39th European Winter Conference on Brain Research

Les Arcs 1800, France

March 17-22, 2019

ewcbr2017@gmail.com

website

EWCBR

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*** SCIENTIFIC REGISTRATION:**

HOTEL DU GOLF-BELAMBRA
Les Arcs 1800, France

Christelle BAUNEZ, Mickael NAASSILA & Christophe BERNARD:
Sunday, March 17: 16:30-19:30 & Monday, March 18: 8:30-10.30; 17-19:30.

*** OPENING OF THE 39TH EWCBR WINTER CONFERENCE**

Christophe BERNARD, President of Promotion des Neurosciences Européennes

Sunday March 17th, 18:30-18:45

Appetizer will precede the dinner

PROGRAMME AT A GLANCE

Young investigator events:

Sunday 17th after diner: Young investigator social

Fun activity with junior researchers (but more senior are also welcome ;-)). The activity will depend on what is possible at the hotel, but I have seen that they have board games so could be for instance a Trivial Pursuit tournament. Or could also be eg Karaoke, billiard… Anything that would allow the young investigators to interact easily!

Tuesday 19th after diner: "Meet-the-PI"

After-diner session in the bar in small groups with 1-2 PIs each. Free topics, but we will provide suggestions for topics (e.g., career path, grants, work-life balance, etc).

SYMPOSIUM 1

(Monday March 18th – 8:30 – 10:30)

« From binge to addiction and from big data and microbiota to brain mechanisms. »

Chairs: Philippe de Timary and Mickaël Naassila

Oliver George (The Scripps Research Institute, La Jolla, CA - From big data to small pathways: multilevel mechanisms of addiction-like behaviors) will highlight recent work form his lab identifying potential mechanisms responsible for addiction-like behaviors to cocaine and alcohol using a multiple levels approach from large behavioral screening to whole brain imaging and optogenetic control of specific neuronal pathways.

Philippe de Timary, (Department of Adult Psychiatry, Academic Hospital Saint-Luc and Institute of Neuroscience, UCLouvain : Gut microbiota, inflammation and Alcohol-Use-Disorders), will present recent convergent data from human and mice studies support the role of the gut microbiota in specific aspects of AUD as well as preliminary data from human studies that support the existence of important brain changes, possibly related to inflammation, during alcohol withdrawal.

Mickael Naassila (INSERM UMR 1247, Amiens, France - Binge drinking and vulnerability to addictive behaviors) will present recent work on binge drinking-like behavior and both decision-making and nucleus accumbens dopamine-related disturbances.

SYMPOSIUM 2

(Monday March 18th – 16:30 – 18:30)

Peripheral immunity in neurocognitive, mental and somatoform disorders

Chair: **Marco Cosentino**

The physiological changes that occur in diseases of the brain such as neurodegenerative diseases and delirium are not restricted to the central nervous system. These diseases are also characterized by systemic physiological alterations that could have contributed to the development of the disease or to its maintenance. Similarly, although no clear peripheral neuronal, metabolic and muscular damages are found in chronic fatigue syndrome, suggesting central underlying mechanisms, this disease is associated with peripheral physiological changes that could contribute to its pathophysiology. In this session, the speakers will highlight the role of the peripheral immune system in the development and/or maintenance of these disorders.

Speakers:

- Peripheral immunity in neurodegeneration
  Marco Cosentino, Center of Research in Medicine Pharmacology, Insubria University, Varese, Italy

- Catecholaminergic modulation of innate immunity and its relevance for neurocognitive diseases.
  Franca Marino, Center of Research in Medicine Pharmacology, Insubria University, Varese, Italy

- How inflammation in arthritis might produce fatigue, cognitive impairment, anxiety and depression.
  Mechiel Korte, Division of Pharmacology, Utrecht University, Utrecht, Netherlands

- Inflammation in chronic fatigue syndrome.
  Martin Jonsjö, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden

Keynote Lecture

(Monday March 18th – 21:30 – 22:30)

