

5TH INTERNATIONAL SYMPOSIUM ON NARCOLEPSY

MONTE VERITÀ, ASCONA
CENTRO STEFANO FRANSCINI
SWISS FEDERAL INSTITUTE OF TECHNOLOGY (ETH)
SWITZERLAND

OCTOBER 10-15 2004

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MICHEL BILLIARD
EMMANUEL MIGNOT**

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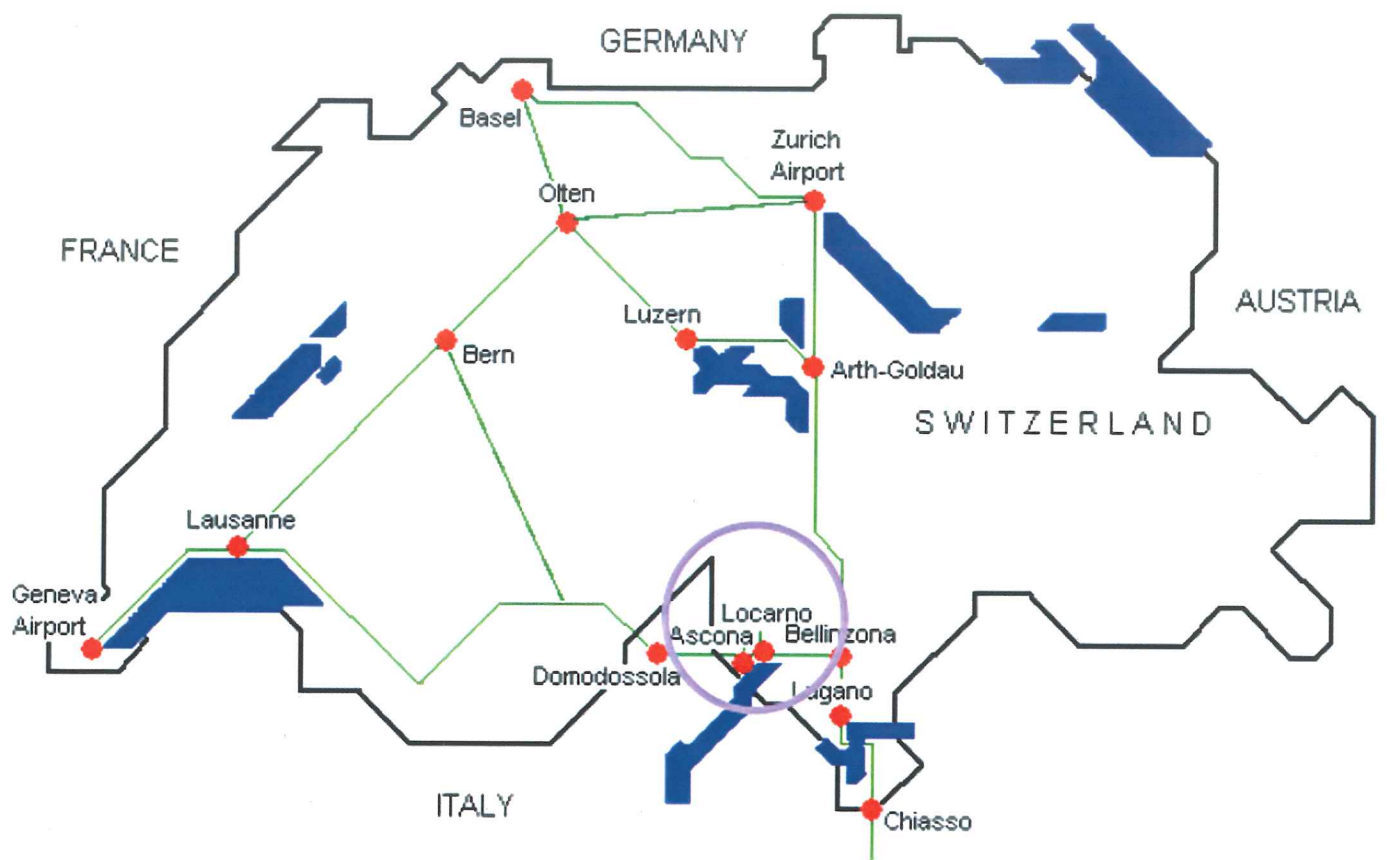
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Preface

It has been almost 30 years since the First International Symposium on Narcolepsy was held in La Grande Motte (France) in 1975, under the leadership of William C. Dement, Christian Guilleminault and Pierre Pas-souant. In this first symposium, a milestone in the area of narcolepsy, the basis of the questions we are still exploring today were laid out. It was recognized that narcolepsy symptoms were intimately related to Rapid Eye Movement (REM) sleep abnormalities. A natural animal model of narcolepsy, canine narcolepsy, was first reported. The first epidemiological and family studies of the condition were described. New classes of pharmacological agents including tricyclics and gammahydroxybutyrate were found to be useful in the treatment of cataplexy, leading to a better codification of narcolepsy therapies.

