Dear members of EBPS,

One question that arises every now and then, is how strictly the ‘E’ in EBPS should be interpreted. That is, to what extent are we a ‘European’ society? The answer can be found in the statements on the aims and origins of our society on our website, written by two of the founder members of EBPS, Ian Stolerman and the late Francis Colpaert. When EBPS was founded in the 1980’s, behavioural pharmacology was a very active research field, but there was no society in Europe to represent it. Therefore, EBPS was founded. However, by no means has our society ever meant to be a purely European matter. Indeed, we have active members all over the globe: a large number from North America, and also from Latin America, Asia, Australia and New Zealand. Today, our President-Elect and General Secretary are based in the USA, and our Communications Officer in Australia. One quite striking – one might even call it romantic – experience that I have recently had during our monthly Zoom meetings of the Executive Committee was that during lunchtime in Europe, we could see the sun rise in North America, while it was already late evening in Australia. This, to me, was an impressive token of the global nature of our society! Therefore, let me emphasize once more that we welcome members from all over the world.

Importantly, it is not just on the basis of geography that EBPS aims to be an inclusive society; EBPS strives to be unbiased in all respects, including gender and ethnicity. For this reason, I am pleased and proud to let you know that EBPS is a signatory of the ALBA Declaration on Equity and Inclusion (see http://www.alba.network/declaration), that was launched at the SfN Global Connectome last month. More on this declaration can be found on the following pages of this newsletter.

This newsletter also contains an introduction to the 2021 EBPS Award winners: Leah Mayo, winner of the Young Scientist Award, and Aldo Badiani, winner of the Distinguished Achievement Award. In addition, there is a journal club article by Andrew Townsend on the effects of treatment with kappa-opioid receptor agonists on fentanyl self-administration, using a drug vs food choice approach in rats.

As EBPS members, we have two exciting events to look forward to in 2021, information about which can also be found here. That is, the postponed workshop on Behaviour to Biomarkers: Reverse Translation will happen online on 5 and 6 March (for more information click here), and our next biennial meeting will take place online from 13-16 July (for more information click here). While the programme for the biennial is nearly finished, registration and abstract submission will open soon, so stay tuned for more updates! Let me also take this opportunity to remind you to renew your membership for 2021, which can easily be done through the EBPS website.

Last, let me spend a few words on the ongoing Covid-19 pandemic. While hopes were high that the availability of vaccines would lift restrictions and make international travel possible again in 2021, the reality forces us not to be overly optimistic. Most likely, it will be for a substantial portion of 2021 that we will face serious restrictions in our personal and professional life.

In the meantime, being a society of committed and enthusiastic scientists, I hope that this sense of community will provide some relief in these challenging times. While the ‘E’ in EBPS may perhaps be a matter of questions and discussion sometimes, there can be no doubt about the ‘S’!

I wish you happy reading.

Best wishes,

Louk Vanderschuren
EBPS President
who have been your mentors in the field and what are some of the best pieces of advice they have given you?

I’ve really enjoyed working with fantastic scientists who, through our interactions, helped shape my career trajectory in different ways. Shelly Flagel gave me my first research opportunity as an undergrad and is still someone I go to for advice regarding non-research matters. I’ve been working with her for six years now, but she invested her time (and patience) to really get me engaged and feel like I was a vital part of the team. This positive culture interweaves drug classes, we expected to obtain the same interest in behavioral pharmacology research, but made me realize the critical role mentoring can have on a young scientist. I first met my eventual PhD advisor, Harriet de Wit, at a poster session during my postdoc, in which we tested this mechanism on rats (Caprioli et al., 2018). I have worked to maintain this translational approach in my research. As a postdoc, my advisor (Markus Heilig) pushed me to keep a clinical perspective in my work, which was challenging since I’m not a clinician. However, now we’re running a clinical trial with the potential to improve clinical care for patients with PTSD, which is incredibly exciting and definitely not something I would have envisioned doing otherwise.

