



'A 2023 full of ESBRA and ESBRA ECI events'

Elena Palma — Chair of ESBRA Early Career Investigators Committee



Dear ESBRA community,

Happy New Year!

Time flies and next month will already celebrate the first anniversary of the ESBRA ECI & Comm Committee! A year since our first meeting and a few achievements under our belt: the organisation of a Social Media Team and an Editorial Team for the promotion of our Society, the launch of the periodic ESBRA Newsletter and some great events at the 2nd World Congress on Alcohol and Alcoholism! In addition, we are organizing a big ECI event for spring 2023 consisting in a sandpit workshop to identify hot topics in alcohol-related research and create collaborative project proposals. Watch this space!-

In the current Issue:

If you weren't in Kraków last September, have a look in the next pages about what you have missed and some of the ECI Committee favourite topics!

Read the interview of the ESBRA President Mickael Naassila with Prof Alexander Louvet about new guidelines for the management of patients with alcoholrelated liver disease jointly published by the French Association for the Study of the Liver (AFEF) and the French Alcohol Society.

Find more about what Jerome and Olli think about the controversial topic of boosting alcohol sales to increase government income via taxes.

And for all the ECI researchers out there, two calls you don't want to miss:

Apply to the prestigious Nordmann award (deadline 31st March 2023)

Become part of the ESBRA ECI & Comm Committee: we are recruiting!

Much has been achieved and many ideas and events are yet to come!

May the 2023 bring everyone more funding for alcohol research and lots of confirmed hypothesis!-

Special

Joint Meeting of ISBRA and ESBRA 2nd World Congress on Alcohol and Alcoholism

Marcin Wojnar & the ESBRA ECI Committee

he <u>congress</u> has been organized in the historic city of Kraków in Poland, one of the most beautiful cities in the world. Kraków is one of the oldest cities in Poland and its Old Town and the Wawel Royal Castle were declared as the first UNESCO World Heritage Site in the world.

The Congress took place in a very convenient *Auditorium Maximum*, a conference and teaching center of the Jagiellonian University.

Despite the potential threat coming from the COVID pandemic as well as a tragic war in Ukraine, it was fortunately possible to organize a hybrid meeting in a form of face-to-face meeting with a possibility for those who could not come in person, to participate in the meeting virtually through the online connection.

The scientific program of the joint meeting of ISBRA and ESBRA was quite impressive, there were 6 plenary lectures with distinguished keynote speakers, 34 symposia containing almost 150 presentations and 57 posters. We were able to hear during the congress about major developments and recent research achievements in the field of studies on alcohol. More room and time were offered this time to the early career investigators who are the future of our societies.

There was also a social event – a Gala Dinner, which was 125 meters underground in the Salt Mine in Wieliczka, another UNESCO Heritage Site. We all experienced not only unforgettable company and palatable food, but most of all a spectacular visit in an extraordinary place – hidden from the world, full of secrets and legends.-

[Marcin Wojnar, Conference President]

~ Conference symposium highlights ~

olecular mechanisms of the individual vulnerability to develop compulsive alcohol seeking and taking: evidence from preclinical research. [Estelle Barbier]

This symposium presented the recent advances in the understanding of the molecular mechanisms of the individual vulnerability to develop Alcohol Use Disorders (AUD).

The first speaker <u>Dr Eric Augier</u> (Linköping University, Sweden) showed that choosing alcohol over the sweet reward (an addiction-like behavior) is in part driven by a decreased expression of the GABA B transporter GAT-3 in the central amygdala (CeA), suggesting that rescuing GABA clearance due to suppressed GAT-3 expression might be a successful therapeutic mechanism in AUD.

The second speaker <u>Dr Esi Domi</u> (University of Camerino, Italy) showed that alcohol taking despite negative consequences (electric footshock) involves the activation of the GABAergic PKCS cells in the CeA and that administration of the GABAB receptor agonist Baclofen decreases compulsive drinking.

The third speaker <u>Dr Lucia Marti-Prats</u> (Cambridge, United Kingdom) discussed the role of the dynorphin/KOR system in the tendency to rely on alcohol to cope with distress and the associated exacerbation of the vulnerability to develop compulsive alcohol drinking.