Chair: **Christophe Bernard**

Prof. Lionel Naccache

Institut du Cerveau et de la Moelle (ICM), Hôpital de la Pitié Salpètrière, Paris, France

"The mechanisms of consciousness"

SYMPOSIUM 3

(Tuesday March 19th – 08:30 – 10:30)

Top-down regulation of the immune system

Chair: **Nicolas Rohleder**

The brain and the immune system interact in a multitude of ways, involving several pathways from the brain to the immune system and back. Dysregulations in brain-immune interactions play an important role in the development and maintenance of a large array of mental and physical diseases in human beings. This symposium focuses on the efferent, top-down brain-immune pathway. The first set of talks by Rainer Straub and Nicolas Rohleder will address regulation of inflammatory mechanisms. Disinhibition of inflammation is a significant factor in the development of cardiovascular and other major diseases affecting human health and longevity. Rainer Straub will focus on anti-inflammatory pathways and specifically address why cAMP-driving neurotransmitters do not have anti-inflammatory effects in chronic inflammation. Nicolas Rohleder will focus on stress as a stimulus activating peripheral inflammation, and will discuss the interactions of psychological and molecular regulatory mechanisms. Manfred Schedlowski and Asya Rolls will address how the brain regulates adaptive immunity. Manfred Schedlowski will focus on the neurobiology of placebo responses and discuss how associative conditioning can be employed as placebo-induced dose reduction strategies in immunopharmacological regimen. Asya Rolls will address by which physiological mechanisms emotions and thoughts can affect physical health. She will talk about how specific brain activity, mainly the reward system, affects the immune response and the ability to fight cancer.

Speakers:

- Why cAMP-driving neurotransmitters aren't anti-inflammatory in chronic inflammation
  Rainer Straub, Department of Internal Medicine, Universität Regensburg, Regensburg, Germany

- Acute stress regulation of peripheral inflammatory mechanisms.
  Nicolas Rohleder, Department of Psychology and Sport Science, Friedrich-Alexander-University of Erlangen-Nürnberg, Erlangen, Germany

- Learned Immune Responses: How to Proceed?
  Manfred Schedlowski, Institute of Medical Psychology and Behavioral Immunology, University Hospital Essen, Essen, Germany

- Activation of the reward system and anti-tumor immunity.
  Asya Rolls, Department of Immunology, Technion – Israel Institute of Technology, Haifa, Israel

SYMPOSIUM 4

(Tuesday March 19th – 08:30 – 10:30)

Epilepsy

Chair: **Claude Wasterlain and René Pumain**

Speakers:

- C. Bernard: Circadian and multidien regulation of seizures.
- C. Wasterlain: Cannabinoids and epilepsy: the science and the hype.
- D. Fujikawa: Why isn't ketamine started for neuroprotection early in the course of status epilepticus?
- O. Paulson: New directions for pre-surgical evaluation of epilepsy: 7 Tesla MR

SYMPOSIUM 5

(Tuesday March 19st – 16:30 – 19:30)

Motivational perspective of fatigue and sickness

Chair: **Julie Lasselin**

Fatigue is a core symptom and is highly disabling in many diseases. The pathophysiological mechanisms of fatigue remain unclear, probably because of the complexity and multidimensionality of this symptom and the difficulty to measure it. Motivational changes are core features of fatigue, as a mere lack of motivation can generate a feeling of fatigue. Changes in motivation for effort is also a hallmark of sickness, along with fatigue. This session will focus on the motivational aspects of fatigue and sickness, and their potential underlying mechanisms, in different populations. The speakers argue for a better comprehension of the motivational changes that occur during fatigue and sickness to understand how these adaptive mechanisms can develop into maladaptive mechanisms in clinical populations.

