# *Review of Clinical Pharmacology and Pharmacokinetics*

**EPITHEORESE KLINIKES FARMAKOLOGIAS KAI FARMAKOKINETIKES**
**ΕΠΙΘΕΩΡΗΣΗ ΚΛΙΝΙΚΗΣ ΦΑΡΜΑΚΟΛΟΓΙΑΣ ΚΑΙ ΦΑΡΜΑΚΟΚΙΝΗΤΙΚΗΣ**
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## *5th Panhellenic Congress of Pharmacology*

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**Επιθεώρηση Κλινικής Φαρμακολογίας και Φαρμακοκινητικής**

***Epitheorese Klinikes Farmakologias kai Farmakokinetikes***

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# GENERAL INFORMATIONS

*REVIEW OF CLINICAL PHARMACOLOGY AND PHARMACOKINETICS*

publishes Applied Pharmacology and Current Therapeutics Reviews, Review Articles on Drugs and Drug Therapy, Original Papers and Practical Therapeutics Articles.

The *scientific standard* of the papers, which are accepted for publication, is controlled by the Editorial Board or by other Experts in the various fields of Pharmacology and Pharmacokinetics.

*Manuscripts*: These should mention, on the first page, the *Title*, *Author(s)* and the *Name of the Institution* at which the work was done. The complete *address* of the author, including Postal area code number, should be given under the rubric *Send reprint requests to*. Papers should follow the general form: *Introduction, Materials and Methods, Results, Discussion* and *References*. Drugs must be referred to by their generic or chemical name, but may be identified by trade name in parenthesis or o footnote. All papers should be submitted in duplicate.

*Summary*: A summary in English (maximum length 200 words) must accompany all manuscripts.

*Key words*: A list of key words should be submitted.

*References*: These should be numbered in the paper and listed under *References* in order of their appearance in the text. The author(s) surname followed by the initials should be given first, then the complete title of the article, the name of the Journal or Magazine (abbreviated according to the Index Medicus), the volume number, page numbers and year of publication in parenthesis.

*Papers should be submitted* to the Editors-in-Chief: Prof. S.T. Plessas or Dr C.T. Plessas.

# 5th Panhellenic Congress of Pharmacology

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## INVITED SPEAKERS



## ORAL AND POSTERS PRESENTATIONS

# Letter from Guest Editor

The progress and contributions of 20th century pharmacology has been immense with over 20 pharmacologists to have received Nobel Prizes. This field of medical studies covers many areas; it is built upon and at the same time incorporates many disciplines such as biochemistry, biology physiology, pathology, anatomy, molecular biology, while the development of new analytical and experimental techniques and instruments has given a new boost in pharmacological research. Yet, although a remarkable progress has been made in developing new drugs and in understanding how they act, the challenges are endless. Integrating a depth of knowledge in many related scientific disciplines, pharmacologists offer a unique perspective to solving drug and chemical related problems which impinge on human health, with ultimate goal the treatment and prevention of major diseases.

The 5th Panhellenic Congress of Pharmacology focuses on four *hot* subjects: Regenerative Pharmacology, Herbal Medicines, Pharmacology of Abuse and Dependence, and Education in Pharmacology.

- *Regenerative Pharmacology* is one of the newest areas in Pharmacology, represents a groundbreaking field of research and has the potential to radically alter the treatment of diseases and disorders.

- *Herbal Medicines* have acquired an important percentage among the drug used; according to WHO 80% of people worldwide rely on herbal medicines for some aspect of their primary health care. This continuously increasing use of plant medicines imposes the need for establishing new regulations.

- *Pharmacology of Abuse and Dependence*, still not a well defined area, presents a lot of challenge for researchers and clinicians.

- *Education in Pharmacology* remains a hot subject in the Medical education, following the knowledge *explosion* of the last decades accompanied by a decreasing reliance on didactic teaching. The crucial question is: how and what should we teach?

We hope that the round table discussions along with the invited lectures, included in this abstract book, will raise new and intriguing ques-

tions that will further stimulate research, and will contribute to new therapeutic approaches and attitudes.

I would like to thank the Editorial Board of *Review of Clinical Pharmacology and Pharmacokinetics* in particular Journal Editors Prof. S.T. Plessas and Dr C.T. Plessas for invitation and for providing the suitable and high-standard forum through which new research findings will become available to the scientific community.

*The Guest Editor*

*Charis Liapi*

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Chair of Hellenic Society of Pharmacology

REVIEW OF CLINICAL PHARMACOLOGY AND
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# Evaluation of the Effects of Different Mood Stabilizers in a Rat Model of Euphoria

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*Key words*: Mood stabilizers, rat model, euphoria

## INTRODUCTION

Psychostimulants, including amphetamine, induce manic symptoms in humans and exacerbate mania in individuals with bipolar disorder. In general, these effects are antagonized by mood stabilizers, like lithium and valproate. Psychostimulants have been reported to facilitate intracranial self-stimulation (ICSS) behavior in rats, which might be well related to the increases in elation and hedonistic drive of bipolar patients. However, the interaction between amphetamine and mood stabilizers in the ICSS model has not been investigated. The present study was designed to compare the effects of acute systemic administration of lithium chloride (LiCl), valproic acid (VPA) and lamotrigine (LTG) on ICSS behavior in rats. Furthermore we studied the effects of LiCl, VPA and LTG on amphetamine-induced potentiation of brain stimulation reward.

## METHODS

Male Sprague-Dawley rats (300-370g) were stereotaxically implanted with a monopolar stimulating electrode aimed at the lateral hypothalamus (LH). The animals were trained to self-stimulate using constant stimulation parameters which maintained near maximal bar-pressing rates. Once the operant response was learned the animals were then trained to self-stimulate during trials in which the stimulation current intensity was held constant and the pulse frequency was systematically reduced from values that supported maximal responding to those that induced extinction. Each pulse frequency was tested during a single 60s trial that was preceded by the noncontigent delivery of three trains of priming stimulation. Between the different trials there was an extinction period of 30s. Drug treatment began when the function relating bar-pressing rate to pulse frequency (the rate-frequency function) was stable for at least three consecutive days. Each drug or vehicle self-stimulation test consisted of a pre- and post-injection rate-frequency function determination. In the first study (acute administration of mood stabilizers), the animals were injected with different doses of LiCl or VPA or LTG while in the second study (acute administration of mood stabilizers + amphetamine) the animals were pre-treated with LiCl or VPA or LTG followed by amphetamine. The significance of the drugs effect was statistically evaluated using one-way (LiCl, VPA or LTG) and two-way (LiCl and AMP, VPA and AMP or LTG and AMP) analysis of variance (ANOVA) followed, by the Bonferroni test for multiple comparisons. The analysis was performed on two aspects of data obtained from the rate-frequency curve, i.e. the ICSS threshold and the maximum rate of responding or asymptote.

## RESULTS AND DISCUSSION

Acute administration of either LiCl or VPA in the highest doses increased ICSS thresholds. On the contrary LTG failed to alter reward at any of the doses tested. Furthermore, in the second study, only LiCl, and not VPA or LTG, attenuated amphetamine-induced potentiation of brain stimulation reward.

The present results might explain the different effects of those common mood stabilizers observed in patients with bipolar disorder, i.e. the fact that lithium is more effective than valproic acid in reducing manic relapses, whereas valproic acid and lamotrigine are more effective during the depressive phases of the disorder. The present results suggest that the ICSS model combined with amphetamine administration will be useful to explore in rats the elation and increased hedonistic drive observed in bipolar patients and ultimately help to identify novel drug treatments for bipolar disorder.

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