EUROPEAN HISTAMINE RESEARCH SOCIETY

Webinars 2021 - 2022

Festive Virtual Poster Event focused on Neuronal Histamine

THURSDAY 16 DECEMBER 2021

12.00-13.30 CET

Organized by Prof. Paul Chazot (Durham, UK) and Dr. Ilona Obara (Newcastle upon Tyne, UK)

Programme

12:00-12:05 ***Introduction***, Paul Chazot (Durham, UK)

12:05-12:20 ***Bed Nucleus of Stria Terminalis as a novel source of extra striatal histamine***

Ricardo Marquez Gomez (Oxford, UK)

12.20-12.35 ***Systematic search for hypothalamic neuropathology in narcolepsy type 1***

Ling Shan (Leiden, The Netherlands)

12.35-12.45 ***Discussion***

12.45-13.05 ***Poster presentations*** (2 min each)

- *Diet prevents social stress-induced maladaptive neurobehavioral and gut microbiota changes in a histamine-dependent manner*, Barbara Rani (Florence, Italy)
- *Chemogenetic activation of histaminergic neurotransmission improves memory expression*, Alessia Costa (Florence, Italy)
- *Unravelling the role of histamine neurons in memory processes through chemogenetics: potential sex differences*, Lola Hardt (Bordeaux, France)
- *3D reconstruction of brain wide neuronal circuits involved in aversive memory following A-fluoromethylhistidine*, Alessandra Franceschini (Florence, Italy)
- *Maternal administration of the histamine H_1 receptor (H1R) antagonist/inverse agonist chlorpheniramine affects rat offspring cerebral cortex development*, Rocío Valle-Bautista (Mexico City, Mexico)
- *Search of the way of MAO-B inhibition by the known histamine H_3 receptor ligands*, Agnieszka Olejarz-Maciej (Kraków, Poland)
- *Dual histamine H3 and sigma-1 receptor ligands as novel pharmacological tools in the treatment of central nervous system disorders with the focus on neuropathic pain*, Katarzyna Szczepańska (Kraków, Poland)
- *An overview of histaminergic signaling in Amyotrophic Lateral Sclerosis*, Savina Apolloni (Roma, Italy)

13.05-13.30 ***Discussion - Concluding remarks***

Paul Chazot (Durham, UK) & Ilona Obara (Newcastle upon Tyne, UK)

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webex by cisco **THURSDAY 16 DECEMBER 2021 AT 12.00-13.30 CET**

Organized by Prof. Paul Chazot (Durham, UK) and Dr. Ilona Obara (Newcastle upon Tyne, UK)

Abstracts

Oral presentations

*Bed Nucleus of Stria Terminalis as a novel source of extra striatal histam*ine

Ricardo Marquez Gomez (University of Oxford, UK, ricardo[dot]marquezgomez[at]dpag[dot]ox[dot]ac[dot]uk)

The Bed Nucleus of Stria Terminalis (BNST) is a limbic system nucleus relevant for anxiety behaviours. We found histamine-positive clusters of axonal projections in the BNSTov locating in the striatal vicinity at postnatal days 9-12 (P9-12), a crucial period for striatal development. Given the low striatal histaminergic innervation at this age range, we explored whether BNSTov could serve as an extra-striatal source of histamine during P9-12. Our results suggest a novel role of histamine as a paracrine modulator of striatal synaptic transmission.

Systematic search for hypothalamic neuropathology in narcolepsy type 1

Ling Shan (Leiden University Medical Centre, Netherlands, l[dot]shan[at]nin[dot]knaw[dot]nl)

Narcolepsy type 1 (with cataplexy) is a rare invalidating chronic sleep disorder caused by a loss of hypocretin neuropeptides, presumed to be due to an auto-immune process. A systematic search for possible involvement of other hypothalamic neurons implicated in sleep-wake regulation has never been performed. We systematically quantified immunohistochemically stained sleep-wake related neuronal populations and the presence of microglia reactions in the hypothalamus comparing narcolepsy type 1 (n=4) with idiopathic hypersomnia (n=1) and matched controls (n=5). Biological clock: there was no difference in the numbers of vasopressin-expressing neurons in the suprachiasmatic nucleus. Sleep promoting neurons: the density of galanin positive neurons in the ventrolateral preoptic nucleus was stable. Arousal related neurons: we confirmed the hallmark loss of hypocretin-1 expressing neurons and the increased numbers of histidine decarboxylase positive histaminergic neurons. The density of choline acetyltransferase-expressing neurons in the nucleus basalis of Meynert was unchanged. Microglial reactions: The presence of ionized calcium binding adaptor molecule 1 tended to be increased in the hypocretin area, but not in any other adjacent area. The human leukocyte antigen-staining was similar in all these areas. These data support the hypothesis that narcolepsy type 1 is associated with loss of hypocretin-1 expressing neurons and the increased numbers of histidine decarboxylase positive histaminergic neurons in the hypothalamus. Results of other arousal nuclei under study will be reported.

Poster presentations

Diet prevents social stress-induced maladaptive neurobehavioral and gut microbiota changes in a histamine-dependent manner

Barbara Rani (University of Florence, Italy, barbara[dot]rani[at]unifi[dot]it)

In this study we demonstrated a new role for brain histamine as a mediator of the beneficial effects of PUFA/vitamin-A enriched diet against the cognitive and neurochemical disruptions caused by chronic stress. To this aim we used Hdc-/- and Hdc+/+ mice. Social defeat stress, a validated model of chronic stress in mice, induced social avoidance, memory impairment, affected long-term-potentiation in the hippocampal CA1 region, caused changes in microbiota profile, oxylipins expression of both Hdc-/- and Hdc+/+ mice. Dietary supplementation since weaning prevented stress-induced deficits only in Hdc+/+ mice. Histamine deficiency prevented almost all of these diet-related beneficial effects.

