### SECOND FRANCE-ISRAEL BINATIONAL CONFERENCE IN NEUROSCIENCE

### "NEUROMODULATION IN HIGH BRAIN FUNCTIONS" "NEUROMODULATION ET FONCTIONS CEREBRALES SUPERIEURES"

Salle de Conférence du Haut-Carré, Agora des Sciences, Talence, Bordeaux, France

Under the high patronage of Valérie Pécresse Minister of High Education and Research

### FINAL REPORT

### **FINNePS**

France-Israel Neuroscience Neurology and Psychiatry Society

October 2007

#### Organizing committee:

Thomas Boraud, CNRS, France (<u>tboraud@u-bordeaux2.fr</u>) Israel Nelken, HUJI, Israel (<u>israel@cc.huji.ac.il</u>) Aline Desmedt, Université Bordeaux 1, France (<u>a.desmedt@cnic.u-bordeaux1.fr</u>) David Hansel, CNRS, France (<u>david.hansel@univ-paris5.fr</u>) Bernard Bioulac, CHU/Université Bordeaux 2-CNRS, France

#### Sponsored by:

Centre National de la Recherche Scientifique, French-Israeli Laboratory of System Neurophysiology and Neurophysics, Interdisciplinary Center for Neural Computation, Hebrew University of Jerusalem, University of Haifa, Weizmann Institute of Science, Ben Gurion University (Be'er Sheva), Université de Bordeaux I, Université Victor Segalen-Bordeaux 2, Université Paris Descartes-Paris 5, Conseil régional d'Aquitaine

#### 2<sup>nd</sup> France-Israel Binational Conference in Neuroscience, Agora des Sciences, Talence, 2007

The second France-Israel Binational Conference in Neuroscience "Neuromodulation in High Brain Functions", which was hold from July 2 to July 4, 2007 in Bordeaux (domaine du Haut Carré, Agora des Sciences, Talence, France) brought together more than a hundred leading French and Israeli researchers - including biologists, physicians, psychologists, physicists and mathematicians - investigating brain functions and dysfunctions.

The thirty invited speakers of the conference were coming from the Hebrew University of Jerusalem, the Weizmann Institute of Science, the University of Haifa, the Technion of Haifa, Bar Ilan University (Ramat-Gan) and Ben Gurion University (Be'er Sheva), the Universities of Bordeaux I, Victor Segalen-Bordeaux 2, University Paris Descartes-Paris 5, Paris Sud-Orsay, Paris XI, Gif sur Yvette, IRCAM, the University of Provence in Marseille and from the University of Joseph Fourier in Grenoble. The talks delivered during the three days of the meeting focused on most recent developments concerning the neurobiological bases of learning, memory, motor control and processing of sensory information. This conference was also the occasion to present some of the implications of fundamental neuroscience for neurology, (e.g. Parkinson disease, amniotrophic lateral sclerosis) as well as psychiatry (e.g. schizophrenia, post-traumatic stress disorder).

In recent years there has been a troubling rise in the number of calls in France and Europe to boycott Israeli academic institutions. This bi-national conference also constituted the opportunity to express clear cut opposition to this unacceptable violation of **academic freedom**.

The research on **learning and memory** is a field in which the cooperation between scientists from France and Israel is especially active. The effects of stress on memory performance constitute a major topic investigated in collaborations between researchers from Bordeaux, the Weizmann Institute and the University of Haifa. While it is well known that emotion can facilitate memory performance, a traumatic experience can result in a pathological memory profile characterized by exacerbated, persistent and maladaptive fear responses. Several of the studies presented during the conference enlightened the boundary conditions for which an emotional experience can promote, or on the contrary alter, memory performance. The neuronal bases of such bidirectional influence of stress on memory (e.g. modified activity in the prefrontal cortex, the hippocampal-amygdalar interaction and the HPA axis) were also discussed.

The two "keynote talks" delivered during the meeting were devoted to issues concerning learning and memory. Prof. Menahem Segal presented results clarifying how changes in shape, size and density of dendritic spines, might constitute the morphological basis of "memory". The possibility of erasing or modifying items in long-term memory through manipulation of certain cell signalling pathways provides a great clinical perspective in treating post-traumatic memories in humans, as shown in the topic of the talk of Prof. Y. Dudai.

Another field of collaborations between France and Israel concerns the neural bases of motor control and in particular the role of the basal ganglia. French physiologists and anatomists are well known for their contribution to the study of the functions and dysfunctions of that structure. The Higher Brain Function Lab at the Hebrew University of Jerusalem is among the leading labs in the world working on basal ganglia and motor cortex. The functions and dysfunctions of the basal ganglia, its role in decision making and in the selection of motor programs have been addressed in a series of three talks during this meeting.

The interactions between different sensory modalities and motor control is a rapidly developing domain of research in neuroscience. Among the topics in that field discussed at the conference were the induction of new cortical representations by sensory-motor learning and the spatio-temporal integration of "tactile representations" within the cortex. Some of the clinical implications of that field were also evoked like for instance the possibility of reorganizing cortical sensory representations to allow blind subjects to recognize objects by processing geometrical shapes transformed into specific soundscapes.

#### 2<sup>nd</sup> France-Israel Binational Conference in Neuroscience, Agora des Sciences, Talence, 2007

Another fruitful collaborative field of research is devoted to **the auditory system**. In particular, a stimulus-specific adaptation in the auditory cortex of cats and rats has been described as well as sensitivity of electrical responses to the short-term history of the stimulation sequence. The concept of predictive information has been presented as a way of theoretically quantifying optimal prediction of the next stimulus in the sequence.

Finally, a coupled of talks, addressed the **cellular mechanisms underlying the firing patterns of neurons**. New results were presented concerning the origin of diversity of firing patterns of GABAergic cortical interneurons. Another presentation focused on the role of calcium and potassium currents in shaping the activity of spinal motoneurons. Boths studies relied on a combination of theoretical (theory of non-linear dynamical systems and bifurcation theory) and experimental approaches.

Last, but not least, the closing ceremony of the conference gave us the opportunity to announce the creation of the **France-Israel Neuroscience Neurology & Psychiatry Society** (*FINNePS*) and to decide that the next bi-national conference in neuroscience will take place in 2009 in Haifa under the auspices of *FINNePS*.

