Abstracts and Biosketches

invited speakers

Second official SIPS conference on placebo studies 2019

Version 1:

11-09-2018

# Keynote Speakers

**Luana Colloca**

### Biosketch

Dr. Luana Colloca is an NIH-funded associate professor at the University of Maryland and a honorary professor at the University of Sydney School of Psychology. Dr. Colloca holds an MD, a master degree in Bioethics and a PhD in Neuroscience. In addition, Dr. Colloca completed a post-doc training at the Karolinska Institute in Stockholm, Sweden and a senior research fellowship at the National Institutes of Health in Bethesda, USA.

Dr. Colloca has conducted several ground-breaking studies that have advanced scientific understanding of the psychoneurobiological bases of endogenous systems for pain modulation in humans. As a result, she has developed an international reputation as a leading scientist for advancing knowledge of the neurobiological mechanisms of placebo effects with an integrative approach including psychopharmacological, neurobiological and behavioral approaches publishing in top-ranked international journals including, *Biological Psychiatry, Pain, JAMA*, among others. The impact of her creative work is clear from her impressive citation rate and more than 100 invited lectures.

### Presentation title

From learning to expectancy violation: Understanding placebo effects to harness them

### Abstract

Expectancies produce positive outcomes and placebo effects in individuals by virtue of anticipations of a benefit and activation of specific endogenous modulatory systems. Based on a well-established proposed conceptual framework, placebo effects are presented as the product of expectancy mechanisms in which conditioned, verbal, and observational cues are centrally integrated to change behaviors and outcomes. Neuroimaging studies that have capitalized on well-established behavioral paradigms within this framework implicate the dorsolateral prefrontal cortex as a key region in producing these effects. However, expectancies of improvements in real-world settings are often violated. The effects of expectancy violation are presented along with the brain mechanism implicated with mismatch processing and abolishment of placebo effects. Finally, strategies to harness placebo effects are discussed including the use of dose-extending placebos as well as vasopressin and oxytocin as promising adjuvants contributing to the enhancement of placebo effects.

## Irving Kirsch

### Biosketch

Irving Kirsch is Associate Director of the Program in Placebo Studies and a lecturer in medicine at the Harvard Medical School (Beth Israel Deaconess Medical Center). He is also Emeritus Professor of Psychology at the Plymouth University (UK), University of Hull (UK) and the University of Connecticut (USA). He has published 10 books, more than 250 scientific journal articles and 40 book chapters on placebo effects, antidepressant medication, hypnosis, and suggestion. He originated the concept of response expectancy. His 2002 meta-analysis on the efficacy of antidepressants influenced official guidelines for the treatment of depression in the United Kingdom. His 2008 meta-analysis was covered extensively in the international media and listed by the British Psychological Society as one of the “10 most controversial psychology studies ever published.” His book, *The Emperor’s New Drugs: Exploding the Antidepressant Myth,* has been published in English, French, Italian, Japanese, Turkish, and Polish, and was shortlisted for the prestigious Mind Book of the Year award. It was the topic of *60 Minutes* segment on CBS and a 5-page cover story in *Newsweek.* In 2015, the University of Basel (Switzerland) awarded Irving Kirsch an Honorary Doctorate in Psychology.

### Presentation title

Hypnosis as a Non-Deceptive Extra-Strength Placebo

### Abstract

Placebos have been shown to be effective for many clinical conditions, but the assumption that deception is needed is a barrier to its use. Recently, studies have shown that placebos can be effective even when presented openly and honestly as placebos. However, clinicians report being uncomfortable asking clients or patients to take “sugar pills.” Hypnosis can provide an alternative means of generating a placebo effect without deception. Similarities between hypnotic suggestions and placebos include the following:

1. Both affect the same clinical conditions
2. Expectancy manipulations can enhance both placebo and hypnotic responding
3. Neither requires the presence of a trance state
4. Hypnotic inductions have no specific components
5. Suggestion is the active ingredient of both

Differences include the greater role of stable individual differences in hypnotic responding than placebo responding and findings showing that hypnotic suggestions can be more effective than placebo pills. Finally, Niels Bagge has developed an intervention in which clients or patients are asked to imagine taking imaginary pills, a procedure that can be implemented with or without inducing hypnosis and that blends open-label placebos with clinical hypnosis.

## Tor Wager

### Biosketch

Dr. Wager is a Professor of Psychology and Neuroscience and a faculty member in the Institute for Cognitive Science at the University of Colorado, Boulder. He received his Ph.D. from the University of Michigan in cognitive psychology in 2003, and served as an Assistant and Associate Professor at Columbia University from 2004-2009. Since 2010, he has directed Boulder’s Cognitive and Affective Neuroscience laboratory. He has a deep interest in how thinking influences affective experiences, affective learning, and brain-body communication. His laboratory also focuses on the development and deployment of analytic methods, and has developed several publically available software toolboxes for fMRI analysis.

### Presentation title

Placebos, expectations, and self-fulfilling prophecies

### Abstract

Placebo effects are improvements in signs and symptoms caused by the context in which a treatment is delivered. They are a natural part of the way our brains work; their mechanisms include learning and neuroplasticity, emotion, social cognition, and expectations and other future-oriented cognition. An underappreciated consequence of placebo effects is their capacity to induce ‘self-fulfilling prophecies’ — positive feedback loops between expectations and experience that can cause resistance to new information and persistent effects of prior beliefs, for good or ill. In this talk, I present a pair of behavioral and fMRI experiments that demonstrate reciprocal positive influences of expectations on pain experience and neurophysiology, and vice versa. This feedback system creates placebo effects that, once established, do not extinguish in spite of a complete absence of primary reinforcement. This empirical study helps provide a foundation for understanding why seemingly innocuous placebo interventions can end up having large and durable clinical effects in some cases.

