





3rd Workshop Inserm- NIDA- NIAAA November 9-10, 2015

> Biopark, 8 Rue de la Croix-Jarry, 75013 Paris

Metro/RER: Bibliothèque François Mitterand



Program

Monday, November 9, 2015

12:00pm - 1:15 pm: Welcome participants (lunch - buffet style)

1:15 pm-1:30 pm: Introductory Remarks: Etienne Hirsch, Director Institute on Neuroscience, Cognitive Science, Neurology, Psychiatry, Inserm

1:30 pm-3:00 pm: Keynote speakers: Discoveries in the field of Addiction Science (30 min talks + 15min Q&A)

1:30 pm-2:15 pm: "New insights into mechanisms of nicotine reinforcement" **Paul Kenny** (Mt Sinai, New York)

2:15 pm-3:00 pm: "From Pregnenolone to AEF0117: the discovery and development of Signaling Specific Inhibitors of the CB1 receptor"

Pier-Vincenzo Piazza (Neurocentre Magendie, Bordeaux)

3:00 pm-4:30 pm: First Round Table Discussion: « Cellular and molecular mechanisms of addiction »

Chair: George Koob, Director, NIAAA

Moderators/Rapporteurs: Joni Rutter (NIDA) & **Jean-Antoine Girault** (Fer à Moulin Institute, Paris)

Invited Panelists:

Brigitte Kieffer (Université McGill, Montréal)

Marina Wolf (University of Chicago, Chicago)

Peter Kalivas (Medical University of South Carolina, Charleston)

Jean-Antoine Girault (Fer à Moulin Institute, Paris)

Veronique Deroche-Gammonet (Neurocentre Magendie, Bordeaux)

Olivier Manzoni (Mediterrenean Institute of Neurobiology, INMED, Marseille)

4:30 pm-5:00 pm: Coffee Break

5:00 pm-6:30 pm: Keynote lectures: Discoveries in the field of Addiction Science (30 min talks + 15min Q&A)

5:00 pm-5:45 pm: "Contributions of Large Scale Studies of Brain Development to Addiction Neuroscience"

Terry Jernigan (University of California, San Diego)

5:45 pm-6:30 pm: "Did the addiction science shed light on the genetic vulnerability of eating disorders?"

Philippe Gorwood (Psychiatrie and Neurosciences Research Center, Paris)

6:30 pm-7:00 pm : Vision & Perspectives for the future

Nora Volkow, Director, NIDA George Koob, Director, NIAAA Yves Lévy, Chairman and CEO Inserm

7:00 pm-7:30 pm: Adjournment/Free Time

7:30 pm-9:30 pm: Dinner

Restaurant « Le Train Bleu » Gare de Lyon, Place Louis Armand, 75012 Paris

Tuesday November 10, 2015

9:00 am-10:30 am: Keynote lectures: Discoveries in the field of Addiction Science (30 min talks + 15min Q&A)

9:00 am-9:45 am: "From binge drinking to alcohol dependence: results of translational studies"

Mickael Naassila (Research group on early life alcohol exposure and vulnerability to dependence, Amiens)

9:45 am-10:30 am: "Prevention and treatment programs for adolescents with addictive behaviors."

Olivier Phan (Mental Health and Public Health, Paris)

10:30 am-11:00 am: Coffee Break

11:00 am-12:30 pm: 2nd Round Table Discussion « Biomarkers of addiction »

Chair: Nora Volkow, Director, NIDA

Moderators/rapporteurs: Peggy Murray (NIAAA) & Mickael Naassila (Research group on early life alcohol exposure and vulnerability to dependence, Amiens)

Invited Panelists:

Laura Bierut (Washington University School of Medicine, Saint Louis)

Dolf Pfefferbaum (Stanford University, Stanford)

Thomas Kash (University of North Carolina, Chapel Hill)

Anne-Lise Pitel (Cognitive Neuropsychology and Functional Neuroanatomy of Human, Memory, Caen)

Jean-Christophe Corvol (Brain and Spine Institute, ICM, Paris)

Bruno Gonzales (Research group NEOVASC – Microvascular Endothelium and Neonate Brain Lesion, Rouen)

12:30 pm - 2:00 pm: Lunch on site

2:00 pm- 2:45 pm: Available Funding Mechanisms for Collaboration (10min each talk, 15min Q&A from audience)

Steve Gust, NIDA Peggy Murray, NIAAA Anne Jouvenceau, Inserm

2:45 pm- 3:00 pm: Award 2015-2016 NIDA-Inserm Fellowships

Dale Weiss, NIDA **Mireille Guyader,** Inserm

3:00 pm-5:00 pm: Conclusion, discussion, next steps

Moderators: Steve Gust (NIDA), Anne Jouvenceau (Inserm)

3:00 pm-3:10 pm: Joni Rutter, Jean-Antoine Girault: Round Table 1 Wrap-Up

3:10 pm-3:20 pm: Peggy Murray, Mickael Naassila: Round Table 2 Wrap-Up

3:20-5:00 pm: How to make this joint Inserm-NIDA-NIAAA endeavor work?

Discussants: Etienne Hirsch, Nora Volkow, George Koob

About Inserm

Research at Inserm covers all fields of health research, from basic research to applied research. It is central to the French health care and public health systems.

Today, Inserm coordinates more than 300 research structures (research units, centres of clinical investigation (CIC) throughout France and it's oversees departments.

Amongst the 13,000 researchers, engineers, technicians and administrative staff working in Inserm laboratories, 5,000 are permanent employees, more than 2,700 have contractual positions and almost 4,500 have positions in universities, teaching hospitals or other research organisations.

Inserm receives one third of its 998 million euro annual budget externally - the highest percentage of external funding as compared to other research institutes. Since 2011, state funding includes allocation for several measures of the National Cancer Research Plan (30 M€). In addition, the research institute ANRS (France Research North & South AIDS-HIV Hepatitis) has been integrated as an independent agency within Inserm with an annual budget of 40 M€ since 1st January 2012. Nearly 90% of Inserm resources are spent on support of research units and infrastructures.

As for results, Inserm is the leading health research institution in Europe in terms of publications, patent filings and participation in European research programmes. Inserm is ranked 2nd amongst health research institutes in the world in publications (roughly 10,000) following the American NIH (National Institutes of Health). Inserm-transfert is a subsidiary of Inserm dedicated to the valorisation of biomedical research discoveries in its labs.

Lastly, Inserm holds presidency of the National Alliance for Life and Health Sciences (Aviesan) which groups together 9 main stakeholders of life and health sciences (Inserm, CNRS, CEA, Inra, Inria, CPU, CHRU, IRD, Institut Pasteur) as well as associate members. Aviesan's major objective is to coordinate the strategic analysis, scientific programming and operational implementation of life and health science research in France. It also supports public policy decisions and facilitates the definition of shared standpoints in terms of European research and international cooperation.

About NIDA

The National Institute on Drug Abuse (NIDA) is a component of the National Institutes of Health, U.S. Department of Health and Human Services. NIDA supports most of the world's research on the health aspects of drug abuse and addiction. The Institute carries out a large variety of programs to inform policy and improve practice.

NIDA's mission is to advance science on the causes and consequences of drug use and addiction and to apply that knowledge to improve individual and public health through:

- Strategically supporting and conducting basic and clinical research on drug use, its consequences, and the underlying neurobiological and behavioral mechanisms involved.
- Ensuring the effective translation, implementation, and dissemination of scientific research findings to improve the prevention and treatment of substance use disorders and enhance public awareness of addiction as a brain disease.

NIDA's strategic priorities are intended to address the full breadth of complexity related to drug use and its health and social consequences across the spectrum from recreational use to problematic use

and substance use disorders (SUDs). SUDs include both behavioral and neurobiological components that are strongly influenced by diverse environmental and social factors. Advances in research technologies and informatics are helping us to understand the complex components and underpinnings of SUDs in unprecedented ways.