More information about the conference 2007 on the conference website: www.inb.u-bordeaux2.fr/siteneuro2/pages/UniteINB/5227Cazalets/France\_Israel\_07.php

### onférence du Haut-Carré, Agora des Sciences, Talence

## 2d/ France - Israel **Neuroscience Binational Conference** 2-4 July 2007 Bordeaux Neuromodulation in High Brain Function

Neuromodulation et Fonctions Cérébrales Supérieures

Under the high patronage of Valérie Pécresse, Minister of High Education and Research

Thomas Boraud, CNRS, France Israel Nelken, HUJI, Israel Aline Desmedt, Université Bordeaux 1, France David Hansel, CNRS, France Bernard Bioulac, Université Bordeaux 2- CHU/CNRS/France

 

d Participants

rous
INSE RM/Université Bordeaux 2, Bordeaux, Frai edi

The Hebrew University of Jerusalem, Jerusalem, Gad
Bar Ilan University, Ramat Gan, Israel

frain
University of Haifa, Haifa, Israel

rgman
The Hebrew University of Jerusalem, Jerusalem, ONRS/Université Bordeaux 2, CHU/CNRS/France

baud
Université Bordeaux 2, CHU/CNRS/France

cazalets
CNRS/Université Bordeaux 2, Bordeaux, France

cheveigné (RCAM/CNRS, Paris, France
Bar Ilan University, Ramat Gan, Israel

many
CNRS/Université Bordeaux 2, Bordeaux, France

bein
Bar Ilan University, Ramat Gan, Israel

many
CNRS/Université Bordeaux 1, Bordeaux, France

coche
CNRS/Université Bordeaux 1, Bordeaux, France

bai
Weizmann Institute of Science, Rehovot, Israel

dai
Weizmann Institute of Science, Rehovot, Israel

university of Haifa, Haifa, Israel
University of Jerusalem, Jerusalem

more
CNRS/Université Paris Sud-Orsay, Paris, France

line
CNRS/Université Paris Sud-Orsay, Paris, France

university of Haifa, Haifa, Israel
University of Haifa, Haifa, Israel

unier
CNRS/Université Paris S, Paris, France

ki
INSERM/Paris XI/Genopole

פכון ויצמו למדע

Thomas Boraud/ Tel +33 (0)5 57 57 47 95 e-mail: tboraud@u-bordeaux2.fr



### **Invited Participants**

A. Amedi	The Hebrew University of Jerusalem, Jerusalem, Israel
I. Bar-Gad	Bar Ilan University, Ramat Gan, Israel
E. Barkai	University of Haifa, Haifa, Israel
H. Bergman	The Hebrew University of Jerusalem, Jerusalem, Israel
P. Burbaud	CHU/Université Bordeaux 2, Bordeaux, France
J.R. Cazalets	CNRS/Université Bordeaux 2, Bordeaux, France
A. de Cheveigné	IRCAM/CNRS, Paris, France
D. Cohen	Bar Ilan University, Ramat Gan, Israel
L. Demany	CNRS/Université Bordeaux 2, Bordeaux, France
G. Di Scala	CNRS/Université Bordeaux 1, Bordeaux, France
Y. Dudai	Weizmann Institute of Science, Rehovot, Israel
C. Feuerstein	Université Joseph Fourier, Grenoble, France
D. Golomb	Ben Gurion University, Be'er-Sheva, Israel
H. Gutfreund	The Hebrew University of Jerusalem, Jerusalem, Israel
R. Lamprecht	University of Haifa, Haifa, Israel
S. Laroche	CNRS/Université Paris Sud-Orsay, Paris, France
P. Magill	Oxford University, United Kingdom
S. Marom	Technion of Haifa, Haifa, Israel
M. Maroun	University of Haifa, Haifa, Israel
C. Meunier	CNRS/Université Paris 5, Paris, France
J. Melki	INSERM/Paris XI/Génopole Evry, Paris, France
J. Micheau	Université Bordeaux 1, Talence, France
B. Poucet	CNRS/Université de Provence, Marseille, France
D. Pressnitzer	CNRS/Ecole Normale Supérieure, Paris, France
G. Richter-Levin	University of Haifa, Haifa, Israel
K. Rosenblum	University of Haifa, Haifa, Israel
M. Segal	Weizmann Institute of Science, Rehovot, Israel
D. Shulz	CNRS, Gif sur Yvette, France
E. Vaadia	The Hebrew University of Jerusalem, Jerusalem, Israel
P. Vidailhet	CHR/Strasbourg, France
D. Zytnicki	CNRS/Université Paris 5, Paris, France

#### Program

#### Monday, July, 2

#### Morning

#### 9h00-9h30 Opening ceremony :

- Mr Alain Boudou (Président de l'Université Bordeaux-1),
- Mr Bernard Bégaud (Président de l'Université Bordeaux-2),
- Mr Bernard Bioulac (Directeur scientifique Adjoint délégué aux Neurosciences du CNRS),
- Mme Sonia Dubourg-Lavroff (Déléguée aux affaires internationales de la ville de Bordeaux)
- Mr Oren Bar-El (Attaché aux affaires économiques et scientifiques de l'Ambassade d'Israël).

#### 9h30-11h15 Neuromodulation and Single neuron learning - Chairperson: Jean-René Cazalets

- Daniel Zytnicki Resonant or not, two amplification modes of physiological inputs by persistent inward currents
- Claude Meunier How persistent inward and AHP currents interact to shape motoneuron discharge
- David Golomb Neuromodulatory regulation of firing patterns in fast-spiking interneurons: a bifurcation theory study

#### 11h15-11h45 Coffee break

#### 11h45-1h30 PM Function and dysfunction of the Basal Ganglia - Chairperson: Pete Magill

- Hagaï Bergman Asymmetric Encoding of Value in the Basal Ganglia
- o Thomas Boraud Motor program selection by incentive values in the Basal Ganglia
- Izhar Bar-Gad Behavioral & neurophysiological changes in the behaving primate following bicuculline injection

#### <u>Afternoon</u>

#### 1h30-3h00 Buffet Lunch and Poster session

#### 3h00-4h45 Learning, Memory and Stress - Chairpersons: Georges Di Scala/Serge Laroche

- Gal Richter-Levin Local circuit activity and plasticity in the dentate gyrus Potential relevance to learning and the effects on stress
- Mouna Maroun The interaction between the prefrontal cortex and amygdala: Relevance to emotional memory.
- Aline Desmedt Switching from adaptive to maladaptive fear responses: the key role of the hippocampus

#### 4h45-5h15 Coffee break

5h15-6h15 *Special talk*: Yadin Dudai introduced by Aline Desmedt - Erasure of Long -Term Memory in Rat Cortex

**8h00 Welcome party and Gala dinner at Mercure-Cité Mondiale, Bordeaux,** featuring a special talk by Hanoch Gutfreund - Physics and Physicists in Brain Research

