Swiss Addiction Research Day

September 27, 2019
Basel, Switzerland

Book of Abstracts

Conference location:
Hotel Pullman Basel Europe, Clarastrasse 43, 4058 Basel

Dear colleagues, dear friends

On behalf of the Swiss Society of Addiction Medicine (SSAM) I have the pleasure to welcome you in Basel to the 7th SWISS ADDICTION RESEARCH DAY. Since its first edition in Zurich in 2004 this day has become the recurring scientific event in our field. The SWISS ADDICTION RESEARCH DAY of the SSAM is a unique opportunity to access the interdisciplinary aspects of addiction research in Switzerland.

This time, the SWISS ADDICTION RESEARCH DAY will be enriched with a Young Investigator Symposium. Young academics will deliver insight into their promising projects.

Traditionally, the RESEARCH DAY of the SSAM has afforded an opportunity to honour superior accomplishments in the field of addiction research. So it shall be again! For the fifth time, the Swiss Addiction Research Award (SARA) will be handed over to excellent scientists in order to honour their outstanding performance.

In the name of the SSAM I would like to thank all participants for their dedication as well as my colleagues of the organizing scientific committee for their active and expert support.

Welcome to Basel, welcome to the SWISS ADDICTION RESEARCH DAY.

Gerhard Wiesbeck
President of the
2019 SWISS ADDICTION RESEARCH DAY

Organizing Scientific Committee:
Barbara Broers (Geneva)
Jean-Bernard Daeppen (Lausanne)
Marcus Herdener (Zurich)
Gerhard Wiesbeck (Basel)
Daniele Zullino (Geneva)

10h00 **Arrival** (registration and coffee)

10h30 **Opening**
G. Wiesbeck

10h45 **Symposium 1: Stigma in Addiction Medicine**
Chair: B. Broers

S1-1 *A conceptual framework on stigma and discrimination*
A. Reyre

S1-2 *Interventions to reduce stigma towards patients with substance use disorder in medical students*
D. Lidsky

S1-3 *Words that stigmatise in addiction medicine: summary of the Pompidou report*
O. Simon

S1-4 *Psychedelic assisted psychotherapy: re-emergence of stigmatised drugs? A literature review*
M. Ljuslin

Global discussion

12h00 **Swiss Addiction Research Award (SARA 2019)**
Chairs: G. Wiesbeck, R. Hämmig

Lectures of the SARA laureates

12h45 **Lunch**

13h30 **Symposium 2: Novel Therapeutic Strategies for the Treatment of Addictive Disorders**
Chair: M. Herdener

S2-1 *Can psychosocial and craving-induced stress responses predict prospective changes in cocaine consumption?*
B. Quednow

S2-2 **Adaptive fMRI neurofeedback stimulation to support smoking cessation**
A. Haugg

S2-3 **Glutamatergic changes in cocaine addiction as a target for pharmacotherapy**
E. Engeli

S2-4 **Serotonergic psychedelics for addictive disorders – a new treatment approach?**
K. Preller

Global discussion

14h30 **Coffee break**

15h00 **Symposium 3: Young Investigators**
Chair: D. Zullino

S3-1 **Longitudinal associations between life satisfaction and cannabis use initiation, cessation and disorder symptom severity in a cohort of young Swiss men**
S. Deligianni

S3-2 **Glial cells and neuroinflammation in addiction. A PET imaging study in tobacco smokers**
S. Tsartsalis

S3-3 **Program areas of WHO Management of Substance Abuse Unit**
D. Krupchanka

S3-4 **Lifecourse of alcohol-related problems among people with alcohol use disorder**
A. Lasserre

Global discussion

16h00 **End**

Abstracts

S1-1 A conceptual framework on stigma and discrimination

Aymeric Reyre[1], Barbara Broers[2]

[1] Division for Penitentiary Medicine

[2] Unit for Dependencies, Division for Primary Care, Geneva University Hospitals, Switzerland

Background: Goffman's conceptualization of stigma in 1963 has been the starting point of a prolific exploration of the consequences of social prejudice on the life of "discredited" persons. Potentially discrediting characteristics include health conditions, and stigma constitutes an important burden for some specific categories of patients. The stigma related to substance use has been suspected to have dire consequences on people's health, affective and professional life or accommodation and research has focused on this important issue by assessing different aspects of stigma such as beliefs about, attitudes or social distance toward people who use psychoactive substances. Doing so, researchers often failed to refer to and to position their work within a comprehensive and accurate theoretical framework of stigma. This results in difficulties to make comparison between studies and to retrieve sound information from the literature.