The discovery of the HLA-narcolepsy association in 1983 rekindled interest in the condition and raised the possibility of immune abnormalities in the disorder. Several international symposia on narcolepsy were then held, including one at Stanford (USA) in 1985, one in Oak Park (USA) in 1989, one in Paris (France) in 1993 and one in Tokyo (Japan) in 1994.

In 1999, the positional cloning of the canine narcolepsy gene and its identification as the hypocretin (orexin) receptor 2 gene was another milestone in the field. A mouse knock-out model for the hypocretin gene was also found to display narcolepsy-like symptoms. In 2000, these discoveries were followed by the report that most cases of human narcolepsy-cataplexy are associated with hypo-

cretin deficiency. Together with the HLA association, these results suggest that narcolepsy may be an autoimmune disorder targeting hypocretin-containing cells in the hypothalamus.

These discoveries are leading to new diagnostic procedures, for example the measurement of cerebrospinal fluid hypocretin-1 levels, and have rekindled research interest in brain mechanisms of hypersomnia. New animal models and novel therapeutic strategies targeting the immune or the hypocretin systems, are being developed. Improved epidemiological surveys, a better definition of the narcolepsy spectrum, the finding of hormonal and metabolic abnormalities in narcolepsy, the identification of non-HLA genes involved in narcolepsy are other areas under active investigation.

The explosion of research in the area of narcolepsy and hypocretin mandated the need for an international body to meet, discuss and report on these new developments. Switzerland, a country with a long tradition in sleep research and sleep medicine, was chosen for this event. The event will take place at the Centro Stefano Franscini in the inspiring and picturesque surroundings of Monte Verità, Ascona (Ticino).

We look forward to meeting you soon in Ascona.

Claudio Bassetti



C. Bassetti

Michel Billiard



M. Billiard

Emmanuel Mignot



E. Mignot

SUNDAY, OCTOBER 10, 2004

Arrival

Welcome Drink	18.00
Dinner	19.00

MONTE VERITÀ, ASCONA
CENTRO STEFANO FRANSCHINI
SWISS FEDERAL INSTITUTE OF TECHNOLOGY (ETH)
SWITZERLAND



MONDAY, OCTOBER 11, 2004

WELCOME ADDRESS (08.00–08.30):

Alexander Borbély, Marco Baggiolini

Historical aspects (08.30–10.30)

Clinical aspects
Immunogenetic aspects
Therapeutic aspects
The hypocretins/orexin as integrators of physiological signals

Chair: A. Borbély, Switzerland

C. Guilleminault, USA
Y. Honda, Japan
Y. Hishikawa, Japan
L. De Lecea, USA

Coffee break

Clinical aspects I (11.00–13.00)

Epidemiology of Narcolepsy: development of the
Ullanlinna Narcolepsy Scale
Epidemiology of narcolepsy
Narcolepsy with cataplexy
Idiopathic hypersomnia

Chair: E. Mignot, USA

C. Hublin, Finland
M. Ohayon, USA
C. Guilleminault, USA
M. Billiard, France

Lunch

Clinical aspects II (14.30–16.30)

The spectrum of narcolepsy
Effect of age on narcolepsy
Sleep paralysis
Narcolepsy in children and adolescents

Chair: T. Pollmächer, Germany

C. Bassetti, Switzerland
Y. Dauvilliers, France
J.A. Cheyne, Canada
S. Nevsimalova, Czech Republic

Coffee break

Neurophysiology I (17.00–19.00)

Neurophysiology of cataplexy and cataplexy-like phenomena
Narcolepsy and abnormal motor activity during sleep
Narcolepsy-like symptoms in a population based sample
Nighttime/daytime PSG evaluation of patients with narcolepsy