NIDA's strategic priorities for the next five years are designed to leverage these advances to translate our increased understanding of the basic science of the brain and behavior into more effective prevention and treatment interventions that can ultimately reduce the negative impacts of drug use on society.

To achieve this mission, NIDA will focus on advancing the following high-level strategic goals:

GOAL 1: Identify the biological, environmental, behavioral and social causes and consequences of drug use and addiction across the lifespan

GOAL 2: Develop new and improved strategies to prevent drug use and its consequences

GOAL 3: Develop new and improved treatments to help people with substance use disorders achieve and maintain a meaningful and sustained recovery

GOAL 4: Increase the public health impact of NIDA research and programs

About NIAAA

The National Institute on Alcohol Abuse and Alcoholism (NIAAA) is one of the 27 institutes and centers that comprise the National Institutes of Health (NIH). NIAAA supports and conducts research on the impact of alcohol use on human health and well-being. It is the largest funder of alcohol research in the world.

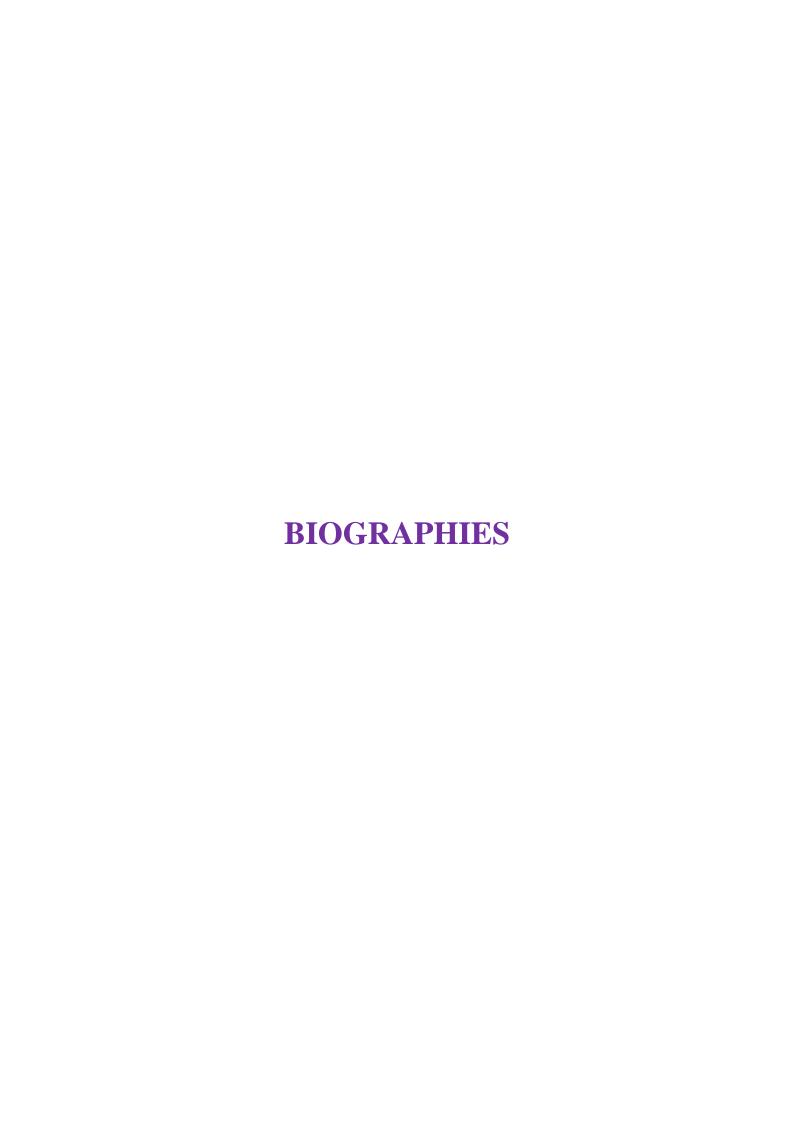
NIAAA leads the national effort to reduce alcohol-related problems by:

- Conducting and supporting alcohol-related research in a wide range of scientific areas including genetics, neuroscience, epidemiology, prevention, and treatment.
- Coordinating and collaborating with other research institutes and federal programs on alcohol-related issues.
- Collaborating with international, national, state, and local institutions, organizations, agencies, and programs engaged in alcohol-related work.
- Translating and disseminating research findings to health care providers, researchers, policymakers, and the public.

Through both research within NIAAA, and by funding grants at institutions worldwide, NIAAA aims to:

- Better understand the health risks and benefits of consuming alcohol, as well as why it can cause addiction.
- Reveal the biological and socio-cultural origins of why people respond to alcohol differently.
- Remove the stigma associated with alcohol problems.
- Develop effective prevention and treatment strategies that address the physical, behavioral, and social risks that result from both excessive drinking, and underage alcohol consumption.

NIAAA-funded discoveries have important implications for improving the health and well-being of all people.





Yves Lévy, MD, PhD,

Professor Lévy is CEO and Chairman of INSERM, the National Institute of Health and Medical Research, since June 2014. He leads also, since July 2014, Aviesan, the French Alliance for Health and Life Sciences. He is Professor of Clinical Immunology at Henri Mondor Hospital/Université Paris Est Créteil since 1996. He obtained his MD in 1986 (Créteil University) and his PhD in Immunology in 1991 (Université Paris 7).

Pr Y. Lévy has developed a research activity in several INSERM units since 1985. He led an INSERM team (U955 Unit) « T cell development in Physiology and in HIV disease

» from 2007 to 2014, focused on HIV physiopathogenesis from upstream to translational researches in the field of immune interventions and vaccines. He served as the Director of the INSERM Unit 899 in Dallas (Texas, USA) from 2010 to 2012. Pr Lévy was, until his appointment at INSERM's direction, the head of the Clinical Department of Immunopathology at Henri Mondor Hospital providing a unique opportunity to connect basic and clinical approaches. In 2011, in the settings of the "Programme Investissement d'avenir", Y. Lévy has created the Labex « Vaccine Research Institute » (VRI). The VRI is aimed to face the challenges to develop effective vaccines against HIV. This research programme is implemented by a large network of 18 teams and key international opinion leaders in this field from different institutions in France and the US through a unique collaborative network and with a central strategic plan.

Since 1990, Pr Lévy is running both basic science and clinical translational researches. He has made contributions to the understanding of the role of cytokines in the development of B cell disorders, the mechanisms of human humoral deficiencies such as Common Variable Immunodeficiencies, the role of Notch and IL-7 on lymphoid stem cell development. As a leading scientist in the field of HIV, he has made seminal contributions on the mechanisms of T cell depletion/dysfunction and on the role of regulatory T cells on immune responses to HIV. These observations led to the development of new immune interventions and vaccines against HIV. He has conducted several national and international phase II/III clinical trials including, antivirals, immunomodulators, cytokine therapies (IL-2, IL-7), therapeutic and prophylactic vaccines. Pr Lévy has been instrumental in designing and implementing early proof-of-concept and Phase 3 clinical trials in France, Europe and internationally in these fields.

Pr Y. Lévy holds the positions of chair of the Immune-based therapies Committee of the ANRS (French Agency of Research Against AIDS and Hepatitis), scientific director of the HIV Vaccine Programme of the ANRS, member of the WHO Vaccine Advisory Committee, the Council of the Global HIV Vaccine Enterprise and other scientific and professional societies. At the institutional level, he was Vice Dean of the Medicine Faculty of UPEC until 2012. He served as Special Councelor of the French Minister of Higher Education and Research from 2012 to 2014.

