Medical Xpress

From the clinics to the bench and back -- phenytoin as a mood stabilizer?

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Phenytoin is a well known antiepileptic agent widely used throughout the world. Recent clinical studies in patients with bipolar disorder have suggested that, as for other anticonvulsant drugs commonly used in the treatment of bipolar patients including valproate and carbamazepine, phenytoin may have mood-stabilizing effects in addition to its well-known anticonvulsant properties.

In a study published in the March 2010 issue of Experimental Biology and Medicine Veronica Mariotti and colleagues utilized DNA microarrays to investigate the molecular underpinnings of the potential mood-stabilizing action of phenytoin by looking at its effect on gene expression in the rat brain.

As compared with untreated animals, rats treated for a month with phenytoin had 508 differentially expressed genes in the hippocampus and 62 in the frontal cortex, including genes involved in GABAergic and glutamatergic neurotransmission, neuroprotection and other genes thought to be crucial for mood regulation. Furthermore, some of these same genes have been shown to be modulated by classical mood-stabilizer agents, like lithium and valproate.

Thus, the findings of this study indicate that chronic phenytoin administration modulates the expression of genes involved in mood regulation and genes that are targets of established mood stabilizers. Dr Mariotti noted that "The results of this study provide preliminary insights into possible molecular mechanisms of action of phenytoin as a

potential mood stabilizer and, more in general, the pathophysiology of bipolar disorders".

The study is the product of a fruitful collaboration between the Molecular Biology Laboratory of Dr. Silvia Pellegrini at the Department of Experimental Pathology, University of Pisa Medical School, Pisa, Italy and the Laboratory of Professors Galila Agam and R.H. Belmaker at the Psychiatry Research Unit at the Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel.

Dr. Steven R. Goodman, Editor-in-Chief of *Experimental Biology and Medicine*, said "Mariotti and colleagues have provided very interesting results on the changes in gene expression in rats treated with phenytoin. There findings shed significant light on the mood altering effects of this antiepileptic drug".

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