Finally, <u>Dr Nathan Marchant</u> (Amsterdam UMC, Netherland) talked about the effects of social reward on choice for alcohol in both male and female rats and found that the preference for social rewards over drugs may not generalize to rats self-administering alcohol.

eurogenomics of alcohol: Molecular signatures of cellular processes in alcohol use disorder models. [Esi Domi]

The symposium on Neurogenomics of alcohol: "Molecular signatures of cellular processes in alcohol use disorder (AUD) models", organized and chaired by Prof Igor Ponomarev and Prof Dayne Mayfield, focused on molecular profiles in specific neuronal and glial cell populations implicated in AUD. The symposium highlighted recent advances in the field such as single cell and single nucleus

RNA sequencing (snRNA-Seq), spatial transcriptomics, and translating ribosomal affinity purification (TRAP) in AUD models. Identification of cell type-specific genes and molecular networks may help develop new tools for cell-specific manipulation of neuronal and glial activity, which may prove to be crucial for the development of novel therapies for the prevention and treatment of AUD.

The session was opened by **Prof Igor** Ponomarev introducing snRNA-Seq and spatial transcriptomics approaches to identify cell-type-specific gene expression changes within the prefrontal cortex after alcohol drinking in mice. Data suggested a large heterogeneity of responses where some of these cell typespecific changes may mechanistically underlie the transition from moderate to high alcohol consumption. The second speaker Dr Nihal Salem, showed transcriptomic changes induced by immune activation in the prefrontal cortex mediating the escalation of alcohol consumption in a mouse model. The third speaker Dr Marion Friske showed overlapping gene expression signatures especially in the immune- and inflammatory pathways as well as formation of excitatory synapses when analyzing snR-NA-Seq data from brain tissues of alcohol-dependent rats and human AUD. The last talk was presented by Prof Estelle Barbier, showing gene expression changes and the role of PKCd-positive neurons in the central nucleus of the amygdala in punishment-resistant alcohol self-administration in rats.

Biomarkers and new targets in Alcohol Use Disorders: translational approaches. [Jérôme Jeanblanc]

It was a pleasure to attend the symposium entitled "Biomarkers and new targets in Alcohol Use Disorders: translational approaches" (Symposium S17). As the name suggests, the speakers came from both the clinical and pre-clinical fields.

The first speaker, <u>Prof Florence Vorspan</u>, presented her latest results concerning the identification of blood biomarkers specific to alcohol withdrawal, such as the neurofilament light chain protein (NfL). The interest of the project lay in the fact that the study is based on clinical studies but also on an animal model of alcohol withdrawal called "Alcohol Deprivation Effect".

Then, <u>Dr Christelle Baunez</u> demonstrated the interest of deep stimulation of the subthalamic nucleus in the reduction of alcohol consumption by operant self-administration and more specifically in a context of social interaction between experimental rats and familiar or unfamiliar conspecifics.

<u>Dr Sami Ben Hamida</u> presented his recent results concerning orphan GPR88 receptors in the control of alcohol consumption in mice in a 2-bottle freechoice intermittent drinking model using specific agonists.

Finally, <u>Dr Vincent David</u> was replaced by his young collaborator <u>Dr Léa Tochon</u>, who recently graduated and presented some of her thesis results. The strength of this work lies in the demonstration of the possibility of studying the role of mutations in the $\alpha 5$ subunit of the nicotinic receptor in vulnerability to alcohol consumption according to the Cloninger typology with social, emotional and cognitive dimensions.

SBRA-JMSAAS joint symposium Mechanisms of alcohol-mediated liver injury. [Elena Palma]

During this conference, the role of mitochondria in alcohol-related organ injury has been highlighted several times. The multiple functions of these organelles are affected not only in the hepatocytes or the liver but may also appear relevant in the context of inter-cellular and inter-organ communication. Also, the importance of EVs, particularly of ExomiR or mitochondria-derived cargo (mtDNA), has emerged in all severity stages of Alcohol-related Liver disease. These messengers put in communication not only the different cell types in the liver, such as hepatocytes, HSCs and macrophages, but an interesting link with skeletal muscles has been suggest-

Furthermore, a few talks have finally emphasised a topic neglected for many years: the gender difference in alcohol-related disorders (including ALD or AUD). An increasing number of studies have started to include both males and females in animal-based investigations or differentiate the presentation of patient results between men and women.