# Invited Speakers

## Fabrizio Benedetti

### Biosketch

Fabrizio Benedetti, M.D. is Professor of Neurophysiology and Human Physiology at the University of Turin Medical School, Turin (Italy), and Director of the Center for Hypoxia at the Plateau Rosà Labs, Plateau Rosà (Italy/Switzerland). He has been nominated member of The Academy of Europe and of the European Dana Alliance for the Brain. He identified some basic mechanisms of placebo responses across a variety of medical conditions.

Recent books: Placebo Effects (Oxford, 2nd Edition, 2014), The Patient’s Brain (Oxford 2010), Placebo (Springer 2014).

Recent awards: Highly Commended Book Award of the British Medical Association in 2009, Seymour Solomon Award of the American Headache Society in 2012, William S. Kroger Award of the American Society of Clinical Hypnosis in 2015.

### Presentation title

Placebo effects at great heights

### Abstract

Placebo effects have been found and described in a variety of systems, ranging from sensory and motor systems to immune and endocrine systems. What has emerged from these studies is that placebos induce powerful psychological effects that can change the physiology of different body functions, and that these changes are very similar to those induced by drugs. However, it is not surprising that there are some limits of these psychological effects in a variety of conditions. For example, can placebo effects occur for functions that are crucial for survival? For instance, can a placebo replace oxygen during respiration? Or, in other words, is it possible to breathe without oxygen by merely using a placebo procedure? Although the answers to these questions may seem quite obvious at first sight, several years ago we started a project to assess the role of placebo effects for critical physiological functions in extreme environmental conditions, where survival is at stake. Indeed, we have investigated the role of placebo effects at high altitudes (3500 m), where oxygen pressure drops to 102 mmHg (159 mmHg at sea level). This corresponds to an oxygen concentration in the air of only 12%, compared to 21% at the sea level. In these extreme conditions, where both physical and cognitive performance deteriorate very quickly, we found that a conditioned placebo procedure can mimic the effects of oxygen, including ventilation, blood pH, heart activity and cyclooxygenase activity, and these effects are still present, albeit to a lesser extent, at altitudes as high as 4500 and 5500 m, where oxygen pressure drops to 92 and 81 mmHg, respectively. Interestingly, opposite effects (nocebo effects) can be elicited as well. A crucial question is to understand the limits of these effects, at altitudes of 8000 m and beyond, where oxygen pressure and concentration approach zero.

**Charlotte Blease**

**Biosketch**

Dr. Charlotte Blease is a philosopher of medicine currently based at the Program in Placebo Studies, Harvard Medical School where she is a Fulbright Scholar and Irish Research Council/Marie Curie Awardee. Dr. Blease has published extensively on ethics and philosophy of science in relation to placebo studies in the BMJ, Journal of Medical Ethics, Perspectives in Biology and Medicine, etc. More broadly, she researchers philosophical issues relating to patient-doctor encounters.

**Title presentation**

Consensus in Placebo Studies - Disagreement is Overstated

**Abstract**

In the relatively nascent field of placebo studies empirical studies have burgeoned. Yet debate about how to define the terms ‘placebo’ and ‘placebo effect’ has not abated. A number of prominent scholars (drawn from medical practice, as well as philosophy, psychology, and anthropology) continue to propose (and defend) different conceptual models for these terms; the perception that conceptual debate persists is often given as one justification for new definitions. Paradoxically – in spite of this lively debate – this paper finds considerable underlying agreement about definitional matters within placebo studies. Drawing on key insights from philosophy of science, and by exploring the nature of scientific consensus and normal scientific research, this paper argues that well-developed placebo concepts form the basis for a placebo paradigm. The paper concludes that conceptual disagreement is overstated.

## Christian Büchel

### Biosketch

Christian Büchel is a full professor of Systems Neuroscience and Head of the Department of Systems Neuroscience at the University Medical Center Hamburg-Eppendorf. He graduated from Heidelberg University as MD. His scientific career continued as a Wellcome Research Fellow at the Wellcome Department of Imaging Neuroscience at UCL in London. From there he moved to Hamburg and headed a research group funded by the Volkswagen Foundation. He is the current director of the Neuroimaging Center NeuroImage Nord and holder of major research grants from the European Research Council, German Research Foundation (DFG), and German Ministry for Science and Volkswagen Foundation. His main scientific interests are the interplay of cognition, pain and emotion with an emphasis on emotional learning in health and disease. He is a member of the Hamburg Academy of Science. Christian Büchel has published more than 150 peer reviewed research articles and was awarded the Jung Award for Medicine, the Gottfried Wilhelm Leibniz-Preis by the German Research Foundation, and the Wiley Young Investigator Award of the Organization for Human Brain Mapping for recognition of his work on effective connectivity in neuroimaging.

