IX Jornadas Olfativas

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EDUCATION THROUGH OLFACTION: A TOUR OF SPACE WITH AROMATOM

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Identifier: 42
Type of communication: ABSTRACT SUBMISSION

Introduction: ‘AromAtom: Discover the Smell of Space’ is a science outreach project, designed to engage the public with what are often seen as difficult subjects – space exploration, astronomy, chemistry and geophysics. Whilst much of the science outreach work done in these areas targets audiences already interested in space, the aim of this project is to reach those audiences who have never engaged with space exploration and astronomy, but who would be enticed by the subject if presented in a creative and evocative manner.

AromAtom utilises the sense of smell to do exactly that, and uses space-smells to hook the audience, and to ignite the curiosity and imagination of children and adults. It takes participants on a journey during which they discover space by smelling odours related to the composition of planetary bodies and molecular clouds, and to the accounts of Apollo and ISS Astronauts.

An Olfactory Encounter with Space: The project takes participants on a guided tour of space using their sense of smell as a guide. This tour has a number of ‘stops’ during which planets and satellites are explored before travelling to the arms of the Milky Way and the Galactic Centre. At each stop, participants are surrounded by images of their location while experiencing a number of smells based on scientific data relating the surfaces and atmospheres of planetary bodies, the geophysical processes that shape planets and satellites, and the molecular composition of dust and gas clouds. At the same time, they are told why and how such odours might be found at different locations in space. Basic astrochemistry, astronomy and geophysical concepts are weaved into the story to help form a realistic idea of what the space-location might be like, and to give context to the olfactory experience.

Target Audience: Science is not just for scientists, AromAtom is for everyone. At its most basic level, its primary goal is to demystify science by presenting it as a fun and accessible experience that anyone can participate in, regardless of age, education, background or disability. It does this by utilizing the most undervalued of the five senses, the sense of smell, and by taking advantage of its ability to evoke emotions and to help recall past events and positive experiences.

Adults. Although participants with diverse scientific interests enjoy the experience and learn new things, the events are designed to reach audiences who do not usually engage with the scientific community, especially those from creative and artistic backgrounds, who often think of science as clinical and boring. The bizarre and unusual space-smells are used not just to enhance the learning experience, but to engage the imagination and prompt participants to ask questions and offer their thoughts and ideas, making the experience inclusive and interactive.

Children. In schools and learning centres children enjoy an educational experience that provides inspiring and engaging activities led by their sense of smell. Through it, they learn about the origin and evolution of the Solar System, get excited about space exploration missions, and are shown that they too can be part of the excitement, become scientists making new discoveries about space, and even train as astronauts. At the same time, teaching staff discover the advantages of using the sense of smell in educational settings, whilst being encouraged to use it in the classroom to create a positive and engaging learning experience for their pupils.

Past Activities: The pilot AromAtom exhibition took place in London on 6 December 2017, and was attended by artists, photographers, engineers, space science students and university lecturers. Since then, further events have been held across the UK, Spain and the USA, including at the 50th Lunar and Planetary Science Conference in Houston, the Bluedot Science Festival at Jodrell Bank Observatory, the Natural History Museum and the Science Museum in London, and the Royal Society.

Additionally, the project has worked with schools in the UK and Spain, with the London Science Museum at their SENsory Astronights for children with special educational needs or disabilities, and with the UK Association of Science and Discovery Centres.

On the role of antennal scales on insect olfaction

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Identifier: 3
Type of communication: ABSTRACT SUBMISSION
Keywords: insect, olfaction, antenna, sensilla, scale

The insect antenna houses olfactory receptor neurons inside porous cuticular microstructures called sensilla. In addition to sensilla, some insects also bear non-sensory cuticular microstructures (scales) on the antennae. It has been theorized that scales aid in olfaction, but solid experimental proof is lacking. In order to provide additional substrate for further predictions, we mapped the position of every sensilla of all sensory modalities (olfactory, gustatory, mechanosensory, and higro-thermo sensory), along with every scale along the male and female antennae of three moth species. Sensilla and scales appear to "compete" for space on the antennal wall. They either segregate on different locations or co-occur forming specific spatial arrangements on the surface of each segment. Sensilla are either fully exposed to the environment or covered (partially or totally) by scales. Males show a proximal and a distal row of sensilla trichodea which suggests that these are devoted to sex pheromone detection. However, pheromone-sensitive sensilla are also known from other areas of the male antennal segments, which calls for a study of the correlation of position and function of moth antennal sensilla. The location of the other sensilla types (auricillica [sensible to plant volatiles], coeleconica [sensible to acids], hygro-thermo and mechano-gustatory) relative to scales suggest a possible role of scales on the function of these sensilla.

Unravelling the olfactory system of the beet armyworm (Spodoptera exigua)

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Identifier: 11

Type of communication: ABSTRACT SUBMISSION

Keywords: odorant receptors, ionotropic receptors, sensilla, olfactory sensory neuron, olfactory-driven behaviour, FISH, SEM, CRISPR-Cas9.

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The beet armyworm, Spodoptera exigua, is a common lepidopteran pest worldwide that feeds on various crops during its caterpillar stage. Insects perceive odorant information from the environment, which influences fundamental behaviours such as food choice, mating, egg-laying and parasitoid or predator avoidance. Consequently, characterizing the olfactory system is crucial for the understanding of the ecology of insect species, and in designing control strategies based on manipulating olfactory-driven behaviours. The main olfactory organs of insects are the antenna and the maxillary palps, which are covered in tiny hairs called sensilla. The sensilla encapsulate and protect the dendrites of the olfactory sensory neurones (OSN), where the Odorant Receptors (ORs) and the antennal Ionotropic Receptors (aIRs) are expressed. Those receptors constitute the main pieces of the olfactory system being responsible for the odorant detection. Two olfactory receptors are required for neuron activation, a single and specific-binding receptor and a coreceptor(s): ORCO (Odorant Receptor Coreceptor) for Odorant Receptors and IR8a or IR25a for Ionotropic Receptors. The binding of the volatiles to these two types of receptors triggers the activation of the olfactory sensory neurons that will transfer information to the high brain centres, which execute the appropriate behavioural response. In order to fully understand how the olfactory system of S. exigua larvae works, it is essential to know it at a physiological, molecular and functional level. First, we studied the morphology of the olfactory organs using the scanning electron microscope (SEM). We observed that the antennae, similar to other insects, are composed of three segments. We found eight sensilla on each antenna and each maxillary palp, being six and three of the olfactory type, respectively. Currently, we are using fluorescence in situ hybridization (FISH) to map the OSN housed in each sensillum, and the corresponding OR and aIR. So far, we have found that ORCO is expressed in every OSN of the olfactory sensilla and IR8 is expressed on the antenna. However, we have not observed expression of IR25 on the olfactory organs of S. exigua larvae. Besides, we are interested in verifying the fundamental role of ORCO in the larval olfactory-driven behaviour. For this, we have knocked out the ORCO gene using the CRISPR-Cas9 genome editing technique. Currently, we are performing behavioural assays comparing the response to an olfactory stimulus of ORCO-knockout and wildtype larvae. Overall, our study provides valuable insights into the olfactory equipment of S. exigua, which will facilitate further studies aimed to deepen into the ecology of this species, and in designing new olfactory-based control strategies.

Contributions of PPL2 dopaminergic neurons to the modulation of olfactory behaviour

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Identifier: 2
Type of communication: ABSTRACT SUBMISSION
Keywords: Dopamine, Mushroom Body, Lateral Horn, Memory

Dopaminergic circuits are involved in learning, motivation, arousal and salience-based decision making, among others. In the fruitfly brain discrete clusters of dopaminergic neurons innervate brain areas associated with innate olfaction and olfactory memory. These clusters have established roles in encoding the valence of a stimulus. However, mammalian literature has identified dopaminergic neurons involved in motivational salience, regardless of the value (positive or negative) of the sensory signal.

Here we investigated the role of PPL2 in both learnt and innate olfactory behaviour. Firstly, we identified a role of PPL2 neurons in associative olfactory memory, enhancing neural responses in memory neurons and modulating memory strength. We addressed how artificial activation of PPL2 neurons affects olfaction at a range of odour concentrations using olfactory Y-mazes, finding that PPL2 activation enhances approach behaviour at low stimulus concentrations, and promotes olfactory aversion at a higher concentrations. Secondly, a connectome-based investigation of PPL2 outputs revealed inhibitory neurons as some of the main post-synaptic targets in both the main memory center of the fly brain (mushroom body) and the area of the brain tipically associated to innate olfaction (lateral horn). Overall, the data presented here suggest a role for PPL2 in olfaction, regardless of stimulus valence, and provides us with targets to further investigate the PPL2 circuit to shed light onto the dopaminergic modulation of behaviour.

GENETIC BASIS OF GLIAL REGULATION OF OLFACTORY RECEPTION IN DROSOPHILA

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Identifier: 36
Type of communication: ABSTRACT SUBMISSION
Keywords: antenna, transcriptomics, Drosophila, glia, olfaction

Glia plays an essential role in the development, homeostasis, and modulation of the activity in the neurons of the central nervous system. However, in the peripheral nervous system, such as that involved in olfactory reception, data are scarcer. In *Drosophila* adults the main olfactory receptor organ is the antenna, where two main types of glia appear, the GH146-type accounting for ~30% and the Mz317-type that represents ~70% of the total glial cells. The GH146-type glia originates in the brain and migrates to the third antennal segment where it wraps the axons of the olfactory sensory neurons (OSNs), which make their first synaptic contact into the brain. MZ317 glia develops in the opposite direction starting from the antenna and surrounds the somas of the OSNs and the axon bundles wrapped by the GH146 antennal glia.