Akira Uchiyama, Japan, presented the role of intestinal microbiota and impact of an antibiotic (rifaximin) on liver injury in a mouse model of obesity and diabetes fed with ethanol. Also, he highlighted the effects of hormonal regulation on the innate immune response in a model of chronic liver disease.

Prof Akiko Eguchi, Japan, presented the analysis of hepatocytes-derived EVs and their effect on inflammation (hepatic macrophages) or fibrosis (HSC) in mouse models of mild ASH and AH, with a particular focus on cargos like miRNAs or mtDNA. She also highlighted the interorgan effects (muscles) of hepatic EVs. Dr Elena Palma, UK, (Twitter) described the effect of ethanol toxicity on mitochondria and the role of these organelles in the pathogenesis of ALD, with a particular focus on the impact on mitochondrial dynamics, megamitochondria formation and mitochondrial fragmentation.

<u>Dr Seddik Hammad</u>, Germany, described the characterisation via transcriptomic and proteomic analysis of a mouse model recapitulating critical features of ACLF, including fibrosis, inflammation, ductular reaction, and multiorgan failure. In particular, using CCl4 as precipitating event allowed the differentiation between good and bad prognoses to mimic patient conditions.

Bacterial infection in Alcoholrelated Liver Disease (ArLD). [Antonio Riva]

This symposium gave an overview of the causes and consequences of increased bacterial infection during ArLD, with a prospective outlook at novel potential therapeutic targets.

Dr Salvatore Piano from University of Padua, Italy, opened the symposium introducing epidemiological data on both bacterial and fungal infections in patients with advanced ArLD, with a special focus on the increasing rates of antimicrobial resistance observed. In the words of Dr Piano, "a judicious selection of empirical antibiotic treatment should be done according to local epidemiology, risk factors for multi-drug resistant bacteria, and severity of infection. Novel strategies should also be developed for preventing infections in patients with ArLD."

Prof Ali Keshavarzian from Rush Medical College, Chicago, the first to report gut barrier alterations in ArLD patients, presented conclusive evidence on microbial dysbiosis and disruption of gut barrier integrity, leading to increased bacterial translocation and systemic dissemination of pro-inflammatory bacterial products, in conjunction with environmental factors such as high-fat diet and disruption of circadian rhythms, two hallmarks of industrial societies and AUD.

Prof Bernd Schnabl from University of California, San Diego, shifted the focus to the intestinal virome, as bacteriophages and human viruses outnumber bacteria and fungi in the intestine, although little is known about their role in ArLD. In fact, viral diversity is increased in patients with ArLD, although the consequences of this phenomenon are unclear, and bacteriophages represent a novel therapeutic target against pathogenic bacteria, which could favour gut barrier restoration and improved outcomes.

The last speaker, <u>Dr Antonio Riva</u> (<u>Twitter</u>) from the Roger Williams Institute of Hepatology, London, presented an overview of the immunological alterations observed in ArLD patients consequent to gut barrier alterations and mi-

crobial translocation, with particular focus on inhibitory immune checkpoint pathways and subsequent unfavourable shifts in antibacterial immune responses. Targeting immune checkpoints appears to be safe in patients with sepsis, which

shares several immune features with advanced ArLD, and pre-clinical in-vitro data would support this novel host-targeted treatment strategy to reconstitute a competent intestinal and immunological environment in these patients.-

~ ECI Social Dinner in Kraków ~

We did it! The first Early-Career Investigators' dinner during the <u>joint ISBRA-ESBRA conference</u> earlier this year in Krakow turned out to be a very successful event.

With almost 50 participants, including the current members of the <u>ESBRA ECIC</u> and <u>ESBRA 'VIPs'</u> Prof Mickael Naassila, Dr Shilpa Chokshi, Dr Karoline Lackner and Prof Steven Dooley, the event brought together young researchers from many European and extra-European countries, including several non -ESBRA scientists affiliated with the International Society (ISBRA).

With their great location, fantastic food and a set limit of one drink per person during the evening, <u>Plac Nowy 1</u>, in the <u>heart</u> of the <u>Kazimierz quarter in Krakow</u>, truly excelled at <u>setting</u>

the stage for a very friendly, happy and productive evening, with lots of chances to get to know like-minded scientists and expand one's professional network.