Methods: We conducted a narrative review of the conceptual literature on stigma, substance use and addiction by searching PsychInfo and Pubmed databases.

Results: In the two last decades, several attempts to formulate a unified and comprehensive theoretical framework have converged, and an articulation of social and psychological mechanisms that are key to the characterization of stigma (labeling, stereotyping, separation and discrimination) has been proposed. Furthermore, social, structural and internalized components of stigma have been described and fruitfully applied to the field of substance use.

Discussion: These conceptual developments help to ordinate and interpret the current literature on substance use related stigma and provide interesting guidance to clinicians and researchers.

S1-2 *Stigma among medical students towards substance use disorder: a systematic review of stigma's assessment and effective educational interventions*

Deborah Lidsky-Haziza, Barbara Broers

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Aims: People suffering from Substance Use Disorder (SUD) are particularly at risk for prejudicial attitudes and discriminatory behaviour, in life in general and in the medical field. The objectives of this systematic narrative review of the literature are to identify and measure medical student's attitude and stigma toward patients with SUD, and identify effective interventions throughout medical education in order to reduce stigma and optimise medical care.

Methods: A review of electronic data-bases was conducted focusing on studies examining stigma among medical students towards people suffering from SUD, and on studies about medical educational interventions in order to improve students' attitude. Search terms were used across databases as Pubmed, Web of Science, Cochrane library and PsycINFO.

Results and discussion: 678 studies were selected, and all abstracts read by two researchers. 139 studies of original articles were included in the analysis. In total, 34 studies met criteria for our review, 17 studies were observational with a qualitative approach of stigma's measure and 17 studies were interventional, with a measure of stigma before and after the intervention.

Stigma among medical students towards patients with SUD was estimated according a huge diversity of questionnaires. The global trends indicate that medical students have a moralist and negative attitude towards people suffering from SUD.

Most of the interventions focused on enhancing knowledge and skills of medical students as well as on improving communication and attitudes with patients suffering from SUD. Globally a combination of traditional didactic learning with clinical exposure including case discussions, practice with peers, motivational interviewing training with standardized patients and interactions with patients recovering from addictions, seem to be the most effective interventions. The results show a decreased medical students' stigma by improving their level comfort in interacting with patients suffering from SUD, in a more non-judgmental, professional and benevolent approach.

Conclusion: Prejudice and stigma in medical students negatively influence the medical care provided to patients suffering from SUD. Effective educational teachings to reduce stigma exist, and should be systematically implemented throughout the medical curriculum.

S1-3 *Words that Stigmatise: the Pompidou Group TDOLEG Report Recommendation on Neutral, Precise and Respectful Terminology*

O. Simon1,2,3,4, R. Haemmig,2,4, R. Stamm3,4,5, V. Junod4,8, M. Roelli1,7, C, Dickson1,7, W. Scholten4,6

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3) Scientific coordination of the TDOLEG project
4) Expert and edition group of the final TDOLEG rapport
5) Drug Section, Federal Office of Public Health (FOPH), Switzerland
6) Consultant, Medicines and Controlled Substances
7) Scientific Collaborator, TDOLEG project
8) Faculty of Law, Geneva and Faculty of Business and Economics (HEC), Lausanne

The Pompidou Group is an intergovernmental organisation affiliated to the Council of Europe, involved in issues related to substance use disorders by bringing together interdisciplinary experts. In most countries, opioid agonist treatment (OAT) is subject to restrictions, which significantly impede access to care. To assist administrative authorities in order to review their regulations, the Pompidou Group mandated a group of health and legal experts to identify criteria for the appropriate regulation of OAT, in line with ethical standards, international law, scientific knowledge and best medical practice. Through discussions and a Delphi survey, the group identified some 60 guiding principles, which were then the subject of a wide public consultation. Endorsed by Pompidou Group member states, the final report identified four key recommendations: (1) Prescription and delivery without prior authorisation schemes, (2) Effective removal of financial barriers to access to care, (3) Coordination and follow-up by a national consultative body, (4) Neutral, precise and respectful terminology.

To prevent prejudice, stigmatisation and discrimination, terms should describe unambiguously the facts, based on scientific knowledge; they respect the personality of persons in treatment, as well as their personal and professional environment. While terminology is to take into account international definitions, recommendations and practices, it must be adapted to the language of each linguistic and/or regional community and must be based on an ongoing debate among healthcare professionals, civil society, the persons in treatment and the competent authorities. Such a debate also promotes the dialogue between different disciplines concerned by the field of substance use disorders. The terminology used in institutional and regulatory documents should be subject to periodic reviews. The use of appropriate language improves scientific quality of articles and increases chances to receive the best treatment and that government policies on psychoactive substance policies will be rational.