Recent studies on *Drosophila* antennal glia Mz317 has shown their role in olfactory perception. Also, we have characterized the differential transcriptional profile of the MZ317-type antennal glia in Drosophila in comparison with other cell types and in the presence and absence of odorant pulses using the Targeted DamID method (TaDa), that allows the study of a single cell group transcriptomics without cell isolation. Moreover, by comparing the genetic expression profile in the presence or absence of intense odorant stimulation we have localized specific gene expression changes related to olfactory function.

All these data have enabled us to compile a selection of candidate genes for further investigation and contributes to understand neuron-glia communication in olfactory signaling. Thus, by analyzing the role of some of these candidate genes by RNAi targeted expression in antennal glia and Ca2+ imaging studies on olfactory receptor neurons we have characterized changes associated to glial modulation of olfactory reception.

Additionally, similarities between the molecular signatures of peripheral glia in Drosophila and vertebrates, will highlight the utility of model organisms in elucidating glial cell functions in complex systems.

Acknowledgements: This work was supported by the Spanish Ministry of Economy, Industry and Competitiveness [BFU2017-85882-P], the University of Oviedo [PAPI-17-PEMERG-2 and PAPI-23-GR-2016-0012], and the Principality of Asturias Government [PA-20-PF-BP19-040] and Fundación Científica Manuel González [APR-22-034]

Olfactory learning and memory in a miniature brain: from elemental to non-elemental problem solving

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Identifier: 41
Type of communication: ABSTRACT SUBMISSION

Honey bees are a well-established experimental model for the study of olfactory processing and learning as they allow coupling controlled olfactory conditioning protocols with access to the nervous system by means of different invasive techniques. In the laboratory, harnessed bees learn efficiently to associate an odorant with sucrose reward. Research on bee memory has led to a widely accepted model in which a single pairing of an odor stimulus with sucrose is unable to form protein-synthesis-dependent long-term memory (LTM) and induces only transient memories. On the contrary, three or more pairings of odor and sucrose induce LTM. By exerting an unprecedented control of appetitive motivation, we show that protein-synthesis-dependent memories are formed already 4 h after the single conditioning trial and persist even 3 days later. These memories (4 h, 24 h, and 72 h) exhibit different dependencies on transcription and translation processes and relate to specific molecular variations in the mushroom bodies (MBs), brain structures that are essential for memory storage and retrieval. These variations are detectable in animals with enhanced appetitive motivation. Besides elemental associations, bees can also master non-elemental (configural), ambiguous associations in which conjunctive representations of events are learned as being different from their elements. We asked if configural olfactory learning requires the MBs and showed that bees with anesthetized MBs distinguish odors and learn elemental olfactory discriminations but not configural ones, such as the negative patterning problem. Inhibition of GABAergic signalling in the MB calyces, but not in the output lobes, impairs patterning discrimination, thus suggesting a requirement of GABAergic feedback neurons from the lobes to the calyces for non-elemental learning.

These results show, on the one hand, that previous studies underestimated the capacity of the bee brain to form robust LTM and that an appropriate control of motivation is mandatory to detect significant variations in memory dynamics. On the other hand, they uncover a previously unidentified role for MBs besides memory storage and retrieval: namely, their implication in the acquisition of ambiguous discrimination problems.

Making semiochemicals practical tools: from fundamental to industrial products.

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Identifier: 40
Type of communication: ABSTRACT SUBMISSION

When the first pheromone was discovered in 1957, a new hope was born for the management of competitive species. Everybody thought that the reign of pesticides was finished. Unfortunately, the gap between the observation of the role of pheromones and other semiochemicals, in native conditions, and the use of the putative compositions, appeared to be so deep and large, that most professionals in agriculture went to think that it was a useless discovery. The disappointment was severe, regarding the management of invertebrate species, but worse with vertebrates. Mammalian pheromones went to be classified in the same category as Loch Ness monsters. Two main causes could be identified for this situation. The first one was related to the sensitivity of chemical analytic methods, but the very main cause was the idea that, as hormones, the pheromones were single compound secretions. This last hypothesis is easily understandable, if we look at the scientific context in the 60s and 70s. The development of molecular biology was promoting the concept of "one function, one molecule". The pheromones, first denominated "pherormones", were logically supposed to follow this rule and the identification of bombykol and of the following first pheromones, seemed to confirm it. Even in mammals, the first descriptions of the salivary boar sexual pheromone was on the same line. Unfortunately, the results obtained with the synthetic copies of those monomolecular pheromones, did not lead to positive results.

The papers published by Silverstein and his team, in the 70s, studying insects' pheromones as well as those from Novotny et al., in 1985, about mice, changed the lead by proving that pheromones were multi-compounds secretions. Our own research led to the description of facial pheromone complex, in cats, with compositions varying from 4 to 7 compounds with precise ratios. This major change in the understanding of the chemical structure of semiochemicals, raised various practical questions. The first one was the way to release the synthetic semiochemicals, having the right composition. The similarity with the technical problems raised in perfume industry, led first to use ethyl-alcohol as a vehicle. Notwithstanding the legal and practical problems raised by the use of this very flammable product; the need to spray the products, once or twice a day, in various places of the environment, appeared as a limitation for the compliance. A more careful analysis of the native secretions, helped in discovering the post-secretion maturation of the pheromones. The methyl-esterification by microbiotic organisms, appeared to be a fascinating process contributing to increase the volatility and dispersion of the pheromone compounds. This observation made possible to prepare a second generation of pheromone products, suitable for the use of electric diffusers. The owners of the animals didn't need any more to renew the applications: it was automatically done for several weeks. Unfortunately, we were still unable to control the composition of the secretion in the air. This challenge has been crucial and has highlighted the relationships between significant variations of the respective ratios of each pheromone compound, and the efficacy of the product.

Between the practical challenges faced on developing pheromone products, one of the most important, is the impossibility to source some compounds. This difficulty is a serious limitation for the identification of the picks during chromatographic analysis, but becomes a critical problem for the preparation of synthetic semiochemicals. One option, currently used in the field of insect control, is to develop methods to synthetize the missing compounds. Another one, is offered by the pharmacophore approach, together with the bioinformatic methods.

Anyway, a continuous cooperation between fundamental sciences, applied or clinical ethology, and industrial chemistry, is crucial for the development of semiochemical products.

Involvement of Glucosamine 6 phosphate isomerase 2 (GNPDA2) Overproduction in β-Amyloid and Tau P301L-driven pathomechanisms

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Identifier: 12
Type of communication: ABSTRACT SUBMISSION
Keywords: GNPDA2, Alzheimer’s disease, neurodegeneration, mass-spectrometry, RNAseq

Introduction: Alzheimer's disease (AD) is a neurodegenerative olfactory disorder affecting millions of people worldwide. Alterations in the hexosamine or glucose-related pathways have been described through AD progression. Specifically, an alteration in glucosamine 6 phosphate isomerase 2 (GNPDA2) protein levels has been observed in olfactory areas from AD subjects. However, the biological role of GNPDA2 in neurodegeneration remains unknown.

Methodology: Transcriptomics, proteomics as well as in vitro (human nasal epithelial cells-NECs) and in vivo models (Tau-P301L transgenic zebrafish embryos) were used.

Results: Using mass-spectrometry, multiple GNPDA2 interactors were identified in human nasal epithelial cells (NECs) mainly involved in intraciliary transport. Moreover, GNPDA2 overexpression induced an increment in NEC proliferation rates, accompanied by transcriptomic alterations in Type II interferon signalling or cellular stress responses. In contrast, the presence of beta-amyloid or mutated Tau-P301L in GNPDA2-overexpressing NECs induced a slow-down in the proliferative capacity in parallel with a disruption in protein processing. The proteomic characterization of Tau-P301L transgenic zebrafish embryos demonstrated that GNPDA2 overexpression interfered with collagen biosynthesis and RNA/protein processing, without inducing additional changes in axonal out-growth defects nor neuronal cell death. In humans, a significant increase in serum GNPDA2 levels was observed across multiple neurological proteinopathies (AD, Lewy body dementia, pro-gressive supranuclear palsy, mixed-dementia, and amyotrophic lateral sclerosis) (n=187).

Conclusion: These data shed new light on GNPDA2-dependent mechanisms associated to the neurodegenerative process beyond the hexosamine route.

LC-MS/MS analysis of microdissected hippocampal human subfields in Alzheimer’s disease

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Identifier: 28
Type of communication: ABSTRACT SUBMISSION
Keywords: Alzheimer's disease, hippocampus, olfactory bulb, proteostasis, microdissection, proteomics

Alzheimer’s disease (AD) is the most widespread neurodegenerative disorder being more prevalent in women. It is clinically characterized by cognitive decline, including anterograde amnesia and spatial disorientation. Through last years, olfactory dysfunction has been described as an AD symptom that may appear before cognitive decline has started. To what extent olfactory bulb-entorhinal cortex-hippocampus pathway is responsible of olfactory memory loss is unknown. Previous stereological and proteomic data have demonstrated specific involvement of hippocampal subregions (cornua ammonis – CA1, CA2, CA3- and dentate gyrus -DG-) in AD. Moreover, immunohistological analysis of OB and hippocampal sections from AD patients of different stages have demonstrated there is an alteration in the cellular proteostasis that may be related to pathological protein aggregation in Alzheimer’s disease. Nevertheless, proteomic analyses focused on single hippocampal subfields have not been carried out. Thus, the aim of this study has been to analyze the different regions of the hippocampus separately and compare the proteomic profiles of each of these areas.