Chemogenetic activation of histaminergic neurotransmission improves memory expression

Alessia Costa (University of Florence, Italy, alessia[dot]costa[at]unifi[dot]it}

To interrogate the function of brain histamine we chemogenetically activated the histaminergic neurons in HDC-Cre mice. Specifically, HDC-Cre mice were injected bilaterally into the TMN with excitatory DREADDs or related control, to transfect histaminergic cells. The mice were then tested for social, spatial and fear memories followed by DREADDs activator Clozapine-N-Oxide (CNO) injection. Here, we observed a memory improvement in all tested tasks when histaminergic cells were chemogenetically activated.

Unravelling the role of histamine neurons in memory processes through chemogenetics: potential sex differences

Lola Hardt (Bordeaux University, France, lola[dot]hardt[at]u-bordeaux[dot]fr

Histamine is a known modulator of memory processes. Previous studies were based on histamine receptors pharmacology or histamine depletion which have inherent limitations, restricting the ability to clearly separate the implication of histamine transmission between consolidation and retrieval. Our study thus used a chemogenetic approach in order to specifically silence histaminergic neurons during either memory formation or retrieval in three different long-term memory tasks, i.e. Object Recognition Memory (ORM), Inhibitory Avoidance (IA) and Social Recognition Memory (SRM), in both males and females. Chemogenetic histamine modulation specifically during training impairs ORM at 48h but not 24h, independently of sex. Similar manipulations during IA training or retrieval have an opposite effect in both sexes at 7 days but not 48h,attenuating retention in males but enhancing it in females. Finally, histaminergic neurons silencing had no impact on SRM assessed at 24h in males (with sex differences as SRM was not effective in females at 24h). Our results confirm the implication of histamine in memory consolidation and further indicate an additional form of implication in later consolidation stages necessary for long-term memory persistence. Moreover, our results stress the complexity of histamine implication in those processes through the discovery of opposite sex effects of histamine neuron inhibition in the aversive memory task.

3D reconstruction of brain wide neuronal circuits involved in aversive memory following a-fluoromethylhistidine

Alessandra Franceschini (University of Florence, Italy, franceschini[at]lens[dot]unifi[dot]it)

The central histaminergic system is an important modulator of memory related to adverse events. Researchers have proved that the histamine neurotransmitter is necessary for long-term memory (LTM) but not short-term memory of step-through inhibitory avoidance (IA). Our aim is to understand how neuronal patterns, involved in formation and storage of fear memory, change with a histamine depletion using whole brain mapping of c-fos expression.

Maternal administration of the histamine H_1 receptor (H1R) antagonist/inverse agonist chlorpheniramine affects rat offspring cerebral cortex development

Rocío Valle-Bautista R (Centro de Investigación y de EstudiosAvanzados del Instituto Politécnico Nacional, México, rociovb26[at]gmail[dot]com)

Histamine increases deep-layer pyramidal neurons (DLPN) differentiation of the neocortex through H1R activation, while chlorpheniramine (Chlor) decreases neuronal differentiation during early corticogenesis in the rat. To explore possible long-term effects of the maternal administration of Chlor during DLPN differentiation, we evaluated postnatal changes on neurons, cytoarchitecture and function of the primary motor cortex in the offspring.

Search of the way of MAO-B inhibition by the known histamine H3 receptor ligands

Agnieszka Olejarz-Maciej (Jagiellonian University, Poland, agnieszka[dot]olejarz[at]uj[dot]edu[dot]pl)

Dual-targeting ligands (histamine H_3 receptor and MAO-B inhibitors) are reported to be a promising approach for the treatment of Parkinson's disease. We chose the most active dual-target ligands from our Library for more detailed MAO-B inhibition studies. For this purpose, the reversibility and modality of the inhibition were examined and results were compared with reference MAO B inhibitor(s) showing a similar inhibition pattern.

Dual histamine H_3 and sigma-1 receptor ligands as novel pharmacological tools in the treatment of central nervous system disorders with the focus on neuropathic pain

Katarzyna Szczepańska(Jagiellonian University, Poland, szczepanskatarzyna@gmail.com)

Recent studies have shown that some clinically evaluated histamine H3 receptor (H3R) antagonists possess nanomolar affinities at sigma-1 receptor (σ1R) binding sites, and therefore we selected twenty representative structures among our previously reported H3R ligands to investigate their affinity at σRs. Most of the tested compounds interact with both sigma receptors (σ1R, σ2R) to different degrees. Interestingly, ligands KSK68 and E377 turned out to be high-affinity histamine H3 and σ1 receptor antagonists with negligible affinity at the other histamine receptor subtypes and promising antinociceptive activity in vivo.

An overview of histaminergic signaling in Amyotrophic Lateral Sclerosis

SavinaApolloni (Fondazione Santa Lucia Istituto di Ricovero e Cura a Carattere Scientifico, Italy, Savina.Apolloni@uniroma2.it)

Amyotrophic lateral sclerosis (ALS) is a late-onset neurodegenerative disease that primarily affects motor neurons. We identified some histamine-related genes that are deregulated in the spinal cord of patients with ALS and we showed that the pharmacological increase of the histamine content in transgenic ALS mice decreases neuroinflammation, reduces death and dendritic spine loss in motor neuron, and increases mice life span. Moreover, by a network-based algorithm for drug repurposing, we identified histaminergic drugs as potential innovative solutions for ALS therapy.