- Using effort-based decision making to study fatigue in disease.
  Marieke van der Schaaf, Donders Institute for Brain, Cognition, and Behaviour, Radboud University, Nijmegen, Netherlands.
- Sickness-induced changes in motivational processes in obesity.
  Julie Lasselin, Stress Research Institute, Stockholm University, Stockholm, Sweden.
- Altered motivational processes in acute and chronic inflammation.
  Leonie Balter, Psychology Department, Clinical Psychology, University of Amsterdam, Amsterdam, Netherlands.
- Motivation for effort expenditure in fatigued cancer patients and survivors.
  Tamara Lacourt, Department of Symptom Research, University of Texas MD Anderson Cancer Center, Houston, Texas, United States.
- Motivational perspective of sleepiness.
  John Axelsson, Stress Research Institute, Stockholm University, Stockholm, Sweden.
- Motivational perspective of disease avoidance and sickness.
  Mats Lekander, Stress Research Institute, Stockholm University, Stockholm, Sweden.

SYMPOSIUM 6

(Wednesday March 20th– 08:30 – 10:30)

Behavioral and neuro-inflammatory mechanisms contributing to pain

Chair: **Annemieke Kavelaars**

This session will focus on different aspects of chronic pain. Dr. Henrik Borsting Jacobsen will start with a presentation on the presence of cognitive dysfunction in patients with chronic pain. He will also present the results of a clinical trial using an intervention based on the relational frame theory to treat the cognitive problems in these patients. Dr. Elsenbruch will introduce the fear avoidance model and current conceptual knowledge about the role of emotional pain-related learning and memory processes in the pathophysiology and treatment of chronic pain. She will present an overview of her brain imaging research implementing classical conditioning paradigms to assess behavioral and neural mechanisms and their modulation by acute stress mediators in different pain models. She will also present recent evidence elucidating the role of salience and specificity to pain modality in healthy individuals and patients with chronic visceral pain. The third speaker in this session, Dr. Eva Kosek, will present an update regarding neuroinflammation in fibromyalgia focusing on inflammatory markers in the cerebrospinal fluid. She will present recent data from positron emission tomography (PET) indicating glia activation in fibromyalgia and discuss the potential importance of neuroinflammation and glia activation for the symptoms and treatment strategies in fibromyalgia. We will end the session by a presentation from Dr. Annemieke Kavelaars, who will add fibroblasts as novel players in the regulation of neuropathic pain. She will present data from rodent studies indicating key role of a protein produced by fibroblast in regulating chronic pain. She will discuss recent findings showing a critical role of the fibroblast–derived protein PI16 in regulation of the endothelial barrier and leukocyte influx in neuropathic pain.

Speakers:

- Parting the clouds: Treating brain fog in fibromyalgia and peripheral neuropathic pain.
  Henrik Børsting Jacobsen, Department of Pain Management and Research, Oslo University Hospital, Oslo, Norway.

- Pain-related fear and safety learning: From methods to mechanisms.
  Sigrid Elsenbruch, Institute of Medical Psychology and Behavioral Immunology, University Hospital Essen, Essen, Germany .

- Neuroinflammation and glia activation in fibromyalgia: new perspectives from recent studies.
  Eva Kosek, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden.

- A novel fibroblast-derived protein regulating neuropathic pain and leukocyte trafficking.
  Annemieke Kavelaars, Department of Symptom Research, University of Texas MD Anderson Cancer Center, Houston, Texas, United States.

SYMPOSIUM 7

(Wednesday March 20th– 08:30 – 10:30)

Circuits and systems of motivation and addiction

Chair: **C Baunez**

Speakers:

- Vincent Pascoli (Univ Geneva, Switzerland) "Circuit remodeling in mouse models of addiction »
- Christelle Baunez (INT, CNRS & Aix Marseille Univ, Marseille, France): STN oscillatory activity as a predictor of compulsive cocaine seeking
- Martine Cador (INCIA, CNRS & Univ Bordeaux, Bordeaux, France) Interoception/habits and dopamine receptor in cocaine addiction
-

SYMPOSIUM 8

(Wednesday March 20th – 16:30 – 19:30)

« Neuroeconomics of individual and social choice »

Chair : **Wolfram Schultz**

This session will focus on neural mechanisms underlying individual and social decision-making. We will present recent data from humans and monkeys during behaviours that are representative of a wide range of everyday choices.