### Presentation title

How expectations shape pain perception

### Abstract

Expectation and experience can shape pain perception in a powerful way. However, the neurobiological mechanisms underlying these effects are still unknown. This talk will focus on potential mechanisms of how expectations can increase (nocebo hyperalgesia) or decrease (placebo hypoalgesia) pain perception. The focus will be on a conceptual framework which posits that pain perception can be seen as the integration (in a Bayesian sense) of expectation (i.e. prior) and incoming data (i.e. stimulus). Importantly, this framework leads to testable hypotheses (e.g. the variance of the expectation should reduce the influence of expectation).

## Ben Colagiuri

### Biosketch

Dr Ben Colagiuri received his PhD in Psychology from the University of Sydney, Australia in 2010. He currently holds a Senior Lectureship and Australian Research Council Discovery Early Career Research Award in the same School. His research aims to understand how expectancies shape human behavior, with a specific interest in placebo and nocebo effects. To date, he has developed a number of novel experimental models to uncover the mechanisms of the placebo and nocebo effect for pain, sleep, nausea, and other conditions. He has published over 40 scientific papers and received state and national recognition for his research, including the Australian Psychological Society Early Career Research Award 2014. His current research is exploring how the placebo effect can be used to improve clinical trial design and clinical practice, with the ultimate aim of enhancing patients’ health and wellbeing.

Website/s:

<http://sydney.edu.au/science/people/ben.colagiuri.php>

<https://bencolagiuri.wordpress.com/>

### Presentation title

Using learning mechanisms to inhibit the development of nocebo nausea.

### Abstract

Nausea is a prevalent and debilitating side effect of many medical treatments. While pharmacological factors undoubtedly contribute to nausea, there is increasing evidence that the nocebo effect also plays a critical role in the development of nausea.  In particular, the formation of associations between the treatment context and the pharmacological agent can lead the treatment context to exacerbate or even induce nausea in and of itself via learning mechanisms. To attempt to combat this, we tested whether pre-exposure to the treatment context prior to treatment could reduce nocebo nausea via latent inhibition. Across two experiments, healthy volunteers underwent nocebo nausea conditioning with Galvanic Vestibular Stimulation (GVS). Critically, some of the participants were randomized to receive pre-exposure to placebo GVS prior to their conditioning in either a deceptive (Experiment 1) or open manner (Experiment 2). In Experiment 1 there was clear evidence of conditioned nocebo nausea that was entirely blocked by pre-exposure to placebo GVS, indicating a latent inhibition effect. In Experiment 2, we replicated the latent inhibition effect for deceptive pre-exposure and found that open pre-exposure was just as successful at blocking the development of nocebo nausea as deceptive pre-exposure. As such, pre-exposure may be an effective method of reducing the development of nocebo nausea and other nocebo effects to reduce the overall burden that side effects cause patients. To this end, the fact that open pre-exposure is as effective as deceptive pre-exposure indicates that latent inhibition can be deployed ethically in clinical practice without violating informed consent.

## Alia Crum

### Biosketch

Dr. Alia Crum is an Assistant Professor of Psychology at Stanford University. She received her PhD from Yale University and BA degree from Harvard University. Dr. Crum’s research focuses on how changes in subjective mindsets—the lenses through which information is perceived, organized, and interpreted—can alter objective reality through behavioral, psychological, and physiological mechanisms. Her work is, in part, inspired by research on the placebo effect, a robust demonstration of the ability of the mindset to elicit healing properties in the body. She is interested in understanding how mindsets affect important outcomes outside the realm of medicine, in domains such as exercise, diet and stress. More specifically, Dr. Crum aims to understand how mindsets can be consciously and deliberately changed through intervention to affect physiological and psychological well-beings. To date, her research has won several awards, most recently, the NIH New Innovator Award. In addition to her academic research and teaching, Dr. Crum has worked as a clinical psychologist for the VA healthcare system and an organizational trainer and consultant, creating, delivering, and evaluating workshops on mindset change and stress management for organizations including UBS, Colgate Palmolive and the United States Navy.

### Presentation title

Harnessing mindset in 21st century medicine

### Abstract

The placebo response has been recognized within western medicine for centuries. Yet—since the advent of the randomized control trial—it has been marginalized as an effect that should be ignored or controlled for.  In this talk I will argue that placebo-like effects can be explained, in part, by the role of mindset—the psychological lens through which information is perceived, organized, and interpreted. First, I will present a selection of studies demonstrating how mindsets can affect health outcomes in various stages of disease including a) influencing the effects of genetic predisposition b) shaping the benefits of of health behaviors such as diet, exercise and stress and c) improving the physiological effects of treatment.  Second, I will discuss how elements of the social context such as the patient-provider interaction can moderate the effect of mindset on health outcomes.  Finally, I will discuss how an improved understanding of mindsets and the social context can empower individuals and healthcare providers to harness the power of mindset to improve health and reduce unnecessary suffering.

## Paul Enck

### Biosketch

Prof. Dr. Paul Enck, Director of Research, Dept. of Internal Medicine VI (Psychosomatic Medicine and Psychotherapy), University Hospital Tübingen, Germany. His main interests are gut functions in health and disease, including functional and inflammatory bowel disorders, the role of the gut microbiota, regulation of eating and food intake and its disorders, of nausea, vomiting and motion sickness, and the psychophysiology and neurobiology of the placebo response, with some emphasis on sex differences. He has published more than 220 original data paper in scientific, peer-reviewed journals, more than 320 review articles and book chapters, and more than 50 science articles for public media. He is board member/treasurer of the European Society of Neurogastroenterology and Motility, the German Society of Neurogastroenterology and Motility, and The Society of Interdisciplinary Placebo Studies, and has served as reviewer for many national and international journals and grant agencies.

