locomotor effects of amphetamine require astroglial CB1 receptors in male, but not female mice. Thus, our results show that astroglial CB1 receptors mediate long-term synaptic depression in the NAc core and suggest that the interaction between amphetamine and the ECS is different in males and females. These results, by revealing unforeseen mechanisms underlying sex-dependent effects of amphetamine, will pave the way to better understanding the diverse impact of psychostimulants in women and men.

Declaration of Interest Statement: None

https://doi.org/10.1016/j.ibneur.2023.08.356

P0352 / #2072

Topic: AS04 Neurons and Glia: Physiology and Inter-Cell Communication

EFFECT OF MICROGLIAL ACTIVATION ON NEURONAL MU-OPIOID RECEPTOR EXPRESSION AND SIGNALLING

Javier Cuitavi [1,2], Pere Duart-Abadia [3,4,5], Julie Sanchez [6,7], Christian M. Sánchez-López [2,8], Jesús Lorente [2], Antonio Marcilla [2,8], Isabel Fariñas [1,4,5], Meritxell Canals [6,7], Lucía Hipólito [1,2]

[1] *University of Valencia, University Institute Of Biotechnology And Biomedicine (biotecmed), Burjassot, Spain*
[2] *University of Valencia, Pharmacy And Pharmaceutical Technology And Parasitology, Burjassot, Spain*
[3] *University of Valencia, Instituto De Biotecnología Y Biomedicina (biotecmed), Burjassot, Spain*
[4] *University of Valencia, Centro De Investigación Biomédica En Red Sobre Enfermedades Neurodegenerativas (ciberned), Burjassot, Spain*
[5] *University of Valencia, Cellular Biology, Functional Biology And Physical Anthropology, Burjassot, Spain*
[6] *School of Life Sciences, Queen's Medical Centre, University of Nottingham, Physiology, Pharmacology And Neuroscience, Burjassot, United Kingdom*
[7] *Universities of Birmingham and Nottingham, Centre Of Membrane Proteins And Receptors (compare), Nottingham, United Kingdom*
[8] *UV-IIS La Fe, Endocrinology, Nutrition And Clinical Dietetics, Valencia, Spain*

Chronic pain is a burden for many health systems and the use of opioid to treat it has massively contributed to "the opioid epidemic", which affects many patients that now suffer from opioid use disorders (OUDs). Neuron-glial interactions have gained momentum in the last few years and seem to play a pivotal role in pain-induced OUDs. Additionally, Mu-Opioid receptors (MORs) are involved in both pain processing and opioid-driven reward, partially due to the action of neuroinflammatory processes. Herein, we present a new interaction between glial and neuronal MORs that might be a target to consider when treating pain-induced OUDs. In this sense, we used primary microglial cell cultures, which were treated with vehicle or 10 ng/mL lipopolysaccharide (LPS) for 24 h. Then, the extracellular medium containing microglial secretome was characterised and stored in two different batches, one of them was left without further manipulation, whereas the other one was used to isolate its soluble fraction, which includes proteins. SH-SY5Y cells, a neuron-like cell line, were treated with the microglial secretome, its soluble fraction, or commercial proinflammatory cytokines for 24 h. After this time, Bioluminescence Resonance Energy Transfer (BRET) assays were carried out to assess agonist-induced MOR signalling, and MOR protein expression was measured by a simple read of total bioluminescence. Results showed that neuroinflammation environments increase neuronal MOR expression and activation. We also tested if MOR-triggered cytokine-enriched NAc dialysates also promote neuronal MOR signalling and expression. Interestingly, we found the same results as in the previous experiment. Altogether these results suggest that opioids could be modulating neuronal MORs by activating glial MORs, which will most likely lead to new therapeutical approaches when treating pain-induced OUDs.