1) Axiomatic tests of economic choice and their neuronal correlates in primate orbitofrontal cortex
Simone Ferrari Toniolo
Department of Physiology, Development & Neuroscience, University of Cambridge, UK

2) Primate amygdala neurones during observational learning
Fabian Grabenhorst
Department of Physiology, Development & Neuroscience, University of Cambridge, UK

3) Primate prefrontal neurones during video competition
Masataka Watanabe
Tokyo Metropolitan Institute for Medical Science

4) Primate coordination and cooperation in formal economic games
Charlotte van Coeverden and Wolfram Schultz
Department of Physiology, Development & Neuroscience, University of Cambridge, UK

5) Human delusions during social fear learning
Predrag Petrovic
Department of Clinical Neuroscience, Karolinska Institute, Stockholm

SYMPOSIUM 9

(Wednesday March 20th – 16:30 – 19:30)

Immunological underpinnings of changes in nervous system structure and function PART 1

Chairs: **Jan-Pieter Konsman and Mats Lekander**

Although the general idea that immune cells and mediators can alter nervous system function and structure is now well-accepted, recent research covered in this session indicates that the domains to which these influences apply are broader than initially anticipated and span both physiology and somatic, in addition to neurologic, disease as well as cognition and psychiatric disorders. Moreover, speakers in this session will show how the mediators and mechanisms involved go beyond the usual suspects of blood-brain barrier breakdown, pro-inflammatory cytokine penetration and immune cell infiltration of the nervous system.

Speakers:

- Lipids tune microglial shaping of neuronal circuits in the developing brain.
  Agnès Nadjar, NutriNeuro laboratory, INRA, University of Bordeaux, Bordeaux, France
- Neuroinflammation and postoperative cognitive decline.
  Regien Schoemaker, University Medical Center Groningen, University of Groningen, Groningen, Netherlands
- Experimental bacterial sepsis can induce encephalopathy and changes in white matter water diffusion and glial cells in the absence of blood-brain barrier breakdown.
  Jan Pieter Konsman, Aquitaine Institute for Cognitive and Integrative Neuroscience, University of Bordeaux, Bordeaux, France
- Functional and structural neuroimaging signatures of inflammation-associated depression.
  Neil Harrison, Brighton and Sussex Medical School, University of Sussex, Brighton, United Kingdom
- Central-nervous-system effects of modulating peripheral IL-6 levels in major depression.
  Paul Hamilton, University of Linköping, Sweden
- Inflammation and emotional learning.
  Harald Engler, Institute of Medical Psychology and Behavioral Immunology, University Hospital Essen, Essen, Germany
- Accelerated aging and cognitive decline after chemotherapy.
  Cobi Heijnen, Department of Symptom Research, University of Texas MD Anderson Cancer Center, Houston, Texas, United States

SYMPOSIUM 10

(Thursday March 21st – 08:30 – 10:30)

Vocal emotions: neural bases and behavioural consequences

Chair : **Didier Grandjean** (Univ Geneva, Switzerland)

Abstract.

Speakers:
Didier GRANDJEAN (Univ Geneva)
« Phylogenetic perspectives of brain mechanisms in primate emotion vocalizations »

Christelle BAUNEZ (INT, Marseille, France)
« Modulation of cocaine intake by ultrasonic vocalizations in rats »

Leonardo CERAVOLO (Univ Geneva)
"Voice perception revisited: parallel functional brain networks process voice and reduce environmental noise"

Damien BENIS (Univ Geneva)
"Differential influences of brain hemisphere and Parkinson's disease side-of-onset on the oscillatory correlates of emotional prosody decoding in the Subthalamic Nucleus".