Tuesday, July, 3

#### Morning

#### 9h00-10h45 Sensory Motor learning - Chairperson: Bernard Bioulac

- Eilon Vaadia Sensorimotor learning induces new representations of instructions and actions by cortical neurons
- o Dana Cohen Skill learning with noisy elements
- Amir Amedi See me, hear me, touch me: multisensory interactions, brain plasticity and sensory substitution in sighted and blind people

#### 10h45-12h45 Brunch and poster session

#### 12h45-3h00 PM Learning and Memory: cellular level - Chairperson: Bruno Poucet

- Edi Barkai Learning-induced post-synaptic enhancement of excitatory and inhibitory synaptic transmission
- Jacques Micheau The ERK/CREB pathway and fear memory consolidation and extinction
- o Koby Rosenblum The taste of memories
- Raphi Lamprecht The roles of cytoskeletal-regulatory proteins in synaptic plasticity and memory formation

#### Afternoon

3h30-8h00 Wine Tour in Saint-Emilion

#### Wednesday, July, 4

#### Morning

#### 9h00-10h45 Large Scale Networks - Chairperson: Eli Nelken

- David Hansel Decision making in the basal ganglia
- o Shimon Marom Representation in networks of cortical neurons
- Daniel Shulz Modulation of spatio-temporal integration in the barrel cortex by stimulation context and timing

#### 10h45-11h15 Coffee break

## 11h15-1h00 PM *Physiopathology of Neurological/Psychiatric Disorders* – Chairperson: Claude

Feuerstein

- o Judith Melki Molecular genetics of human motor neuron disorders
- Pierre Vidailhet Imaging episodic memory deficits in schizophrenia
- o Pierre Burbaud Deep brain stimulation: data, prospective and hopes

#### Afternoon

#### 1h00-2h15 Buffet Lunch and Poster session

#### 2h15-4h00 Tuning in the Auditory System - Chairperson: Alain de Cheveigné

- Israel Nelken Between sensory responses and memory: context sensitivity and predictive information in auditory cortex
- Laurent Demany Auditory change detection
- o Daniel Pressnitzer Temporal dynamics of auditory scene analysis

#### 4h00-4h30 Coffee break

**4h30-5h30** *Special talk:* Menahem Segal introduced by David Hansel - Anatomical basis of memory: lessons from cultured neuron

#### 5h30-5h45 Closing remarks

2<sup>nd</sup> France-Israel Binational Conference in Neuroscience, Agora des Sciences, Talence, 2007

### Pictures gallery of the 2007 meeting

### First day



Opening ceremony with (from left to right): A. Boudou, F. Nagy, O. Bar-El, T. Boraud, B. Bioulac, M. Jaber & S. Dubourg-Lavroff



Three symposia preceding the keynote talk given by Pr Y. Dudai



Buffet lunch in the garden



Views from the Poster sessions

2<sup>nd</sup> France-Israel Binational Conference in Neuroscience, Agora des Sciences, Talence, 2007



Welcome party and gala dinner dinner at Mercure-cité mondiale, Bordeaux



Gala dinner, featuring a special talk by H. Gutfreund (bottom right)



**E. Barkai** Two symposia and...the famous questions from M. Segal



Departure to the wine tour in Saint-Emillion



Best of the wine tasting...



Visit of Saint-Emillion



Three symposia preceding the keynote talk given by Pr M. Segal



Closing remarks and announcement of the creation of the French-Israeli Neuroscience Neurology & Psychiatry Society (*FINNePS*) by David Hansel

#### 2<sup>nd</sup> France-Israel Binational Conference in Neuroscience, Agora des Sciences, Talence, 2007



Best of the team in charge of the 2007 meeting...at work!

Lehitraot in 2 years in...Haifa!

#### **Abstracts - Symposia**

#### Monday, July, 2 AM - Neuromodulation and Single Neuron Learning

## Resonant or not, two amplification modes of physiological inputs by persistent inward currents

Marin Manuel, Claude Meunier, Maud Donnet and **Daniel Zytnicki** UMR 8119 CNRS–Université Paris-Descartes, Paris, France

Why do motoneurons possess two persistent inward currents (PICs), a fast sodium current and a slow calcium current? We investigated how these PICs amplify proprioceptive inputs in spinal motoneurons of anaesthetized cats using dynamic clamp. We showed that their action depends on the presence of a resonance (around 10 Hz) created by the  $I_b$  current. A fast PIC enhances the resonance and amplifies the dynamic component of  $I_b$  inputs elicited by ramp-and-hold muscle stretches. In contrast, in non-resonant motoneurons, a fast PIC easily triggers plateau potentials that lead to a dramatic amplification of the static component. The slow PIC may switch a motoneuron from resonant to non-resonant by counterbalancing  $I_b$ , thus conditioning the action of the fast PIC. Our results suggest that, according to the neuromodulation level, PICs adapt the integrative properties of motoneurons to the motor task. Since an abnormal expression of PICs was demonstrated in an animal model of spasticity, we will discuss the potential implication of our results for understanding this pathology.

## How persistent inward and AHP currents interact to shape motoneuron discharge

Marin Manuel, **Claude Meunier**, Maud Donnet and Daniel Zytnicki UMR 8119 CNRS–Université Paris-Descartes, Paris, France

Spinal motoneurons are endowed with persistent sodium and calcium currents. These persistent inward currents (PICs) amplify synaptic input and may induce a bistability of the neuronal discharge, where a down-state (quiescence or low frequency discharge) coexist with a higher frequency up-state. It is widely believed that bistability is due to the dendritic component of the calcium current, which is activated only when membrane depolarization is sufficient to counterbalance voltage attenuation between the soma and the remote dendritic location of the PIC. However, in vivo dynamic clamp experiments in anesthetized reveal that the somatic component of sodium and calcium PICs may also induce bistability. This is evidenced by a conterclockwise hysteresis of the current-frequency curve in response to triangular current ramps. Using simple models of motoneurons, we show that bistability arises from the competition between the positive feedback elicited by PICs and the negative feedback due to the afterhyperpolarization (AHP) current that regulates the discharge. Transition from the down to the upstate occurs when the PIC starts to grow faster with the injected current than the AHP current. The amplification of the frequency modulations induced by sinusoidal currents is also controled by the balance between the AHP current and PICs. The propensity of motoneurons to bistability depends on the strength of the competing currents, on kinetic parameters (time constant of the PIC, AHP relaxation time, velocity of the current ramp) and on spike threshold accommodation. This suggests that monoaminergic neuromodulation controls bistability by acting on the AHP and on both types of PICs.