Chair: M. Silber, USA

S. Overeem, Netherlands
J. Montplaisir, Canada
M. Szklo-Coxe, USA
M. Mitler, USA



TUESDAY, OCTOBER 12, 2004

Neurophysiology II (08.30–10.30)

Vigilance tests in narcolepsy
Homeostatic aspects of narcolepsy
Circadian and ultradian aspects of narcolepsy
Neurophysiology of vigilance in narcoleptics

Chair: P. Achermann, Switzerland

J. Mathis, Switzerland
R. Khatami, Switzerland
F. Ferrillo, Italy
R.J. Broughton, Canada

Coffee break

Hypocretin/Orexin I (11.00–13.00)

Hypocretin/orexin: Molecular characteristics of hypocretin/orexin and MCH neurons
Hypocretin/orexin: in vitro studies
Role of hypocretin/orexin in normal behavior
Role of hypocretin/orexin in neurobiology: sleep and metabolism

Chair: S. Nishino, USA

C. Peyron, France
M. Muhlethaler, Switzerland
J. Siegel, USA
E. Mignot, USA

Lunch

Hypocretin/Orexin II (14.30–16.30)

CSF hypocretin-1/orexin A studies, USA and European experience
Hormonal abnormalities in hypocretin/orexin deficient narcolepsy
Metabolic abnormalities in narcolepsy
Human narcolepsy a neurodegenerative disease

Chair: T. Scammell, USA

Baumann, Switzerland / Mignot, USA
G. Lammers, Netherlands
T. Pollmächer, Germany
T.C. Thannickal, USA

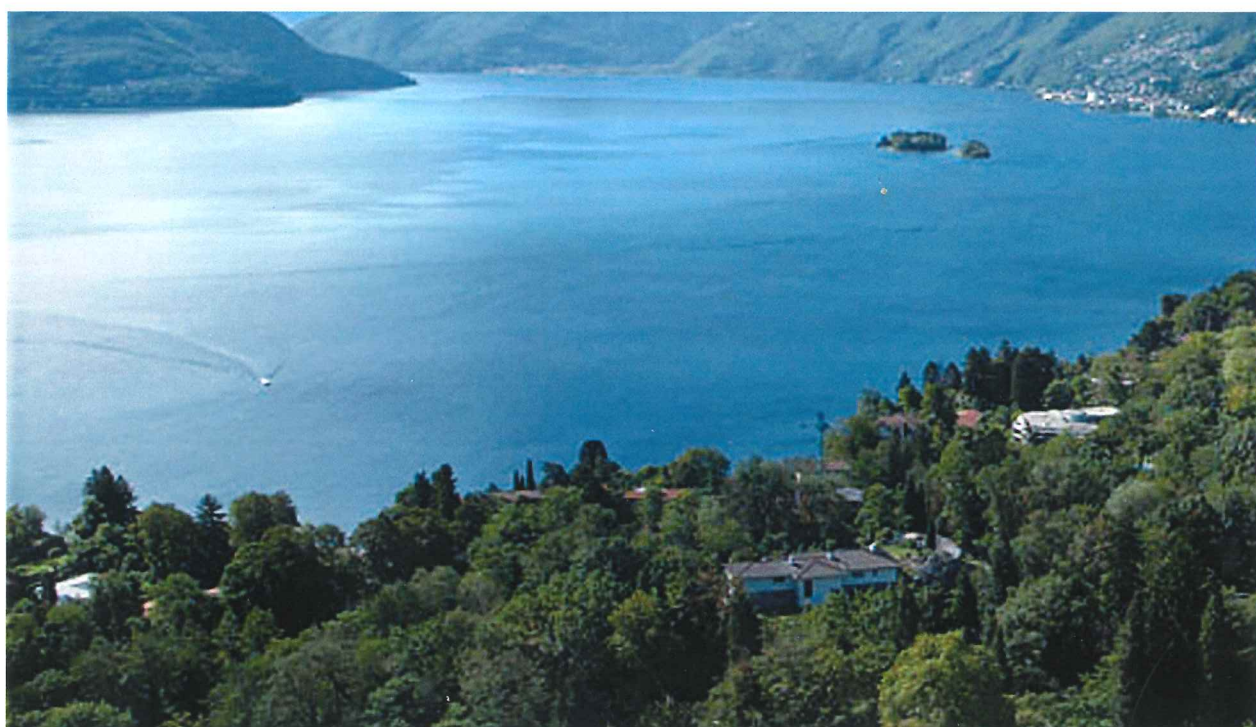
Coffee break

Animal models of narcolepsy (17.00–19.00)