SYMPOSIUM 11

(Thursday March 21st – 08:30 – 10:30)

Immunological underpinnings of changes in nervous system structure and function PART 2

Chairs: **Jan-Pieter Konsman and Mats Lekander**

Although the general idea that immune cells and mediators can alter nervous system function and structure is now well-accepted, recent research covered in this session indicates that the domains to which these influences apply are broader than initially anticipated and span both physiology and somatic, in addition to neurologic, disease as well as cognition and psychiatric disorders. Moreover, speakers in this session will show how the mediators and mechanisms involved go beyond the usual suspects of blood-brain barrier breakdown, pro-inflammatory cytokine penetration and immune cell infiltration of the nervous system.

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  Cobi Heijnen, Department of Symptom Research, University of Texas MD Anderson Cancer Center, Houston, Texas, United States

SYMPOSIUM 12

(Thursday March 21st – 16:30 – 19:30)

Pain: novel mechanisms and treatments

Abstract : Chronic pain is common. It affects nearly 20% of the adult population and has a major impact on these people's lives. While we have many analgesic drugs available, the very large majority of drugs taken for pain relief are of only two categories: aspirin-like drugs and opiates. These, and other existing pharmacotherapies, have limited efficacy and very significant side effects.

This symposium will review a number of recent advances in our understanding of the mechanisms of chronic pain. These relates to changes taking place in the peripheral innervation of diseased tissues, the central processing of pain-related signals in the spinal cord and the descending control pathways that regulate spinal processing. In addition several of the talks will highlight the therapeutic opportunities to treat pain based on our new understanding of mechanisms.

Speakers:

1) *Mateusz Kucharczyk, London Uk : "Bone cancer pain: why does it hurt so much?"
2) Stefan Lechner, Heidleberg, Germany "The molecular basis of mechanosensitivity in 'silent' nociceptors"
3) Stephen McMahon, London UK "IL6 as a mediator of neuropathic pain"
4) *Beatrice Oehler, London, UK "D-4F apoA-I mimetic peptide, a promising peptide ameliorating TRP channel mediated hyperalgesia in rodents"
5) Jiri Palecek, Prague "Modulation of spinal cord synaptic transmission in a model of chemotherapy induced pain"
6) Katarzyna Starowicz, Krakow, Poland "Gene expression patterns in the rat knee cartilage in response to cannabinoid-based treatment"

*these are PhD students and should be eligible for reduced registration rates

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SYMPOSIUM 13

(Thursday March 21st – –16:30 – 18:30)

Role of the microbiome and nutrition in eating, mood and cognitive disorders

Chairs: **Christoph Rummel and Sophie Layé**

Research on the influence of nutrition on eating disorders, mood and cognition has revealed new insights into the mechanisms and mediators that are involved. Related to the specific composition of dietary intake, also a role for the microbiome has recently been demonstrated in such responses while causative relationships remain under discussion. In this session, we will present and discuss various aspects on how nutrition can influence brain health and function or its neuropsychiatric vulnerability in a rather broad perspective. In this scope, the following related topics will elaborate how the gut-brain axis or neuropsychiatric vulnerability are altered by the microbiome or intestinal permeability, respectively. Appetite regulation pertains to another tightly related research topic that in particular emerged with the discovery of the appetite and body weight regulating hormone leptin and worldwide increasing rates of obesity and related health risk factors. A presentation on hormone reactive immunoglobulins will broaden the complex network of food intake regulation in health and disease. In addition, new data on the fact that dietary modulation can alter cognition and cognitive/mood disorders including dementia in late-life will be presented. As such, polyunsaturated fatty acids and in particular n-3 fatty acids contribute to the complex balance of pro- and anti-inflammatory processes that also alter function of the healthy and diseased brain. Some of recently defined metabolites of polyunsaturated n-3 fatty acids, for example, pertain to new cutting edge targets for novel therapeutic approaches in the future to "resolve" brain diseases.

