## Author's Accepted Manuscript

The role of branched chain amino acid and tryptophan metabolism in rat's behavioral diversity: Intertwined peripheral and brain effects

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www.elsevier.com/locate/euroneuro

 PII:
 S0924-977X(15)00227-8

 DOI:
 http://dx.doi.org/10.1016/j.euroneuro.2015.07.009

 Reference:
 NEUPSY11067

To appear in: *European Neuropsychopharmacology* 

Received date: 16 February 2015 Revised date: 8 June 2015 Accepted date: 14 July 2015

Cite this article as: Eyal Asor, Shiri Stempler, Avi Avital, Ehud Klein, Eytan Ruppin, Dorit Ben-Shachar, The role of branched chain amino acid and tryptophan metabolism in rat's behavioral diversity: Intertwined peripheral and brain effects, *European Neuropsychopharmacology*, http://dx.doi.org/10.1016/j. euroneuro.2015.07.009

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## **ACCEPTED MANUSCRIPT**

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The role of branched chain amino acid and tryptophan metabolism in rat's behavioral diversity: Intertwined peripheral and brain effects

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Short title: Tryptophan and branched amino acids in rat behavior

Abstract

Previously, we showed that a transient early-in-life interference with the expression of multiple genes by mithramycin (MTR) followed by later-in-life exposure to chronic stress, leads to a "daring" and novelty seeking behavior in rats. In this study we searched for molecular changes that contribute to this behavioral alteration.We applied a non-hypothesis driven strategy using whole genome cDNA array analysis (WGA) followed by Genome Scale Metabolic modeling analysis (GSMM). Gene expression validation was performed by qRT-PCR and immunoblotting. Brain and serum amino acids levels were measured by HPLC. WGA data directed us towards metabolic pathways and GSMM pointed at branched chain amino acids (BCAA) pathway. Out of 21 amino acids analyzed in the prefrontal cortex of MTR+Stress rats only tryptophan, whose brain levels depend on serum BCAA levels,

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