### Presentation title

Nocebo effects beyond clinical trials, and why we should be careful in labelling them

### Abstract

In placebo-controlled trials, reports of adverse events (AE) in the placebo arm of such trials have given rise to the name "nocebo effects", but the situation is far less clear in medical routine, when a patient receives a drug and reports AE that are unlikely the consequence of the drug. The following instances may - at least in part - characterize the occurrence of such nocebo effects: 1) A patient may have an underlying condition whose natural history produces some symptoms (such as a headache), that the patient *misattributes* to the drug. 2) The patient may be have warned about AE in patient information sheets (drug leaflets), and this negative expectation could then produce the event. 3) The patient may have consulted the internet and other electronic sources to search for the available and most appropriate therapy for his/her condition, and has received conflicting information, or contradictory evidence about safety and AE of the prescribed drug. 4) Nocebo effects were induced by medical information and decision making in switching patients with a successful therapy from a branded to a generic drug, or from a biologic to a biosimilar for non-medical, economic reasons. 5) The patient may have a relative or friend with a similar condition who has experienced AEs with the same or a similar drug - this effect (placebo/nocebo by proxy) is so far mainly investigated in children and their parents.

The presentation will summarize the evidence for two out of these five options; for the remaining options, the current database is yet too poor for a thorough review. Strong nocebo effects have been noted with

(a) internet-based patient information related to adverse events, as is the case in statin therapy. It was found that statins for therapy of high cholesterol levels are increasingly reported to provoke AE in many internet fora and chat rooms recently. Increased AE are reported in unblinded studies while evidence from blinded placebo-controlled trials is missing. It has also been noted that the non-compliance to statin therapy is the higher, the more information is available on the internet.

(b) The second case will be made for nocebo effects occurring with the switch from a successful treatment of inflammatory diseases such as rheumatism and inflammatory bowel disorders by a biologic (originator) drug to a biosimilars, especially when the initial therapy is successful. This mimics effects seen with the switch from a branded to a generic drug. I has been shown that different health care systems require different solutions to prepare a patient for such a switch for non-medical, economic reasons. The presentation will also touch upon potential counter-measure to prevent such nocebo effects to occur.

The final point I will address is why in these, but also in other cases of presumed nocebo effects it is advisable to not label such expectancy-induced effects nocebo effects for individual patients, since different from nocebo effects in placebo-controlled trials (see above), AE after taking a "real" drug can always, even if extremely unlikely, be the consequence of the drug and not of the expectation, and these two can rarely be separated. Labelling AE symptoms as "nocebo" is violating the autonomy of the patient and undermining a trustworthy doctor-patient relationship.

## Jens Gaab

### Biosketch

Jens Gaab is a psychologist and psychotherapist. After completing his studies in psychology at the University of Trier, he enjoyed his PhD and Postdoc at the University of Zurich, Switzerland. Since 2011, he is Associate Professor for Clinical Psychology and Psychotherapy at the Department of Psychology of the University of Basel, Switzerland, where he and his team is determined and eager to examine the placebo and its effects in different settings, populations and interventions, to explore the relationship between placebo and psychotherapy and to test ethically acceptable ways to harness the placebo and its effects.

### Presentation title

Placebo and Psychotherapy

### Abstract

Psychotherapy is a psychological intervention, which has a long track record and which has been shown to have proven and clinically significant effects in a multitude of psychological disorders and problems. But let’s face it: The same can be said about the placebo. But does this resemblance suffice to equal both interventions? On the basis of conceptual, empirical and ethical arguments and findings I will argue that the aforementioned interventions share many features and processes (and thus placebo can of course be a placebo!), but that it is possible for psychotherapy to be anything but placebo. However and therefore, the current reciprocal non-consideration of both interventions should best be ended, which would have important consequences on psychotherapy practice and research.

## Andrew Geers

### Biosketch

Andrew L. Geers, Ph.D. is a Professor Psychology at the University of Toledo (USA) and completed his degree at Ohio University. His research focuses on the advancement and application of social psychology theory within health and medical contexts. This research typically concerns (1) how beliefs/expectations shape the outcome of medical treatments and interventions (placebo/nocebo effects), (2) the causes and consequences of optimistic or pessimistic evaluations of future events, (3) the effects of involving individuals in their own health care decision making and (4) how to increase the initiation and maintenance of healthy behavior. He has published numerous empirical and conceptual review articles and his research has been funded by the National Institutes of Health.

Link to my research webpage: <https://utsocialpsychology.wordpress.com/>

### Presentation title

A social psychological process approach for understanding placebo effects

### Abstract

An underlying goal of research on placebo effects is to develop a deeper understanding of the phenomenon so as to strategically incorporate it into patient care. Because placebo effects are strongly influenced by a patient’s subjective interpretation of the clinical encounter and the interpersonal context surrounding treatment, clarifying the various psychological processes at play should aid translation of research findings to clinical interventions that encourage placebo responses and discourage nocebo responses. In this talk, I will review and describe an empirically-supported multi-process model that can serve as a framework for research into the psychology of placebo effects. From this approach, the success or failure of treatment-relevant information in producing placebo effects depends to a large extend upon the specific communication variables at play, and most importantly, upon the processes by which those variables operate. This model leads to predictions regarding many facets of placebo effects, such as their directionality, durability, and likelihood to alter subsequent behaviors. The proposed conceptualization could help in synthesizing prior theoretical approaches regarding the occurrence of placebo effects and in addressing several unanswered questions in the placebo literature. The model also suggests steps that practitioners might take to amplify the placebo component of medical treatments and interventions. Research relevant to the model will be described and directions for future research will be highlighted.