Speakers:

- Microbiota and the gut-brain axis.
  Anna Andreasson, Stress Research Institute, Stockholm University, Stockholm, Sweden

- Role of hormone-reactive immunoglobulins in regulation of stress and appetite in normal and pathological conditions.
  Serguei Fetissov, Neuronal and Neuroendocrine Communication & Differentiation, University of Rouen, Rouen, France

- The role for n-3 fatty acids in the modulation of brain-controlled sickness responses during systemic LPS-induced inflammation.
  Christoph Rummel, Institute for Veterinary Physiology and Biochemistry, Justus-Liebig-Universität Gießen, Gießen, Germany

- Dietary polyunsaturated fatty acids, role in mood and cognitive disorders.
  Sophie Layé, NutriNeuro laboratory, INRA, University of Bordeaux, Bordeaux, France

POSTERS

Site of action of brain neurosteroid - pregnenolone sulfate - at the N-methyl-D-aspartate receptor.

*L. VYKLICKY[1], B. KRAUSOVA[1], B. KYSILOV[1], J. CERNY[1], V. VYKLICKY[1], T. SMEJKALOVA[1], M. LADISLAV[1], H. CHODOUNSKA[2], E. KUDOVA[2];

[1]Institute of Physiology CAS, Prague, Czech Republic; [2]Institute of Organic Chem. and Biochem. CAS, Prague, Czech Republic

N-methyl-D-aspartate receptors (NMDARs) play a key role in excitatory synaptic transmission, and their dysfunction underlies some neurological and psychiatric disorders. Receptor hypofunction has been implicated in autism, schizophrenia, and various forms of intellectual disability, and compounds with a positive allosteric effect at NMDARs may have a beneficial effect in these diseases. The aim of this study was to characterize the site of action for pregnenolone sulfate (PE-S), an endogenous neurosteroid that has a positive allosteric effect at NMDARs.

We have used patch-clamp technique to study PE-S effect at recombinant GluN1/GluN2B receptors. Our results show that PE-S did not compensate for the diminution of NMDAR responses induced by cholesterol depletion, indicating that cholesterol and PE-S potentiation are mediated by distinct sites. Dose-response analysis of the positive allosteric effect of PE-S at NMDAR indicates that at biologically relevant concentrations the steroid exists in micelle form and together with the effect of methyl-γ-cyclodextrin indicates that the steroid acts at the NMDAR transmembrane domain. The steroid positive allosteric effect was observed only for PE-S added from the extracellular, not from the intracellular site. To identify the PE-S site, we sequentially replaced amino acid residues at the outer segment of the transmembrane helices M1 and M4 of both the GluN1 and GluN2B subunits. Single alanine substitution mutations included: GluN1(Q559A to V572A; T809A to V825A) and GluN2B(S555A to I568A; D814A to A830T). Relative effect of PE-S (100 μM) varied considerably from that found for the wild type receptors (104 ± 4 %; n = 158) and mutated receptors (spanning from inhibition -33 ± 2 % (n = 7) for GluN1/GluN2B(M824A) to augmented potentiation 507 ± 112 % (n = 4) for GluN1/GluN2B(G815A)). The effect of PE-S at GluN1/GluN2B(D816A; Y823A; and M824A) receptors was significantly reduced compared to WT and at GluN1(G815A; M818A; and G822A)/GluN2B receptors was significantly increased compared to WT.

Electrophysiological results together with computational methods indicate that PE-S binds to the cavity between the M1 and M4 membrane domains of the GluN2B subunit of the closed conformation of the channel. Following receptor activation M1/M4 helices rearrange, including the steroid binding site – this explains why the effect of PE-S is disuse-dependent. Together our study has identified a novel site at the NMDAR by which endogenous neurosteroid PE-S augments the activity of the receptor.

Supported: Czech Science Foundation (GACR): 19-01300S, PharmaBrain: CZ.02.1.01/0.0/0.0/16_025/0007444; Technology Agency of the Czech Republic: TE01020028 CZ.02.1.01/0.0/0.0/16_025/0007444; TN01000013/01.

Is R(+)-baclofen the best option for the future of baclofen in alcohol dependence pharmacotherapy? Insights from the preclinical side.