We identified twenty-three problematic terms and their possible alternatives. Elimination of the term "substitution therapy" is an emblematic example of this issue. The term "substitution", being ambiguous as to the nature and function of opioid agonist medicines, is to be avoided in favour of alternatives focused on the real characteristics of opioid agonist medicines.

Pompidou Group. (2018). Opioid Agonist Treatment. Guiding principles for legislation and regulations. Expert group on the regulatory framework for the treatment of opioid dependence syndrome and the prescription of opioid agonist medicines. Strasbourg.

Scholten, W., Simon, O., Maremmani, I., Wells, C., Kelly, J.F., Hämmig, R., Radbruch, L. (2017) Access to treatment with controlled medicines: Rationale and recommendations for neutral, respectful, and precise language. Public Health, Volume 153, 147-153

S1-4 *Psychedelic assisted psychotherapy: re-emergence of stigmatized drugs? A literature review*

Michael Ljuslin
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Psychedelics are psychoactive substances that powerfully alter perception, mood, and cognitive processes. Despite the published adverse reactions, they are now considered physiologically safe and do not produce dependence or addiction. Known and used for millennia, their human use predates written history, and they were employed by early cultures in a variety of sociocultural and ritual contexts. Although there has been a western interest for over half a century in the therapeutic use of classic hallucinogens to treat substance use disorders and other selected psychiatric disorders, medical research with these drugs was halted in the early 1970s, leaving many questions unanswered.

In the past two decades, a3fter extensive research about the possible harmful effects of those substances, clinical research on the potential therapeutic uses of classic hallucinogens and associated substances has resumed, focusing mainly on conditions for which current recommended treatment have low efficacy or none. To date, trials were conducted with various types of classic psychedelics for substance abuse, LSD and psilocybin for the treatment of fear and anxiety in people suffering from terminal illnesses, MDMA for resistant PTSD, ketamine for resistant unipolar depressive disorder, and several substances for obsessive-compulsive disorder and cluster headaches, with results that appear very promising. Nevertheless, further research is needed to explore the therapeutic application for these conditions and provide evidence for their efficacy. Indeed, such research is underway in several countries including Switzerland. This review aims to give an overview of the current research in substance abuse disorders and theories underlying the putative therapeutic mechanisms of action, including psychological and pharmacological aspects.

S2-1 *Can psychosocial and craving-induced stress responses predict prospective changes in cocaine consumption?*

Ann-Kathrin Kexel, Bruno Kluwe-Schiavon & Boris B. Quednow

Experimental and Clinical Pharmacopsychology, Department of Psychiatry, Psychotherapy and Psychosomatics, Psychiatric Hospital of the University of Zurich

It is assumed that an increased susceptibility to stress plays an important role in the development, maintenance, and relapse of cocaine addiction. However, previous research applying laboratory stress paradigms to cocaine users exclusively investigated hormonal responses but so far neglected potential changes in the expression of stress-related genes. It is furthermore unclear how individual stress responses of the hypothalamic–pituitary–adrenal (HPA) axis and expression of stress-related genes can predict positive or negative changes in cocaine use intensity. We therefore investigated the effects of psychosocial stress (Trier Social Stress Test) and drug craving-related stress on the HPA axis and the peripheral expression of stress-related genes in 50 regular cocaine users and 40 matched healthy controls at baseline and at a 4-months follow-up. Cocaine use intensity was determined by hair testing at both time points. We expect to find changes in the physiological stress response on the endocrinological and gene-expression level in cocaine users at baseline and propose that stress susceptibility predicts changes of cocaine use at the follow-up. Preliminary data of the study will be presented at the conference.

S2-2 *Adaptive neurofeedback stimulation to support smoking cessation*

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5) University College London, United Kingdom;
6) McGill University, Canada

Aim: Controlling craving is key to quit smoking. To help smokers tolerate craving cues better, we trained them with neurofeedback to downregulate cue-induced craving activation in the anterior cingulate cortex (ACC). Neurofeedback training was accomplished using a novel adaptive real-time fMRI neurofeedback paradigm where the intensity of the displayed nicotine cues was dynamically coupled to ongoing ACC activity.