Fresh-frozen human hippocampal tissue blocks from AD and non-AD cases of women were cryostat sectioned, collected on specific slides and Nissl stained. Areas of interest (CA1, CA2, CA3 and DG) were microdissected and collected in separate tubes. Tissue extracts were trypsin-digested to obtain peptide pulls. Later, peptide mixtures were cleaned and desalted prior to mass-spectrometry analysis using Orbitrap Exploris™ 480 Mass Spectrometer with the aim to identify specific protein subsets of each hippocampal region. According to preliminary data, differential proteomic profiles are expected in the studied hippocampal fields.

The study was sponsored by the UCLM/ERDF (2022-GRIN-34200 to NPND), Spanish Ministry of Science and Innovation (grant no. PID2019-108659RB-I00) to AMM and Autonomous Government of Castilla-La Mancha/ERDF (grant no. SBPLY/21/180501/000093) to AMM and IUB.

We especially appreciate the generous contribution of patients and the collaboration of the Spanish ISCIII Biobank platform and the Netherlands Brain Bank (eNBB).

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EVALUATION OF THE OLFACTORY CAPACITY IN CHRONIC KIDNEY DISEASE PATIENTS UNDERGOING HEMODIALYSIS IN THE MEXICAN POPULATION

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Identifier: 26
Type of communication: ABSTRACT SUBMISSION
Keywords: olfactory function, odor discrimination, odor identification, chronic kidney disease patients, hemodialysis

Chronic kidney disease (CKD) is a health condition with a high incidence worldwide. In Mexico, CKD constitutes the third cause of death among metabolic diseases and has been strongly associated with diabetes and hypertension. CKD is diagnosed when the kidney function is compromised due to a deficient glomerular filtration for more than three months, increased accumulation of uremic toxins and systemic inflammatory status. CKD patients have a decreased olfactory function that directly affects their quality of life and importantly can alter their feeding behavior promoting malnutrition, which is one of the principal causes of mortality in the disease. Interestingly, CKD patients show elevated concentrations of prolactin, and experimental evidence suggests that hyperprolactinemia alters olfactory function. Detecting early olfactory dysfunctions in CKD patients that could correlate with other biochemical or endocrine alterations offers a good opportunity to identify a biomarker that helps the opportune diagnosis and treatment that could impact the patient’s quality of life. In the present project, we evaluated a population of 36 CKD (18 women and 18 men) patients and 40 control subjects between 18 and 60 years old. All patients received treatment with hemodialysis. Metabolic and routine biochemical parameters of the disease were verified; additionally, prolactin levels were evaluated before hemodialysis treatment. Olfactory function was assessed for odor discrimination, odor identification and olfactory memory formation before and after hemodialysis treatment. As expected, urea and creatinine levels were significantly increased, and albumin concentration decreased in CKD patients. No differences among women and men were found in these parameters. The patient’s weight and the body mass index were decreased, especially in the women group. Prolactin levels were elevated in CKD patients, being higher in women than in men. For the olfactory assessment, odor discrimination and identification were significantly reduced in CKD patients. In both olfactory assessments, women were the most affected group. For the olfactory memory test, no deficits for the CKD patients were detected. The hemodialysis treatment did not improve the performance of the CKD patients in any of the olfactory tests evaluated. Interestingly, women patients that were the most affected on olfactory capacity evaluations, showed the lowest body weight and the highest levels of prolactin compared to men patients. These results suggest a sexual dimorphism in the olfactory capacity in CKD that could be explained by the hormonal imbalance and the metabolic alterations promoted by the disease. The compromised olfactory capacity of the CKD patients could promote or be a consequence of the metabolic and hormonal alterations. To our knowledge this constitutes the first evaluation in Mexico to show that CKD patients have a compromised olfactory capacity. Further analysis and clinical evaluations need to be performed to unravel the relation of the CKD and the olfactory sense.

Supported by UNAM-DGAPA-PAPIIT IN214822, IA202218, IA200820, IN204718, IN205423 and CONAHCYT A1S8948.

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OLFACTORY AND ENDOCRINE DYSFUNCTIONS IN MICE MODEL OF KIDNEY DISEASE

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Identifier: 25
Type of communication: ABSTRACT SUBMISSION
Keywords: olfactory alterations, detection and discrimination, prolactin, adenine, Kidney disease,

Kidney disease (KD) is an important public health problem. Mexico has a high prevalence of KD and the most common causes of this pathology are diabetes and hypertension. KD is characterized by functional and structural abnormalities of the kidneys, and its classification is according to cause, severity, and duration of those abnormalities. KD patients report olfactory alterations, which can lead to unbalanced feeding behaviors. Additionally, alterations in prolactin (PRL) circulating levels have been reported with a high prevalence in KD patients, and evidence shows that PRL can modulate the olfactory function. However, the onset and evolution of the pathophysiology of the olfactory and PRL alterations have been little addressed in KD. In the present work, a KD model was generated in adult C57BL/6J female mice by intragastric adenine administration (50 mg/kg, n=10) for four weeks to evaluate olfactory capacity and PRL levels. The KD was confirmed by metabolic, biochemical, and morphological parameters. To determine possible olfactory alterations, we used two behavioral tests, the Buried Food test (BFT) and the Habituation/Dishabituation test (HDT), to evaluate the mouse's ability to smell and locate food using volatile cues, and to evaluate their ability to detect and differentiate odors (discrimination and memory processes), respectively. The tests were performed before the adenine treatment and every second week to evaluate the olfactory capacity during the progression of the disease. The morphology of the olfactory epithelium (OE), a structure in which olfactory processing begins by odorant detection, was analyzed at the end of the treatment. Circulating levels of PRL were determined by ELISA weekly during the progression of the KD. As expected, serum creatinine and urea levels were significantly increased in the adenine-treated group. Additionally, hematoxylin-eosin histological kidney sections were analyzed and showed significant differences in tubular dilation that confirm renal damage. For the behavior, all female mice before adenine treatment showed intact olfactory capacity by finding the buried food and discriminating among the odors. For the BFT, from the second to the fourth week, adenine-treated mice showed alterations on the detection of volatile cues by displaying different latencies to find the hidden food compared to the control mice. Interestingly, the adenine-treated mice also showed significant differences on the capacity of discriminating odors in the HDT test over time, starting two weeks after adenine treatment and becoming more pronounced at four weeks. Globally, our behavioral data indicates that adenine treatment alters the olfactory function in female mice in a progressive manner, by disrupting the volatile detection and discrimination abilities. For the OE, no changes in the olfactory epithelial thickness or cell density were detected. Opposite to expected, peripherical levels of PRL decreased in adenine-treated mice at least for the first four weeks on the pathology. Further experiments are needed to unravel the olfactory dysfunction and the PRL regulation in a KD mouse model.

Supported by UNAM-DGAPA-PAPIIT IN214822, IA202218, IA200820 e IN204718, IN205423 y CONAHCYT A1S8948.

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Impact of Early Social Recognition Impairment on Memory Functions in Alzheimer's Disease Triple Transgenic Mice

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Identifier: 27
Type of communication: ABSTRACT SUBMISSION

Although social recognition is severely impaired in Alzheimer's disease, it has been difficult to study in animal models. Our study focuses on the relationship between spatial and social memory deficits in triple transgenic Alzheimer's disease (3xTgAD) mice. The results reveal early-onset social recognition deficits in 6-8 month female 3xTgAD mice in a test based exclusively in chemosensory cues. The whole-brain serial analysis of the immunofluorescence for beta-amyloid and TAU proteins at 3, 6, 9 and 12 months, shows the evolution from the initial presence of intracellular beta-amyloid in the hippocampus to extensive extracellular deposits. Calcium imaging techniques were employed to elucidate the functionality of dCA1 place cells in reaction to chemical signals from conspecifics, uncovering a decrease in neuronal activity among older subjects. These findings elucidate the consequent relationship between early social recognition deficits and subsequent alterations in hippocampal memory circuits, antecedent to significant beta-amyloid accumulation. By associating reduced operational efficiency of dCA1 place cells with preliminary social recognition deficits, our research contributes to clarify the mechanisms underlying the failure of an appropriate integration of the "who" and "where" components of episodic memory along the progression of Alzheimer's disease.

Funding: Ministry of Science, Innovation and Universities, PID2022-141733NB-I00/AEI/10.13039/501100011033/ FEDER, UE. A Teruel-Sanchis is a predoctoral fellow of the FPU20/02632 program of the same Ministry.

Neuropathological stage- and sex-dependent proteome and phosphoproteome imbalance in the Nucleus Basalis of Meynert in Alzheimer´s disease

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Identifier: 22
Type of communication: ABSTRACT SUBMISSION
Keywords: Nucleus basalis of Meynert, Alzheimer's disease, Sexual Dimorphism, Braak stage, Proteomics.

Introduction: The Nucleus basalis of Meynert (NbM) is considered one of the main centers of cholinergic innervation of the cerebral cortex. Cholinergic neurons present in the NbM integrate information from different subcortical regions that is projected to the frontal cortex, hippocampus, amygdala, or olfactory bulb[1]. In fact, substantial NbM damage is evident for neurological disorders accompanied by marked smell loss (such as Alzheimer´s disease, AD), and is absent or less evident for diseases with little or no olfactory deficit[2]. NbM plays an indispensable role in the subcortical regulation of memory, attention, and arousal state in which cholinergic abnormalities occur as early as asymptomatic or at prodromal stages of AD[3]. Moreover, recent evidence suggests that neuropathological changes of the entorhinal cortex are preceded by degeneration of the cholinergic NbM in AD models. Based on these data, deep brain stimulation has been gradually acknowledged as a potential therapy for AD, making the NbM a promising target for modulating the AD-associated neural network dysfunction. However, the intrinsic molecular imbalance that occur at the level of the NbM during AD progression is largely unknown.