Pr Lévy has published around 190 articles and chapter books in international peer-reviewed scientific journals (NEJM, Lancet, Cell, Molecular Cell, J.Exp Med, PNAS, J.Clin Investigation, Blood).



Etienne Hirsch, PhD,

Dr Hirsch is a neurobiologist involved in research on Parkinson's disease and related disorders. He obtained his PhD in 1988 from the University of Paris VI (Pierre et Marie Curie).

Dr. Etienne Hirsch is currently the director of the Insitute for Neurosciences, Cognitive sciences, Neurology and Psychiatry at INSERM, the National Institute of Health and Medical Research, and the French alliance for life and health science Aviesan, the associate director of the research center of the Institute of Brain and spinal cord (ICM), head of "Experimental therapeutics of Parkinson disease" at the ICM at Pitié-Salpêtrière hospital in Paris and since

November 2014 in charge of the research aspects of French national plan on neurodegenerative disorders.

His work is aimed at understanding the cause of neuronal degeneration in Parkinson's disease and is focused on the role of the glial cells, the inflammatory cytokines and apoptosis but also on the consequences of neuronal degeneration in the circuitries downstream to the lesions.

Dr. Etienne Hirsch is member of several advisory boards including, French Society for Neuroscience (past-President), Scientific Advisory board at INSERM. He obtained several prizes including Tourette Syndrome Association Award in1986, Young researcher Award, European Society for Neurochemistry in 1990, Grand Prix de l'Académie de Sciences, Prix de la Fondation pour la recherche biomédicale « Prix François Lhermitte » in 1999, Chevalier de l'ordre des palmes académiques in 2009, Prix Raymond et Aimée Mande of the French National academy of Medicine in 2011, Member of the French National Academy of Pharmacy in 2011. He is author of more than 200 peer reviewed articles.



Nora D. Volkow, M.D.,

Dr Volkow became Director of the National Institute on Drug Abuse (NIDA) at the National Institutes of Health in May 2003. NIDA supports most of the world's research on the health aspects of drug abuse and addiction.

Dr. Volkow's work has been instrumental in demonstrating that drug addiction is a disease of the human brain. As a research psychiatrist and scientist, Dr. Volkow pioneered the use of brain imaging to investigate the toxic effects of drugs and their addictive properties. Her studies have documented changes in the dopamine system affecting the actions

of frontal brain regions involved with motivation, drive, and pleasure and the decline of brain dopamine function with age. She has also made important contributions to the neurobiology of obesity, ADHD, and the behavioral changes that occur with aging.

Dr. Volkow was born in Mexico, attended the Modern American School, and earned her medical degree from the National University of Mexico in Mexico City, where she received the *Premio Robins* award for best medical student of her generation. Her psychiatric residency was at New York University, where she earned the *Laughlin Fellowship Award* as one of the 10 Outstanding Psychiatric Residents in the USA.

Dr. Volkow spent most of her professional career at the Department of Energy's Brookhaven National Laboratory (BNL) in Upton, New York, where she held several leadership positions including Director of Nuclear Medicine, Chairman of the Medical Department, and Associate Director for Life Sciences. In addition, Dr. Volkow was a professor in the Department of Psychiatry and Associate Dean of the Medical School at the State University of New York (SUNY)-Stony Brook.

Dr. Volkow has published over 500 peer-reviewed articles and more than 90 book chapters and non-peer reviewed manuscripts. She has also edited three books on the use of neuroimaging to study mental and addictive disorders. *Time* magazine recently named her one of the "Top 100 People Who Shape our World" and *Newsweek* magazine included her as one of 20 people to watch in 2007. She was listed in *Washingtonian* magazine's 2009 and 2011 "100 Most Powerful Women" feature, and named "Innovator of the Year" by *U.S. News & World Report* in 2000.

During her professional career, Dr. Volkow has been the recipient of multiple awards, including her selection for membership in the Institute of Medicine in the National Academy of Sciences and the **2009 International Prize from the French Institute of Health and Medical Research** for her pioneering work in brain imaging and addiction science.



George Koob, Ph.D.

Dr. George Koob, an internationally-recognized expert on alcohol and stress, and the neurobiology of alcohol and drug addiction, began his tenure as Director of the National Institute on Alcohol Abuse and Alcoholism (NIAAA) on January 27, 2014. As NIAAA Director, Dr. Koob oversees a wide range of alcohol-related research, including genetics, neuroscience, epidemiology, prevention, and treatment.

Even before beginning as NIAAA Director, Dr. Koob had a longstanding relationship with the Institute. Throughout his career, he received funding from NIAAA and other NIH institutes for many significant research projects. Importantly, he also led a 10-year, NIAAA-funded, multi-institutional consortium dedicated to identifying the molecular basis of alcoholism.

Dr. Koob received his Ph.D. in Behavioral Physiology from Johns Hopkins University in 1972. He spent most of his career at the Scripps Research Institute, where he served as the Director of the Alcohol Research Center, and as Professor and Chair of the Scripps' Committee on the Neurobiology of Addictive Disorders. Early in his career, he served as a researcher in the Department of Neurophysiology at the Walter Reed Army Institute of Research and in the Arthur Vining Davis Center for Behavioral Neurobiology at the Salk Institute for Biological Studies. He was a post-doctoral fellow in the Department of Experimental Psychology at the University of Cambridge.

Dr. Koob began his career studying the neurobiology of emotion, including how the brain processes reward and stress. His contributions advanced our understanding of the anatomical connections of emotional systems and the neurochemistry of emotional function. This background led to investigations into why certain alcohol drinkers transition to addiction while others do not, and how the brain and body respond to alcohol consumption.

Dr. Koob's work has significantly broadened our understanding of the neurocircuitry associated with the acute reinforcing effects of alcohol and other drugs of abuse, and of the neuroadaptations of the reward and stress neurocircuits that lead to addiction. In addition, he has validated key animal models for addiction associated with alcohol and drugs and identified the major role that brain stress systems play in the development of addiction. Dr. Koob is the author of more than 650 peer-reviewed scientific papers, and the co-author of *The Neurobiology of Addiction*, a comprehensive review of the most critical neurobiology of addiction research conducted over the past 50 years.

Dr. Koob is the recipient of many prestigious honors and awards, including the Daniel Efron Award for excellence in research and Axelrod Mentorship Award from the American College of Neuropsychopharmacology, the Distinguished Investigator and Marlatt Mentorship Awards from the Research Society on Alcoholism, the Mark Keller Award from NIAAA, and the Neuronal Plasticity Prize of the Foundation Ipsen.

Keynote Speakers:

Paul Kenny
Pier-Vincenzo Piazza
Terry Jernigan
Philippe Gorwood
Mickael Naassila
Olivier Phan



Paul Kenny, Ph.D.

Dr Paul Kenny is the Ward-Coleman Professor and Chairman of the Department of Pharmacology & Systems Therapeutics at the Icahn Schools of Medicine at Mount Sinai in New York. Dr. Kenny is also Director of the Experimental Therapeutics Institute at Mount Sinai. He received a degree in biochemistry from Trinity College Dublin and his Ph.D. in psychopharmacology from King's College London. He

completed his post-doctoral training in neuropharmacology The Scripps Research Institute in La Jolla, California. Research in Dr. Kenny's laboratory is focused on the molecular neurobiology of drug addiction, obesity and schizophrenia. Dr. Kenny is also involved in efforts to develop novel small molecule therapeutic agents for the treatment of drug addiction and other psychiatric indications, and is the co-founder of Eolas Therapeutics, Inc. Dr. Kenny is a handling editor for the Journal of Neuroscience and a member of the National Advisory Council on Alcohol Abuse and Alcoholism (NIAAA). Dr. Kenny has won numerous awards for his research, including the Jacob P. Waletzky Memorial Award, Society for Neuroscience and the Tom Connor Distinguished Investigator Award, Neuroscience.