Methods: 64 smokers who wanted to reduce their weekly cigarette consumption or quit smoking completely were randomly assigned to either the experimental group (EG; N=32) or the control group (CG; N=32). Subjects in the EG were trained to downregulate their ACC activity, whereas in the CG feedback was linked to activity in the angular gyrus, an area not associated with nicotine craving. Before and after ten neurofeedback training runs, clinical and behavioral assessments were performed, including a five-week follow-up assessment.

Results: For subjects in the EG, average number of weekly consumed cigarettes decreased from 83.02 to of 43.27 ($p = 0.0001$). 75% of the EG subjects reduced cigarette consumption, with 18.75% of them quitting smoking completely. Craving related to nicotine cues decreased considerably and correlated with decreased cigarette consumption ($p < 0.01$). In the CG, weekly cigarette consumption decreased from 83 to 70.17 ($p = 0.16$). Here, 55.55% of the subjects reduced cigarette consumption and 11.11% quit smoking completely.

Conclusion: Adaptive neurofeedback training supports smoking reduction/cessation. This reduction is achieved through reduced craving when being confronted with nicotine cues. Overall, our results suggest that brain-controlled adaptive nicotine cue exposure stimulation might be promising novel therapeutic tool in addiction.

S2-3 *Glutamatergic changes in cocaine addiction as a target for pharmacotherapy*

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Aim: Craving, as triggered by drug-related cues, is at the heart of addiction. Animal models describe that chronic cocaine administration leads to decreased glutamate levels in the nucleus accumbens (NAcc), whereas cue-induced reinstatement of substance-seeking is accompanied by enhanced glutamatergic transmission[1]. However, little is known about such neurometabolic alterations in cocaine addiction in humans. We thus aim at investigating potential changes within the glutamate homeostasis in the NAcc of cocaine-addicted individuals (CAI) during rest and cue-induced cocaine craving by means of a tailored proton magnetic resonance spectroscopy (^{1}H-MRS) protocol for small voxels[2].

Methods: To overcome previous methodological hurdles, non-water suppressed metabolite cycling ^{1}H-MRS was performed in 26 CAI and 30 healthy controls (HC). Glutamate concentrations were assessed in the NAcc during a neutral and a craving state that was triggered with audio-visual cocaine stimuli. Subjective craving was rated on a visual analogue scale. Further, ^{1}H-MRS was performed twice to assess potential restoring effects of N-acetylcysteine on glutamate. This short-term challenge of 2400mg/d on two consecutive days was administered in a randomised, placebo-controlled design.

Results: Our technical adjustment of the ^{1}H-MRS protocol substantially increased the spectral quality of the metabolite measures in the Nacc. We observed significantly decreased glutamate concentrations in CAI compared to HC during the neutral state. While during the presentation of cocaine stimuli, we found elevated glutamate concentrations in the Nacc of CAI. Also the CAI's ratings on the visual analogue scale showed elevated craving after the cocaine stimulus in relation to all

previous ratings. Contrary to expectations, the N-acetylcysteine neither showed an effect on craving nor on glutamate levels.

Conclusion: Despite the small voxel size, our dedicated ^{1}H-MRS protocol achieves high data quality and, thus, finally allows a reliable detection of glutamate in the human NAcc. For the first time this reveals that, in accordance with animal models, glutamatergic alterations in the NAcc occur in CAI and might play a decisive role in the development and maintenance of cocaine addiction. Hence, the glutamatergic system is a target for future pharmacological treatment approaches, in which glutamate could potentially serve as a predictive biomarker for treatment response.

References
1. Kalivas, P. W. The glutamate homeostasis hypothesis of addiction. *Nature reviews. Neuroscience* **10,** 561–572 (2009).
2. Hock, A. *et al.* Towards metabolic profiling of the neurocircuitry of mood: small-voxel, non-water-suppressed 1H-MRS in the nucleus accumbens, amygdala and cingulate cortex at 3T. *Joint Annual Meeting ISMRM-ESMRMB* (2014).

S2-4 Serotonergic psychedelics for addictive disorders – a new treatment approach?

Katrin H. Preller

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Addiction is a significant public health concern. Despite increased effort, pharmacological treatment options in substance use disorders remain scarce and, if available, show limited efficacy.

After the discovery of the psychotropic effects of the serotonergic psychedelic compound Lysergic acid diethylamide (LSD), it was used in the treatment of alcohol addiction in the 1950s and 60s with several studies suggesting reductions in craving and alcohol use. However, after being placed in Schedule I, research on the clinical potential of psychedelic compounds stopped almost completely.