## Jeremy Howick

### Biosketch

I investigate medical questions that require input from philosophy and clinical epidemiology. These include: the ontology, effects, and ethics of placebo treatments in clinical trials and clinical practice, the benefits and harms of informed consent, the extent to which basic science and mechanism research is required for clinical advancements, and the problem of too much medicine. With over 60 academic publications (including two books), I have been funded by the Medical Research Council and the National Institutes of Health Research (both in the United Kingdom) and my research has been used to shape policy. I am also a dedicated teacher who has won four teaching awards. More recently I have expanded my public engagement activities and give regular talks to lay audiences, my social media platform has over 5000 followers, and I have a forthcoming popular science book (April 2017) called [*Doctor You*](https://www.hodder.co.uk/books/detail.page?isbn=9781473654211), which explains the science behind the problem of too much medicine for a lay audience.

### Presentation title

Effects of placebos without deception compared with no treatment: a systematic review and meta-analysis

### Abstract

Our aim was to address the clinical efficacy of open-label placebos compared with no treatment by systematic review, and meta-analysis where possible.

We searched the Cochrane Injuries Group's Specialised Register, The Cochrane Central Register of Controlled Trials (CENTRAL), Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations (OvidSP), EMBASE (OvidSP), and clinical trials registers and screened reference lists. We ran the most recent search on April 27 2015. All randomised controlled trials of any medical condition, which had both open-label placebo and no-treatment or treatment as usual groups were included. Two authors independently applied the selection criteria and extracted data. The risk of bias of included studies was assessed using theCochrane criteria. We used random-effects model for meta-analysis.

After removing duplicates we screened 348 publications, assessed 24 articles for eligibility and identified 5 trials (260 participants) that met our inclusion criteria. The clinical conditions were: irritable bowel syndrome (IBS), depression, allergic rhinitis, back pain and attention deficit hyperactivity disorder (ADHD). The overall risk of bias was moderate. All 5 trials were eligible for meta-analysis. We found a positive effect for non-deceptive placebos (standardized mean difference (SMD) 0.88, 95% CI 0.62 to 1.14, *P*<0.00001, I2= 1%).

Open-label placebos appear to have favorable clinical outcomes, compared to no treatment or no additional treatment. Caution is warranted when interpreting the results due to the limitations including the small number of trials and lack of blinding. Larger definitive trials are now warranted to explore the potential patient benefit of open-label placebos.

This protocol has been registered on PROSPERO (2015:CRD42015023347).

## Karin Jensen

### Biosketch

I am a clinical psychologist and neuroscientist specializing in brain imaging and pain. My studies have focused on the learning aspects of placebo analgesia, such as associative learning, and included psychophysical measurements as well as neuroimaging experiments. My research line includes studies of on the non-conscious aspects of treatment expectations.

### Presentation title

What is minimally required to elicit placebo effects?

### Abstract

Today, little is known about the placebo response in patients with limited cognitive abilities, such as intellectual disability (ID). The aim of this talk is to discuss recent data on placebo mechanisms in patients with impaired cognitive function, as well as experimental studies investigating how implicit cognitive processes may shape placebo responses.

## Ted Kaptchuk

### Biosketch

Ted is a professor of medicine at Harvard Medical School and director of the Harvard-wide Program in Placebo Studies & Therapeutic Encounter hosted at the Beth Israel Deaconess Medical Center. He is also a professor of global health and social medicine.

### Presentation title

Things Not Usually Said: Unorthodox Views About Placebo

### Abstract

When we SIPS people give talks they are designed either to persuade the medical community we have something important to contribute (public talks) or share experimental details and new findings with our colleagues (intra-professional). For this talk, Ted will share some of his private ruminations, emergent thoughts and percolating ideas. His talk will touch on overlooked aspects of his studies, unconventional ideas about placebo mechanisms, qualitative data that dramatically changed his research models and overlooked differences between clinical and laboratory studies. The talk will be deliberately provocative to foster our community’s self-examination and foster open discussion and innovative approaches especially with young researchers as they join our community.

**John Kelley**

**Biosketch**

John M. Kelley, Ph.D. is Professor of Psychology at Endicott College and the Deputy Director of the Program in Placebo Studies and the Therapeutic Encounter at Harvard Medical School. In addition, he is a licensed psychologist in the Psychiatry Service at Massachusetts General Hospital, and he has a private practice in psychotherapy. His research interests include: (1) investigating the placebo effect in medical and psychiatric disorders, and (2) understanding how the patient-clinician relationship affects healthcare outcomes in medicine and psychiatry. Professor Kelley has served on ten US National Institutes of Health (NIH) research grants. His research has also been funded by the Robert Wood Johnson Foundation, the Arnold P. Gold Foundation, the David Judah Fund, the Josiah Macy, Jr. Foundation, and the Risk Management Foundation.