Methods: Label-free quantitative (phospho)proteomics and bioinformatic workflows were applied in 52 post-mortem NbM derived from controls with no known neurological history (n=16) and AD (n=36) subjects. Specifically, AD group was divided in Braak stage I-II (with no discernible or a few isolated NFTs) (n=19), Braak stage III (with low/moderate numbers of NFTs) (n=9) and Braak stage IV-VI (with high numbers of NFTs) (n=8).

Results: 5913 proteins and 36.247 phosphorylation sites were identified in this region. At proteome level, 70, 238, 224 and 441 differential expressed proteins (DEPs) were detected in Braak-I, Braak-II, Braak-III and Braak-IV-VI stages, respectively. There were 4 DEPs in common across stages and few common disrupted biological processes such as transport regulation, synapse organization and neuron projection development. This proteomic alteration was accompanied by 474, 529, 416 and 728 differential phosphorylation sites across Braak stages (being 25 phosphorylation sites commonly affected). An upstream kinase analysis pointed out that PKA protein kinase A (PKA), P21/Cdc42/Rac1-Activated Kinase 1 (PAK1) and Cyclin Dependent Kinase 5 (CDK5) are activated across Braak stages. Preliminar analysis considering the sex variable indicates that: i) protein expression and signaling differences exist in the NbM between control women and men (62 DEPs & 284 phosphosites), ii) there are 50% more DEPs in AD women than in AD men (318 vs 148 DEPs), iii) the functional profile is clearly different across sexes and iv) the NbM phosphorylation-mediated rewiring is more severe in AD men than AD women (1028 vs 291 phosphorylation sites).

Conclusions: Proteome and phosphorylation-based signal transduction imbalances were observed at the level of NbM in AD. These alterations induced a disruption in NbM protein interaction networks in a Braak-stage dependent manner as well as widespread sex-dependent pathway perturbations. Ongoing drug repositioning workflows will help us to define potential compounds with capacity to reverse these pathological omics signatures, proposing novel therapeutic approaches to be used in AD treatment.

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Analysis of volume, neurodegeneration, astrogliosis and microgliosis in the human olfactory bulb in Huntington disease

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Identifier: 37
Type of communication: ABSTRACT SUBMISSION
Keywords: Neurodegeneration, olfactory bulb, huntington disease, astrogliosis and microgliosis

Many neurodegenerative diseases such as Alzheimer's and Parkinson's diseases course with prodromal hyposmia in parallel with early and preferential aggregates of proteinopathies, amyloid-β and tau and α-synuclein, respectively, in the olfactory bulb. Neurodegeneration, astrogliosis and microgliosis have been also observed being often sexually dimorphic (Flores-Cuadrado et al., 2021, npj Parkinson's Disease 7:11; Ubeda-Banon et al., 2024, under review). Huntington disease, however, a rare and strictly genetic neurodegenerative disease that also course with olfactory deficits and huntingtin deposits in the olfactory bulb have not been thoroughly studied from this perspective. Therefore, the present report aims at analyzing the volume, neurodegeneration, astrogliosis and microgliosis in the human olfactory bulb in Huntington disease from a sex perspective.

Fomalin-fixed human olfactory bulb from patients suffering Huntington's (n=6), Alzheimer's (=6) and Parkinson's (n=4) or no suffering these diseases (n=3) will be sectioned using a freezing microtome. Sections will be Nissl-stained, or immunostained against pathologic (huntingtin), neural (calcium binding proteins or somatostatin), astroglial (GFAP) or microglial (Iba-1) markers. Stereological unbiased procedures will be used to quantify volume, neurodegeneration astrogliosis and microgliosis among bulbar layers as well as in the bulbar anterior olfactory nucleus.

The study was sponsored by the UCLM/ERDF (2022-GRIN-34200 to NPND), Spanish Ministry of Science and Innovation (grant no. PID2019-108659RB-I00) to AMM and Autonomous Government of Castilla-La Mancha/ERDF (grant no. SBPLY/21/180501/000093) to AMM and IUB.

We especially appreciate the generous contribution of patients and the collaboration of the Spanish ISCIII Biobank platform.

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Bone marrow-derived cell distribution in the telencephalon of a mouse model for multiple sclerosis

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Identifier: 20

Type of communication: ABSTRACT SUBMISSION

Keywords: Bone marrow-derived cells, distribution, cell morphology, Experimental Autoimmune Encephalomyelitis, central nervous system, telencephalon.

Neurodegenerative diseases pose significant challenges for society due to limited treatments. Among the potential therapies, cell therapy stands out as a particularly promising one. We know that **bone marrow-derived cells** (BMDC) can infiltrate the central nervous system in different ways. In the cerebellum, these cells can fuse with Purkinje cells, while in other areas like the olfactory bulb, it has been described that BMDCs can undergo **transdifferentiation**, that means, changing from one cell type to another. Under physiological conditions, the number of incorporated BMDCs is low, however, the number increases in different pathologies, such as multiple sclerosis.

Research to date has focused on studying the possible neuroprotective effects of BMDCs. Nevertheless, we need to understand the distribution of these cells in the brain to be able to fully exploit their therapeutic potential. To achieve this, we have studied the distribution of BMDCs in the brain of mice with **Experimental Autoimmune Encephalomyelitis** (EAE), a model for multiple sclerosis. We have compared BMDCs distribution on three main telencephalic regions (**hippocampus, olfactory bulb, and cerebral cortex**) using immunofluorescence and confocal microscopy.

Our results show that BMDCs are **distributed heterogeneously** among the three regions, being the hippocampus the area with the lowest cell density. This distribution is also different within the same region, depending on the cell layers. Furthermore, we described that most BMDCs had **different morphologies** and that some of them were positive for the **microglia/macrophage** marker Iba1. All these results help to understand BMDCs infiltration in the brain, bringing us closer to their use in cell therapy.

Support: MIU (FPU2020); MICINN (PID2022-140456NB-I00) (PID2022-140525NB-I00); USAL, FENS/IBRO-PERC Exchange Fellowship, Programa Interreg VIAEspaña-Portugal (POCTEP) 2021-2027 (Cross-3DTool-4ALS).

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IMMATURE NEURONS IN THE OLFACTORY TUBERCLE IN MOUSE MODELS OF X-LINKED NEURODEVELOPMENTAL DISORDERS

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Identifier: 13
Type of communication: ABSTRACT SUBMISSION
Keywords: Rett Syndrome, MECP2, Fragile X Syndrome, FMR1, Neurogenesis

Rett syndrome and fragile X syndrome are X-linked neurodevelopmental disorders that cause intellectual disability, communication impairment and autistic features. Rett syndrome, which affects mostly females, is caused by mutations in *Mecp2*, a gene encoding the epigenetic reader methyl-CpG-binding protein 2 (MeCP2), whereas fragile X syndrome, predominantly affecting males, is caused by mutations in the *Fmr1* gene, which encodes the RNA-binding protein FMRP. Despite their distinct aetiology, both disorders involve two proteins crucial for neural maturation, whose interaction might contribute to the overlapping symptoms of these conditions. Recently, we identified a population of immature neurons expressing the marker doublecortin in layer I of the olfactory tubercle. The density of these immature neurons is increased in young adult *Mecp2*-null male mice as compared to WT controls. Thus, in this study we sought to better characterize this population and to investigate its dynamics with age. To do so, we detected doublecortin by immunofluorescence in brain coronal sections of infantile, adolescent, and young adult *Mecp2*-null, *Fmr1*-null and WT male mice, and studied the ultrastructure of these neurons by electron microscopy. We show that these immature neurons can be found in close apposition to astrocytes in the outer edge of layer I, especially when organized in clusters resembling migratory chains. Some of these clustered cells co-express the proliferation marker Ki67, and their ultrastructure further suggests that they are immature neurons. Also, deeper in layer I and rarely in layer II, they can be found isolated with relatively complex dendritic arborization. Interestingly, the number of immature neurons and the distribution of neurons across maturation stages can be altered by mutations in these neurodevelopment-related proteins. These findings corroborate and expand our previous data and suggest that the olfactory tubercle retains a postnatal neurogenesis potential, which is affected by neurodevelopmental disorders. Funded by Spanish Ministry of Science and Innovation (grant PID2019-107322GB-C22 funded by MCIN/AEI/10.13039/501100011033) and Fondo para la Investigación en Síndrome de Rett (FinRett 2022).

Dysregulation in the GnRH system might contribute to pubertal and olfactory impairment in Rett syndrome

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Identifier: 19

Type of communication: ABSTRACT SUBMISSION

Keywords: Mecp2, Gonadotropin Releasing Hormone, Kisspeptin, hypòthalamus, olfactory bulbs, neurodevelopmental disorders

Rett syndrome (RTT) is a rare neurodevelopmental disorder that affects mostly females. RTT is mainly caused by mutations in the X-linked gene methyl CpG-binding protein 2 (MECP2) and is characterised by a period of normal development followed by a loss of acquired skills and a range of neurological and behavioural symptoms. However, certain aspects such as dysregulation of altered puberty onset are prevalent in RTT yet understudied. Since altered pubertal trajectories along with olfactory deficits are characteristic in other neurodevelopmental disorders, we sought to investigate them in patients and a mouse model of RTT. In a pilot study, we found a high percentage of RTT patients showing delayed menarche. Consistently, we found delayed puberty in *Mecp2*-null males, previously shown to display atypical social and olfactory behaviour. Gonadotropin Releasing Hormone (GnRH) neurons play a crucial role in regulating reproductive cycles and are involved in olfactory processing to a lesser extent. During early development, these neuroendocrine cells originate from the olfactory placode and migrate to their final destinations in the adult mammalian brain, including the olfactory bulbs, septum and hypothalamus. Immunofluorescence detection of GnRH in adolescent and young adult *Mecp2*-mutant mice suggest a dysregulation of this system. Our study offers a preliminary insight into how MECP2 deficiency may affect this regulatory pathway essential for coordinating reproduction and social behaviour, learning and memory. Funded by Fondo para la Investigación en Síndrome de Rett (FinRett 2022) and Spanish Ministry of Science and Innovation (grant PID2019-107322GB-C22 funded by MCIN/AEI/10.13039/501100011033).