Pier Vincenzo PIAZZA, MD, PhD,

Dr. Pier Vincenzo Piazza is Director of the Neurocentre Magendie, INSERM - Bordeaux France

Dr. Piazza, 53 years old, is a renowned and awarded scientist. Dr. Piazza has provided groundbreaking contributions to the understanding of behavioral pathologies and in particular addiction, introducing new visions of the disease, new approaches to study it and uncovered several of its molecular mechanisms.

Dr. Piazza has published many influential papers in high profile journals and currently ranks within the 1 % most cited scientists in the fields of "Neuroscience and Behavior" and "All Science".

Dr. Piazza has obtained several awards. For example, he was, in 2003, the first recipient of the Jacob Wallesky Award that is attributed by the American Society of Neuroscience for innovative research of drug addiction and alcoholism. More recently he has also obtained the Camille Woringer award from the French Foundation for Medical Research, for his work on brain diseases and in 2015 the Lamonica prize of neurology from the biomedical research foundation.

Dr. Piazza holds as director of research "classe exceptionelle", the higher level of the French research system. He is also the founder and director of the Neurocentre Magendie in Bordeaux, a research center of the INSERM (the French equivalent of NIH).

Dr. Piazza is also the cofounder of three biotech companies Fluofarma in 2003, Aliénor Farma in 2008 and Aelis Farma in 2013. Aelis Farma focuses on developing signaling specific inhibitors of the CB1 receptor as therapeutic drug that have been discovered by Dr. Piazza group. The development of this new pharmacological class, one of the most promising treatments of cannabis addiction, is today Dr. Piazza principal focus and challenge.



Terry L. Jernigan, Ph.D.

Dr. Terry Jernigan trained as a clinical and experimental neuropsychologist, and since the late 1970s has studied the human brain using imaging. This work has focused on brain development and aging, neurodevelopmental disorders, neuropsychiatric and substance use disorders, and neurodegenerative disorders. Since 2008 her central research interest has been the developing human mind and brain, and she has pursued this interest in collaboration with an interdisciplinary team as Director of the Center for Human

Development at the University of California, San Diego. She also directs the Coordinating Center for the PING Project — a publicly shared imaging genomics data resource with imaging, neurocognition, and whole genome genotyping data from over 1500 children aged 3 to 20 years. She co-directs (with Sandra Brown) the Coordinating Center for the recently initiated Adolecent Brain Cognitive Development (ABCD) Study.

She is a member of the National Advisory Board on Drug Abuse and the NIH Council of Councils and serves on the scientific advisory boards of several research organizations in the US and Europe.



Philip Gorwood, MD, PhD

Professor Gorwood studied medicine from 1982-1988, and specialised in psychiatry in 1988. He is currently full Professor of Psychiatry at Sainte-Anne Hospital and Head of the CMME department [Clinique des Maladies Mentales et de L'Encéphale, with 60 beds], teaching at the Paris-Descartes University. He is also Head of the Team 1 at INSERM (Institut National de la Santé et de la Recherche MEdical) research unit 894 (Center of Psychiatry and Neuroscience) devoted to genetic vulnerability of psychiatric and addictive disorders.

Professor Gorwood has published over 240 scientific

articles (h-index=43) and 24 book chapters. He has served on 16 editorial boards for journals in psychiatry, neuroscience and genetics, and is editor-in-chief of the journal European Psychiatry (IF=3.2) and the Resource Centre "Progress in mind: focus on alcohol use disorder" developed by Elsevier.

He is now treasurer and member of the Core Organising and Scientific Committee (COSC), Executive Committee (EC) and board of the European Psychiatric Association. He joined the scientific advisory (SAB) board of the ECNP for addictive disorders in 2009. Philip Gorwood is the vice-president of the Federation de Recherche sur l'Alcool (FRA).

In 1992, Professor Gorwood received the Lilly 'First Communication' award and later in 1997, the French Association for Biological Psychiatry 'Best Communication of the Year' award. In 1999, he received the Association of European Psychiatry 'Young Researcher' award; and in 2000 the French National Academy of Medicine for the best research.



Hobby * Triathlon. Personal bests: 2h13 for the Olympic distance in Paris 2012; 5h24 for half-Ironman in Cambraie 2011; 11h11 for Ironman in Barcelona 2011.



* Trail: Personal bests: Ecotrail-2013, 30Km, 3h15; Fontainbleau-2013, 52 Km, 7h30; Millault-Trail 2013: 73Km, 13h10; Diagonale des fous-2014:172Km, 56h24.



Mickael Naassila, PhD

Professor Naassila is the head of the dept of physiosiology of the Pharmacy School of the Université de Picardie Jules Verne in Amiens. He received his PhD in Neurosciences at the University of Rouen studying the mechanisms of action of acamprosate and the role of neuronal nitric oxide synthase in alcohol dependence (post-dependent rats). During his postdoctoral training at the Pharmacology & toxicology dept of the Pharmacy school at the University of Kansas, he studied the transcriptional and post-translational effects of alcohol on NMDA receptor subunits. Since coming at the University of Picardie Jules Verne in 2000, he has

been working on the effect of early life ethanol exposure (in utero and/or adolescence) on the vulnerability to develop alcohol dependence. He was also involved in different clinical projects on the genetic vulnerability to develop a severe phenotype of alcohol dependence and alcohol liver disease. He is the leader of the European project ALCOBINGE (http://www.alcobinge.org/) on both the cognitive and emotional impact of binge drinking in young people and on the use of preclinical model to mimic this phenomenon in rodents to uncover neurobiological mechanisms underlying long term vulnerability to alcohol abuse. He is also the leadpartner of a national grant form the ANR (SENSIBALCO project, http://anrsensibalco.jimdo.com/) to study the role of the behavioural sensitization to the stimulant effects of alcohol in addictive behaviour. Currently he is the head of the Research Group on Alcohol & Pharmacodependences (INSERM unit ERi 24, https://grap.u-picardie.fr/), one of the very rare research group in France seeking to elucidate neurobiological bases of alcohol dependence in relevant animal models of the disease and in humans. The animal model of alcohol addiction used in the lab is the chronic intermittent exposure to ethanol vapours known for inducing both physical and psychological dependence in rats. Pr Naassila is member of the board of the ESBRA (http://www.esbra.com) and is the President of the Société française d'alcoologie (>800 acting as members, http://www.sfalcoologie.asso.fr). He is also acting as the President of the Addictions Group of the Health Regional Agency (Picardie; previous Alcohol Task Force). He received the "fight against alcoholism" award from the national Academy of Medicine in 2011. mickael.naassila@Inserm.fr @Equipe_eri24

https://www.facebook.com/GRAP-361186414030016/



Doctor Olivier Phan, M.D., Ph.D.

Dr Phan is actually:

- ➤ Head of Hospital Service and Medical Practitioner at the following institutions:
 - Head Consultant of Centre for adolescents and addictive behavior, Center Pierre Nicole, French Red Cross, 27 rue Pierre Nicole, 75005 Paris;
 - Head Consultant of Addiction unit for Adolescents, Dupré clinic for child psychiatry, Students of France Health Foundation, 30 avenue du Président Franklin Roosevelt, 92 Sceaux;
 - Provider of head of the advanced consultations at the Justice Educational Center of Beauvais.
- Lead Supervisor and Trainer of medical staff for the research Project INCANT (International Cannabis Need of Treatment): implementation of this Project seeking to validate the MDFT (Multi-Dimensional Family Therapy) method in Europe for cannabis smoking adolescents. (The Project is financed by the International Mission Against Drugs and Dependency (Toxicomanie), and Clinical Research Program of Hospitals of France (PHRC) Programme Hospitalier de Recherche Clinique).
- Consulting physician and member of the Research Addictive Behavior Unit at the House of Adolescents, Boulevard de Port Royal Paris (Research Unit of the Professor Bruno Falissard and the Professor Henri-Jean Aubin).

