Ketamine and the promise of novel rapidly acting antidepressant treatments

Prof. Gerard Sanacora

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Several large-scale real world studies have recently illuminated the limitations of the existing treatments for mood disorders, showing relatively low rates of sustained remission and a substantial number of patients who receive little benefit from the treatments. Moreover, those who did achieve remission required weeks of treatment to get there. The field of depression research has learned to be circumspect about putative new breakthroughs; fifty years of research has not produced drugs that are more effective than the original tricyclic antidepressants or monoamine oxidase inhibitors. Yet, a series of recent studies suggesting a novel class of drugs may rapidly lead to mood improvement in previously treatment-refractory patients has captured great attention. The unique effects of ketamine broke new ground by suggesting that antidepressants need not require several weeks to produce meaningful clinical improvement. In addition, the fact that ketamine's effects appear related to its effects on glutamate signaling rather than modulation of monoaminergic signaling also points to novel targets for future drug development. However, there remain many unanswered questions regarding the underlying mechanism of rapid antidepressant action and the true clinical utility associated with this novel class of treatments. Several of these pressing issues are addressed in this presentation.

Mr. Eliahu Khanbaba Youdim was born in Teheran and educated in the French Alliance School in Teheran. He was fluent in 5 languages. He became a successful businessman during the second world war, dealing mostly in commerce with England. When Iran nationalized its oil company, the relations between England and Iran deteriorated and Mr. Youdim's company, as others, collapsed. This had a profound effect on his mental state and triggered the development of sever depression, which could not be treated in Iran. He travelled to England for treatment in 1957, though the only therapy available at that time was electroshock treatment. On this occasion both Prof. Moussa Youdim and his brother, Abner Youdim attended English high schools. Although Eliahu Youdim recovered, he never went back to work or touched money and he suffered from recurrent depression throughout his life.

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המכון הלאומי לפסיכוביולוגיה בישראל
The National Institute for Psychobiology in Israel

Joint International Symposium on Depression featuring

The Annual Eliahu Youdim Memorial Lecture

Ketamine & the promise of novel rapidly acting antidepressant treatments

Prof. Gerard Sanacora

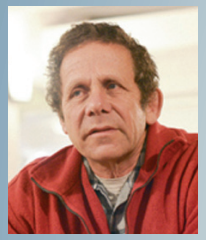
Mishkenot Sha'ananim, Yamin Moshe, Jerusalem

Sunday, March 9, 2014 16:00-18:00

Dopamine and Glutamate antagonist models of human disorders - a window for understanding and treatment

Hagai Bergman

The Hebrew University - Hadassah Medical School and the Edmond and Lily Safra Center (ELSC) for Brain Research, Jerusalem, Israel



The basal ganglia (BG) use actor/critic architecture enabling multi-objective optimization of behavioral policy. The dopamine neurons (and other BG modulators, critics) encode the mismatch between prediction and reality; whereas the BG main axis (actor) provides the connection between state and action.

In Parkinson's disease (PD), dopamine depletion in the striatum leads to synchronous oscillations of the BG main axis neurons expressed as PD clinical symptoms. The efficacy of first-line dopamine replacement therapy is exhausted within 5-10 years amongst most PD patients, at which stage Deep Brain Stimulation (DBS) has become mainstay treatment. Recently, we showed that closed-loop stimulation of the BG output stage triggered by cortical spikes has a significantly greater effect on akinesia and BG oscillations than standard open-loop and matched-control DBS paradigms.

Recent clinical observations found that NMDA antagonists such as ketamine exert an immediate robust antidepressant effect. Long standing clinical data have accumulated suggesting dissociative and even psychotic exacerbations may also be associated with the use of this class of agents, serving as a well-established basis for modeling schizophrenia symptoms. An integrative view of dopamine-glutamate interactions will be presented, furnishing possible insights into these apparently discrepant observations. Our recent studies have revealed ketamine-induced robust spontaneous gamma (30-50 Hz) oscillations in the primary motor cortex and the central nucleus of the basal ganglia - the external segment of the globus pallidus (GPe). This unique spectral signature, could therefore serve as a neural target for closed-loop adaptive DBS and may pave the road towards novel treatment methods for severe mental disorders.

Program:

16:00 Chair: Prof. Ronen Segman
Director,
National Institute for Psychobiology in Israel

Opening Remarks and Introduction
Prof. Elliot Gershon
Chairman, Board of Trustees
National Institute for Psychobiology in Israel

The Annual Eliahu Youdim Memorial Lecturer

Gerard Sanacora, MD, PhD
Guest Lecturer
Yale University School of Medicine, USA

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17:00 Coffee Break

17:30 Hagai Bergman, MD, PhD
Hebrew University Hadassah Medical School and The Edmond and Lily Safra Center (ELSC) for Brain Research, Jerusalem

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