Can SARS-CoV-2 hitchhike on the olfactory projection and take a direct and short route from the nose into the brain?

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Identifier: 43
Type of communication: ABSTRACT SUBMISSION

Anosmia, the loss of smell, is a common and often the sole symptom of COVID-19. We reasoned that the neurotropic or neuroinvasive capacity of SARS-CoV-2, if it exists, should be most easily detectable in individuals who died in an acute phase of the infection. Procuring high-quality fresh tissue samples from the human olfactory mucosa and olfactory bulb has proved challenging, both from living patients and during an autopsy. We have developed a protocol for rapid postmortem bedside sampling of these structures, using an endoscopic endonasal surgical technique that we adapted from skull base surgery. The procedure leaves no visible incisions and enables a rapid response and logistic flexibility in a variety of hospital settings including a ward. Compared to a typical autopsy, the protocol drastically reduces the postmortem interval — in our experience with a cohort of 138 cases, the median was 89 minutes — thereby contributing to preserving the tissue samples in pristine condition. Our cohort included 115 COVID-19 patients who died a few days after infection with SARS-CoV-2, enabling us to catch the virus while it was still replicating. We found that sustentacular cells are the major target cell type in the olfactory mucosa. We failed to find evidence for infection of olfactory sensory neurons. We postulate that transient insufficient support from sustentacular cells triggers transient olfactory dysfunction in COVID-19 and that olfactory sensory neurons would become affected without getting infected. Confocal imaging of sections stained with fluorescence RNAscope and immunohistochemistry also afforded the light-microscopic visualization of extracellular SARS-CoV-2 virions in tissues. We failed to find evidence for viral invasion of the parenchyma of the olfactory bulb and the frontal lobe of the brain. Instead, we identified anatomical barriers at vulnerable interfaces, exemplified by perineurial olfactory nerve fibroblasts enwrapping olfactory axon fascicles in the lamina propria of the olfactory mucosa. This poorly characterized cell type appears to seal olfactory axon fascicles hermetically from invasion by SARS-CoV-2 virions. We speculate that this barrier may also be effective against some of the many other pathogens that infect the nasal mucosa and could threaten the brain. In conclusion, SARS-CoV-2 appears to be stopped dead in its tracks by several anatomical barriers at vulnerable interfaces, even in extremely weak individuals with an abysmal level of defense who lost the battle.

A Comparative Transcriptomic Landscape of Neural Progenitors in the Developing Brain

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Identifier: 6
Type of communication: ABSTRACT SUBMISSION
Keywords: Neural Progenitor Cells (NPCs) NG2-glia Radial Glial Cells (RGC) Development Molecular profile

The intricate process of brain assembly begins with a pool of Neural Progenitor Cells (NPCs). Initially, neuroepithelial cells give rise to Radial Glial Cells (RGC), which then generate neurons, astrocytes, NG2-glia, and oligodendrocytes in partially overlapping waves. Recent studies have revealed the diversity among progenitors, ranging from lineage-specific limitations to spatial or temporal factors. Our focus is on the remarkable potential of NG2-glia. These cells not only act as progenitors but also exhibit the ability to differentiate into oligodendrocytes, astrocytes, and even neurons in the adult mouse brain. Our previous studies identified NG2-progenitors during development, contributing to the generation of diverse neural cell lineages, such as neurons, astrocytes, oligodendrocytes and NG2-glia.

However, their precise identity remains a mystery: are they a distinct subtype or merely a transitional stage within the NPC pool? To address this question, we targeted using StarTrack and compared the derived cell progeny of two distinct progenitor populations: NG2+ and GFAP+ progenitor cells. Then, we performed an RNA-sequencing of the cells derived from these embryonic progenitors. This analysis revealed that the molecular profile of the embryonic derived-progeny from NG2-progenitors exhibited both similarities and differences compared to those derived from GFAP+ progenitors. Our results not only provide new data on the lineage potential contributing to NPC heterogeneity but also emphasize the existence of NG2-progenitors within the NPC pool.

This work was supported by the Spanish grant PID2022-136882NB-I00, funded by MICIU/AEI/ 10.13039/501100011033.

The role of NG2 cells in the mouse olfactory bulb.

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Identifier: 7
Type of communication: ABSTRACT SUBMISSION

Over the past years, it has become more evident that the functional role of each glial cell type is significantly richer and more complex than previously thought. Additionally, well-known glial cell types like oligodendrocytes, astrocytes, ependymal cells, and microglia, NG2-glia emerge as a distinct class of glial cells. Distributed uniformly throughout the adult brain in a grid-like pattern, NG2-glia represent a significant glial populations in the CNS. These cells exhibit specific electrical properties, proliferation rates, and responses to injury, and possess the remarkable ability to differentiate into myelinating oligodendrocytes and other neural cells, including neurons. Furthermore, they persist in the adult brain as a resident, self-renewing population with considerable progenitor potential. Notably, NG2-glia lack gap junction coupling and display high input resistance, along with voltage-dependent sodium and potassium conductance. Moreover, NG2 glial cells establish bidirectional synaptic connections with neurons, underscoring their dynamic role in neural circuitry. This project aims to elucidate the interplay between neuronal and NG2 glial cells in the olfactory pathway, particularly within the olfactory bulb. Employing viral tracing and STED for super-resolution imaging of NG2 glia synaptic connections, our investigation seeks to uncover the structural and functional contributions of NG2 cells. By enhancing our understanding of these interactions, our findings will advance the development of more accurate models of olfactory neural networks, providing insights into the broader olfactory bulb circuitry and the role of diverse glial cells in shaping postnatal olfactory circuits' plasticity. Supported by the Spanish grant PID2022-136882NB-I00, funded by MICIU/AEI/ 10.13039/501100011033.

Semi-Automated Time-Lapse Analysis of Postnatal Subventricular Progenitors

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Identifier: 8
Type of communication: ABSTRACT SUBMISSION

The subventricular zone (SVZ) of the mouse harbors a neurogenic niche that continually generates cells throughout life. The adult neurogenesis plays a crucial role in supplying the adult olfactory bulb with new interneurons. Our previous research has indicated that this postnatal cell population gives rise not only to neurons destined for the olfactory bulb but also to glial cells that migrate to surrounding areas. However, the initial postnatal events in this neurogenic niche, particularly regarding GFAP and other nature progenitors, remain poorly understood. To address this gap, we conducted time-lapse microscopy studies of the derived cell progeny from GFAP-expressing progenitors compared to other progenitors, using a ubiquitous promoter for labeling at early postnatal stages up to P11. Given the complex morphologies and non-nuclear staining of the images, we employed Cellpose 2.0 to train a segmentation model tailored to our needs. This model was subsequently applied to Cell-ACDC to segment all frames of the time lapse image sequencing, creating masks that were then utilized for cell detection and tracking with the ImageJ plugin TrackMate. TrackMate provides us information on cell division, merge events, fluorescence intensity, and basic cell morphology. With data provided by TrackMate, we conducted an in-depth investigation to ascertain potential correlations between the movement speed/distance traveled of different progenitors and their division patterns. Through this approach, we semi-automated time-lapse microscopy analysis and elucidate the proliferative properties and migration patterns of these distinct postnatal progenitors. This work was supported by the Spanish grant PID2022-136882NB-I00, funded by MICIU/AEI/10.13039/501100011033.

Postnatal plasticity in the olfactory system of the juvenile swine brain

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Identifier: 23
Type of communication: ABSTRACT SUBMISSION
Keywords: postnatal neurogenesis, piriform cortex, amygdala, rostral migratory stream, doublecortin

Swine are known for having an excellent sense of smell, which plays a crucial role in complex social interactions, including sexual receptivity, conspecifics discrimination, and social-status recognition. In terms of cerebral areas, they have enlarged and highly complex olfactory structures, which makes them an ideal model to study dynamics in these areas, such as the postnatal plasticity in the olfactory bulbs (OB) and other olfactory areas. In other mammals, a large proportion of OB interneurons are produced postnatally in the subventricular zone and reach OB by following the rostral migratory stream (RMS). The RMS is considered the predominant source of periglomerular neurons expressing tyrosine hydroxylase (TH) and calretinin (CR), and granule cells expressing GABA and CR. It has been proposed that these newly incorporated neurons could be substrates for olfactory learning and discrimination, having an impact on emotional states and survival chances. Our aim was to investigate the postnatal plasticity in olfactory areas of juvenile swine brains. We used immunohistochemistry to study the distribution of immature cells expressing the microtubule-associated protein doublecortin (DCX) in the OB, the periventricular zone of the olfactory ventricle (ov), the piriform cortex (Pir), and the amygdala. With double and triple immunofluorescence, we studied DCX+ co-expression with the cell proliferation marker Ki-67, and different mature phenotype markers including CR and TH. Some cells co-expressed Ki-67 and DCX, suggesting that they were proliferating. In horizontal and sagittal sections, chains of migratory-like DCX+ cells were observed parallel to the lateral ventricle forming the RMS. In the OB, DCX+ cells were abundant in the granular and glomerular cell layers and most of them co-expressed CR. In the Pir, chains of migrating immature cells were observed crossing radially layer III and appeared to incorporate to the cortical layer II, which showed a high density of immature neurons. In the pallial amygdala, DCX+ cells formed large patches in the lateral part of the basal complex of the amygdala (BCA), while they were dispersed in the rest of BCA. Some of these cells in the Pir and the BCA co-expressed DCX and CR, with various intensities of either DCX or CR, from high DCX/low CR to low DCX/high CR, suggesting different degrees of maturation. The high level of immature neurons found in Pir and BCA of this species is in contrast with that described in other mammals with highly developed olfactory system (such as rodents), but is in line with that found in different pallial areas of other gyrencephalic species.