**Presentation title**

Lumping and Splitting: Toward a Taxonomy of Placebo and Related Effects

**Abstract**

The placebo effect is closely related to many other constructs, including most prominently, conditioning and expectancy, but also natural history, regression to the mean, priming, mindset, context effects, the meaning response, specific and non-specific clinical effects, placebo-related effects, the patient-clinician relationship, and the common factors in psychotherapy. How are these various constructs related to one another? To what degree do they overlap, and to what degree do they diverge? To form a better theoretical understanding of these constructs and to foster improved empirical research, is it better to lump these constructs together in some fashion? Or will progress best be served by maintaining the splits between the constructs? Or would it perhaps be most effective to employ some mixture of lumping and splitting? In this talk, I will address these and related questions with two major goals: (1) to delineate and clarify the relationship between these constructs; and (2) to suggest some possible re-alignments in the way in which we conceptualize the relationships among these constructs that might prove useful in fostering research on placebo and related effects. In addition, clarifying the interconnections between the placebo effect and other related constructs has the potential to spark innovative cross-fertilizations between related areas of research.

## Regine Klinger

### Biosketch

Regine is the head psychologist of the section „Pain Medicine and Pain Psychology“ at University Medical Hospital Hamburg-Eppendorf (UKE), Center for Anesthesiology and Intensive Care Medicine, Department of Anesthesiology . In her working field the research models „Placeboanalgesia“, „Nocebohyperalgesia“ and “Placeboresponses in Itching” play an important role. Regine is head of several placebo research projects which are part of the DFG-Research group „Expectation and Conditioning as Basic Processes of the Placebo and Nocebo Response: From Neurobiology to Clinical Applications”. The transfer of research results to clinical application in ethical borders is one of her utmost aims: she describes and proposes several approaches how to exploit placebo mechanisms to improve pharmacological and non-pharmacological pain interventions in a more systematic manner than what naturally occurs in clinical settings.

### Presentation title

Clinical application of analgetic placebo effects?

### Abstract

A number of meta-analyses have demonstrated the efficacy of placebo analgesia, however, high variance is apparent in different study designs. The placebo phenomenon is a complex psychobiological process consisting of learning and expectancy components acting on neurophysiological systems, and its efficacy has been confirmed empirically in a range of fields such as pain and the immune system. Inert substances such as sugar pills can trigger placebo analgesia, and these effects can also enhance the response to active treatments. In the lecture different research approaches to placebo analgesia, different facets of the placebo phenomenon and the underlying mechanisms will be described. The central question will be: Does clinical application of placebo effects make sense? To answer this question two presumptions are necessary: (1) placebo research results must be transferable to patients; (2) that placebo effects must be deliberately applied, so that we can boost the efficacy of pain treatment. These 2 presumptions will be explicated. Proposals of clinical application will be discussed to make better use of placebo analgesia in clinical practice to optimize treatment outcome and to provide patients with an additional placebo-based benefit. The discussion will focus on ways of effectively translating these findings from laboratory to clinical settings and daily clinical practice.

## Karin Meissner

### Biosketch

Karin Meissner, MD, is Head of the Placebo Research Group at the Institute of Medical Psychology at the Ludwig-Maximilians-University Munich and since 2016 also a full professor of Integrative Medicine at the University of Applied Sciences and Arts in Coburg. Her research interests include meta-analyses of placebo effects in clinical trials, psychobiological correlates of placebo effects in nausea and appetite regulation, and mechanisms of placebo effects on autonomic organ functions. She is also interested in the evaluation of CAM treatments to optimize the care of chronically ill patients. Her research has been funded by the German Ministry for Science and the German Research Foundation (DFG).

Link: <http://www.imp.med.uni-muenchen.de/research/placebo_research-meissner_lab/index.html>

### Presentation title

Differential effectiveness of placebo treatments

### Abstract

The size of placebo effects depends on various contextual factors, including the type and characteristics of the placebo intervention. Several systematic reviews provided evidence that more intense placebo interventions are associated with larger placebo effects than less intense ones. For example, sham acupuncture and sham surgery were associated with significantly higher placebo response rates than oral placebos in 79 randomized placebo-controlled studies of migraine prophylaxis (Meissner et al., JAMA Int Med 2013). Similarly, a review of 149 randomized trials on knee osteoarthritis showed intra-articular and topical placebo interventions to induce larger improvement than oral placebos (Bannuru et al., Ann Intern Med 2015). However, a systematic review of 12 studies allowing a direct comparison of different placebo treatment modalities within the same study did not reveal consistent evidence for greater effectiveness of more intense placebos (Fässler et al., J Clin Epidemiol 2015). Likewise, in an experimental paradigm we recently found no evidence for a differential effectiveness of more and less intensive placebo interventions in the treatment of nausea (Meissner et al., submitted). Thus, while there is accumulating evidence from indirect comparisons of placebo groups in clinical trials that the placebo effect size varies systematically according to type of intervention, evidence from studies allowing a direct comparison still challenges this view. Possibly, not only the type of treatment, but also other closely related contextual factors, such as treatment duration and the amount of attention provided by doctors and nurses, contribute to the observed differences of placebo effectiveness across treatment modalities. Implications of the results for the design and interpretation of clinical trials will be discussed.