PUBLICATIONS

Over 60 publications on issues relating to Multidimensional Family Therapy in treating addictive behavior of adolescents, consumption of cannabis, cocaine, opiates, poly-consumption of various substances by young adults, binge-drinking, vide-game addictions, trauma-related neuroses, BMC

Round Table 1 Moderators/Rapporteurs

Joni Rutter Jean-Antoine Girault



Joni Rutter, Ph.D.,

Dr Rutter is Division Director for the new Division for Neuroscience and Behavior at the National Institute on Drug Abuse, since October 1 2015. This division was created after the reorganization of NIDA to integrate its research portfolio, promote translational research and increase efficiencies. The new structure incorporates research on clinical neuroscience, brain development and behavioral treatment development into existing and newly formed components of

NIDA divisions. Joni Rutter was previously Division Director for the Division of Basic Neuroscience and Behavioral Research (DBNBR), after serving as acting director of DBNBR since 2011, leading her staff to build strategic directions for the science supported by the division.

Dr. Rutter's career spans 15 years of excellent basic and clinical research in human genetics and the study of genetic and environmental risk factors in the fields of cancer and addiction. She has earned a national and international reputation for her diverse and unique expertise in more than 50 publications in journals, and she received several scientific achievement awards, including a SmithKline Beecham Student Award in Pharmacology, a Janssen Research Foundation Young Investigator Award, and a Fellowship Achievement Award from the National Cancer Institute. Rutter has also built, supported, and maintained the NIDA Genetics Consortium, a group of more than 20 investigators who study addiction genetics.

Prior to joining NIDA in 2003, Dr. Rutter received her Ph.D. from the Department of Pharmacology and Toxicology, Dartmouth Medical School, Hanover, New Hampshire. Upon completing her doctoral degree, she remained at Dartmouth Medical School as a research associate for a short period of time. She then accepted a fellowship at the National Cancer Institute within the Division of Cancer Epidemiology and Genetics to fortify her training in human genetics. Her scientific objective is to integrate genetic principles with the study of how drugs and chemicals act on the brain.



Jean-Antoine Girault, MD, PhD,

Dr Jean-Antoine Girault is an Inserm Research Director.

He was trained in Biochemistry and Medicine in Paris. After laboratory of Jacques Glowinski at the *Collège de France*, and then worked as a post-doctoral fellow and an assistant professor at the Rockefeller University (New York) with Paul Greengard. In 1990 he came back to France as an Inserm scientist and headed a research group at *Collège de France* until 1999. In 2000, he created a novel Inserm unit at the *Fer à Moulin* site in Paris, and in 2007 became head of the newly created *Institut du Fer à Moulin*, a research institute

investigating the development and plasticity of the nervous system and affiliated with Inserm and the Pierre & Marie Curie University (UPMC, Sorbonne Universités).

Dr J.A. Girault also coordinated the creation of the Paris School of Neuroscience in 2007 and directed it until 2010. Since 2012 he has been heading the Bio-Psy "Laboratory of excellence" (Biology for Psychiatry), a network of basic and clinical research groups aiming at strengthening and combining neuroscience and psychiatry research in Paris area. He is currently president of the French Society for Neuroscience.

Dr Jean-Antoine Girault's research interests are mostly focused on the basal ganglia and more specifically on the intracellular signaling mechanisms underlying long term adaptations and dysfunction in striatal neurons. He contributed to the description of signaling pathways mediating short and long term effects of dopamine and glutamate on these neurons. Over the recent years his group has been interested in the mechanisms by which neurotransmitters signal to the nucleus and control nuclear transcriptional and epigenetic responses. Girault's lab, co-headed with Denis Hervé, explores how the striatal signaling pathways are recruited in response to drugs of abuse and how this recruitment contributes to the establishment of addiction. They also investigate the similarities and differences between drug-induced adaptations and those which result in L-DOPA-induced dyskinesia in the Parkinsonian brain.



Brigitte L. Kieffer, PhD,

Dr Kieffer is the Scientific Director of the Douglas Research Centre at MCGill University. She is also Professor of Psychiatry and the Monique H. Bourgeois Chair in Pervasive Developmental Disorders at the Faculty of Medicine of McGill University.

Dr. Kieffer graduated from the University of Strasbourg, where she later became a Professor. She then went on to become Research Director at the Institut national de la santé et de la recherche médicale (Inserm) in France. She developed her main research activity at the Institut de génétique et de biologie moléculaire et cellulaire (IGBMC) in Strasbourg in 2001 and directed this institute from 2012 to 2013.

Between 2001 and 2012, she received three major awards from the U.S. National Academy of Sciences and the French Académie des sciences. She was also named a member of the European Molecular Biology Organization (EMBO) and was made as a Chevalier (Knight) of the Legion of Honour by the President of the French Republic. In December 2013, she was elected Membre of the French Académie des sciences.

Dr. Kieffer lends us her international reputation and expertise in molecular neurobiology, particularly in the field of opiate receptors. Her work had a major impact on research in addiction, mood disorders and other mental illnesses such as autism.



Marina Wolf, Ph.D.

Dr Wolf is Professor and Chair of the Department of Neuroscience at the Chicago Medical School of Rosalind Franklin University of Medicine and Science. She has been a pioneer in studying the role of neuronal plasticity in drug addiction.

Dr. Wolf received her Ph.D. in Pharmacology in 1986 from Yale University. From 1987-1990, she trained as a Postdoctoral Fellow at the Center for Cell Biology at Sinai Hospital of Detroit. After completing her postdoctoral training, Dr. Wolf was Assistant Professor of Psychiatry at Wayne State University until moving in 1992 to the Chicago

Medical School. Dr. Wolf's research has been supported by the National Institute on Drug Abuse (NIDA) since 1992. Her current grants include two R01 Awards from NIDA. She has previously been the recipient of a Merit Award and a Senior Scientist Research and Mentorship Award (K05) from NIDA. She has also received support from the National Institute of Mental Health, the Pharmaceutical Manufacturer's Association Foundation (PMAF), and the National Alliance for Research on Schizophrenia and Depression (NARSAD).

Dr. Wolf has served as a member of the NIDA Advisory Council and the NIH Council of Councils. Other honors include Phi Beta Kappa, predoctoral and postdoctoral fellowships from NSF, PMAF and NIH, and election as a fellow of the American College of Neuropsychopharmacology (ACNP). She presently serves as Chair of an NIH study section, as well as on the NIDA Board of Scientific Counselors and the Council of the ACNP.



KALIVAS, PETER W. PhD

Dr Kalivas is a neuroscientist best known for his work to elucidate the brain molecules and neurocircuitry that underlie addiction. This work is highlighted in over 400 publications and as editor of 6 books that focus on the cellular mechanisms and brain circuitry mediating psychiatric disorders. He has received national and international awards including a Merit Award from the National Institute of Drug Abuse, the Efron Award from the American College of Neuropsychopharmacology, the Governor's Award for Research (South Carolina) and the ISPEN

Foundation Prize in Neuroplasticity, he is an Honorary Professor of Neuroscience at Nanjing Medical University and the University of Cordoba, as well he is a Distinguished University Professor at both the Medical University of South Carolina and Washington State University. He is a member of the Scientific Advisory Board for the National Alliance for Research in Schizophrenia and Depression, President of the American College of Neuropsychopharmacology (2014), and serves as editor or is on the editorial board of 6 major journals in the field of neuroscience. He received his Ph.D. in Pharmacology from the University of Washington in Seattle in 1980, and during a postdoctoral fellowship at the University of North Carolina in Chapel Hill (1980-82) he became oriented towards the role that brain circuitry plays in the regulating behavior. In his first faculty position at Louisiana State University in New Orleans (1982-84) and during a more extensive tenure at Washington State University (1984-98) he studied the cellular and molecular underpinnings of the brain circuits mediating addiction. This research perspective constitutes a primary contribution he continues to make to the field of neuroscience as Professor and Chair of the Department of Neuroscience at the Medical University of South Carolina in Charleston (1998-present).