Funding: MICIU/AEI/10.13039/501100011033 Grant No. PID2019-108725RB-100. JF has a predoctoral contract from FPU (Ministerio de Educación, Formación Profesional y Deportes FPU22/03133)

Sexual dimorphism in the Otp neurons of the medial extended amygdala

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Identifier: 24
Type of communication: ABSTRACT SUBMISSION
Keywords: medial extended amygdala; sexual dimorphism; gonadal hormones receptors; glutamatergic neurons; Otp cells

Social behaviors, such as mating, parental care and aggression, show strong variations between sexes. The medial extended amygdala (EAme) is one of the major brain regions involved in modulating these sexually dimorphic behaviors, and, for doing this, it requires information of social cues. In rodents, one of the most important sensory pathways mediating social behavior is olfaction: the EAme receives vomerolfactory and olfactory information from the main and accesory olfactory bulbs, the piriform cortex and other amygdalar olfactorecipient areas, and integrates this information to mediate behavioral responses. The EAme shows anatomical and molecular sexual dimorphism in many species. In the mouse, such dimorphism is subtle and became evident when studying molecularly defined neuron subpopulations (1). In the EAme, this approach was mainly focused on its GABAergic neurons, controlling mating and aggression. However, the EAme also contains an important subpopulation of glutamatergic neurons. Recently, our group found that most of these neurons originate in a new embryonic domain that coexpresses the transcription factors Otp and Foxg1 (2). Our aim was to investigate if these Otp neurons present sexual dimorphism in size, number and expression of gonadal hormones' receptors and to investigate the connectivity of these neurons.

To that aim we used Otp-eGFP and Otp/Cre transgenic mice. To study cell morphology we used immunohistochemistry against GFP and analyzed the images with Fiji (Image J). We observed that in the posterodorsal medial amygdala (MePD), a subnucleus well known for receiving vomeronasal information and mainly regulating sexual behavior, the volume occupied by Otp neurons and the size of their somas were significantly larger in males than in females, but their number was not different, this was similar to the results observed for the whole area (3). Moreover, using FISH against mRNA of estrogen receptors (Er$/alpha$ and Er$/beta$) or androgen receptor (Ar) combined with immunofluorescence against GFP, we observed that, in both sexes, the majority of Otp neurons of the EAme express gonadal hormones' receptors. For studying the specific projections of Otp neurons we injected Cre-dependent viral vectors in the medial amygdala of Otp/Cre mice. What we observed is that Otp neurons of the medial amygdala, including MePD, project to similar targets as the ones already described for the whole medial amygdala, including the BSTM, other amygdalar areas, septum and several hypothalamic subdivisions, which are part of the social behavior network (4).

Our results suggest that the Otp neurons of the mouse MePD contribute to the sexual dimorphism of EAme and might be involved in sexually dimorphic behaviors by projecting to different areas of the social behavior network.

Funding: MICIU/AEI/10.13039/501100011033, Grant No. PID2019-108725RB-100, AGA had an FI AGAUR (2021 FI_B00353) contract and has an Ajuts al Personal Investigador en Fromació predoctoral contract.

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Pheromones and mother-pup attachment

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Identifier: 21
Type of communication: ABSTRACT SUBMISSION
Keywords: Chemical communication, vomeronasal, mouse, behaviour, analytical chemistry, maternal behaviour, infanticide

In nature, adult rodents either take care of pups they might find (parental behaviour) or kill and eat them (infanticide). However, female lab mice strains show spontaneous maternal care, with increased motivation during motherhood (peripartum), because of the action of pregnancy hormones (sexual steroids and lactogens)
Although male infanticide behaviour is known to depend on chemosignals, the specific role of pup-derived chemosignals in eliciting motivated maternal care is still unclear. Therefore, we have combined a series of experiments to check the working hypothesis that pup pheromones detected with the vomeronasal organ (VNO) become rewarding for females during motherhood, thus resulting in pup(goal)-directed maternal behaviours.
First, we demonstrated that pup volatiles are attractive and rewarding for lactating mothers (induce place-preference), but only elicit transient investigation (novelty effect) in virgin females. Late-pregnant females show persistent attraction to pup-derived odours, thus suggesting hormone-dependent reward of pup chemosignals in female mice. The use of egr-1 expression indicates that pup- stimuli activate the VNO of adult females (both virgin and late-pregnant). Moreover, pup-induced neural activity (cFos expression) is increased in late-pregnant, as compared to virgin females, in key centres of the olfactory (piriform cortex), vomeronasal (posteromedial cortical amygdala), sociosexual (ventrolateral PAG) and motivational (AcbC) brain circuits.
To identify the pup volatiles involved in pup reward, we used GC-MS based untargeted metabolomics to analyse the volatolome of neonatal pups (3-4 day-old, which induce maternal care) and pups at the age of weaning (20-22 day-old, do not elicit maternal care). Volatolome is much richer in neonatal pups than at the time of weaning. We identified 11 volatiles that are emitted almost exclusively during the neonatal period, being good candidates for pup-derived pheromones eliciting maternal care (e.g. reward). Among them, durene (1,2,4,5-tetramethylbenzene) had been shown to activate the VNO of adult mice. We further tested the response of VNO cells to these putative pheromones using calcium imaging techniques and proved that they significantly activate populations of isolated VNO cells in vitro.
Then, we exposed adult female mice (mothers or virgins) to pup dummies (3D printed using a soft material with a texture recalling pup skin) swabbed with either vehicle or pup wash. We analysed their behaviour towards the dummies (licking-grooming and attacks) for 5 min. For this test, mothers must be separated from their pups, and consequently paid little attention to the dummies. Virgin females attacked vehicle-swabbed dummies, but attacks are significantly reduced when dummies are coated with pup wash. Licking-grooming was barely observed.
These data suggest that pup-derived chemosignals can act as reward-inducing pheromones during peripartum, thus inducing pup(goal)-directed maternal behaviours and reduce pup-directed attacks in virgin females. The specific identity of these pheromones, among a list of volatile candidates, and the vomeronasal receptors involved in their detection are currently being investigated.
This work has been funded by the Spanish Ministry of Science (PID2019-107322 GB-C21) and Universitat Jaume I de Castelló (UJI-B2016-45).

Are pup-derived odours necessary to maternal sensitization of virgin female rats?

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Identifier: 35
Type of communication: ABSTRACT SUBMISSION

Motherhood is a critical period in the lifespan of a female mammal, in which motivated pup directed (maternal care) and non-pup directed behaviors (maternal aggression) are displayed to ensure the survival and protection of the offspring. In mice, pregnancy-related hormones alter vomeronasal and olfactory sensory processing, as well as the activity pattern of social and motivational brain circuitry. These changes, likely trigger an increase of motivated pup-directed behaviors while decreasing other conducts, such as exploration of non-social objects.

Pup-naïve virgin female mice show spontaneous maternal care, which increases and improves after continuous exposure to pups, when we call them “godmothers”. By contrast, pup-naïve virgin rats avoid pups and only become maternal after 7-8 days of continuous exposure to pups. Here, we explore the possibility that the model of godmothers (continuous exposure to pups with their dam during the whole postpartum) also works for sensitizing virgin rats.

To do so, we performed an ethological analysis of the social and maternal behavior of female rats in several conditions: pup-naïve virgins, godmothers, pregnant females and postpartum lactating rats. To this end, pregnant and virgin Sprague-Dawley female rats were housed together in pairs until postpartum day 6 (pregnant-mother with virgin-godmother). In both females we explored anxiety-related behaviors (auto-grooming and digging), and social interactions between them (sniffing/grooming behavior and time in touch) during early pregnancy (E3 and E4), late-pregnancy (E19 and E20) and postpartum period (P4, P5 and P6). Likewise, we explored maternal behavior of both female rats during the postpartum period (P4 to P6), by assessing time in-nest, on-nest and off-nest, pup licking/grooming, approach to pup and pup retrieval. Maternal behavior of the lactating rats was assessed before and after a dam-pup short separation period, whereas the maternal response of virgins was assessed in the presence and absence of the dam.

Globally, our results reveal that dams decrease social interaction with other known adult female rats from early pregnancy. Otherwise, virgin female rats mostly initiated social interactions with the dam (pregnant or lactating rat), but, during postpartum they reduced social interactions with them. Maternal behavior was fully displayed by dams in the postpartum period, with no changes after a brief pup separation period. However, virgins did not display maternal behavior at all, even after 6 days, when they were expected to be fully sensitized according to the mouse godmother paradigm. In the absence of the dams, virgins approach to pups but never retrieve them. This suggests that exposure to distal pup-derived odours is not enough to maternally sensitize virgin female rats. Access to proximal pup-derived stimuli (vomeronasal or somatosensory) seems prevented by the presence of the dam in the godmother model for rats. These stimuli would be needed for maternal sensitization.

This work has been funded by the Spanish Ministry of Science (PID2019-107322 GB-C21) and Universitat Jaume I de Castelló (UJI-A2019-14). CPG is a predoctoral fellow of Generalitat Valenciana (GV/2020/173).