# Neuromodulatory regulation of firing patterns in fast-spiking interneurons: a bifurcation theory study

#### David Golomb

Faculty of Health Sciences, Department of Physiology, Ben-Gurion University, Beer Sheeva, Israel

Neuromodulators control the firing patterns of fast-spiking (FS) cortical interneurons. For instance, application of dopamine prevents the delay period that many fast-spiking cells exhibit in response to step current injection. Dopamine attenuates the slowly-inactivating potassium current in FS cells, whereas serotonin and metabotropic glutamate receptors decrease the sodium current by shifting its inactivation curve towards more hyperpolarizing potentials. To study how those neuromodulators regulate the firing properties of FS neurons, we construct a minimal, single-compartment conductancebased model of FS cells that includes transient sodium, delayed-rectifier potassium and slowly inactivating, d-type potassium conductances. The model is analyzed using nonlinear dynamical system theory. For small sodium window current, the neuron exhibits high-frequency tonic firing. At current threshold, the spike response is almost instantaneous for small d-current conductance, and\_ it is delayed for larger d-conductance. Subthreshold oscillations appear during the delay period. As the dconductance further increases, the neuron stutters. In contrast, when the sodium window current is large, the neuron always fires tonically. Near threshold, the firing rates are low, and the delay to firing is only weakly sensitive to noise; subthreshold oscillations are not observed. We propose that neuromodulators can transform the type of firing pattern of FS neuron by moving the parameter set of the neuron through a bifurcation point.

#### Monday, July, 2, AM - Function and dysfunction of the Basal Ganglia

#### Asymmetric Encoding of Value in the Basal Ganglia

Hagai Bergman

Hebrew University, Department of Physiology, Hadassah Medical School, Jerusalem, Israel

Experimental and theoretical studies1 depicts the basal ganglia as a reinforcement learning system. Events that are better than predicted (e.g., rewards or cue predicting future rewards) are encoded by increase in the discharge of dopaminergic neurons; whereas events that are worse than predictions (e.g., reward omission) are encoded by suppression of the tonic dopaminergic discharge. The phasic dopamine changes lead to cellular learning at the cortico-striatal synapses and to reshaping of the state-action maps. However, the low level of the tonic discharge rate of dopaminergic neurons impose natural limits for their encoding of negative events. Here we show that activity of 475 neurons in five distinct areas of the basal ganglia (striatal TANs, midbrain Dopaminergic neurons, GPe, GPi and SNr) is modulated strongly by reward expectancy but only slightly by expecting aversive outcomes. We found that in a probabilistic classical conditioning task the basal ganglia activity reflects the level reward expectancy. However, the probability of aversive outcome is poorly encoded in basal ganglia activity; furthermore this activity is similar to activity when no outcome is expected. Our results demonstrate the asymmetry of the basal ganglia activity in response to reward versus aversion. This asymmetry indicates that the basal ganglia is part of the reward system and suggests that the reward and the aversive neural systems are implemented in different brain regions.

#### Motor program selection by incentive values in the basal ganglia

Benjamin Pasquereau, Agnes Nadjar, Bernard Bioulac, Christian Gross, **Thomas Boraud** CNRS UMR 5227, Université Bordeaux 2 & Laboratoire Franco-Israelien de Neurophysiologie et Neurophysique des Systèmes, Bordeaux, France

In visually-guided behavior, decision-making is a distributed neural process which involves the basal ganglia (BG), which presumably act as a 'helper system'. A consistent amount of data suggested that dopamine provides information about action value to the striatum, one of the main input structure of the BG. In a recent electrophysiological study in behaving monkeys, we showed that the encoding of movement parameter by the neurons of the BG is modulated by the value of the action to perform during a center-out reward probability based free choices motor task. It provides a mechanism by which motor program selection could be performed under dopamine control. However, interpretation of our data necessitates a revaluation of the classical model of BG functioning. We proposed here a comprehensive model of the Cortex-BG-thalamus-cortex loop based on anatomical and electrophysiological data which highlight the role of the BG in the selection of motor program based on the action value. We also discuss the consequences of this model in the physiopathology of movement disorder associated to the BG such as Parkinson's disease.

### Behavioral & neurophysiological changes in the primate following bicuculline injection Izhar Bar-Gad

Gonda Brain Research Center, Bar-Ilan University, Ramat-Gan, Israel

Obsessive compulsive disorder (OCD), attention-deficit hyperactivity disorder (ADHD), choreic dyskinesia and Tourette syndrome are a group of severe disorders which, despite their different clinical manifestation, have been associated with a common neuronal pathway: the cortico-basal ganglia loop. Within this loop, information propagates in multiple parallel limbic, associative and motor pathways leading to discrete domains within the different nuclei of the basal ganglia. Most of the nuclei of the basal ganglia use GABA (gamma-aminobutyric acid) as their primary neurotransmitter both as projection to other nuclei and as collaterals within the same nucleus. Localized bicuculline injection to the three domains within the globus pallidus external segment (GPe), one of the nuclei of the basal ganglia, in the primate enables reproduction of stereotypy, hyperactivity and movement abnormality characteristic of the aforementioned disorders (Grabli et al., 2004). Thus, hinting to some common neurophysiological basis of these disorders differing only in the domain of abnormal activity. In addition, other studies have shown that tics, characteristic to Tourette syndrome which is related to these disorders, may be evoked following bicuculline injections to another basal ganglia nucleus, the putamen (Crossman et al., 1988). In our study we use extracellular multi-electrode recording to characterize the changes in firing patterns of multiple single neurons and to uncover the neuronal interaction within small neuronal network following alteration of the GABAergic modulation via bicuculline injection. Our results demonstrate that local blocking of GABAergic transmission leads to the formation of oscillatory intermittent high-frequency activity within both segments of the globus pallidus. Moreover, neurons within the injected domain transition from uncorrelated firing to a synchronized firing pattern. The observed changes in neuronal activity are highly correlated to the behavioral symptoms as assessed by the limb kinematics and the behavioral assessment. This role of GABAergic transmission within the cortico-basal ganglia loop provides unique insight into the information encoding within this circuit and to the breakdown of normal activity leading to the severe clinical symptoms.

#### Monday, July, 2, PM – Learning, memory and Stress

## Local circuit activity and plasticity in the dentate gyrus – Potential relevance to learning and the effects on stress

**Gal Richter-Levin**, Mouna Maroun, Orly Yarom, Rachel Levy The Brain and Behavior Research Center, University of Haifa, Haifa, Israel

Studies have shown that, depending on its severity and context, stress can affect learning and memory formation. Most related studies concentrate on the impact of stress on synaptic plasticity and long-term potentiation (LTP) of principle cells. We have recently demonstrated within the dentate gyrus that modifications also take place at the level of complex interactions of interneurons with the principle cells, i.e. at the local circuit level. So far, no research has been done to establish the possible effects of stress on local circuit activity and plasticity. We set out to examine the possible alterations in local circuit activity and plasticity following exposure to stress. Local circuit activity and plasticity were measured by using frequency dependant inhibition (FDI), commissural modulation and paired pulse stimulation protocols following exposure to stress. A 15 minute-forced swim stress or Juvenile stress did not alter FDI but Commissural-induced inhibition and paired-pulse inhibition were significantly higher in stressed rats both before and after applying theta burst stimulation. Theta burst stimulation reduced inhibition in both control and stressed animals. These findings indicate that the exposure to stress induced plasticity of aspects of local circuit activity (increased inhibition), independently of the plasticity induced by theta burst stimulation (reduced inhibition). The results further suggest that stress differentially affects subsets of local interneurons. It is possible that these alterations underlie some of the behavioral consequences of the stress experience.