## Winfried Rief

### Biosketch

Rief, Winfried, Professor of Clinical Psychology and Psychotherapy, Philipps University of Marburg, Germany. Head of the Clinic for Psychological Interventions. License for psychotherapy and supervision. Dr. Rief worked for many years in hospital settings (e.g., Roseneck Hospital for Psychosomatic Medicine, Prien a. Ch.). He is specialized in placebo- and nocebo effects, perception and coping with somatic symptoms, optimization of clinical studies and interventions. He was guest professor at Harvard Medical School, Boston (2004/2005), University of Auckland Medical School (2002), and University of California San Diego (2009/2010). Additionally, he was nominated for the expert committee of WHO/APA for the revision of the classification of mental disorders according to DSM-5, and he is co-chairing the WHO working group on chronic pain diagnoses in ICD-11. Dr. Rief is elected coordinator for grant applications to the German Research Foundation and he is spokesperson of the DFG-research unit on placebo and nocebo mechanisms. His publication record summarizes more than 450 articles, in particular in the field of behavioral medicine and somatoform disorders. He received the Distinguished Researchers award in Behavioral Medicine in 2014.

### Presentation title

Why Changing Dysfunctional Expectations in Clinical Practice is Challenging

### Abstract

During the last decade, psychological and neurobiological mechanisms that are involved in the development of placebo and nocebo responses have been identified. While clinical trials used to reduce placebo mechanisms, clinical practice should try to make use of them for the benefit of the patient. Expectation and learning mechanisms are the major psychological factors contributing to placebo and nocebo effects. Examples will be presented how optimizing patients’ expectations leads to improved outcome in different clinical conditions. However, to better understand the persistence of dysfunctional expectations in patients, we need a model for understanding mediators of expectation change in the case of expectation violation. We introduce the concept of “cognitive immunization” to understand expectation persistence, and we will present examples how dysfunctional expectations can be changed in patients, even if they have a tendency for persistence of negative expectations.

Finally, implications for optimizing psychological interventions in general will be highlighted, and first examples confirm the clinical potential of successfully applying our model of expectation change.

## Manfred Schedlowski

### Biosketch

Manfred Schedlowski is Professor and Director of the Institute of Medical Psychology and Behavioral Immunobiology at the Medical Faculty, University of Duisburg-Essen, Germany. Born 1957 in Hannover, Germany, he obtained his degree in Psychology and his PhD at the Department of Medical Psychology, Hannover Medical School, Germany. Since October 1997, Manfred Schedlowski is Full Professor and Director of the Institute of Medical Psychology and Behavioral Immunobiology at the Medical Faculty, University Essen-Duisburg interrupted by a research stay as Professor of Psychology and Behavioral Immunobiology at the Swiss Federal Institute of Technology (ETH) in Zürich, Switzerland (2004-2007). Manfred Schedlowski’s current primary focus of research is the neurobiology of placebo and nocebo responses, in particular the mechanisms and clinical relevance of behavioral or Pavlovian conditioning of immune and neuroendocrine functions.

**Presentation title**

Teach the T cells: Learned Immunosuppressive Placebo Responses

**Abstract**

Akin to other physiological responses, immune functions can be modified in humans through associative conditioning procedures as part of learned placebo responses. The potential clinical applicability of learned immunosuppressive responses has been convincingly demonstrated in rodents, where conditioned immune responses significantly reduced the mortality in animals with inflammatory autoimmune disease, significantly reduced allergic responses or prolonged the survival time of transplanted vascularized organs. In an established taste-immune learning paradigm in rodents and humans, the calcineurin-inhibitor and immunosuppressant cyclosporine A (CsA) as an unconditioned stimulus (US) is paired with a gustatory stimulus as a conditioned stimulus (CS) during acquisition. Subjects are re-exposed to the CS during evocation, inducing immunosuppressive responses similar to the drug effects. However, it is unclear so far, whether learned immune responses can be produced in patient populations already on immunosuppressive regimen. In a recent study, we demonstrated in renal transplant patients who were already on immunosuppressive treatment, that learned immunosuppressive placebo responses increased efficacy of immunosuppressive medication reflected by significant reduction of T cell proliferative capacity. These data demonstrate, that behavioral conditioning of drug responses may be a promising tool that could be used as a placebo-based dose reduction strategy in ongoing immunopharmacological regimen the aim being to limit unwanted drug side effects and to improve treatment efficacy.

## Lene Vase

### Biosketch

Lene Vase received her PhD in experimental psychology in 2006 and she is currently a professor at the Department of Psychology and Behavioural Sciences, School of Business and Social Sciences, Aarhus University, Aarhus, Denmark. Her research focuses on how psychological interventions or dispositions may enhance or decrease the experience of pain with a special focus on placebo analgesia and nocebo hyperalgesia effects. Recently, she has investigated how knowledge of placebo and nocebo mechanisms may improve the test of new treatments in Randomized Controlled Trials. She has published more than 60 papers and book chapters and given several presentations at conferences world-wide. She has numerous international collaborations and she was awarded the EU Innovative Medicines Initiative grant EUROPAIN together with leading pain laboratories in the Europe. She is currently Associate Editor on PAIN and part of the steering committee for the Society for Interdisciplinary Placebo Studies.