Canine narcolepsy (familial and sporadic canine narcolepsy)
Lessons from sleepy mice
Behavioral and neurophysiological studies of the Hypocretin System
Input and output systems of orexin/hypocretin producing neurons:
Implications in the regulation of energy homeostasis/behavioral states

Chair: I. Tobler, Switzerland

E. Mignot, USA
J. Willie, USA
T. Kilduff, USA
T. Sakurai, USA



WEDNESDAY, OCTOBER 13, 2004

Environmental factors in narcolepsy and neurologic hypersomnias

(08.30–10.30)

Chair: M. Billiard, France

Autoimmune studies in narcolepsy

Secondary narcolepsy and hypersomnia with hypocretin/orexin

Posttraumatic and poststroke hypersomnia

Environmental factors in narcolepsy

M. Silber, USA

T. Kanbayashi, Japan

C. Bassetti, Switzerland

M. Billiard, France

Coffee break

Genetics of human narcolepsy (11.00–13.00)

Chair: M. Tafti, Switzerland

HLA, present status

Non-HLA genes involved in narcolepsy

Mutation screening of hypocretin system genes in narcoleptics

L. Lin, USA

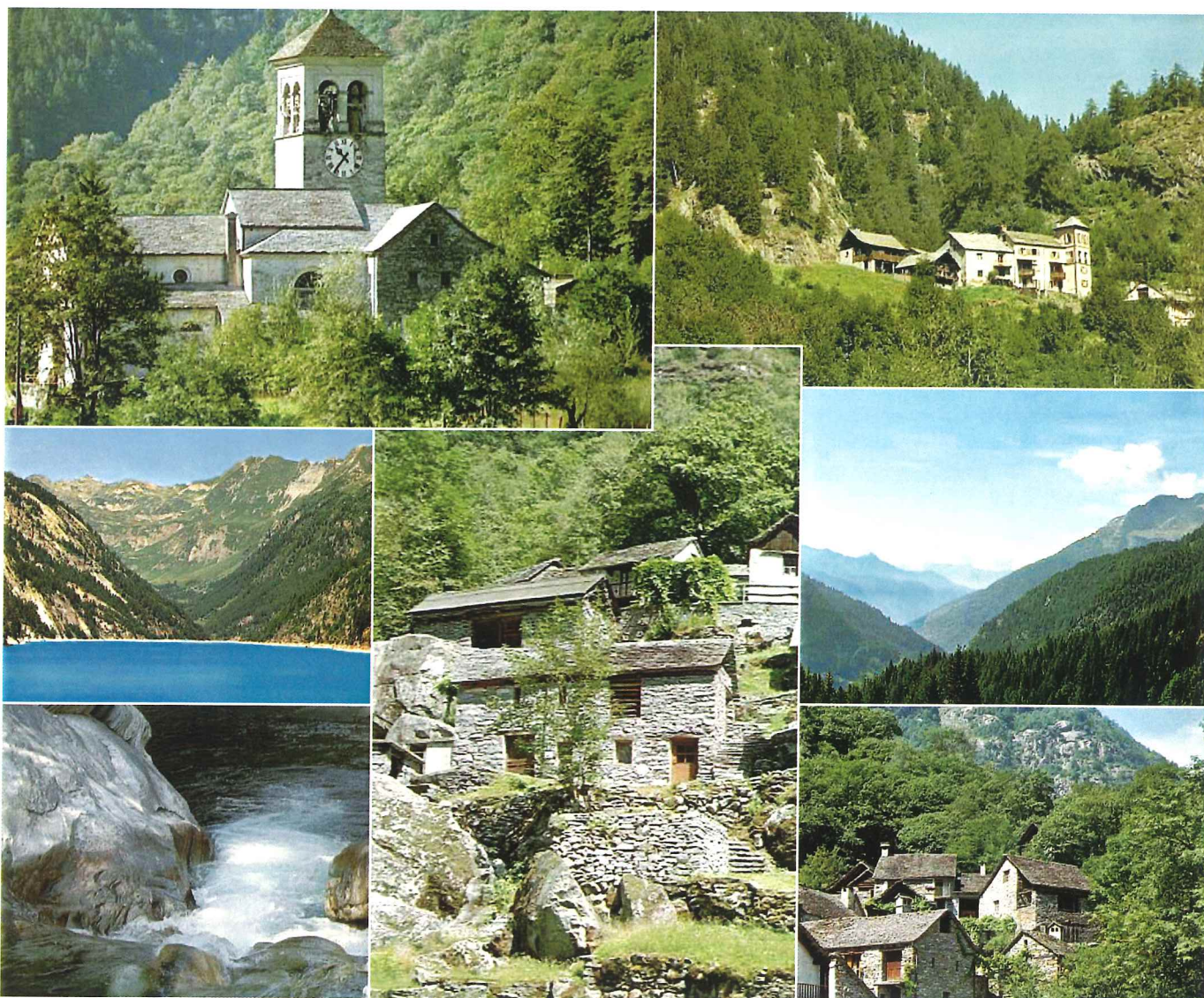
M. Tafti, Switzerland

J.H. Faraco, USA

Lunch

Social program

Trip to Valle Maggia (14.00–22.00)



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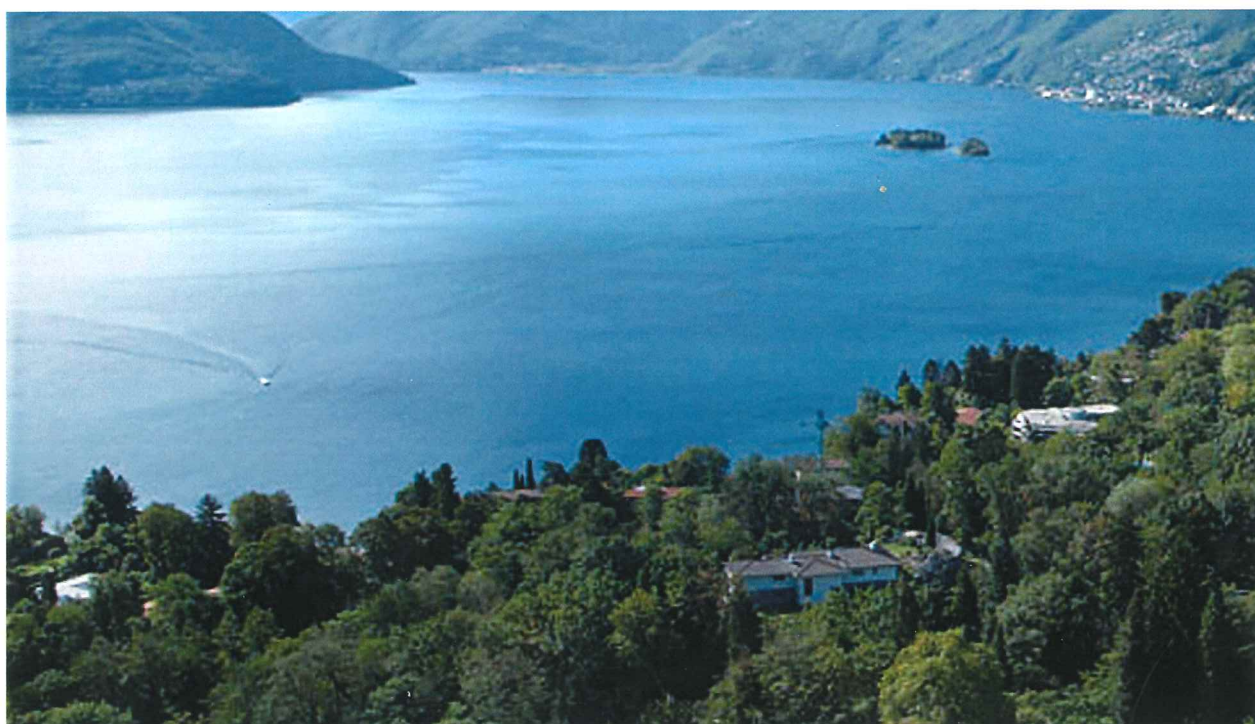
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T. Kanbayashi, Japan
C. Bassetti, Switzerland
M. Billiard, France

Coffee break

Genetics of human narcolepsy (11.00–13.00)

HLA, present status
Non-HLA genes involved in narcolepsy
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Chair: M. Tafti, Switzerland