## The interaction between the prefrontal cortex and amygdala: Relevance to emotional memory

#### Mouna Maroun

The department of Neurobiology and Ethology, University of Haifa, Haifa, Israel

Extensive research has shown that emotional aspects of an experience exert complex effects on the way information is processed and stored. Although stress can impair memory, stress can also generate longterm memory trace that lasts for years, as in the pathological case of post-traumatic stress disorder (PTSD). It has been suggested that pathological fear and anxiety may be the manifestation of abnormal modulations in basolateral amygdala (BLA) and ventromedial prefrontal cortex (vmPFC) activity and their interaction. Accordingly, symptoms reflect amygdala hyperresponsivity to fear-related stimuli, with a concomitant lack of 'top-down' prefrontal inhibition. Lack of vmPFC inhibition over the amygdala has been associated both in humans and rodents with deficits in extinction of fear responses, a major characteristic of PTSD. Using behavioral stress and electrophysiological recordings in the vmPFC-BLA circuit we deciphered LTD/LTP mechanisms that may contribute to the dichotomy in which stress induces long-lasting memories and on the same time impairs the recall of particular aspects of the experience. We have found that under normal conditions, LTD in the vmPFC-BLA is favored over LTP, and exposure to a stressful event induces LTP and inhibits LTD. We suggest that LTD in the BLA may represent memory of safety and LTP represents the memory of fear. These observations are further supported by the finding from our laboratory that exposure to stress impairs extinction of fear, a task dependent on an intact prefrontal cortex. The existence of bi-directional changes in plasticity in this circuit could be suggested as the mechanism by which the vmPFC and the BLA interact to form memories of safety and of fear. Impairments in this bidirectional changes could constitute the mechanism of exaggerated fear responses following exposure to stressful events.

# Switching from adaptative to maladaptative fear responses: the key role of the hippocampus Aline Desmedt

UMR CNRS 5228, Université de Bordeaux 1, Bordeaux, France

In classical fear conditioning, subjects adaptively select among environmental stimuli those that predict an aversive event. When a discrete conditioned stimulus (CS, a tone) is systematically paired with the unconditional stimulus (US, a footschock), subjects display a preferential conditioned fear response to this discrete CS, which is processed as the main predictor of the aversive US. In contrast, when the CS has no or low predictive value (e.g. CS-US unpairing), a major fear response to contextual cues is observed. While neural bases of tone and contextual fear conditioning have been extensively studied, mechanisms subserving the appropriate selection/consolidation of environmental stimuli (tone vs. context) that best predict an aversive event are still elusive. I will present a set of experiments showing, in mice, that the hippocampal cholinergic signal and hippocampal corticosterone contribute to these selection/consolidation processes leading to adaptive fear responses.

First, our experiments show, that levels of hippocampal cholinergic neurotransmission during training constrain the patterns of ERK1/2 activation in the amygdala and actually determine the selection of the best predictor of the aversive event. Decreasing the hippocampal cholinergic signal not only impairs contextual conditioning but also mimicks conditioning to the discrete tone. Conversely, increasing this cholinergic signal not only disrupts tone conditioning, but also promotes contextual fear conditioning. Hence, these findings highlight that alterations in the hippocampal cholinergic neurotransmission are sufficient to produce a subjective appraisal of emotionally laden stimuli that does not match their predictive values for aversive events.

Second, we specified the boundary conditions under which the influence of corticosterone (CORT) on memory consolidation may switch from a facilitating effect to a deleterious effect. Under mild footshock intensity, post-training intra-hippocampal infusions of CORT dose-dependently enhance adaptive conditioned fear responses. However, beyond a critical dose (20 ng), fear responses become maladaptive, i.e. independent on the conditioning procedure.

Altogether, these findings support a key role for the hippocampus in the switch from adaptive to maladaptive fear responses.

#### Tuesday, July, 3, AM - Sensory motor learning

## Sensorimotor learning induces new representations of instructions and actions by cortical neurons

Eilon Vaadia

Hebrew University, Department of Physiology, Hadassah Medical School, Jerusalem, Israel

The talk describes our studies of internal representations of sensorimotor learning and its implications for inference of reaching movements from the electrical activity in the brain. First, we found that sensorimotor learning generates new neuronal representations and improves the information content about instructions and required actions by populations of motor cortex neurons. We then developed new algorithms to extract this information from local filed potentials (LFP) and single unit activity. We use these algorithms as the core of brain machine interface that proves efficient in inferring arm movements from brain activity. These results shed light on the role of motor cortex in learning and contribute to the development of brain machine interface for clinical applications.

#### Skill Learning with noisy elements

#### Dana Cohen

Gonda Brain Research Center, Bar-Ilan University, Ramat-Gan, Israel

Neurons are noisy entities yet a prolonged movement practice during motor skill learning leads to stereotypical performance with low variability. To understand neural coding, we must understand how inaccurate neural activity gets translated into the performance of accurate movement. For that purpose rats were trained for over 2 months to move left and right in response to specific auditory cues. Neural activity from motor cortex was recorded using chronically implanted microelectrode arrays. Analyzing the data, we aimed at finding neuronal features that will match the behavior. This means that the distance between these features will be smaller when movements are similar and larger when movements are different. We looked at a range of features: firing frequency during movement, time to first spike after movement initiation and firing order across neurons. Such a finding would support the overarching hypothesis that neuronal variability is countered by having neuronal networks that are sensitive to specific features of their input. All tested features but the neural order of firing exhibited a clear distinction of neural activity during opposite movements to the left and to the right. However, we were not able to identify subgroups of neurons working in synch during similar movements. The lack of clear relationship between the similarity across movements and the similarity across neural activity during similar movements suggests that there are many solutions to the neural computation perform during similar movements.

### See me, hear me, touch me: multisensory interactions, brain plasticity and sensory substitution in sighted and blind people Amir Amedi

Berenson-Allen Center for Noninvasive Brain Stimulation, Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Harvard, USA.