Our ESBRA VIPs answered loads of questions, including many useful tips for career development, and we hope to see more and more collaborations stemming from this and all the future events that the ESBRA ECIC is planning to organise.

We are very thankful to the ESBRA Board of Directors for supporting this event, and we are looking forward to our next ESBRA Early-Career Investigator Social Dinner, which will take place during the <u>ESBRA 2023 conference in Graz, Austria</u>. We wish you a great 2023!

Check this space for more information, coming soon!-



ESBRA Nordmann Award 2023 . The European Society for Biomedical Research on Alcoholism (ESBRA) is pleased to announce the 2023 ESBRA Nordmann Award to recognise the significant contribution of an early career investigator in alcohol-related biomedical research. The applicant should be a European researcher, maximum in the 10th year after obtaining a PhD (with time allowed for parental leave in line with EU standards - 1.5 years per child for mothers and respective time taken off for fathers), who has undertaken most of the research in European institutions. The application has to be recommended by a letter from an active ESBRA member. The award consists of 3000 Euro and a certificate, and the winner will be presented during the 19th ESBRA Biannual Meeting 2023 (31 August - 03 September 2023) in Graz, Austria. Applications should include: (1) Curriculum Vitae, including a list of publications; (2) List of most significant publications; (3) An original text of 5 pages maximum with a summary of already published results and ongoing projects.

ESBRA Helmut Seitz Award 2023. We are happy to announce that "The Helmut Seitz Award of The European Society for Biomedical Research on Alcoholism" donated by the Manfred Lautenschläger Foundation will be continued for 2023. The Award will be granted to a well-established alcohol researcher who has contributed strongly to the understanding of alcohol-related and alcohol-associated diseases or the development of treatment strategies in alcohol-associated diseases. The recipient of the Award must have devoted most of his academic and research career to alcohol research. Potential awardees can be either nominated by ESBRA members or potential candidates can apply directly. The award consists of 25000 Euro, and the winner will be presented during the 19th ESBRA Biannual Meeting 2023 (31 August – 03 September 2023) in Graz, Austria. Applications should include: (1) a formal application letter; (2) Curriculum Vitae; (3) a list of publications.

New guidelines

Interview with Alexandre Louvet

Mickael Naassila — ESBRA President

In a recent issue of Liver international, the French Association for the Study of the Liver (AFEF) publishes joint guidelines with the French Alcohol Society about management of patients with alcohol-related liver disease. Alexandre Louvet, hepatologist in Lille, France, has served as a coordinator of these recommendations.

What these new recommendations are about?

"These clinical guidelines rely on an evidence-based level of recommendation and aim to summarize how patients with alcohol-related liver disease should be managed. Over the last years, the AFEF has published several recommendation texts to give strong rationale to hepatologists for adapting clinical care of patients suffering from various liver diseases. The present text is not only a list of evidence-based recommenda-

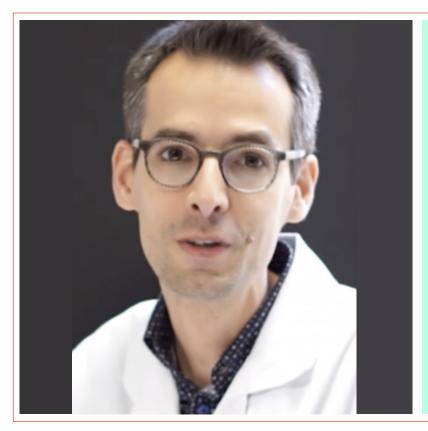
tions elaborated in French and then translated into English, it also represents one of the rare occasions for which addiction specialists and hepatologists have discussed, voted and modified recommendations to fit the actual clinical management of patients with excessive drinking."

What are the main topics?

"Main topics covered include screening of alcohol in the general population, how to detect alcohol consumption during a medical interview, impact of binge drinking on the liver, alcohol and comorbidities, assessment of fibrosis and steatosis, alcoholic hepatitis, etc. In fact, these joint guidelines have been designed to help addiction specialists manage patients with alcohol-related liver disease and to help hepatologists better understand addiction management."

How these new recommendations are useful for clinical practice?

