



**Department of Psychiatry**

**Columbia University, College of P&S**

**NYS**

**Psychiatric Institute**

# **DIVISION OF BRAIN STIMULATION AND THERAPEUTIC MODULATION**

**JOURNAL CLUB**

**MOHAMED ALY, M.D.**

**VISITING FELLOW**

**DIVISION OF BRAIN STIMULATION AND THERAPEUTIC MODULATION**

**and**

**ANGEL PETERCHEV, PH.D.**

**INSTRUCTOR IN CLINICAL PSYCHIATRY**

**DIVISION OF BRAIN STIMULATION AND THERAPEUTIC MODULATION**

**will discuss the following papers on ECT topics:**

Chen F, Madsen TM, Wegener G, Nyengaard JR. Repeated electroconvulsive seizures increase the total number of synapses in adult male rat hippocampus. *Eur Neuropsychopharmacol.* 2009 Jan 26.

Spellman T, Peterchev AV, Lisanby SH. Focal Electrically Administered Seizure Therapy: A Novel form of ECT Illustrates the Roles of Current Directionality, Polarity, and Electrode Configuration in Seizure Induction. *Neuropsychopharmacology.* 2009 Feb 18.

## **Wednesday April 1, 2009**

**1:00 PM to 2:00 PM**

**Location: New York State Psychiatric Institute, 1051 Riverside Drive, Room 6601 (Board Room)**

(Enter Kolb Annex, 40 Haven Ave., walk through atrium, across bridge over Riverside Dr. to new NYSPI 6<sup>th</sup> floor, walk south along main corridor to end )

(See over for speaker brief biography, paper abstracts)

### **ABOUT MOHAMED ALY, M.D.**

Dr. Mohamed Aly is a native of Egypt, and received his training in medicine and psychiatry there. He is Assistant Lecturer of Psychiatry, El-Minia University, Egypt. <http://www.minia.edu.eg/> In 2008-09, Dr. Aly is a Visiting Fellow with the Division of Brain Stimulation and Therapeutic Modulation, Columbia University.

### **PAPER FOR JOURNAL CLUB**

Chen F, Madsen TM, Wegener G, Nyengaard JR. Repeated electroconvulsive seizures increase the total number of synapses in adult male rat hippocampus. *Eur Neuropsychopharmacol.* 2009 Jan 26. [Epub ahead of print]

The underlying mechanism of the therapeutic effect of electroconvulsive therapy (ECT) is still unclear. Here we investigated whether repeated electroconvulsive seizures (ECS), an animal model of ECT, in rats induce neuroplastic changes in the subregions of the hippocampus. ECS or sham treatment was given daily for 10 days to adult male rats. Stereological principles were employed to quantify volumes and the number of neurons and synapses. Volumes of granule cell layer (GCL) and Hilus in Dentate Gyrus of the hippocampus were significantly larger in the ECS treatment group. The neuron numbers in GCL, synapse numbers (including total synapses, spine synapses, and both perforated and nonperforated spine synapse subtypes) and synapse height in CA1 were significantly increased in the ECS treatment group. Our results indicated that repeated ECS induces neurogenesis, synaptogenesis and remodelling of synapses in rat hippocampus. This could provide a potential mechanism to explain the therapeutic effect of ECS.

### **ABOUT ANGEL PETERCHEV, PH.D.**

Dr. Peterchev is Instructor in the Division of Brain Stimulation and Therapeutic Modulation. He received an A.B. degree in physics and engineering sciences from Harvard University, Cambridge, MA, in 1999 and M.S. and Ph.D. degrees in electrical engineering from the University of California at Berkeley in 2002 and 2005, respectively. He completed postdoctoral training in transcranial magnetic stimulation (TMS) at Columbia University in 2007.

Dr. Peterchev's current research is focused on the development of technology and application paradigms for brain stimulation. His interests include pulsed power circuits and coil design for TMS, brain stimulation modeling, and simultaneous delivery of TMS with functional magnetic resonance imaging (fMRI) and electroencephalography (EEG).

### **PAPER FOR JOURNAL CLUB**

Spellman T, Peterchev AV, Lisanby SH. Focal Electrically Administered Seizure Therapy: A Novel form of ECT Illustrates the Roles of Current Directionality, Polarity, and Electrode Configuration in Seizure Induction. *Neuropsychopharmacology.* 2009 Feb 18.

Electroconvulsive therapy (ECT) is a mainstay in the treatment of severe, medication-resistant depression. The antidepressant efficacy and cognitive side effects of ECT are influenced by the position of the electrodes on the head and by the degree to which the electrical stimulus exceeds the threshold for seizure induction. However, surprisingly little is known about the effects of other key electrical parameters such as current directionality, polarity, and electrode configuration. Understanding these relationships may inform the optimization of therapeutic interventions to improve their risk/benefit ratio. To elucidate these relationships, we evaluated a novel form of ECT (focal electrically administered seizure therapy, FEAST) that combines unidirectional stimulation, control of polarity, and an asymmetrical electrode configuration, and contrasted it with conventional ECT in a nonhuman primate model. Rhesus monkeys had their seizure thresholds determined on separate days with ECT conditions that crossed the factors of current directionality (unidirectional or bidirectional), electrode configuration (standard bilateral or FEAST (small anterior and large posterior electrode)), and polarity (assignment of anode and cathode in unidirectional stimulation). Ictal expression and post-ictal suppression were quantified through scalp EEG. Findings were replicated and extended in a second experiment with the same subjects. Seizures were induced in each of the 75 trials, including 42 FEAST procedures. Seizure thresholds were lower with unidirectional than with bidirectional stimulation ( $p < 0.0001$ ), and lower in FEAST than in bilateral ECS ( $p = 0.0294$ ). Ictal power was greatest in posterior-anode unidirectional FEAST, and post-ictal suppression was strongest in anterior-anode FEAST ( $p = 0.0008$  and  $p = 0.0024$ , respectively). EEG power was higher in the stimulated hemisphere in posterior-anode FEAST ( $p = 0.0246$ ), consistent with the anode being the site of strongest activation. These findings suggest that current directionality, polarity, and electrode configuration influence the efficiency of seizure induction with ECT. Unidirectional stimulation and novel electrode configurations such as FEAST are two approaches to lowering seizure threshold. Furthermore, the impact of FEAST on ictal and post-ictal expression appeared to be polarity dependent. Future studies may examine whether these differences in seizure threshold and expression have clinical significance for patients receiving ECT. *Neuropsychopharmacology* advance online publication, 18 February 2009; doi:10.1038/npp.2009.12.