Restoration of sight in a blind person imposes great clinical and scientific challenges. Despite intensive efforts, recovery of vision using neuroprostheses has not been achieved. A major reason for this failure might be that the brain in the blind undergoes profound plastic changes and we do not know enough about vision and about how to communicate with this altered cortex to generate meaningful visual perception. In this presentation, I will discuss new findings regarding the nature of sensory representations for visual, tactile and verbal memory information in sighted, blind and week long blindfolded subjects. These studies show that interactions between sensory modalities are critical to our understanding of sensory representations in the brain, specifically in the occipital cortex. These findings also show that massive brain plasticity is possible even in the adult visual cortex. Here, I will also highlight the role of Transcranial Magnetic Stimulation (TMS) as a tool to assess the functional relevance of these plastic changes. Finally, I will discuss the use of sensory substitution devices (SSD) in the context of blindness. In SSD, visual information captured by an artificial receptor is delivered to the brain of a blind person using non-visual sensory information via a human-machine interface. Here I will show that the use of an auditory-to-visual sensory substitution device called "The vOICe" yields successful performance on object recognition tasks, and specific recruitment of visual structures both in blind and sighted experts. Specifically, part of the Lateral-Occipital-Complex (LOtv) is activated when objects are recognized by vision or touch. Both sighted and blind individuals who recognize objects by extracting shape information from "The vOICe" soundscapes also activated LOtv. Recognizing objects by their typical sounds or learning to associate specific soundscapes with specific objects fail to activate this region. This suggests that LOty rather than being driven by the sensory information modality is driven by the presence of shape information. We also studied shape versus location processing of visual geometrical shapes transformed into soundscapes. We found specific recruitment of the ventral visual stream (used in sighted to perceive form) to shape soundscapes. The dorsal stream (used in sighted to perceive space) was recruited in the location task. These results support a meta-modal theory of the brain, in which cortical regions are defined by the computation they apply rather than by their dominant sensory modality input. I will close by discussing the importance of "The vOICe" as a device to be used for daily activities (e.g. object recognition and localization) and its potential use to 'guide' the visual cortex to 'read' and interpret visual information arriving from a retinal prosthesis.

#### Tuesday, July, 3, AM – Learning and memory: cellular level

# Learning-induced post-synaptic enhancement of excitatory and inhibitory synaptic transmission

#### Edi Barkai

Departments of Biology and Neurobiology, Faculty of Sciences, Haifa University. Haifa, Israel

The brain, much as other biological complex systems, maintains homeostasis for stability and survival. Thus, homeostatic plasticity must occur in neurons and neuronal networks under various physiological processes, such as learning and memory. To fully understand how large neuronal ensembles undergo permanent changes while maintaining their functionality, three components of the total neuronal excitability and the manner by which their action is combined must be fully described: the excitatory synaptic drive mediated mainly by glutamate receptors, the intrinsic neuronal excitability, and synaptic inhibition mediated by GABA receptors. The purpose of the present study was to explore if and how excitatory and inhibitory synaptic inputs onto pyramidal neurons are co-modified after olfactory learning to balance each other's effects. Rats were trained in four-arm maze to discriminate between odors in pairs. As previously shown, rats require 6-8 consecutive training days to learn to distinguish between a pair of odors, but to learn a second pair of odors only requires 1-2 training days (rule learning). Piriform cortex brain slices were prepared 4-5 days after rule- learning. Whole-cell voltageclamp recordings were obtained from layer II pyramidal neurons at 300C, with Vm held at -80mV. Intracellular recordings were performed with sharp electrodes at 360C. The averaged amplitude of the minimal (quantal) spontaneous AMPA-receptors mediated events was significantly larger (P<0.01) in neurons from trained rats (8.2 + 2.9 pA, n=18) compared to neurons from pseudo-trained (6.1 + 1.0 pA, n=14,) and naïve rats (5.7+1.4, n=15). Thus, the single quantum increases after rule-learning. Accordingly, the averaged amplitude of the spontaneous events was significantly larger in neurons form trained rats. In contrast, the frequency of spontaneous events was similar in both groups, indicating that the probability of release is not modified after learning. To evaluate changes in inhibitory synaptic transmission, intracellular recordings with sharp electrode were made from layer II pyramidal neurons. IPSPs were evoked by electrical stimulations applied in layer III, in the presence of APV and DNQX, to block glutamatergic synaptic transmission. The averaged fast IPSP's reversal potential was significantly lower in neurons from trained rats (-77.1 mV+5.3, n=16 for trained vs. -70.4+7.2, n=17 for naive and -69.6+5.2, n=16 for pseudo trained, p<0.01), indicating enhancement of inhibitory synaptic efficacy. Our data support the notion that olfactory learning is accompanied by long-lasting post-synaptic modifications of excitatory and inhibitory synaptic transmission onto piriform cortex pyramidal neurons. These co-modifications allow enhancement of excitatory synaptic transmission between pyramidal neurons, while preventing the cortical network from entering into a hyper-excitable state, where in which strengthening of undesired synaptic connections may occur.

Supported by grants from the Israel Science Foundation and the US-Israel Binational Science Foundation.

#### The ERK/CREB pathway and fear memory consolidation and extinction.

P. Trifilieff, L. Calandreau, C. Herry, P. Vanhoutte, J. Caboche, A. Desmedt, N. Mons, and **J. Micheau** CNRS 5228, University of Bordeaux I, Bordeaux, France

The purpose of this series of experiments was to explore how neurobiological processes within brain structures are contributing to long-term memory formation according to the kind of information processing. Using fear conditioning, we have shown that the ERK/CREB pathway is differentially activated in the hippocampus and amydala nuclei depending on the nature of the memory representation (CS-US pairing *vs* CS-US unpairing procedures). With immunocytochemistry, we found in CA1, CA3, LA and BLA a biphasic pattern of ERK1/2 and CREB activation after contextual conditioning and only an early transient or no activation after cue conditioning. The blockade in the CA1 of either of the two peaks of activation by intrahippocampal injection of U0126, a MEK inhibitor, was shown to affect selectively the retention of contextual conditioning by impairing contextual fear. Moreover, the MEK inhibition in the CA1 was accompanied by a reduction in p-ERK1/2 immunoreactivity in BLA, providing evidence for the functional coupling between the hippocampus and the amygdala. Finally, we showed that although cue conditioning did not induce any modification of the phosphorylation state of ERK1/2 in the BLA, extinction consolidation on the contrary required ERK/CREB signaling pathway in this nucleus. Taken together, these cellular consolidation processes might reflect system consolidation implementation.