You’re the mother of beautiful twins and a first-generation, Native American scientist. That is no mean feat! What are some of the challenges you faced and what would you like to tell young scientists about this experience? 

I had no idea being a scientist was an actual career option until well undergrad, so I’ve always felt a bit behind the curve in my career planning. I grew up in a rural area, on a Native American reservation, and I thought the moment the moment the college. I didn’t have access to a lot of the resources and information that others had, and often didn’t even know enough to ask. Even when I did do well, I always felt underdetermined. I vividly remember getting my first travel award in grad school and a colleague told me, “I wish I could claim I was Native American so I could get an easy travel award.” It took me a long time to begin to realize how important it was to have role models in my family have attended that the latter somehow made the former ‘less’.

I think my biggest challenge was always my lack of knowledge about what academia was and how to navigate it. Even though I’m fortunate to have met really supportive people along the way, it can be hard to ask for help when you don’t know what you don’t know. When I applied to grad school, I took the GRE on the very last day that it was possible to still get the results in time because I didn’t know that it took much more time to get the results (or that it cost so much). I’m glad these sorts of gate-keeping methods are being dropped in lots of schools, but I think we have to be careful about what replaces them. How can we bridge the gap between the gap in academic opportunities and the knowledge that many students lack about the relationship to the opportunities they had access to? Or better yet, how do we broaden accessibility to opportunities so that they aren’t only available for a select few? Providing paid undergrad- education initiatives are aware of them is key. I don’t have all the answers, but I’d like to see a world where students who are interested in science, regardless of their background, have equal access to opportunities. I believe we have a long way to go to ensure that everyone has access to the education they need to succeed in science, and that we are making progress in this direction.

EBPS Young Investigator Award

Dr Leah Mayo
LinQping University

How has the journey been so far in setting up your own lab in Linkoping?

When I envisioned starting my own lab, I definitely didn’t think it would occur just a few months after becoming a mother (to twins!) in the midst of a global pandemic, but here we are! Nevertheless, I’m really impressed with how the lab has adapted to continually changing circumstances with such a positive outcome. We have come together as a team of researchers who each bring their own skills and interests, while being kind and supportive team members. Even though everything is more challenging than anticipated, I’m really lucky to be working alongside really fantastic people. They really deserve the credit for allowing me to navigate these circumstances and still manage to have fun with science.

What are the main research programs you are leading?

Our primary focus right now is a clinical trial evaluating a novel cannabinoid-related compound in the treatment of post-traumatic stress disorder (PTSD). This is a direct extension of the work I did during my postdoc, in which we tested this mechanism on ‘resident’ rats (Caprioli et al., 2020). We are also exploring the potential utility of cannabinoid-related therapies more broadly.

You’ve had a long and successful career in addiction neurosciences. Could you tell us about some of your most memorable moments?

Memorable moments come in many forms and shapes. The first experiment. The first encounter with a beloved mentor. The first international meeting. The first job. Getting tenure. For some reason however ‘memorable moment’ makes me think first and foremost of the moment in which data analysis provided an answer to a critical scientific question, pointing the way to a new line of investigation or confirming a pet hypothesis. I can think of four of these moments, all related to the same line of research.

