New research discovers key to survival of brain cells

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Nicolas G. Bazan, MD, Ph.D, Boyd Professor and Director of the Neuroscience Center of Excellence at LSU Health Sciences Center New Orleans, and David Stark, an MD/Ph.D student working in his lab, have discovered how a key chemical neurotransmitter that interacts with two receptors in the brain promotes either normal function or a disease process -- determining whether brain cells live or die. The work is published and highlighted in the September 28, 2011 issue of the *Journal of Neuroscience*.

These findings reveal how receptor signaling takes place between receptors of synapses (gaps between neurons through which chemical or electrical signals pass permitting cells to "talk" to each other) and the mechanisms involved in initiating disease. The receptors, called NMDARs, are located both inside and outside of the synapses. Activation of the NMDRs inside (synaptic) allows the synapse to adjust response to signals and activation of the synaptic NMDRs is also required for survival of the cell. In contrast, activation of the receptors outside the synapse (extrasynaptic) leads to cell death.

The LSUHSC research team believed that activation of the extrasynaptic NMDRs promotes the pathological effects of cyclooxygenase 2 (COX-2), a protein known to contribute to inflammation associated with neurotoxicity. They found that activating the synaptic NMDRs greatly increased levels of COX-2, but not of the chemical (arachidonic acid) upon which COX-2 acts. Conversely, activating the extrasynaptic NMDRs increased the levels of arachidonic acid, but not COX-2. The researchers discovered, however, when synaptic and extrasynaptic NMDARs were sequentially activated, the levels of both COX-2 and arachidonic acid increased, as did neurotoxic inflammation.

"We have discovered a fascinating relationship regarding the "conversations" that occur between these two receptors in the brain," said Dr. Nicolas G. Bazan, Professor and Director, LSUHSC Neuroscience Center of Excellence.

"In this paper, we demonstrate how these signals affect cell functions and how they lead to diseases, including stroke, epilepsy and other neurodegenerative disorders. Targeting mechanisms that couple sequential synaptic then extrasynaptic NMDAR stimulations may lead to new anti-inflammatory/neuroprotective approaches."

The research was supported by grants from the National Institutes of Health, National Institute of Neurological Disorders and Stroke, National Center for Research Resources, and the National Center for Complementary and Alternative Medicine.

"I have a very gifted and talented young MD/Ph.D student in my lab, David Stark, who has a National Institutes of Health award, performed exemplary experiments and co-authored the paper with me," said Dr. Bazan.

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