Effects of motherhood on the response of female mice to male pheromones

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Identifier: 9
Type of communication: ABSTRACT SUBMISSION
Keywords: pheromones, darcin, MUP20, motherhood, maternal aggression

Motherhood constitutes a period of dramatic changes in the life of females that prepare them for ensuring offspring survival. In mice, these changes include reducing social interactions with adult conspecifics, thus restricting their social life to taking care of the pups. In fact, during the peripartum period, mothers furiously attack unknown adults, especially intact adult males, what is known as maternal aggression (Lonstein and Gammie 2002).

There is evidence indicating a key role of male-derived sexual pheromone MUP20 (darcin) in maternal aggression (Martín-Sánchez et al. 2015a, 2015b). Therefore, darcin has different effects throughout females' lifespan, eliciting attraction during adulthood (Roberts et al. 2010, 2012) and aggression only during peripartum. This suggests changes in the central processing of MUP20 and/or in its detection by vomeronasal organ (VNO) cells associated with motherhood. This study aims to understand these changes and how they are related with switching females' response to males during motherhood, from attraction to aggression.

To do so, we exposed virgin females and dams to clean (control) or male-soiled bedding and after 90 min, brains and VNO were processed for cFos and pS6 immunohistochemistry respectively. This way, we combined analysis of female's chemoinvestigation time of the male-soiled bedding with assessment of the patterns of activity (cFos expression) of the sociosexual, motivational and chemosensory brain networks (olfactory and vomeronasal), including the VNO (pS6). The results indicate that motherhood seems to reduce VNO sensitivity, as dams show less activation of the VNO despite having similar exploration times. As for the brain nuclei, when analysed individually, we find differences between groups, between stimulus or both. Moreover, analysis of neural activity in the whole chemosensory-motivational-sociosexual brain network, indicates sharp changes in the pattern of male chemosignals-induced activation with motherhood.

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The mouse as model to study vomeronasal organ alterations in domestic animals

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Identifier: 5
Type of communication: ABSTRACT SUBMISSION

The vomeronasal organ (VNO) is a sensory structure responsible for chemical cues detection and involved in mammals'communication. VNO alterations can severely impair social interactions in cats and farm pigs.

To identify the causes of these changes, we used the mouse model, investigating the effect of the environmental living conditions to identify some of the factors which could explain the social difficulties previously observed in farm pigs.

Therefore, we compared the VNOs from mice housed in normal conditions to mice housed in confined conditions. The confined condition induced more VNO alterations than normal housing ($p<0.0001$) and the non-sensory epithelium was more inflamed ($p=0.0016$), while no differences were observed in the sensory epithelium ($p=0.2251$). Moreover, confined conditions induced a decrease of the olfactory marker protein positivity (OMP) ($p<0.0001$), while Gαi2 protein expression remained unchanged ($p=0.9789$).

Then, we investigated the aging effect on mouse VNOs, observing cellular degeneration ($p<0.0001$), glycogen accumulation ($p<0.0001$), decrease of OMP positivity ($p<0.0001$) and of Gαi2 expression ($p<0.0001$) from 10 months of age. A behavioral study confirmed a decrease of the detection capabilities, showing that aging mice adopted less fear behaviors in presence of an alarm cue ($p<0.0001$). These findings highlighted the importance of age in social groups and better explained the social impairments encountered in aging animals.

These results on the mouse model permitted to better identify one of the causes of vomeronasalitis in farm animals, contributing to improve farm animal conditions and welfare. The study on aging also allowed to discover another cause of VNO alteration.

Stable representation of male features by the mouse AOB during the estrus cycle

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Identifier: 29
Type of communication: ABSTRACT SUBMISSION

The vomeronasal system plays a major role in directing social behaviors, and reproductive behaviors in particular. In most social contexts, the relevance of a given stimulus, and thus the appropriate response, depend on the subject's own state. For example, the response of a female mouse to a male stimulus will depend not only the stimulus, but also on her own reproductive state. This implies that at some stage of the processing pathway, stimulus induced neuronal responses should reflect the female's state. In this work, we set out to investigate how male stimuli are represented by neuronal activity in the first processing stage of the vomeronasal system, namely, the accessory olfactory bulb (AOB), and whether representations change under different reproductive states. To this end, we measured responses to male urine from three strains, in three different male physiological states. Our analysis reveals that the estrus cycle does not modulate either the general response features of AOB neurons, nor their responses to male signals directly relevant for mating. Regardless of the estrus state, we also analyzed the "receptive field" properties of AOB neurons, and found little evidence for preferred representations of either male strain or male physiological state. Our results are consistent with other studies showing that AOB representations of chemosensory stimuli are globally stable, and unlikely to be a major site of state dependent processing.

First Immunohistochemical Demonstration of the Expression of a type-2 Vomeronasal Receptor, V2R, in a Non-Rodent Mammalian Model

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Identifier: 18
Type of communication: ABSTRACT SUBMISSION
Keywords: vomeronasal organ; V2R; G-proteins; Canidae; immunohistochemistry

The vomeronasal system serves as a pivotal element in mammalian sensory biology, allowing the perception of chemical signals essential for social communication via the activation of three receptor families, namely V1R, V2R and FPR. In rodents, V1R expressing neurons are localized in the apical neurons of the vomeronasal organ whereas V2Rs, in the basal ones. Moreover, the expression of V1Rs and V2Rs is tightly linked with that of the G-protein alpha-subunits, Gαi2 and Gαo, respectively. This dichotomy is maintained in the accessory olfactory bulb, thus defining two distinct labelled lines for pheromone transduction. Accordingly, the exploration of the evolutionary pathways of V1Rs and V2Rs across all mammalian species remains a main challenge, juxtaposing available genomic data against emerging immunohistochemical evidence. However, recent investigations, in contrast to what is predicted by the currently annotated genomic sequences, have revealed a marked expression of Gαo in the vomeronasal neuroepithelium of wild canids, including wolves and foxes. In the present study, the employment of a specific antibody raised against the mouse V2R2, a member of the C-family of vomeronasal receptors, V2Rs, has enabled the detection of this receptor in the VNO of fox and wolf, but, unexpectedly, it has revealed the lack of expression in the dog. This may reflect the impact of domestication on the regression of the VNS in this species, in contrast to their wild counterparts, and underscores the effects of artificial selection on sensory functions. Thus, these findings suggest a more refined chemical detection capability in wild species.

Vomeronasal organ alterations: first descriptions and effects on animal behaviour and welfare

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Identifier: 4
Type of communication: ABSTRACT SUBMISSION
Keywords: Vomeronasal organ, pathology, behaviour, chemical communication, domestic animals

The vomeronasal organ (VNO) is responsible for chemical cues detection and, therefore, for animal chemical communication. Since VNO pathologies and their behavioural effects were only recently described, this communication aims to present our studies on VNO spontaneous changes. From 2009, we studied by histopathology VNOs from different species. These studies were conducted according to IRSEA Ethics Committee. In a study on 20 cats, we observed that 70% were affected by VNO chronic inflammation. The χ^2-test revealed that the sensory epithelium inflammation was associated with intraspecific aggression ($P=0.038$). In 38 pigs, we observed that the bilateral vomeronasalitis was associated with an increase in aggressions ($P<0.001$). Immunohistochemistry showed that an inflamed VNO has less neurons and cannot assure a normal intraspecific chemical communication, contributing to the presence of aggressive behaviours. Moreover, we observed that free-range pigs presented more changes than intensive farm pigs, suggesting that dust and microparticles are the main causes of porcine vomeronasalitis, more than the accumulation of farm gases, also considering that digging and rooting are natural behaviours of pigs, which can facilitate microparticles access into VNOs from the mouth. A preliminary study showed that also sheep can be affected by vomeronasalitis, with 25% presenting a bilateral and 25% a unilateral inflammation. Other observations showed vomeronasalitis also in rabbits and dogs. Overall, these findings open the way for novel and different perspectives. For pets, studies should investigate the possibility of diagnosing VNO changes in living animals, while, for farm animals, perspectives mainly concern the impact on animal welfare.

Comments on the mechanisms of semiochemical communication in a domestic dog in the context of reproductive behaviour.

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Identifier: 38
Type of communication: ABSTRACT SUBMISSION
Keywords: dogs; urine; proteome; estrus; chemical signals

In mammals, chemical communication plays a key role in recognizing the status of other individuals of the same species. This may refer to issues such as gender, age, current mental condition (stress) or physical condition (metabolic disease). In the case of sexual behaviour, specific chemical signals emitted by glands located in various parts of the body convey information to males, enabling them to both locate and determine the reproductive status of the female. Moreover, in dogs, some males can recognize the most fertile days during estrus and limit their determined sexual behaviour (mating attempts) only to the most fertile period during estrus. This suggests that the pheromone signal emitted by the female during estrus is not uniform, which may be related to both a change in the composition of the emitted signal as well as a change in the concentration of the substances included in it. Interestingly, this chemical signal can be modified by the influence of saprophytic bacterial flora. In turn, modification of this flora (e.g. its elimination through antibiotic therapy) may affect the composition of the oestrous signal. In chemical communication, many animal species have demonstrated the importance of not only volatile substances but also, for example, less volatile components contained in urine. This group certainly includes well-studied rodent proteins, including (MUP). Research recently published by our team indicates that in the urine of bitches during estrus, an increased concentration of various types of proteins can be observed - those playing a role in fertilization processes (sperm maturation), those involved in immune processes, and those related to semiochemical communication, belonging to the group of lipocalins and performing a transport function for pheromones.