Victor Echeverry-Alzate1, Jérôme Jeanblanc2, Pierre Sauton2 and Mickaël Naassila2
1 present address - Laboratory of Psychobiology, Dept. of Psychobiology & Behavioral Sciences Methods, School of Psychology. Complutense University of Madrid. Hospital Regional Universitario de Málaga, Neuropsychopharmacology Group. Spain
2 INSERM U1247 – Research Group on Alcohol & Pharmacodependences (GRAP), Université de Picardie Jules Verne, Amiens, France

For several decades, studies conducted to evaluate the efficacy of (±)-baclofen in the treatment of alcohol dependence yielded contrasting results and animated debate at the international level regarding the benefit / risk balance of the drug. Human and animal studies recently questioned the use of the racemic drug in patients since a potential important role of the different enantiomers has been revealed with an efficacy thought to reside with the active R-enantiomer. Here we conducted experiments in the post-dependent rat model of alcohol dependence to compare the efficacy of R(+)-baclofen to that of (±)-baclofen on ethanol intake, seeking and relapse. We found that R(+)-baclofen was more effective than (±)-baclofen in reducing ethanol intake and seeking during acute withdrawal and also in reducing ethanol intake during relapse after abstinence. Here we used also an original population approach in order to identify drug responders. We found a significant proportion of responders to S(-)-baclofen and (±)-baclofen, displaying an increase in ethanol intake and this increasing effect was not seen in the R(+)-baclofen group. At an intermediate dose of R(+)-baclofen, devoid of motor side effects, we identified a very large proportion of responders (75%) with a large decrease in ethanol intake (90% decrease). Increasing the dose of R(+)-baclofen and (±)-baclofen was associated with an increase in the number of responders. R(+)-baclofen and (±)-baclofen were effective in reducing sucrose intake. Finally, alcohol dependent animal were less sensitive to R(+)-baclofen than non dependent animals thus suggesting lower sensitivity of GABA-B receptor induced by alcohol dependence. Our study has important clinical implication since it suggests that the wide variability in the therapeutic responses of patients to (±)-baclofen may come from the sensitivity to the R(+)-baclofen but also to the one of the S(-)-baclofen that can promote an increase in ethanol intake.

The Cocaine and Oxycodone Biobanks: Two repositories of biological samples from genetically characterized outbred rats that exhibit compulsive-like escalation of cocaine or oxycodone self-administration

Lisa Maturin, Marsida Kallupi, Abraham Palmer, Leah Solberg Wood, Giordano de Guglielmo, Olivier George
The Scripps Research Institute

Identification of the mechanisms that underlie compulsive cocaine or oxycodone use in animal models is a major goal for understanding the genetic risk factors for addiction and facilitating the identification of novel druggable targets. A key issue for the field is the lack of a repository that contains biological samples from behaviorally and genetically characterized rats. We introduce the Cocaine Biobank (www.cocainebiobank.org) and the Oxycodone Biobank (www.oxycodonebiobank.org), two repositories of biological samples from a unique, genetically diverse strain of outbred heterogeneous stock (HS) rats that have been behaviorally and genetically characterized using next-generation sequencing, state-of-the-art behavioral screening, and a variety of preservation techniques. Male and female rats are trained to self-administer cocaine (0.5 mg/kg/inf) in daily 6 h sessions or oxycodone (0.15 mg/kg/inf) in dialy 12 h sessions and tested using progressive-ratio responding and responding despite adverse consequences (contingent footshocks), and measures of analgesia, hyperalgesia and irritability-like behaviors. Results show high individual variability with vulnerable and resistant rats that is likely to facilitate the detection of gene variants and the molecular and cellular mechanisms of addiction. Preservation techniques include perfusion, snap-freezing, and cryopreservation maximize the compatibility of these tissue banks with cellular, molecular, and anatomical methods. The Biobanks provides free access to over 20 organs. The use of the Biobanks have the potential to have a sustained impact on the field of addiction they will identify novel druggable targets, provide a comprehensive analysis of compulsive drug use in both males and females, and provide unique data/tissue repository that will facilitate follow-up and replication studies.

ATTENDEES DIRECTORY

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