First, the discovery of previously neglected, dopamine-independent, environmental influences on drug reward (Badani et al., 1998). In the mid-90s, when I was a post-doctoral fellow in Terry Robinson’s laboratory at the University of Michigan, we conducted a series of studies showing that the psychomotor effects of amphetamine and cocaine in the rat are a function of the setting surrounding drug administration (Badani, Anagno- taras & Robinson 2005; Badani, Brownow & Robinson 1995). The exhilarating moment came when we demonstrated, using a combination of in-vivo microdialysis and in-situ hybridization of c-fos mRNA (still a novel technique at the time), that the response of striatal circuitry to amphetamine is modulated by the setting independent of dopaminergic transmission (Badani et al., 1998, 1999). In particular, we found that the ‘indirect’ projection pathway of the striatum is activated by amphetamine only in rats for which the testing apparatus was a distinct non-home environment (novel ‘non-resident’ condition) but not in rats that had lived extensively in the same apparatus (home or residen- dent condition). To a pharmacologist like me, this was an epiphen- any, as it showed that the dopaminergic response to drugs depends not only on pharmacokinetics but also on previously neglected environmental fac- tors. Also striking was the realization that the coupling between the behavioral effects of psychostimulants and dopaminergic transmission is less tight than previously thought. After more than 20 years the field has not yet come to terms with these findings, presumably because they challenge entrenched no- tions concerning the role of the dopaminergic system.

Second, the realization that unitary models of drug reward are wrong (Caprioli et al., 2008). After moving to the Sapienza Uni- versity of Rome, I began to investigate the role of setting in drug reward using self-administration procedures. As for the psychomotor effects, we found that the reinforcing effects amphetamine- like reinforcing effects are setting dependent. I came to Shelly with zero experience but really me engaged and feel like I was a vital part of the team. This positive culture interweaves drug classes, we expected to obtain the same interest in behavioral pharmacology research, but made me realize the critical role mentoring can have on a young scientist. I first met my eventual PhD advisor, Harriet de Wit, at a poster session during my postdoc, in which we tested this mechanism on rats (Caprioli et al., 2018). I have worked to maintain this translational approach in my research. As a postdoc, my advisor (Markus Heilig) pushed me to keep a clinical perspective in my work, which was challenging since I’m not a clinician. However, now we’re running a clinical trial with the potential to improve clinical care for patients with PTSD, which is incredibly exciting and definitely not something I would have envisioned doing otherwise.

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Fourth, imaging drug memories as a function of setting in real world drug users and showing once again that cocaine and heroin are a long way off drug use and that drug use is just one example of a more complex set of drug use behaviors. The unequivocal key finding was that substance use disorder prefer to use heroin at home and co- caine outside the home because these drugs are more pleasant in those settings. How can we address this question? If the effective state induced by heroin and cocaine in humans do not change as a function of setting, can we also observe a parallel change in the activity of relevant brain circuitry? We tried to get an answer to these questions by developing a novel task to measure the emotional response to these drugs and then using a combination of fMRI to monitor neural activity during drug imagery (re-creating the setting of drug use). The results were consistent with our working hypothesis but still most astonishing in their clarity. The majority of participants reported a strong preference for heroin from mostly pleasant at home to mostly unpleasant outside the home. The opposite shift was observed for cocaine; that is, most participants who found cocaine pleasant outside the home found that drug unpleasant at home. We predicted that we would find a double dissociation, as a function of drug and setting imagery, in the activity of the fronto-striatal-cerebellar network, in summary, we found that the same setting can influence in
What advice do you have for the early- and mid-career researchers who are new in EBPS? Be truth-seekers, this is the job of scientists. Test hypotheses, do not feel compelled to confirm them. ‘Negative’ data are more important than ‘positive’ data (hence, registered studies should become the rule). Build your career around problems, not techniques. Be courageous: when necessary challenge the mighty and powerful. Be courageous: run ‘risky’ experiments. Be persistent. Be dedicated. Be caring of your students and associates. Be decent. Easier said than done.

**ALBA Declaration**

We are proud to be amongst the early signatories for the ALBA Declaration on Equity and Inclusion, reflective of our shared beliefs that “diversity is a fundamental component of excellence in brain sciences, and that access to education, training, resources, mentorship and jobs should be based on an individual’s potential, not on their sex, gender identity, sexual orientation, disability, age, socioeconomic status, ethnicity, race, nationality, religion, or culture.”

