ДНС Друштво за неуронауке Србије
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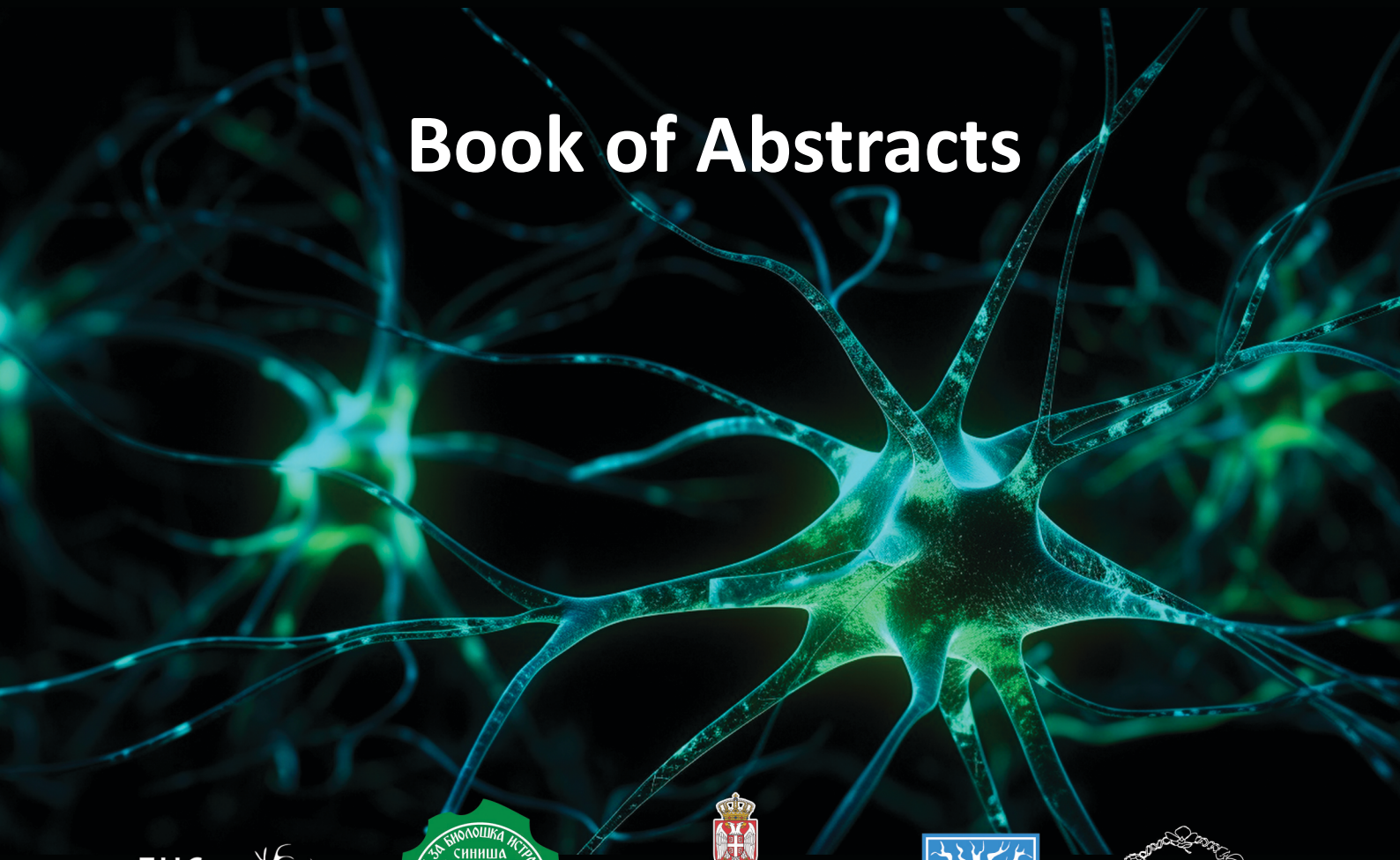
Congress Serbian Neuroscience Society

31 May - 02 June
Belgrade Youth Center
Belgrade



Book of Abstracts

ДНС SNS

Институт за биолошка истраживања Синиша Станковић ИБИСС Универзитет у Београду

Република Србија Министарство науке, технолошког развоја и иновација

Универзитет у Београду Медицински факултет University of Belgrade Faculty of Medicine

Labena

PROMEDIA Laboratory supply specialists

ZEISS

8th CONGRESS OF SERBIAN NEUROSCIENCE SOCIETY with international participation

31 May – 2 June 2023. Belgrade, Serbia - BOOK OF ABSTRACTS

Published by:
Serbian Neuroscience Society
Bulevar despota Stefana 142, 11060 Belgrade, Serbia

Editors
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Technical editor:
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Graphic design:
Olga Dubljević, Irina Veselinović

ISBN: 978-86-917255-4-9

Ketamine ameliorates fear extinction learning in adolescent males via hippocampal mTOR signaling

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Adolescence is a developmental stage characterized by impaired fear extinction learning, which is a significant contributing factor for the high incidence of fear-related disorders observed across this period. Ketamine is a noncompetitive N-methyl D-aspartate receptor antagonist that targets glutamatergic transmission and mammalian target of rapamycin (mTOR) signaling pathway, synaptic plasticity mediators known to be involved in fear extinction processes. Therefore, we aimed to explore ketamine's potential to boost fear extinction of adolescent males, as well as to identify the associated molecular mechanisms. Adolescent male mice (C57BL/6) received an i.p. ketamine injection (10 mg/kg) 1h prior to each cued fear extinction session for 4 consecutive days. Protein expression levels of synaptic plasticity markers in hippocampal synaptosomal fractions were subsequently detected by Western blot analysis. Our results revealed that ketamine significantly improved overall fear extinction learning, as well as extinction memory consolidation/retention. Our data also showed that ketamine upregulated protein kinase B (Akt), mTOR and glutamate receptor 1 (GluR1) protein levels in the hippocampus. Interestingly, we detected no changes in the levels of extracellular signal-regulated kinase 1/2. These results suggest that ketamine ameliorates longterm fear extinction of adolescent males via hippocampal Akt-mTOR-GluR1 signaling, highlighting this pathway as an important therapeutic target for improving extinction learning in the adolescent population.

Acknowledgment: This work was supported by the Ministry of Science, Technological Development and Innovations, Republic of Serbia, Grant Number 451-03-47/2023-01/ 200017.