Véronique Deroche-Gamonet, PhD

Dr Deroche-Gamonet is Research director, Psychobiology of addiction, NeuroCentre Magendie, CRIU862, Bordeaux.

Key coordination activity

OptoPath project: Platform for instrumental and procedural innovation in experimental psychopathology (Investissement d'Avenir French grant - 8 research teams / 2 neuroscience institutes / 3 industrial partners) (2011-2019) (http://optopath.equipex.u-bordeaux.fr/en).

Main domain of research: Experimental psychopathology, Psychobiology, Drug addiction, Animal models.

I have been conducting experimental research on drug addiction since the early 90s. I always challenged the classical experimental preparations used to model drug addiction. This led to the development of a multisymptomatic DSM-IV-based animal model of cocaine addiction. This model allowed evidencing that addiction could result from a default of counter-adaptations to early cocaine-induced effects, rather than from specific drug-induced alterations.

A new challenge is the coordination of the *OptoPath* project for an innovative platform in experimental psychopathology based on cutting edge exploratory techniques and a dimensional transnosographic approach of key psychopathologies, i.e. addiction, obesity, PTSD, and aging-related memory deficits.



Manzoni Olivier, Ph.D.

Dr Manzoni is an Inserm Research Director, head of the team "Pathophysiology of synaptic plasticity" at the Mediterranean Institute of Neurobiology (INMED)

The entire scientific career of Dr Manzoni has been devoted to the study of synaptic pathophysiology. He initially combined biochemical and imaging methods to discover new intracellular and intercellular messengers produced by two essential classes of receptors expressed at excitatory central synapses: NMDA and mGluRs. Following post-doctoral fellowships at UCSF and the Vollum Institute, he started his own independent group that focused on synaptopathies. Early on, his group discovered that the endocannabinoid signaling system underlies a form of long lasting synaptic plasticity in the Nucleus accumbens. Remarkably, this type of synaptic depression has since proven to

be one of the most common forms of synaptic plasticity in the CNS. Moreover, his work has revealed that it is a common synaptic correlate of neuropsychiatric diseases. Notably, Dr Manzoni discovered that endocannabinoid synaptic plasticity is altered in mice models of western diets (unbalanced n-3/n-6 polyunsaturated fatty acids), Fragile X and drugs of abuse including cocaine and cannabis. The general strategy of his team is to elaborate structural and functional portraits of the normal and diseased synapse in order to identify synaptic modifications and discover new endophenotypes of neuropsychiatric diseases. Since its inception Manzoni's research group has shown a consistent ability to pursue independent lines of research and reach its scientific goals.

Round Table 2 Moderator/rapporteur

Margaret M. Murray, Michael Naassila



Margaret M. Murray, PhD

Dr. Murray is Director of the Global Alcohol Research Program, National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health. Dr. Murray directs NIAAA's efforts in international research collaboration spanning each of the Institute's priorities in biomedical, epidemiological, prevention and treatment research. This includes serving on U.S. Science and Technology Committees, NIH and government wide initiatives in global health, and representing NIAAA to multilateral organizations such as the World Health Organization, the Organization for Economic Cooperation and Development and National Academies of Science

committees. She is primarily responsible for facilitating collaborative relationships at the individual institute and scientist level. Dr. Murray is a member of the Institute of Medicine's Forum on Global Violence Prevention.

In 2014, Dr. Murray was assigned to represent NIAAA on the Coordinating Committee for Collaborative Research on Addiction at the NIH, or CRAN.

Dr. Murray is also responsible for the Institute's research translation initiatives in health professions education. She is co-author of *A Medical Education Model for the Prevention and Treatment of Alcohol-Use Disorders*, a twenty module curriculum and faculty development course for medical school faculty in the primary care specialties. The model has been translated into five languages and implemented in eight countries. She led the development of a model curriculum for social work educators, *A Social Work Education Model for the Prevention and Treatment of Alcohol Use Disorders* that is currently being disseminated and tested by NIAAA, and is also involved in a similar project in nursing education.

She has published in the areas of screening and brief intervention for alcohol use disorders in primary health care settings, evaluation of international faculty development programs and homelessness and alcohol and drug problems.

Dr. Murray received a BA degree in English from St. Mary's College of Maryland, a public honors college. She holds PHD and MSW degrees in social policy from Catholic University in Washington, DC and certificates in epidemiology and biostatistics from Johns Hopkins University School of Public Health.

Dr. Murray served as adjunct faculty in the graduate Social Work program at the Catholic University of America and Howard University where she taught courses in the history of Social Welfare Policy in the United States.



Laura Jean Bierut, M.D.

Dr Laura Jean Bierut is the Alumni Endowed Professor of Psychiatry at Washington University School of Medicine in St. Louis. Dr. Bierut graduated from Harvard Radcliffe College with a bachelor's degree in biochemistry and molecular biology. She earned her medical degree and completed psychiatry residency at Washington University School of Medicine. Dr. Bierut was elected to the Alpha Omega Alpha Honor Medical Society, and she has been honored by the American Psychiatric Association and Washington University for her efforts to teach and mentor medical students, residents, post-doctoral trainees, and junior faculty.

Dr. Bierut has built a successful research program devoted to understanding the genetics of substance dependence with funding from the National Institutes of Health (NIH). She serves on the Advisory Counsel for the National Institute on Drug Abuse (NIDA) and is a member of the NIH Big Data to Knowledge (BD2K) Multi-Council Working Group. She is also an active member of the NIDA Genetics Consortium, a national group of scientists who are leading NIDA's efforts to understand genetic causes of substance dependence. Dr. Bierut led the initial studies which found that the α 5 nicotinic receptor subunit genes on chromosome 15 and the α 6 β 3 nicotinic receptor subunit genes on chromosome 8 increase a smoker's risk for nicotine dependence. In collaboration with other groups, it has since been demonstrated that the same genetic variants that contribute to smoking in the chromosome 15 region also influence the development of lung cancer and chronic obstructive pulmonary disease. Dr. Bierut's research team is currently studying the relationship between *CHRNA5-CHRNB4* variants and smoking cessation, with the goal of using genetic information for precision medicine with smoking cessation patients. In recognition of Dr. Bierut's research contributions, she was awarded the 2014 Alton Ochsner Award Relating Smoking and Disease.



Adolf Pfefferbaum, M.D.

Dr. Pfefferbaum is Distinguished Scientist at SRI International, Menlo Park, CA and Professor Emeritus, Stanford University School of Medicine, Stanford, CA. He received his M.D. from the University of California School of Medicine, San Francisco, CA. His program of research has focused on advancing a mechanistic understanding of the effects of chronic alcoholism on the brain using a variety of *in vivo* neuroimaging and electrophysiology approaches. Throughout his career, Dr. Pfefferbaum has actively contributed to the development of advanced magnetic

resonance imaging (MRI) science that has led to identification of selective brain structural and functional changes disrupted with continued hazardous drinking and recovery with sustained sobriety. His studies of alcohol use disorder span the age range from adolescence to senescence. In addition to naturalistic studies of human alcoholics, he has an active, translational program of neuroimaging research using rodent models of voluntary alcohol self-administration and high dose involuntary alcohol administration. Dr. Pfefferbaum has been PI or co-investigator on numerous NIH-funded grants, including an NIAAA Merit Award, and more than 300 publications have resulted from this funding.