L. Lin, USA
M. Tafti, Switzerland
J.H. Faraco, USA

Lunch

Social program

Trip to Valle Maggia (14.00–22.00)



THURSDAY, OCTOBER 14, 2004

Treatment I (08.30–10.30)

Behavioral management
Stimulants/amphetamines
Sodium Oxybate: Mechanisms of action
Sodium Oxybate: Clinical experience

Chair: Ch. Hess, Switzerland

R.J. Broughton, Canada
S. Nishino, USA
W. Houghton, USA
J. Black, USA

Coffee break

Treatment II (11.00–13.00)

Modafinil: Mechanisms of action
Modafinil: The US experience
Modafinil: The European experience
Antidepressants/MAOI

Chair: S. Nevsimalova, Czech Republic

T. Scammell, USA
M. Thorpy, USA
M. Billiard, France
S. Nishino, USA

Lunch

Treatment III (14.30–16.30)

Comorbidity in narcolepsy
Driving and narcolepsy
Psychosocial and legal aspects in narcolepsy
Perspectives for new treatments

Chair: M. Thorpy, USA

G. Mayer, Germany
J. Krieger, France
A. Siegel, Switzerland
E. Mignot, USA

Coffee break

Social program

Trip to Ascona (17.00–19.00)

Poster session (21.00–22.30)

Chair: M. Billiard, E. Mignot, E. Werth



FRIDAY, OCTOBER 15, 2004

Workshop I: Diagnostic guidelines (08.30–10.00)

Chair: E. Mignot, USA

Bassetti, Billiard, Broughton, Guilleminault, Honda, Lammers, Mignot, Murray, Nobili, Pollmächer, Silber, Thorpy

Coffee break

Workshop II: Treatment guidelines (10.30–12.00) (including EFNS task force)

Chair: M. Billiard, France

Bassetti, Black, Broughton, Billiard, Dauvilliers, Honda, Kanbayashi, Lammers, Mayer, Mignot, Montplaisir, Pollmächer, Scammell, Silber, Sonka, Thorpy

Lunch

Workshop III: (13.30–15.00) Psychosocial and legal aspects

**Chair: R. Broughton, Canada
A. Siegel, Switzerland**

Billiard, Broughton, Bruck, Guilleminault, Krieger, Lammers, Mathis, Nevsimalova, A. Siegel

Coffee break

Workshop IV: (15.30–17.00) European Narcolepsy Research Network

**Chair: C. Bassetti, Switzerland
G. Lammers, Netherlands**

Bassetti, Baumann, Billiard, Dauvilliers, Ferini-Strambi, Geisler, Khatami, Lammers, Mayer, Nevsimalova, Overeem, Peyron, Pollmächer, Sonka, Tafti

End of Symposium



Participants

Peter	Achermann	Switzerland
Marco	Baggiolini	Switzerland
Claudio	Bassetti	Switzerland
Christian	Baumann	Switzerland
Michel	Billiard	France
Steffen	Birkmann	Germany
Jed	Black	USA
Konrad	Bloch	Switzerland
Stavros	Boufidis	Switzerland
Alexander	Borbély	Switzerland
Roger	Broughton	Canada
Dorothy	Bruck	Australia
Elisabeth	Brandauer	Austria
James Allan	Cheyne	Canada
Yves	Dauvilliers	France
Luis	De Lecea	USA
Mali	Einen	USA
Tatiana	Evsiukova	Norway
Juliette H.	Faraco	USA
Luigi	Ferini-Strambi	Italy
Franco	Ferrillo	Italy
Susanne	Frigerio	Switzerland
Rolf	Fronczek	Netherlands
Heidemarie	Gast	Switzerland
Peter	Geisler	Germany
Anita	Guggenheim	Switzerland
Adrian	Guggisberg	Switzerland
Christian	Guilleminault	USA
Lucie	Hanriot	France
John	Harsh	USA
Mona Skard	Heier	Norway
Christian	Hess	Switzerland
Yasuo	Hishikawa	Japan
Yutaka	Honda	Japan
Makoto	Honda	Japan
William C.	Houghton	USA
Christer G.M.	Hublin	Finland
Meggy	Jäger	Switzerland
Vankova	Jitka	Czech Republic
Michel	Jouvet	France
Takashi	Kanbayashi	Japan
Minae	Kawashima	Japan
Harriet	Keller Wossidlo	Switzerland
Ramin	Khatami	Switzerland
Thomas S.	Kilduff	USA
Lois E.	Krahn	USA
Jean	Krieger	France
Gert Jan	Lammers	Netherlands
Ling	Lin	USA
Johannes	Mathis	Switzerland
Geert K.A.	Mayer	Germany