Due to many studies showing that psychedelics can be administered safely in a clinical setting and the unsatisfying results obtained with currently available medication, interest in the effects of psychedelics in the treatment of substance use disorders has recently returned. First preliminary studies show that one or two doses of psilocybin, the main active compound of the so-called magic mushrooms and a serotonin 2A/1A receptor agonist, induced robust decreases in drinking, with a pre-post effect size of $d > 1$ persisting at a final 9-month follow-up visit. Furthermore, another study investigating the effects of two to three doses of psilocybin in combination with cognitive behavioral therapy for smoking cessation showed that 12 of 15 participants were abstinent at 6-month follow-up and 10 participants remained abstinent at 12 months after treatment.

While these results are very promising with regard to the clinical potential of psychedelics in the treatment of substance use disorders, the current preliminary studies suffer from small sample sizes and the lack of placebo conditions. We are therefore conducting a randomized, placebo-controlled clinical trial testing the efficacy of psilocybin in alcohol use disorder. If larger, controlled studies support the clinical efficacy of psilocybin in the treatment of substance use disorders, this may reveal a novel treatment approach based on single or only few supervised administrations of a pharmacological agent in combination with psychotherapy.

S3-1 Longitudinal associations between life satisfaction and cannabis use initiation, cessation and disorder symptom severity in a cohort of young Swiss men

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Abstract: Motivations for cannabis use may include coping with negative well-being. Life satisfaction, a hallmark of subjective well-being, could play a role in cannabis use among young adults. This study aims to assess whether life satisfaction (SWLS) at age 21 is associated with cannabis initiation and cessation between the ages of 21 and 25, and with cannabis use severity (CUDIT) at age 25. Data were drawn from a cohort of young Swiss males. Associations of life satisfaction with initiation, cessation and severity were assessed with logistic and zero-truncated negative binomial regressions. Age, family income, education, alcohol and tobacco use at age 21 were used as adjustment variables. From a sample of 4,778 males, 1,477 (30.9%) reported cannabis use at age 21, 456 (9.5%) initiated use between age 21 and 25, and 515 (10.8%) ceased by age 25. Mean (SD) SWLS was significantly higher among non-users at age 21 (27.22(5.35) vs. 26.28(5.80), $p<.001$). Negative associations between life satisfaction at age 21 and cannabis use initiation (OR=0.98, p=.029) and severity at age 25 (IRR=0.97, $p<.001$) were no more significant in adjusted analyses (OR=0.98, p=.059 and IRR=0.99, p=.090). Life satisfaction at age 21 was not associated with cannabis cessation (OR=0.99, p=.296). Results suggest that the predictive value of life satisfaction in cannabis use is questionable and may be accounted for by other behaviors such as tobacco and alcohol use.

S3-2 Glial cells and Neuroinflammation in Addiction. A PET imaging study in tobacco smokers

Dr. Stergios Tsartsalis

Department of Psychiatry, Geneva University Hospitals

Epidemiological studies suggest that tobacco smoking is associated to an increased risk of developing various neuropsychiatric disorders. A direct toxicity of tobacco in the Central Nervous System (CNS) is proposed in recent studies and a potential causal link between tobacco smoking and the pathophysiology of neuropsychiatric disorders could be neuroinflammation. Indeed, some evidence exists that tobacco smoking alters the function of glial cells, notably microglia and astrocytes, and induces an inflammatory reaction in the CNS. Molecular imaging with Positron Emission Tomography (PET) is the ideal tool to evaluate this phenomenon *in vivo*, using radiotracers that bind to the 18 kDa Translocator Protein (TSPO), a component of the mitochondrial membrane that is overproduced by activated microglia and astrocytes. In this presentation, the development of a molecular imaging study to assess glial function in tobacco smokers using PET is described, both from a clinical and translational standpoint.

S3-3   *Program areas of WHO Management of Substance Abuse Unit*

Dr. Dzmitry Krupchanka

Medical Officer WHO, Management of Substance Abuse (MSB)

Presentation will overview activities of Management of Substance Abuse Unit, Department of Mental Health and Substance Abuse, WHO in key dimensions of work, including: implementation of the Global strategy to reduce the harmful use of alcohol; strengthening public health aspects in addressing the world drug problem; normative guidance and technical support to countries; generation and dissemination of new evidence through international research projects; monitoring and evaluation.

S3-4   *Lifecourse of alcohol-related problems among people with alcohol use disorder*

Dr. Aurélie Lasserre

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