Thomas Kash, Ph.D.

Dr. Kash earned his BS in Chemistry at the State University of New York College of Environmental Science and Forestry in 1999. Following this, Dr. Kash worked briefly at the medical department at Brookhaven National Labs under the guidance of Dr. Andrew Gifford before joining Dr. Neil Harrison's lab at Cornell University Graduate College of Biomedical Science in New York City. While a student in Dr. Harrison's lab Dr. Kash worked on understanding the structure and function of ligand-gated ion channels, in particular GABA-A receptors. In 2004, Dr. Kash moved to Dr. Danny

Winder's lab at Vanderbilt University in Nashville, TN and began working on understanding how alcohol and peptides can modulate function in the extended amygdala. In 2009, Dr. Kash started his lab at the Bowles Center for Alcohol Studies at the University of North Carolina at Chapel Hill where he has continued his efforts to understand how modulation of neuronal circuits can alter behavior. Research in the Kash lab has focused on understanding how stress and alcohol abuse can alter neuronal function in brain regions that regulate cognitive and emotional behavior. This is performed using a robust multidisciplinary approach ranging from chemogenetics, electrophyiology and single-cell genetic analysis. The major drive is to understand how modulation of neuronal circuits can ameliorate pathological behavior associated with neuropsychiatric conditions.



Pitel Anne-Lise, PhD

During her PhD, conducted at Caen in France under the supervision of Francis Eustache and Hélène Beaunieux (2003-2007Dr Pitel was working on memory disorders in alcohol dependent patients with and without Korsakoff's syndrome. Then, she spent 3 years in California at Stanford University as a post-doctoral fellow supervised by Adolf Pfefferbaum and Edith Sullivan (2008-2011). She investigated alcohol-related brain abnormalities using structural MRI, DTI and fMRI. Since 2012, Anne Lise Pitel is an assistant professor at the University of Caen Lower-Normandy in France and works in the U1077 Inserm research unit.

Dr Pitel has now been working on neuropsychology and neuroimaging of alcoholism for more than ten years, has received several awards from France and the US and has published around 40 original articles in international journals. Her fields of research focus on cognitive dysfunction and altered brain structure and function in alcoholics. The objectives of her studies are to better understand the physiopathology of alcohol-related disorders in order to prevent the development of debilitating and definitive neurological disorders and to favor cognitive and brain recovery.



Corvol Jean-Christophe, MD, PhD,

Jean-Christophe Corvol is Professor of Neurology at the Pitié-Salpêtrière Hospital, head of the Clinical Research Center for Neurosciences at the Brain and Spinal cord Institute (ICM), co-chair of the French clinical research network for Parkinson's disease and movement disorders (NS-Park), and researcher in the team of neurogenetics at the ICM (head Pr A. Brice). JC Corvol has a training in both Neurology and Pharmacology (MD in 2003), he has done a PhD (2005) on dopaminergic signalling in the laboratory of JA Girault (Institut du fer à moulin, Paris) and a post-doc at UCSF in the neurogenetic laboratory of J. Oksenberg (San Francisco, USA).

His field of interest is genetic modifiers and pharmacogenetics in Parkinson's disease. The approach is transversal, combining transcriptomic experiments in experimental models, candidate genetic association studies in well-phenotyped cohorts, imaging-genetic studies, and genome wide association studies. JC Corvol has published 90 original articles in peer review journals (H index=29). He is member of the scientific committee for neuroscience at INSERM, member of the French societies for Neurology, Pharmacology and Neurosciences, and member of the International Movement Disorder Society.



Bruno Gonzalez, PhD

Dr Bruno J Gonzalez is senior researcher in the National Institute for Medical Research (Inserm, France) and the head of the NeoVasc Laboratory "Microvascular Endothelium and Neonatal Brain Lesions", ERI28, Rouen, Normandy University, France. Since its creation in 1999, the research axis of the team is the neonatal handicap. In particular, research is focused on pathologic neurodevelopment in preterm and term neonates with a particular attention to

neurovascular defects, considering as working hypotheses that (1) microvessels participate to injurious mechanisms with age-dependent specificities; (2) microvessels may become the target of therapeutic actions since they are much more easily accessible to drugs and (3) microvessels release factors that may become markers of suffering tissues. Main objectives are to perform a molecular, cellular and functional characterization of the microvessel and the endothelial cell from the immature brain, to characterize interactions between endothelial and neural cells regarding neurodevelopment (GABA interneurons) and pathology (alcohol, benefit/risks of medications) and to transpose to clinical research with the development of protective strategies and identification of biomarkers. To reach these goals, the structuration of the NeoVasc Laboratory is based on a strong interaction between clinicians and academic researchers. Among marked results obtained in the last five years, it can be mentioned the demonstration that (1) brain microvessels present phenotypic and functional age specificities (Lecointre et al., J Cereb Blood Flow Metab., 2014; Henry et al., Neurobiol Dis., 2013), (2) in utero alcohol exposure impairs brain angiogenesis (Jégou et al., Annals Neurol., 2012), (3) NMDA antagonists such as anesthetics disrupt long term integration and differentiation of GABA interneurons (Aligny et al., Cell Death Disease, 2014), (4) the follow-up of preterm cohorts is required to evaluate long term neurological disabilities and effects of neuroprotection strategies (Marret et al., PLoS One 2013, Marret & Bénichou, JAMA 2015) and that (5) placenta is a provider of biomarkers of brain defects (Lecuyer et al., patent Inserm transfert, Normandy University and Rouen hospital, n° FR1555727, 2015).

Available Funding Mechanisms for Collaboration

Steve Gust, NIDA
Peggy Murray, NIAAA
Anne Jouvenceau, Inserm



Steven W Gust, Ph.D.

Dr. Steven W. Gust directs NIDA's International Program, which coordinates the Institute's global research, research training, and education efforts. In addition he serves as the Institute liaison within NIH and other U.S. agencies, foreign governments, and international, regional, and nongovernmental organizations. Before assuming leadership of the NIDA International Program, Dr. Gust served as deputy and acting director of the Institute's Office on AIDS and as a special assistant to the director responsible for research on the medical uses of marijuana. He joined NIDA in 1986 in the Clinical and Behavioral Pharmacology Branch, Division of Clinical Research, and has served as chief of

the Research Section for the NIDA Division of Applied Research Workplace Performance Research Branch. Before joining the Government, Dr. Gust also conducted research at the University of Minnesota and the Minnesota Department of Health. He has served on the Surgeon General's Advisory Group on the Health Effects of Smokeless Tobacco; the Transportation Research Board Committee on Alcohol, Other Drugs, and Transportation; and the White House Health Care Reform Task Force.



Anne Jouvenceau Ph.D.

Since September 2014, Dr Anne Jouvenceau is the head of the international Affairs of Inserm.

For the past 2 years, she has been the Health and Life Sciences Advisor for the Minister of Higher Education and Research, Geneviève Fioraso.

Born in 1970, she completed a PhD in biology of aging of the UPMC (1997) and was certified to direct research by the Paris-

Descartes University (2007).

After a 4-year post-doctorate fellowship, part in the UK at Eli Lilly and University College of London and part in France at Inserm in Paris, she was appointed at Inserm as a full time researcher in 2002. She was then promoted as a scientific policy officer at the multi-organization thematic institute of neurosciences, cognitive sciences, neurology and psychiatry of Aviesan (National Alliance for the life sciences and health) where she successfully officiated from 2008 to 2012.