Alba means sunrise in several languages (e.g., Spanish, Italian) and is a name for the ALBA network. ALBA represents an emerging energy to help catalyze movement towards a definitive change that will allow all brain scientists an equal opportunity to thrive and contribute to the advancement of scientific knowledge.

In my opinion, the major problem is not with ‘translation’ but with the problems that a variety of problems exhibit. For example, we know a lot about the mechanisms of drug reward, but we are not able to recover from their addiction on their own while others do not. Finally, there is still a dearth of therapeutic options for addiction. Certainly, we do not have effective medications, except for substitution treatments in the case of opioid addiction.

We know extremely little about the neurobiological mechanisms responsible for individual differences in the vulnerability to addiction, and why an individual became addicted to one drug but not to others. We also do not know why some people are able to recover from their addiction on their own while others do not. Finally, there is still a dearth of therapeutic options for addiction. Certainly, we do not have effective medications, except for substitution treatments in the case of opioid addiction.

**EBPS Workshop - Data Blitz**

We are excited about our upcoming EBPS-CANBiD workshop on March 5th and 6th and even more excited about the data blitz presentations by our trainees! For the full program click here.

**Session 1 - Strategies for Biomarker Discovery**

The affective bias test and 50kHz USVs as graded measures of positive affective state in rat. Justyna K. Hinchcliffe, University of Bristol, Bristol, UK.

Predicting venlafaxine remission in late-life depression using genome-wide and clinical data. Victoria S. Marshe, University of Toronto, Toronto, ON, Canada.

Waist circumference is associated with treatment response to Cognitive Behavioural Therapy for Depression in Females: A Canadian Biomarker Integration Network for Depression (CAN-BIND) Study. Brett D. M. Jones, University of Toronto, Toronto, ON, Canada.

Genomic Associations of Remission and Relapse of Psychotic Depression Treated with Sertaline Plus Olanzapine: the STOP-PD II Study. Xiaoyu Men, University of Toronto, Toronto, ON, Canada.

**Session 2 & 3 - Biomarkers of Addiction & Relapse**

Pharmacogenetics of Lethal Opioid Overdose. Leen Magan, Centre for Addiction and Mental Health, Toronto, Canada.

Lack of effect of different pain-related manipulations on opioid self-administration, choice, and reinstatement of drug-seeking. Sarah M. Claypool, NIDA, Baltimore, MD, USA.

Hedonic Taste Reactivity to Sucrose in Differentially Rared Rats Altered by Mu Opioid Receptor Functioning. Dylan A. Laux, Kansas State University, KS, USA.

Effect of chronic delivery of the mixed MOR/NOP agonists BU08026 and AT-201 on relapse to heroin seeking and taking in a rat model of opioid maintenance. Lindsay Altdorfer, NIDA, Baltimore, MD, USA.

Traumatic childhood and substance use disorders: a translational approach for the identification of peripheral biomarkers. Clarissa Catala, Sapienza University of Rome, Rome, Italy.

Environmental Enrichment Alters Amphetamine Intake and Cue-Induced Relapse Following Extended-Access Amphetamine Self-Administration. Troy D. Fort, Kansas State University, KS, USA.

Expression of nicotinic receptors on supramammillary neurons projecting to the medial septum. Youseke Arima, NIDA, Baltimore, MD, USA.

Effect of access duration on operant responding for social interaction with a peer in male and female rats. Jules M. Chabot, NIDA, Baltimore, MD, USA.

**Future EBPS Meetings**

**EBPS Workshop 2022**

Our biennial workshops are held every two years, with a focused theme. Aside from being an opportunity for experts in the specific field to share their vision and provide direction, it is also a chance for early career researchers to present their research findings and expand their academic networks. If you’ve got an idea for what the next workshop should be on, where it should be held and if you’d like to play a key role in its organisation, submit your proposal with the subject line “EBPS Workshop” to the general secretary by May 1, 2021.