### Presentation title

Placebo effects and expectations across therapeutic interventions

### Abstract

Placebo effects are well-documented in relation to pharmacological treatments but recently placebo effects have also been investigated in relation to psychological treatments, music therapy, acupuncture and surgical interventions. Across these therapeutic interventions large placebo effects have been documented and expectations of treatment effect appears to be a central to the placebo effect as well as to the efficacy of the active treatment. In this talk the conceptualization of placebo effects and expectations will be debated and it will be illustrated how different types of interventions can be placebo controlled and how that may help us better understand the factors that contribute to treatment efficacy.

## Andrea Evers

### Biosketch

Evers is full professor of Health Psychology at Leiden University and chair of the unit of Health, Medical and Neuropsychology. She is affiliated to the Leiden University Medical Centre and the Leiden Institute for Brain and Cognition. Evers graduated (PhD) Cum Laude and obtained several personal awards and highly prestigious grants for her innovative, interdisciplinary and translational research on psychoneurobiological mechanisms and treatments for somatic conditions. She has received several grants for excellent researchers, including an NWO VENI (2004) and VIDI grant (2009), Aspasia (2010) as well as ERC Consolidator grant (2014) and an ERC Proof of Concept grant (2015) as well as awards, such as the PB Boeke Prijs (2004), Goslingsprijs (2004) and the Herman Musaph Award (2012) for her research group. In 2011 she became professor of Psychobiology of somatic conditions at Radboud university medical centre and founder and chair of the interdisciplinary Radboud expert centre of Psychology & Medicine. In 2014, she became Professor of Health Psychology at Leiden University and chair of the department Health, Medical and Neuropsychology. In 2013, she was elected as a member of the Young Academy of the Royal Netherlands Academy of Sciences (KNAW). She currently is co-chair of the Interdisciplinary trace of the Young Academy of the KNAW. Evers also has diverse clinical registrations: she is registered as Clinical Psychologist (BIG), supervisor Cognitive Behavioral Therapist and Healthcare Psychologist (BIG). She is member of the editorial (advisory) board of various international journals, such as Pain, Itch, European Journal of Pain and International Journal of Psychology. Evers is member of the international Board IASP (International Association for the Study of Pain) SIG (Special Interest Group) on PLACEBO (since 2012). She was also a cofounder of the international placebo society SIPS (Society of Interdisciplinary Placebo Studies) in 2014 and is scientific chair of the first official world conferences of the SIPS in Leiden, 2017.

### Presentation title

Use of placebo for innovative treatment strategies in somatic conditions

### Abstract

Physical complaints, such as pain or itch, can be effectively altered by placebo and nocebo effects due to induction of positive or negative expectations. The major clinical challenge remains whether experimentally laboratory findings of induced physical complaints, such as pain or itch, of short duration in healthy subjects can be generalized to patients in a clinical setting and used as therapeutic strategies to improve treatment outcomes. There is some preliminary evidence that patients with chronic physical complaints, for example of itch or pain, are more sensitive to expectation learning processes, in a way that expectations regarding the physical sensations elicit stronger patterns of nocebo or placebo responses in patients compared to healthy subjects. Treatment outcomes might be maximized by making optimally use of placebo effects in clinical practice, by using both conscious and automatic strategies of optimizing expectancy effects, for example, by applying conditioning principles for therapy adherence, adjusting environmental cues to the preferred outcome or replacing regular pharmacological treatments partly by expectancy interventions. Moreover, the role of individual characteristics in placebo and nocebo responsiveness can be used to personalize interventions and to optimize treatment outcomes. This knowledge can help improve therapeutic interventions by enhancing adequate favorable expectations and reducing exaggerated unfavorable expectations in patients suffering from chronic somatic conditions.

## Keith Petrie

### Biosketch

Keith Petrie, PhD is Professor of Health Psychology at Auckland University Medical School in New Zealand. His research group does work on patients’ perceptions of illness, treatment adherence, as well as the placebo and nocebo response. Keith Petrie and his colleague John Weinman developed the Illness Perception Questionnaire, which is widely used internationally. Professor Petrie’s research in the placebo and nocebo area has recently focused on improving patient expectations about treatment and reducing the nocebo response. Keith Petrie has been awarded numerous prizes and fellowships for his research, including a Fulbright Fellowship to Harvard University, the Gluckman Medal and a Distinguished International Scholar Award from the American Psychological Association. He has been elected as a Fellow of the Association of Psychological Science and the Academy of Behavioural Medicine Research. In 2015 he was made a Fellow of the Royal Society and was the recipient of the Durie Medal, which is awarded to New Zealand’s pre-eminent social scientist.

### Presentation title

Handle with Care: The Nocebo Response in the Clinical Environment

**Abstract:**

The nocebo effect has a major influence on the outcome of medical treatment but it is relatively understudied and unrecognized, compared to its more glamorous counterpart, the placebo effect. Understanding the mechanisms involved in the nocebo response is key to reducing its negative outcomes in clinical settings, which include increased symptom burden, unnecessary hospitalization and treatment, non-adherence and impaired patient quality of life. The misattribution of physical symptoms is at the heart of the nocebo response and I will discuss the key factors involved in this process. I will also present some of our recent studies in different clinical areas focused on understanding the development and reduction of the nocebo response. These include the role of the media in intensifying the nocebo response following a recent nationwide medication switch. I will also discuss how subtle differences in clinician framing of drug information and response can influence patient expectations and willingness to change to new treatment. New research on the role of the internet and technology in promoting nocebo responding will be presented. The talk will also cover some new work on how the nocebo response can be reduced in clinical investigations and treatments.