD je pozorována zvýšená reaktivita sympatického nervového systému a zvýšený obsah prozánětlivých cytokinů (IL-6, IL-1 β , IL-8).

Nevýhodou simulace PTSD u zvířat jsou obtíže s interpretací výsledků výzkumu a překrývání příznaků PTSD s příznaky jiných poruch. Další rozvoj metodiky experimentů a metod výzkumu biomarkerů je cestou k objevení nových aspektů vývoje PTSD.

Klíčová slova: Posttraumatická Stresová Porucha, Biomarker, Předklinické Metody, Klinické Metody, Stres, “Two-hit” hypotéza, Alostatická Zátěž

Addition

Chapter 1.; page 1:

1.1 Introduction of the problem and setting the aims

A traumatic event such as a serious road accident, sexual assault, terrorist attack or war, a natural disaster can lead to psychological trauma. Most people cope with the trauma and return to everyday life. However, some people develop psychological disorders, one of which is PTSD.

Post-traumatic stress disorder (PTSD) originally referred to disorders observed among military people. It was first widely used as a diagnosis during the First World War. Subsequently, PTSD was no longer attributed exclusively to the environment of military personnel. At the moment, there is a large number of studies relating to civilians who have developed trauma.

A person diagnosed with PTSD may have sleep disorders and nightmares, increased irritability, feel guilty and look for the cause of problems in themselves, and may not experience positive emotions. Symptoms

of PTSD have a destructive effect on the patient himself and affect loved ones, leading to a break in social ties and loss of work (American Psychiatric Association, 2013).

PTSD is a complex disease affecting various regulatory systems of the body, but despite many studies, the aetiology of PTSD development is not clear today. Various preclinical and clinical methods allow tracking biomarkers associated with changes in the body after an injury to solve this problem. The study of biomarkers will bring us closer to understanding the aetiology of PTSD, direct further pharmacological research for drug development, and identify risk groups of people, preventing the development of PTSD.

The introductory part of the paper discusses the definition and impact of stress on the human body. For understanding the physiological processes that occur in response to stressors, the HPA axis is considered, followed by a description of the “Two-Hit” hypothesis, as a possible theory of the origin of PTSD. The second chapter examines the current definition of PTSD and the risk factors that contribute to the development of PTSD. The third chapter provides preclinical and clinical methods for studying biomarkers related to memory and regulatory disorders. The fourth chapter describes the most studied biomarkers related to memory systems, hormonal regulation, the immune system, genetic and epigenetic predisposition, and the functioning of the autonomous nervous system. The fifth chapter describes the problems of research and conclusions.

The purpose of this thesis is to generalize the available knowledge about the most studied biomarkers and methods of their detection for the study of the aetiology of PTSD development.

Prague, 2021