Declaration of Interest Statement: None

https://doi.org/10.1016/j.ibneur.2023.08.357

P0353 / #1650

Topic: AS04 Neurons and Glia: Physiology and Inter-Cell Communication

DIRECT AND INDIRECT AIR POLLUTION EFFECTS ON SYNAPTIC TRANSMISSION LINKED TO THE DEVELOPMENT OF NEURODEGENERATIVE DISEASE

Sara Di Girolamo [1], Giulia Terribile [1], Paolo Spaiardi [2], Gerardo Biella [2], Slvia Sesana [3], Francesca Re [1,3], Giulio Sancini [1,3]

[1] *University of Milano-Bicocca, Department Of Medicine And Surgery, Monza, Italy*
[2] *University of Pavia, Department Of Biology And Biotechnologies, Pavia, Italy*
[3] *University of Milano-Bicocca, Nanomedicine Center, Monza, Italy*

In recent years, human epidemiological and animal studies show how the Central Nervous System (CNS) is emerging as an important target for adverse health effects of air pollution (AP), where they may be strongly associated with neurodegenerative disorders, such as Alzheimer's disease (AD). Specifically, different studies demonstrate how exposure to AP induces synaptic plasticity impairment, both directly and indirectly. Our first aim is to investigate how AP modifies and invalidates delicate and complex mechanisms on which synaptic plasticity depends, including multiple neurotransmission signals, whose function is at the base of memory process. For this purpose, we exposed mouse brain slices to *Diesel Exhaust Particles* (DEP) (Reference Material), which constitute an important component of AP and can mimic its effects on CNS. We performed electrophysiological experiments through the *Whole-Cell Patch Clamp* technique on pyramidal neurons of the neocortex. DEP induce a widespread decrease of *spontaneous Excitatory and Inhibitory Post Synaptic Currents* (sEPSCs/sIPSCs) frequency with critical alterations on the pre-synaptic neurotransmitter release. Furthermore, we executed *in vitro* experiments through the *Calcium Imaging* technique on different neuronal support cells belonging to the Neurovascular Unit (NVU), which can modulate neurotransmission indirectly. DEP cause a strong decrease of the calcium wave response in different NVU cells. Hereafter, our second aim is based on preliminary results that highlight the effects of multifunctional liposomes (mApoE-PA-LIP) as a putative therapeutic tool for AD treatment. In particular, mApoE-PA-LIP can enhance NVU cells activity and ameliorate mouse model memory impairment. Thus, we tested the direct and indirect effects of mApoE-PA-LIP on synaptic transmission before and after DEP exposure with both *ex vivo* and *in vitro* experiments. In

conclusion, AP produces significant direct and indirect modifications on physiological mechanisms of neurocommunication linked to the development of AD, for which mApoE-PA-LIP could be promoted as a strategy to counteract neurotransmission impairment.

Declaration of Interest Statement: None

https://doi.org/10.1016/j.ibneur.2023.08.358

P0354 / #3731

Topic: AS04 Neurons and Glia: Physiology and Inter-Cell Communication

DECIPHERING THE ROLE OF THE NOVEL INTERNEURON POPULATION PTHLH IN THE MOUSE STRIATUM

Mónica Díez Salguero [1], Lisbeth Harder [2], Meritxell Llorca-Torralba [3,4], Marla Herr [2], Juan Manuel Barba Reyes [1], Esther Berrocoso [3,4], Jens Hjerling-Leffler [2], Ana Muñoz Manchado [1,2]

[1] *University of Cádiz, Dep. Of Pathological Anatomy, Cell Biology, Histology, History Of Science, Forensic And Legal Medicine And Toxicology. Inibica (institute Of Biomedical And Innovative Research Of Cadiz., Cádiz, Spain*
[2] *Karolinska Institutet, Department Of Medical Biochemistry And Biophysics, Stockholm, Sweden*
[3] *Ciber of Mental Health (CIBERSAM), ISCIII, Cb/07/09/0033 Group, Madrid, Spain*
[4] *Institute of Research and Innovation in Biomedical Sciences of Cádiz (INiBICA), Neuropsychopharmacology And Psychobiology Research Group, Cadiz, Spain*