Participants

Emmanuel	Mignot	USA
Merril M.	Mitler	USA
Jacques	Montplaisir	Canada
Michel	Muhlethaler	Switzerland
Brian J.	Murray	Canada
Sona	Nevsimalova	Czech Republic
Seiji	Nishino	USA
Lino	Nobili	Italy
Maurice M.	Ohayon	USA
Sebastiaan	Overeem	Netherlands
Markku	Partinen	Finland
Christelle	Peyron	France
Dante	Picchioni	USA
Thomas	Pollmächer	Germany
Takeshi	Sakurai	Japan
Thomas	Scammell	USA
Rüdiger	Schulze	UK
Rosalia	Silvestri	Italy
Adrian M.	Siegel	Switzerland
Jerry	Siegel	USA
Michael H.	Silber	USA
Hans	Sjöholm	Norway
Karel	Sonka	Czech Republic
Michael	Summers	Switzerland
Mariana	Szklo-Coxe	USA
Mehdi	Tafti	CH
Thomas C.	Thannickal	USA
Michael J.	Thorpy	USA
Irene	Tobler	Switzerland
Naoji	Tsukimori	Japan
Philipp	Valko	Switzerland
Jolanta	Vanagaite Vingen	Norway
Esther	Werth	Switzerland
Jon T.	Willie	USA

A Brief History of Monte Verità

Those interested in cultural and historical aspects may enjoy reading this: around the turn of the century the Locarno/Ascona area attracted a large number of politically and culturally active individuals, e.g., the Russian anarchist Mikhail Bakunin (later leading to an anarchist/communist/social-democratic scene), the Russian baroness Antonietta de Saint-Léger (she set up the botanic garden on the Brissago islands), and the Austrian dancer and choreograph Rudolf von Laban (dancing school, later continued by famous dancers such as Charlotte Bara). Activities on Monte Verità included the project of a theosophical monastery, a sanatorium (which grew out of a vegetarian cooperative), and the above mentioned dancing school. During the first world war, Ascona attracted a large number of immigrants who moved between Zürich and sunny Ticino. In 1918, along with many others, the Dadaist Hugo Ball and the expressionist painter Alexei von Jawlensky joined the scene in Ascona. In 1923, the first hotel was established on Monte Verità through a group of Bohemians. In 1926, the enterprise was taken over by the Baron Eduard von der Heydt, the banker of the former Emperor Wilhelm II and collector of contemporary and non-European art. (See the collection of [Chinese] art distributed over the building. A lot more of the collection is in Wuppertal, Germany and in the Rietberg Museum in Zürich.) Financed through von der Heydt, the Hotel Monte Verità was built in the famous „Bauhaus“ style by the architect Emil Fahrenkamp in 1927. (Bauhaus: unification of art with modern technology, a style created at the „Hochschule für Bau und Gestaltung“ [construction and design] in Weimar. Famous proponents were the artists: Albers, Bayer, Gropius, Schawinsky, Schlemmer, Bill, Klee, Kandinsky...).

With the creation of the new regime in Germany in 1933, a second wave of immigrants arrived in Ascona, among them Else Lasker-Schüler and Erich Maria Remarque. In 1945, the peace treaty of Ascona was established between the commands of the Italian and allied armies. In the wake of the German „Wirtschaftswunder“ (economic boom, although perhaps Americans might call it the Marshall plan) Ascona flourished. In 1964, after the death of von der Heydt, the property on Monte Verità was handed over to the canton Ticino. In 1975, the Sala Balint was dedicated to the psychoanalyst Michael Balint. In 1989, the Monte Verità was transformed into a scientific congress center. A contract with the Swiss Federal Institute of Technology (ETH) guarantees a seminar activity for 20 weeks of the year within the set-up of the Centro Stefano Franscini. Who was Stefano Franscini? He lived from 1796 to 1857, established the public school system in the canton Ticino and was the first member of the Swiss federal council representing the canton Ticino. He was a strong proponent of a national technical university.

You can find a historical review in the museum in Casa Anatta (on campus, open 14.30–18.30, closed on Monday).

Edition April 2004



Stefano Franscini (1796–1857)