**EBPS Conference 2023**

EBPS Conferences present members with an opportunity to visit a new country, present and share their research findings and to follow the affective bias test and 50kHz USVs as graded measures of positive affective state in rat. Justyna K. Hinchcliffe, University of Bristol, Bristol, UK.

Predicting venlafaxine remission in late-life depression using genome-wide and clinical data. Victoria S. Marshe, University of Toronto, Toronto, ON, Canada.

Waist circumference is associated with treatment response to Cognitive Behavioural Therapy for Depression in Females: A Canadian Biomarker Integration Network for Depression (CAN-BIND) Study. Brett D. M. Jones, University of Toronto, Toronto, ON, Canada.

Genomic Associations of Remission and Relapse of Psychotic Depression Treated with Sertaline Plus Olanzapine: the STOP-PD II Study. Xiaoyu Men, University of Toronto, Toronto, ON, Canada.

**Session 3 – Reverse Translation to Novel Therapeutics and Mechanisms of Action**

Reverse Translation: Role of Genetic and Environmental Circadian Disturbances in Alcohol Drinking Behavior - From Bedside to Bench and Back. Hanneh Ansija, Ludwig Maximilian University, Munich, Germany.

Characterization of NHE-7-resistant depression and exploitation of experimental ketamine treatment on clinical and psychosocial outcomes. Aleksander Biorac, Queen’s University, Kingston, ON, Canada.

Modeling spontaneous THC withdrawal symptoms in mice. Andrew J. Kesner, NIAAA, Rockville, MD, USA.

**Session 5 – Emerging Role of the Microbiome in Mental Health**

The Safety, Efficacy, and Tolerability of Microbial Ecosystem Directed Therapy (MIDT) in Treatment-Resistant Depression and an Open-label Study of MIDT in a Subset of Subjects with Generalized Anxiety Disorder and/or Generalized Anxiety Disorder: A Phase 1, Open-Label Study. Arthi Chinnaya Meyyappan, Queen’s University, Kingston, ON, Canada.

Investigation of the role of the microbiome-gut-brain axis in schizophrenia and clozapine-induced weight gain: A pilot study. Jonathan Liu, Centre for Addiction and Mental Health, Toronto, ON, Canada.

The Binging Baboons of Baltimore: Long-Term Chronic Alcohol Self-Administration Leads to Changes in the Fecal Microbiome, Gut Metabolome in Non-Human Primates. Daria Piacentino, NIDA, Baltimore, MD, USA.

The gut microbiome as a biomarker for a microbiota-dependent stress response. Sarah-Jane Leigh, University College Cork, Ireland.

Future EBPS Meetings
Misuse of mu opioid receptor (MOR) agonists contributes to the worldwide opioid overdose crisis. Remarkably, MOR agonists of another opioid receptor are under investigation as a tool to curb the misuse of MOR agonists. Whereas MOR agonists generally function as reinforcers, MOR agonists do not function as reinforcers and can promote conditioned aversive effects. It has been hypothesized that these seemingly opposing effects of MOR and KOR agonists could be used to develop a non-contingent MOR/KOR agonist pain-management regimen with less abuse liability than currently available MOR-agonist based anecstics (e.g., morphine, oxycodone).

Consistent with this hypothesis, KOR agonists decrease rates of MOR agonist self-administration under a variety of conditions. However, one interpretation of these findings is that traditional drug self-administration procedures rely on rate-based schedules of reinforcement. This is an important consideration when evaluating the abuse-limiting effects of KOR-agonists, because KOR agonists similarly decrease rates of drug- and food-maintained responding under rate-based schedules of reinforcement. Thus, the possibility remains that KOR agonists decrease rates of MOR agonist self-administration through undesirable, non-selective effects on operant responding (e.g., sedation).