#### The Taste of Memories

#### Kobi Rosenblum

Dept Neurobiology & Ethology, Center for Brain and Behavior, Haifa University, Haifa, Israel

Our research exploit the advantages and the special characteristics of taste learning: a learning/memory paradigm that facilitates highly quantified results in a single trial; and well characterized neuroanatomy and biochemistry of the relevant cortical area during learning, consolidation and retrieval. We used tastes that are highly soluble in water and which, therefore, have somatosensory quality dimensions (temperature and texture) that are mainly sensorially similar, differing taste qualities, but no other sensory dimensions. In addition, since taste learning is simple and takes place in the animals' home cage, there are very few parameters that impinge on the learning session itself. We find that temporal interaction between two novel taste inputs can be positive (enhancing) or negative (interfering) depending on the time, novelty and directionality. Biochemically, we find that both initiation and the elongation phases of translation are regulated during taste memory consolidation in the taste cortex. Moreover, modifying genetically some of these identifies translational factors can attenuate as well as enhance learning. Our recent results shed new light on the "off-line" processing of sensory information mediated by the cortex during memory consolidation.

## The roles of cytoskeletal-regulatory proteins in synaptic plasticity and memory formation

Raphael Lamprecht, Claudia R. Farb, Daniel S. Margulies, Sarina M. Rodrigues, Mian Hou, Luke R. Johnson and Joseph LeDoux

Department of Neurobiology and Ethology, Department of Biology, University of Haifa, Haifa, Israel

The actin cytoskeleton has been shown to be involved in synaptic transmission, adhesion and morphogenesis but its role in memory is not well understood. In the present studies we investigate whether proteins that regulate various functions of actin cytoskeleton in neurons are involved in synaptic and structural plasticity and in memory formation. Profilin is an actin polymerization-regulatory protein that affects spine structural stability. We show that fear conditioning leads to the movement of profilin into dendritic spines in lateral amygdala (LA) and that these spines undergo enlargements in their postsynaptic density. The myosin light chain kinase (MLCK) phosphorylates the myosin light chain and induces actomyosin contractility leading to the modulation of neurotransmitter receptors, vesicle release and neuronal morphology. Inhibition of MLCK with the specific inhibitor ML-7 facilitates the induction of long-term potentiation in the auditory thalamus-LA pathway. Microinjection of ML-7 into the LA enhances short- and long-term fear memory acquisition but not fear memory consolidation or retrieval. Together these results show that proteins that regulate the actin cytoskeleton are involved in synaptic and structural plasticity and fear memory formation in LA.

#### Wednesday, July, 4, AM – Large Scale Networks

### Decision making in the basal ganglia

David Hansel

UMR 8119 CNRS–Université Paris-Descartes, Paris, France & Laboratoire Franco-Israelien de Neurophysiologie et Neurophysique des Systèmes, Bordeaux, France

Experiments performed in normal animals suggest that the basal ganglia (BG) are crucial in motor program selection. BG are also involved in movement disorders. In particular, BG neuronal activity in parkinsonian animals and patients is more oscillatory and more synchronous than in normal individuals. We propose a new model for the function and dysfunction of the motor part of BG. We hypothesize that the striatum, the subthalamic nucleus, the internal pallidum (GPi), the thalamus, and the cortex are involved in closed feedback loops. The direct (cortex-striatum-GPi-thalamus-cortex) and the hyperdirect loops (cortex-subthalamic nucleus-GPi-thalamuscortex), which have different polarities, play a key role in the model. We show that the competition between these two loops provides the BG-cortex system with the ability to perform motor program selection. Under the assumption that dopamine potentiates corticostriatal synaptic transmission, we demonstrate that, in our model, moderate dopamine depletion leads to a complete loss of action selection ability. High depletion can lead to synchronous oscillations. These modifications of the network dynamical state stem from an imbalance between the feedback in the direct and hyperdirect loops when dopamine is depleted.

#### Representation in networks of cortical neurons Shimon Marom

Faculty of Medecine, University of Technion, Haifa, Israel

Over the years, the question of how objects are represented in the activity of neuronal networks has been a source for rich discussions and hot debates. No matter what the nature of neural representation scheme turns out to be, it should conform to constraints dictated by the physiology of excitable membranes. Perhaps the most severe constraint in that respect is the wide range of timescales (milliseconds to minutes) that are characteristic of membrane excitability, leading to inherent nonstationarity.

## Modulation of spatio-temporal integration in the barrel cortex by stimulation context and timing

Daniel E. Shulz, Vincent Jacob and Julie Le Cam

Unité de neurosciences intégratives et computationnelles, CNRS, Gif sur Yvette, France

Rats localize objects and discriminate textures by scanning the objects' surface with their facial vibrissae. The exploratory movements of the vibrissae generate spatio-temporally complex sequences of tactile contacts. The neural responses of the somatosensory system to these "tactile scenes" have not yet been explored. Here, we delivered biologically inspired complex tactile stimuli to the rat's facial whiskers using a new stimulator composed of 25 independent piezoelectric actuators adapted to the 5 rows and the 5 caudal arcs of the whisker pad. We used the stimulator to build spatio-temporal receptive fields (ST-RF) using sparse noise stimulation and forward correlation techniques. Most units showed multivibrissal ST-RFs with different degrees of asymmetry and elongation. We have further tested tactile scenes composed of sequences of locally invariant stimulations (i.e. a rostro-caudal deflection of each whisker) that differed in their multivibrissal spatiotemporal pattern. The patterns corresponded to a wave of contacts that would be generated by a bar moving at a constant speed (1.25 m/s) in 8 different directions across the mystacial pad. We calculated direction-tuning curves defined only by the multivibrissal component of the movement. We observed in 75% (n=65) of the neurons a significant direction anisotropy indicating that the system extracts collective properties of the stimulus and globally integrates a tactile scene. It is known that exposure to natural tactile scenes under certain conditions can induce modifications in the extent of cortical receptive fields. These plastic changes could be governed by hebbian plasticity rules, like spike timing-dependent plasticity (STDP) in which a synaptic potentiation is induced when the afferent activity precedes the postsynaptic firing by a few tens of ms, while a synaptic depression is observed when the two activities occur in the opposite order. This rule has not been explored in the somato-sensory cortex in vivo. Here, we have applied a backward pairing protocol during extracellular recordings and a more standard forward pairing protocol during whole cell recordings in the barrel cortex where we controlled the relative timing between the postsynaptic activity of a neuron and the afferent activation through whisker stimulation. In both cases we observed a synaptic plasticity that depended on the relative timing of pre- and post-synaptic activity as expected from the SDTP rule and that can sustain the spatial reorganization of receptive fields that are often associated to behavioral learning.