Striatal interneurons are a diverse group of neurons that represent around 5% of the total neuronal population, the other 95% are projecting neurons known as MSNs (medium spiny neurons). Despite their small number, the interneurons are essential in the basal ganglia regulation as they integrate incoming information from different brain areas and act on MSNs activity to modulate the output information. A recent study from Muñoz-Manchado et *al.* (Cell Reports, 2018) revealed an abundant GABAergic striatal population of *Pthlh*-expressing interneurons. These Pthlh-expressing interneurons are characterised by a variable *Pvalb* expression level and a broad continuum of intrinsic electrophysiological properties, which correlates both with *Pvalb* levels and a regional pattern within the striatum with differential input areas (Bengtsson et *al.*, 2020). In a more recent study of our group we show also that PTHLH constitute one of the largest interneuron populations of the human dorsal striatum (Garma et *al.*, https://www.biorxiv.org/content/10.1101/2023.03.22.533839v1). With the purpose to understand the role of this novel interneuron population on the basal ganglia circuit we have designed the Pthlh^{cre}::R26R-tdTomato mouse line. We have used quantitative FISH to histologically characterise the dorsal striatum of this line, finding that around 90% of Pthlh cells are labelled with the reporter gene *tdTomato*, making it a proper tool to investigate the role of the Pthlh population in the striatal circuit. We will also confirm these results studying the electrophysiological properties of the cells expressing the reporter gene. Moreover, we aim to investigate the role of the Pthlh population in the circuit using the DREADDs technology. This tool will allow us to modify the *Pthlh*-expressing cells activity using our transgenic mouse. We will run a complete behavioural pipeline in order to assess both cognitive and motor functions.

Declaration of Interest Statement: None

https://doi.org/10.1016/j.ibneur.2023.08.359

P0355 / #3289

Topic: AS04 Neurons and Glia: Physiology and Inter-Cell Communication

JOINT MODULATION OF INTERPEDUNCULAR NUCLEUS NEURONS ACTIVITY BY NGF AND RELAXIN-3 - POSSIBLE ROLE IN CONTROL OF STRESS AND ANXIETY RELATED BEHAVIOURS

Sylwia Drabik, Aleksandra Trenk, Anna Gugula, Patryk Sambak, Angelika Kaleta, Gabriela Stopka, Anna Blasiak

Institute of Zoology and Biomedical Research, Jagiellonian University, Department Of Neurophysiology And Chronobiology, Krakow, Poland

Interpeduncular nucleus (IPN) is a highly complex and evolutionary-conserved, midbrain structure lying at the posterior end of the interpeduncular fossa. It is anatomically divided into seven subnuclei, which neuronal populations express different chemical markers. IPN is densely innervated by medial habenula (MHb) originating, cholinergic fibers which are known to mediate the aversive effects of nicotine and nicotine withdrawal, fear and anxiety and novelty preference. Another important source of IPN innervation comes from nucleus incertus (NI) – a highly stress-sensitive structure involved in the control of anxiety, arousal and stress responses, and the source of relaxin-3 (RLN3) neuropeptide, the highly specific ligand for relaxin family peptide receptor 3 (RXFP3). Interestingly, IPN is characterized by a high level of expression of the nerve-growth factor (NGF) receptor TrkA, and NGF was shown to control stress- and anxiety-related behaviours. Taken together these data we hypothesise that IPN-NI axis is involved in stress response control and remains under the modulatory influence of NGF. Multiplex *in situ* hybridization allowed us to characterise the distribution of mRNA for TrkA, and its co-expression with RXFP3 as well as with vGAT1 and GABA- neurons marker). Multielectrode array recordings revealed both excitatory and inhibitory effects of NGF administration on IPN neurons. Moreover, during whole-cell patch clamp recordings we observed NGF evoked inward whole-cell current in IPN cells. Finally, viral based neural tract-tracing of NI neurons innervating IPN shown a distinct innervation pattern in septal area and ventral hippocampus. Obtained results proved GABAergic nature of TrkA/RXFP3 co-expressing IPN neurons. NGF administrations confirmed its ability to modulate activity of IPN neurons. Moreover, tract-tracing results suggest that NI-IPN axis is involved in stress response. **Founding:** National Science Centre, Poland (UMO-2018/30/E/NZ4/00687); National Science Centre, Poland (UMO 2021/41/N/NZ4/04499)

Declaration of Interest Statement: None

https://doi.org/10.1016/j.ibneur.2023.08.360