NIDA-Inserm Postdoctoral Fellows

The National Institute on Drug Abuse (NIDA) and Institut National de la Santé et de la Recherche Médicale (Inserm) have established a binational postdoctoral research exchange fellowship program.



Andrew Scheyer, PhD, INMED, Marseille

Having arrived only at the beginning of September, my post-doctoral position with Dr. Manzoni, funded by this fellowship, is still in quite early stages. Thus far, my fellowship period has largely been adjustment, preparation and model generation. Specifically, due to the protracted nature of our research (in vivo exposure to CBR agonists, then offspring development) I began the process of generating animals for research

immediately upon entering the lab. In the meantime, I have also been collecting comparative data for future studies by assessing the nature of GABAergic synaptic transmission during the transitional periods which occur during the first several weeks after birth. This has allowed me to lay a foundation for the future of my studies, as well as familiarize myself with the protocols and standards used in the lab. Moving forward, we intend to continue the lab's characterization of the synaptic consequences of prenatal exposure of THC or it's pharmacological analogue, WIN. My experience until now has convinced me that my position here will be fruitful and remain fascinating throughout.



Yann Pelloux, PhD

Drug addicted individuals often compulsively use drugs despite the adverse consequences associated with such use. I previously developed a rat model of compulsive cocaine use, operationalized by the maintenance of cocaine seeking despite intermittent mild foot shocks. In addition to the characterization of some underlying neural dysfunctions, I have uncovered some key brain structures involved in this pathological behavior such as the basolateral amygdala. However, the fundamental psychological processes underlying compulsive cocaine seeking

remains to be identified. An important question is whether the cause of compulsive drug seeking is the inability to update drug related behaviors in the face of punishment, or the inability to retrieve/maintain this information to guide future behavior.

The INSERM/NIDA fellowship has given me the opportunity to work within Yavin Shaham's lab, in collaboration with Geoffrey Schoenbaum's team. These two teams are renowned for their expertise in the behavioral and electrophysiological analysis of addictive disorders in animal models. Thanks to their support, I will be evaluating the response to punishment of two brain structures previously shown to be involved in compulsive cocaine seeking: the basolateral amygdala and the dorsal striatum. This project aims to understand how risky situations are encoded in the brain and whether the compulsive use of cocaine originates from the miscoding of risk. Since my arrival on September 1, I developed a behavioral procedure that is suitable for the electrophysiological evaluation of neural responses to risk, a critical first step in achieving the goals of this project. Further progress has also been made towards setting up the electrophysiological recording. By identifying the cause of compulsive drug use, this project will help to clarify the most pertinent therapeutic strategy.



Vivien Zell, PhD,

University of California, San Diego

Ventral tegmental area glutamate neurons co-release

GABA and promote positive reinforcement (work

submitted for publication, currently being peer-reviewed).

The primary goal of the initial proposal was to identify how VTA glutamate-releasing neurons contribute to mesolimbic circuit function at molecular, physiological and behavioral levels. Within the first year of this fellowship we made

significant advancements on the characterization of this neuronal population.

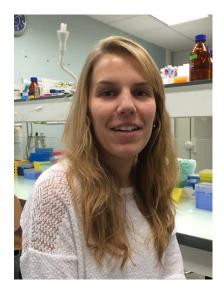
Using VGlut2-Cre genetic mouse lines to induce glutamate neuron-specific expression of ChR2 in the VTA we were able to: (1) assess the role of glutamate neuron cell body and terminal stimulation on behavior and (2) understand the output of these neurons to three target nuclei: the lateral habenula (LHb), the ventral pallidum (VP) and the shell of the nucleus accumbens (NAc). We discovered the existence of GABA co-release from VTA glutamate neurons in the VP and the LHb (but not the NAc) and characterized its impact on the postsynaptic neuron excitability.

- 1. Using operant tasks, we showed that VTA glutamate cell body stimulation produces strong positive reinforcement. But when we used the real-time place preference test, we monitored a modest aversion while stimulating the VTA glutamate neuron terminals in the VP, LHb and NAc. To further characterize these seemingly contradictory results, I performed *in vitro* electrophysiological recording of the postsynaptic neurons in the VTA (local connections: VTA^{>VTA}), but also in the VTA-glutamate neurons projection structures: VTA^{>NAC}, VTA^{>LHb} and VTA^{>VP}.
- 2. Using whole-cell patch clamp recordings in slices I was able to record AMPA light-evoked EPSCs in the VTA, NAc, LHb and VP (recorded at -60 mV of holding potential; these currents were abolished by addition of 10 μ M DNQX). In the same recording conditions, I discovered a co-release of the inhibitory GABA neurotransmitter from VTA glutamate neurons at VTA $^{\rightarrow LHb}$ and VTA $^{\rightarrow VP}$ synapses (recorded at 0 mV of holding potential in presence of DNQX; this current was abolished by addition of 10 μ M of GBZ). The measure GABA/Glutamate ratio is significantly greater at the VTA $^{\rightarrow LHb}$ synapse when compared to the VTA $^{\rightarrow VP}$ synapse.

Whereas this phenomenon has been recently reported in the LHb, little is known about its significance and its impact on the postsynaptic cell excitability. Current clamp recordings using a cell-attached configuration showed that VTA-glutamate neurons terminal stimulation produced a significant net reduction of action potential firing frequency in LHb (inhibition) and a significant net increase of firing frequency in the VP (excitation). This difference is consistent with the GABA/AMPA IPSC/EPSC ratio which is significantly greater at the VTA JLHb synapse.

Taken together, our results strengthen our knowledge on this newly discovered mode of cotransmission in the LHb and describe its existence for the first time in the VP. Our study has been submitted for publication this year (October 2015) and is currently under peer-review.

Several other projects are still under development under the NIDA-Inserm International Fellowship. Using a wide array of approach in the lab of Dr. Thomas Hnasko including CV-TRAP, DREADDs, Single-cell PCR as well as optogenetics coupled with behavioral assays and *in vitro* electrophysiology, we aim at refining the characterization of VTA Glutamate neuron population in terms of intrinsic properties and information transmission and modulation to several key brain regions being of interest in goal-directed behavior.



Céline Nicolas, PhD

In 2011, at the end of my master degree, I obtained a governmental doctoral grant due to top 3 ranking. I therefore entered a PhD program in neuroscience for 3 years at the University of Poitiers, under the direction of Marcello Solinas in the Experimental and Clinical Neurosciences Laboratory, directed by M. Jaber. In December 2014, I defended my thesis untitled "Long-term alterations induced by chronic cocaine intake revealed by anatomical, metabolic and behavioral approaches" and I am currently an associate researcher in the same University and laboratory. My research has been focused on the characterization of the neurological modifications induced by

drugs of abuse, in particular cocaine, and responsible for the persistence of addiction, as well as the quest for new strategies to reduce the risks of relapse.

I chose to join Dr Ikemoto's laboratory as a postdoctoral fellow in order to expand my scientific background, improve my skills and learn novel state-of-the-art techniques in integrated neurosciences. The choice of this laboratory is determined by highly qualified environment and expertise in optogenetics, electrophysiology in vivo and behavior neuroscience. During the training in Dr Ikemoto's lab, I expect to expand my methodological repertoire in a way that is highly complementary to the methods I learned during my graduate career. This will allow me to gather a very wide panels of modern neurosciences approaches and in the longer term to develop my own independent line of research. I have proposed a project with Dr Satoshi Ikemoto, which brings all these scientific and technical approaches to investigate how habitual cocaine use alters the way in which individuals respond to stressful events. We propose to examine the role of central amygdala (CeA) neurons projecting to the bed nucleus of the stria terminalis (BNST) in such behavior of cocaine-experienced rats a day or a month after cocaine withdrawal.

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