"Screening for alcohol is crucial in clinical practice, especially for the general practitioner and for the specialist in digestive diseases. Talking about alcohol with our patients is simultaneously very simple and very complex and we hope these recommendations give the best validated approach to adapt the multidisciplinary care we can offer to them. Special attention has been paid to make these guidelines as practical as possible, taking into account that some firm evidence still lacks for several topics. We have also chosen to state the unmet needs for both clinical research and medical management that seemed important for us to address in the next years. We truly hope that these recommendations will be disseminated outside the French-speaking areas and that they will be helpful for hepatologists and addiction specialists."-



New alcohol guidelines of the French Association for Liver Studies (AFEF): https://afef.asso.fr

These guidelines have been published in Liver International

https://onlinelibrary.wiley.com/doi/10.1111/liv.15221

Link to download the French version of the guidelines:

https://afef.asso.fr/wp-content/ uploads/2021/01/AFEF Prise-en-charge -de-la-maladie-du-foie-liee-a-lacool.pdf

Videos on youtube:

https://youtu.be/OPs09amiMC0 https://youtu.be/RZXOGE7-SwY

Alexandre Louvet is Professor of Hepatology in the Gastroenterology Department of the University Hospital of Lille, France. Prof Louvet is also Associate Editor for the prestigious <u>Journal of Hepatology</u> (IF 2021 30.083). Email: <u>alexandre.louvet@chru-lille.fr</u>

Opinions & News in the Alcohol World

Boosting alcohol sales to raise more taxes is a bad idea: insights from behavioural economics

Jérôme Jeanblanc & Olli Kärkkäinen

n July, 2022, <u>Japan launched a contest</u> for new business ideas to increase alcohol consumption in the younger population. The fact is nowadays, young Japanese drink less alcohol than the elderly ones and this has some economic consequences. Tax revenues decrease and some companies are at risk of bankruptcy.

Such an initiative is misguided, as making people drink more seems both drastic in terms of public health, and a very short-term solution to fix low tax revenues. Indeed, in most countries the economic cost of alcohol use exceeds the income from the taxes related to the sale of alcohol beverages (example : France about €4 billion in tax revenues vs €120 billion in associated costs per year ; Expertise collective INSERM : Réduction des dommages associés à la consommation d'alcool).

Among the different ideas that can be proposed, the Japanese government suggests working on reducing the price of alcoholic beverages through the use of price promotions and discounts. It is already well known that the price of commodities will modify the buyer's behavior. This science is called behavioral economics and was first introduced in the 18th century by economists such as Adam Smith (1723 - 1790) and later developed by Vilfredo Pareto (1848 - 1923). After a decrease in interest in the early 1900's a revival of this theory occurred in the 1960's with the rise of cognitive psychology, but Hursh (1980, 1984) described the integration of microeconomic principles with behavior analysis and the ways in which behavioral economic principles could be applied in both animal and human models of consumption.

In short, behavioral economics examines the relationship between price and consumption, or *demand*, and several indices quantify aspects of demand (Hursh & Roma, 2016). For example, the extent to which price increases produce decreases in consumption is labeled demand *elasticity*, while "unconstrained" consumption, or consumption at zero price, is termed demand *intensity*. Other indices include maximum expenditure (Omax), and the

price at which Omax occurs, or Pmax. Omax and intensity, in particular, are strongly associated with alcohol use and severity (Martinez-Loredo et al., 2021; Zvorsky et al., 2019).

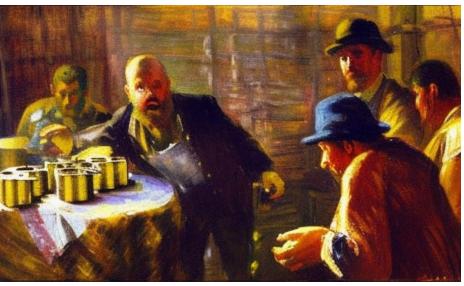
Demand analysis has been a useful tool to examine consumption of alcohol among young adults, among whom binge drinking is prevalent. Prof. Margaret Martinetti and her colleagues have used the hypothetical Alcohol Purchase Task (APT) (Murphy & MacKillop, 2006) to study demand for alcohol in university students from the U.S. and France (Martinetti et al., 2019), and have examined demand for alcohol-related commodities, such as "bottomless cups" (Morrell et al., 2021). They also created a modification of the APT, the APT Choice (Martinetti et al., 2019), that includes a non-alcoholic option at a fixed low price. Taken together, her work along with that of many others, reveals that low alcohol prices are associated with binge-level consumption, but that consumption decreases when drinks are more expensive.