One strategy to minimize the influence of non-selective effects on abuse-liability assessment includes the use of concurrent schedules of reinforcement. Here, the experimental subject is provided a choice of two or more options (e.g., choice between drug injections or food), and the primary dependent measure is behavioral allocation between the options. Behavioral allocation is relatively insensitive to non-contingent pretreatments. In this way, the influence rate is reduced because choice procedures are well suited to evaluate the effects of drugs with rate-decreasing effects (e.g., KOR agonists) on reinforcement. Using choice procedures, previous work has shown non-contingent (i.e., experimenter administered) pretreatment with KOR agonists to fail to decrease choice of cocaine over non-drug alternatives (1, 2). In contrast, when provided a choice between a MOR agonist and a MOR agonist mixed with a KOR agonist, choice of the KOR-agonist containing option is decreased (3). Collectively, these results from previous choice studies suggest that KOR agonists would only be expected to decrease the abuse liability of MOR agonists if administration of the KOR agonist was contingent upon self-administration of the MOR agonist, which could be achieved by formulating MOR and KOR agonists into a single medication.

However, previous reports of dysphoric, psychotomimetic, and sedative effects following KOR agonist administration to humans introduces a potential obstacle to the clinical utility of this approach. Namely, these unpleasant KOR-agonist effects could contribute to medication non-compliance, resulting in inadequate pain management in the case of a combined MOR/KOR agonist analgesic. One strategy for minimizing these untoward side effects is to use a KOR agonist with a less severe side-effect profile, such as naltralina. Naltralina has been available for the treatment of uremic pruritus in Japan since 2009, and is the only selective KOR agonist approved for clinical use. No reports of psychiatric side effects have been published, providing evidence that naltralina is well tolerated in humans.

As part of my dissertation with Dr. Kevin Freeman at the University of Mississippi Medical Center, we found that contingently administered naltralina decreased oxycodone self-administration in rats when the two drugs were self-administered as a mixture (4). While encouraging, this study used a rate-based (i.e., oxycodone only) schedule of reinforcement to investigate whether KOR agonists do not function as reinforcers and can promote conditioned aversive effects. Therefore, it remained unclear whether naltralina decreased rates of MOR agonist self-administration through a non-selective effect on operant responding. My desire to address this issue lead me to post-doctoral fellowship where I received an internal grant from the Post-Doctoral Association of Virginia Commonwealth University. The goal of this project was to compare the effects of naltralina and U50,488 (a “traditional” KOR agonist with depressive properties) on fentanyl-versus-food choice in male and female rats. KOR agonists were administered either 1) contingently with each fentanyl injection or 2) non-contingent pretreatments administered by the experimenter.

We found that both naltralina and U50,488 decreased choice of fentanyl over food when the KOR agonists were self-administered contingently as a mixture of fentanyl/KOR agonist (contingent naltralina results are summarized in the left panel). However, only a subset of the rats responded when the choice was between the high unit doses of the KOR agonist/fentanyl mixtures and food, suggesting KOR-induced decrease in fentanyl choice may correspond with undesirable effects that impair motor function. When administered as non-contingent pretreatments, the KOR agonists did not significantly attenuate fentanyl self-administration up to KOR agonist doses that decreased rates of operant responding for both fentanyl and food (non-contingent naltralina results are summarized in the right panel).

These results illustrate that the effects of KOR agonists on behavior are more complex than their interactions with receptors. Non-contingent administration of the KOR agonists was found to produce non-specific decreases in self-administration of both fentanyl and food, which does not support the use KOR agonists as stand-alone Substance Use Disorder Medications. However, if delivery of the same KOR agonist was the consequence of fentanyl self-administration by the subject, choice of fentanyl decreased. A potential translational implication of this finding is that alternative KOR agonist could be repurposed to decrease the abuse liability of a MOR agonist. However, given that naltralina and U50,488 produced abuse-limiting and potentially desirable side effect profiles similar to those observed in this study, these data suggest that KOR-activated abuserside-effects may contribute with side effects, which are better assessed in humans and/or non-human primates.