## Wednesday, July, 4, AM – Physiopathology of Neurological and psychiatric disorders

#### Molecular genetics of human motor neuron disorders Judith Melki

INSERM et Université de Paris XI, Evry, France

NA

#### Imaging episodic memory deficits in schizophrenia Pierre Vidailhet

CHU de Strasbourg, Strasbourg, France

NA

#### Deep brain stimulation: data, perspectives and hopes Pierre Burbaud

CHU de Bordeaux et UMR 5227, Université Bordeaux 2, Bordeaux, France

Bilateral high frequency simulation (HFS) is recognized as a treatment of choice for various movement disorders including advanced levodopa-responsive forms of Parkinson's disease (PD), generalized dystonia (GD), and essential tremor. (ET) More recently, new indications in the field of psychiatry has emerged. Different targets are used depending on diseases and their presumed pathophysiology: subthalamic nucleus (STN) for PD, internal globus pallidus (GPi) and ventral intermediaire nucleus (VIM) of the thalamus in ET. Although the rationale for the use of HFS is rather rough and its mechanisms largely unknwon, it is clearly accepted that this technique leads to a drastic reduction in the severity of of movement disorders. This technique represent an enormous hope for medicacely intractable conditions threathening the vital pronostic. In this talk, we will present some exemples of clinical benefit in various forms of PD and GD and expose the risks and complications of this technique. A new field is now emerging in the treatment of Tourette's syndrom and psychiatric conditions such as resistant depression and obsessive compulsive disorders. We will report our experience and discuss new therapeutic strategies.

#### Wednesday, July, 4, PM – Tuning in the Auditory system

# Between sensory responses and memory: context sensitivity and predictive information in auditory cortex

Israel Nelken

Edmund Safra Campus, Givat Ram Dept. Neurobiol, Life Sci Inst, Jerusalem, Israel

Electrical responses in auditory cortex show sensitivity to the short-term history of the stimulation sequence. I will describe stimulus-specific adaptation in the auditory cortex of cats and rats. I will introduce the concept of predictive information as a way of theoretically quantifying optimal prediction of the next stimulus in the sequence, and show how this concept may account for some of the more complex features of context sensitivity in auditory cortex. Finally, I will describe our initial attempts to relate context sensitivity and neuromodulation.

#### Auditory change detection

Laurent Demany

CNRS UMR 5227, Université Bordeaux 2, Bordeaux, France

The auditory "objects" which have to be identified in speech or music are not static sounds but sound sequences. Thus, a crucial task of human listeners is to bind successive sounds. Recent psychophysical studies from our laboratory suggest that the auditory system binds successive sounds that differ from each other by means of automatic spectral-change detectors. In support of this view, we have found that it is possible to perceive an ascending or descending pitch change between two pure tones while the pitch of the first tone is not consciously audible (due to an informational masking effect). This phenomenon is observable even if the two successive tones are separated by several seconds of silence or by a loud noise burst. Auditory change detection appears to be based on an "echoic" memory that is quite different, in several respects, from the "iconic" memory used for visual change detection. In particular, the storage time of echoic memory appears to be at least 20 times longer than the storage time of iconic memory.

#### Temporal dynamics of auditory scene analysis

#### Daniel Pressnitzer

CNRS - Université Paris Descartes 5 & Département d'Etudes Cognitives, Ecole Normale Supérieure, Paris, France.

Auditory scene analysis (ASA) is by nature a dynamical phenomenon. ASA function is to group together sensory information originating from a same sound source, and to segregate information coming from different sources. The mechanisms involved have to be versatile enough to accommodate changes in the auditory scene, or even to explore alternate organization possibilities when the sensory information is ambiguous. In this talk I will present psychophysical and physiological data using longduration ambiguous auditory streaming stimuli, for which perceptual bistability can be observed. Strong similarities are observed in the temporal dynamics of auditory and visual bistability, but the two can cooccur independently. We also recorded responses to long streaming sequences at an early stage of the auditory pathways, the ventral cochlear nucleus. The single-units firing rates showed dynamical changes compatible with behavioral responses obtained in human listeners with the same stimuli. To account for these experimental findings, I will propose that neural mechanisms aimed at resolving ambiguities when grouping or segregating perceptual scenes could share common functional principles in different sensory modalities, but are implemented in a distributed fashion in various neural loci.

#### Abstracts – Special talks

## Monday, July, 2, PM – Erasure of Long-Term Memory in Rat Cortex Yadin Dudai

Department of Neurobiology, The Weizmann Institute of Sciences, Rehovot, Israel

Items in long-term memory are assumed to become consolidated shortly after their retrieval into a state that is resistant to amnesic agents. The textbook account is that consolidation occurs just once per item. However, ample data from several systems and memory paradigms have recently revitalized the notion that memories can undergo reconsolidation upon reactivation in retrieval. This provides a window of opportunity to modify or even erase items in long-term memory, a possibility of great theoretical as well as clinical potential (e.g., in treating post-traumatic memories). I will present evidence that in rat cortex, long-term associative taste memory can be quickly erased even weeks after its encoding and consolidation, in the absence of explicit reactivation of the memory, by specifically targeting the protein kinase PKMzeta. This finding bears marked implications on our understanding the mechanisms of persistence of long-term memory.

## Wednesday, July, 4, PM – Anatomical basis of memory: lessons from cultured neuron

#### Menahem Segal

Department of Neurobiology, The Weizmann Institute of Sciences, Rehovot, Israel

Despite extensive research over the past century on the morphological basis of memory, there is still no clear understanding of what are the permanent changes that take place once a 'memory' is established in the connection between neurons. The prime candidate for a 'memory store' is the dendritic spine, where changes in shape, size and density have been reported following enriched environment and specific learning experiences. We have used cultured hippocampal neurons to explore possible changes in morphology and functions of dendritic spines following exposure of the neurons to enhanced activation of the network. We compared such changes to those produced by pairing of activity in preand postsynaptic neurons, conditions that are similar to those used in the brain to produce long term enhancement of synaptic connections. Several changes in dendrites and spines could be found following a brief exposure to a conditioning stimulation. First and foremost, the excitatory connections among neurons are strengthened, such that activation of a single neuron produces a larger postsynaptic current in the follower neuron. On the other hand, a connection between inhibitory neuron and an excitatory one is markedly weakened. This means that the balance between excitation and inhibition in the network is shifted to more excitation. Second, the individual synaptic current is modified for a long time following a brief conditioning. Lastly, the dendritic spines are rearranged such that some spines are enlarged, some are formed and some are pruned. In addition, glutamate receptors are diffusing into the spines, in a manner that is dependent on intracellular calcium variations. These studies lead to the identification of several elementary processes that underlie learning and memory in the brain.