Prof. Martinetti notes that the APT Choice measure may be useful in the study of "substitutes" for alcohol in American and European cultures. For example, she and her colleagues at the GRAP Laboratory in Amiens, France found that both American and French university students demonstrated a decrease in alcohol demand when the non-alcoholic option was available (Martinetti et

al., 2019). Although the APT Choice requires additional replication, her recent U.S. findings further support its utility: Ortelli and Martinetti (Ortelli and Martinetti, 2021) found that the non-alcoholic option reduced alcohol demand, particularly among younger university students involved in fraternity and sorority organizations. She hopes that these findings will inform harm-reduction efforts among high-risk students and young adults.

Reducing alcohol prices is likely to increase consumption among the young population, potentially creating a new generation of life-long consumers, who may then be more vulnerable for AUDs. Interestingly, some countries, such as Scotland (2018), England and Wales (2020), have introduced a minimum unit pricing for alcohol with promising results in the reduction of alcohol consumption in young population. WHO published a report in June 2022 on this topic named: No place for cheap alcohol — The potential value of Minimum Pricing for protecting lives.

So, in most countries, economic interests are likely to prevail over the health of young populations. Some countries have decided to introduce a minimum price for alcoholic drinks. The latest studies on the impact of alcohol on young people, as well as data from the field of behavioral economics, clearly show an interest in increasing the price of alcohol to reduce its consumption.-



"The alcohol tax collector", Antonio Riva © via StableDiffusion

ESBRA Early-career Investigators Committee (EECI)

Call for new members to join the ESBRA Early-career Investigators committee

Are you an early-career investigator engaged in alcohol-related research in Europe and would like to connect with other ECI? Would you like to raise awareness about alcohol? Are you interested in organizing events/webinars/symposium and in outreach activities?

The <u>ESBRA Early-career Investigators & Comm (EECI) committee</u> is now launching a call for new members to join the EECI committee. The term for these members is for two years from 1st April 2023 to 1st April 2025.

The EECI Committee was established in February 2022 after the idea of ESBRA President Prof. Mickael Naassila to improve the promotion of ESBRA society. The EECI Committee is currently formed by 9 ESBRA members with different backgrounds and interests, coming from 7 European countries (France, UK, The Netherlands, Sweden, Italy, Finland, Russia) with a common mission "To enhance engagement and create opportunities for collaborations within the ESBRA community to further advance alcohol-related biomedical research in Europe."

The EECI Committee aims to promote research conducted by ESBRA members, especially by early -career scientists and clinicians within the Society; enhance the visibility of ESBRA through social media platforms (Social Media team); spread communication to facilitate collaborations, through a periodic Newsletter; provide regular opportunities for networking amongst EECI members; boost educational activities in alcohol-related research; attract new European ECI with interest in this field to be part of ESBRA.

Eligibility criteria:

- Applications are sought from young, independent scholars who combine the highest level of research excellence with a demonstrated passion for delivering impact.
- The candidate must have a background in alcohol-related research.
- The candidate must be living in a European country.
- The candidate must become an ESBRA member when accepted as a EECI Committee member (or be already a member at time of application).

Your application should include:

- a letter of motivation and your aspirations to join the EECI, including what you would bring and a brief proposal/suggestion on what you would like to see realised by the EECI committee.
- an updated CV (2-pages) including the most relevant scientific publications (up to 5), and relevant skills including experience with newsletters, science communication, organizing events, social engagement, and outreach.

The call is open until 15th March 2023. Send your application to the ESBRA office (office@esbra.com). For questions, please do not hesitate to contact the EECI committee chair Elena Palma (e.palma@researchinliver.org.uk).

The new EECI members will be announced in the EECI newsletter published in April 2023.



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How to become a member of ESBRA:

https://www.esbra.com/membership

ESBRA calendar:

https://www.esbra.com/calendar

Job opportunities:

https://www.esbra.com/job-announcements

ESBRA awards:

https://www.esbra.com/awards

Further links:

https://www.esbra.com/links

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