Institute of Molecular Biology and Biotechnology (IMBB)

Foundation for Research and Technology-Hellas (FORTH)

PRESS RELEASE

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IMBB-FORTH Researchers reveal how stress and nutrient deprivation influence complex brain functions such as learning and memory

The findings of the study published today in the premier international scientific journal *Cell Metabolism*, reveal an intricate molecular mechanism that regulates neuronal metabolism in the adult mammalian brain.

IMBB-FORTH Researchers, Dr. Vassiliki Nikoletopoulou and Dr. Nektarios Tavernarakis (Professor at the Medical School, University of Crete, and Chairman of the Board, FORTH), together with collaborators Prof. Kyriaki Sidiropoulou (Department of Biology, University of Crete), Prof. Yannis Dalezios (Medical School, University of Crete), and Dr. Emmanouela Kallergi (IMBB), now demonstrate that nutrient deprivation differentially affects the process of autophagy in different brain areas.

Autophagy is an important, evolutionarily conserved catabolic pathway that degrades proteins, lipids and other macromolecules, as well as superfluous or defective cellular organelles. In most tissues, autophagy is regulated by the availability of nutrients as well as by stress. Impairment of autophagy in the brain leads to autistic behaviours in mouse models and causes defects in synapses, the contact point structures, facilitating the communication between neurons. Notably, autistic individuals carry mutations in autophagy genes. However, despite its essential role, regulation of autophagy in the brain remained poorly characterized.

The new data shows that in the cortex and hippocampus, which are areas devoted to cognitive functions and memory, nutrient deprivation causes unexpected suppression of autophagy, mediated by increased levels of the signalling molecule BDNF. BDNF is a major trophic factor for neurons of the brain and has a pivotal role in the strengthening of synapses that underlie memory and learning. Suppression of autophagy by BDNF is necessary for the synaptic strengthening and enhancement of memory. Hence, fasted animals exhibit improved memory that is dependent on the BDNF-autophagy axis. These findings establish autophagy as a novel, key mechanism that regulates inter-neuronal communication by degrading

specific components of synapses, identified in this work. Characterization of the molecular pathways that regulate autophagy in the brain is crucial for understanding how environmental stressors and genetic factors deregulate autophagy during neurodevelopment and compromise neural health.

The study of the IMBB investigators published today reveals an elegant molecular mechanism, by which nutrient availability influences neuronal physiology and behaviour. The tight evolutionary conservation of the regulatory factors involved in this highly coordinated response suggests that similar pathways operate in humans. These insights could be effectively utilized towards the successful development of novel, targeted and personalized interventions targeting numerous devastating human pathologies, such as autistic spectrum disorders, depression and bipolar syndromes, as well as learning disabilities.

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Relevant links: http://www.cell.com/cell-metabolism/ & http://www.elegans.gr/