Another extremely important issue in the chemical communication process is the signal detection mechanism. The traditional approach included the detection of odours by the MOB and pheromones by the VNO. Currently, it seems that both systems are involved in the process of detecting chemical signals enabling the identification of estrus in bitches. In many works however, schematically presenting the structure of the VNO in dogs, its structure seems to be oversimplified, suggesting that the only place of contact of the VNO with the environment providing semiochemical signals, is the entrance to the ductus incisivus, located near the incisive papilla in the mouth. Relying on such a simplified scheme may lead to the conclusion that only chemical signals suspended in the liquid phase are available to receptors located in the dog's VNO. Although substances available in the liquid phase (e.g. in urine) can certainly be collected by the dog by licking, it seems that the VNO may also be involved in the process of detection of the volatile substances, through part of the ductus incisivus, which communicates the VNO with the external environment in the nasal cavity, even though this opening of this structure is completely not visible in this area.

The proposed presentation describes interesting features of the mechanism of the semiochemical communication process in dogs, in the context of reproductive behaviour, based on the published own results.

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Influence of human putative sex pheromones on brain activity monitored by rsfMRI.

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Identifier: 39
Type of communication: ABSTRACT SUBMISSION
Keywords: human; pheromones; androstadienone; rs-fMR, brain activity

The existence of semiochemical communication among animals does not raise any doubts. The presence of similar substances in humans, despite some doubts and controversial opinions, is also postulated. Many studies using various substances suspected to be human putative pheromones have been examined till now. Most studies focused on changes in interpersonal perception and mood or evaluated behavioural or physiological effects. Moreover, brain imaging was also performed including fMRI or PET examination. The issue of the existence and activity of VNO in humans was a field of discussion also. The aim of our study was the evaluation of the brain activity stimulated by the androsta-4,16-dien-3-one, a human putative pheromone.

Ten women aged 23-25 with declared heterosexual preferences were included in the study and scanned before and during olfactory stimuli. The experiment was carried out with the use of the MR 3T apparatus and the MR-compatible olfactometer. In the course of the research, volunteers were presented with various substances, including androsta-4,16-dien-3-one (La Croy, RSA), postulated as a human putative pheromone. Using the functional connectivity analysis method based on regions of interest, only after the presentation of the aforementioned stimulus, changes in the connectivity of the right angular gyrus network (stimulation) and changes in the parietal network of the left posterior cortex were demonstrated. Moreover, in response to the androstadienone, the centres located in the area of the frontal lobe were inhibited.

Our results seem particularly interesting taking into account the fact that the frontal lobe centres responsible for the so-called higher mental activities such as planning, assessing the situation, predicting the consequences of actions and controlling emotions arising in the limbic system are located. In addition, this part of the brain is responsible for controlling social behaviour, memory processes and concentration.

The obtained results indicate a similar reaction in all the volunteers, however, further research is needed on a larger group of volunteers, including people with different sexual preferences.

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A neural circuit for identity coding in mice.

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Identifier: 32
Type of communication: ABSTRACT SUBMISSION
Keywords: Individual recognition, identity codebar, MUPs, territorial behavior, vomeronasal.

Mice, as territorial animals, possess an adept spatial navigation ability that is dependent on the integration of stimuli from multiple sensory modalities. A critical information type for navigation is derived from the patterns of major urinary proteins found in conspecific urine, which mark territories and carry the identity of the conspecific owner. This information is integral to the "who" aspect of episodic memory. Our research has pinpointed a neuroanatomical pathway that incorporates individual recognition information into the complex socio-spatial memories within the hippocampus. At the heart of this pathway lies the posteromedial cortical amygdaloid nucleus, acting as the primary conduit for vomeronasal information to be relayed to the hippocampus. We recorded single-unit extracellular activity within this nucleus, employing a head-fixed paradigm where female mice were introduced to various male-derived stimuli. These stimuli ranged from the urine of different males, a synthetic blend of these urines, urine from one male overlaid on another, and to the urine of the female mouse under examination. The selection of these stimuli aims to unravel the encoding of complex natural processes, such as individual recognition, countermarking, and self-perception. To analyze our large-scale dataset, we applied tensor decomposition methods for neural activity analysis, supplemented by CEBRA low-dimensional embeddings and decoding accuracy techniques. Tensor decomposition analysis uncovered that within the cortical amygdala, there exists a dual mechanism: one that responds to a wide spectrum of stimuli and another that is activated specifically by certain stimuli, illustrating a balance between generalization and precise recognition. Likewise, CEBRA embeddings revealed distinct global activity patterns corresponding to each type of urine, enabling the differentiation between individuals. Furthermore, decoding accuracy examination demonstrated that neurons responding to conspecific stimuli subtly alter their responses upon repeated exposures to the same stimulus, indicating the presence of a learning process within the cortical amygdala.

Funded by the Ministry of Science, Innovation and Universities, PID2022-141733NB-I00/AEI/10.13039/501100011033/ FEDER, UE.

ELECTROPHYSIOLOGICAL PROFILE OF NEURONAL POPULATIONS IN THE POSTEROMEDIAL CORTICAL AMYGDALA.

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Identifier: 30
Type of communication: ABSTRACT SUBMISSION
Keywords: PMCo, interindividual recognition, social behaviour

Rodents establish interindividual relationships based on the recognition of volatile and nonvolatile urine molecules, which are detected by the vomeronasal organ. The resulting signals are processed by the accessory olfactory bulb (AOB), which sends projections to several amygdaloid nuclei, including the posteromedial cortical nucleus (PMCo). PMCo, due to its embryonic origin, its specific reelin-mediated laminar organization, and its direct connection to the AOB, is considered the primary vomeronasal cortex. The aim of this study was to characterize the electrophysiological nature of the neurons located in PMCo, in order to better understand their role in the processing of chemosensory information. During recordings, different rodent urines were used as olfactory stimuli and multi-electrode probes were used to record neuronal activity. To carry out the characterization, features such as firing rates and neuronal waveforms were analyzed, allowing the identification of features such as rhythmicity or amplitude of neuronal responses. Preliminary results indicate significant heterogeneity in PMCo neural responses to specific signals, suggesting a complex decoding mechanism that facilitates the recognition of social and territorial cues.

Decoding the Neural Mechanisms of Pheromone Perception in Social Memory Formation

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Identifier: 33
Type of communication: ABSTRACT SUBMISSION
Keywords: Social Memory, Hippocampus, Pheromones, Identity, Single Unit

Social memory serves as a cornerstone for navigating the intricate social landscapes of gregarious species, underpinning critical behaviours such as mate selection and territoriality. Notably, in male mice, the deposition of urine marks, imbued with pheromonal signals, acts as a mechanism for delineating territorial boundaries and attracting mates, thereby playing a pivotal role in social hierarchies and reproductive success. These pheromonal cues are detected by the vomeronasal organ (VNO), which relays this signal through the accessory olfactory bulb (AOB) to the posteromedial cortical nucleus of the amygdala (PMCo). The latter is integrating the pheromonal information into the hippocampal formation, particularly, the vCA1 region, crucial for the storage and retrieval of social memories. Therefore, this pathway is likely facilitating the formation of distinctive engrams that encode social memories. Despite advancements in understanding the sensory processing of pheromones, the neural circuitry mediating the integration of these cues into social memory engrams remains poorly understood. Our research aims to elucidate this circuitry by mapping the neural activity patterns induced by social and chemosensory stimuli, employing behavioural paradigms and c-Fos activation mapping to pinpoint the specific vomeronasal and hippocampal interactions. Additionally, the electrophysiological analysis of vCA1 neurons response to familiar vs unfamiliar conspecifics will help elucidate the neural dynamics underlying social memory. This study not only advances our understanding of the neural substrates of social cognition but also highlights the complex interplay between sensory processing and memory in social behaviour.

Funding: Ministry of Science, Innovation and Universities, PID2022-141733NB-I00/AEI/10.13039/501100011033/ FEDER, UE. CASV is an “Atracció al talent” program predoctoral fellow at the University of Valencia.

Cutting-edge progress in computational modelling of olfactory and vomeronasal receptors in mammals

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Identifier: 14

Type of communication: ABSTRACT SUBMISSION

Keywords: Semiochemicals, Vomeronasal receptors (VRs), Olfactory receptor (ORs), Molecular dynamic simulation (MDS), Bioinformatics

The chemical cues and other odorant molecules are detected by the peripheral vomeronasal receptors (VRs) in the vomeronasal organ (VNO) and olfactory receptors (ORs) in the main olfactory epithelium for enhancing socio-sexual communication in mammals. Specifically, semiochemicals are secreted by different glands and trigger emotional and behavioural responses, which play a significant role in the welfare of animals. At present, VRs do not have any experimental structures and a few cryo-electron microscopy structures of humans are available. Therefore, an in-silico approach is necessary to study the sequence and structural annotation of VRs and ORs in animals. We have applied several approaches to build the models for these receptors, such as template-based comparative structural modeling, machine learning, threading, and ab initio methods. In the last two decades, substantial research has led to the invention of computational models like AlphaFold2, which provide structural predictions close to experimental accuracy. However, the other structure prediction algorithms, such as ESMFold, predict high-resolution structures 60x faster from primary protein sequences, while Robetta is more accurate for membrane-compatible topology than AlphaFold. Besides, structural validation is crucial for ensuring the accuracy and reliability of models. It is essential to verify the polypeptide backbone conformation (dihedral angles), folding, and stability through molecular dynamic simulation (MDS) with compatible membranes for models. Here, we highlight recent significant advances in computational analysis that have accelerated the determination of protein structures, hence providing biological insights into structures of VRs and ORs that are currently unknown.

Preliminary results on computational analysis of vomeronasal type-2 receptors (V2Rs) in mammals

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Identifier: 15
Type of communication: ABSTRACT SUBMISSION
Keywords: Vomeronasal type-2 receptors (V2Rs), Sequence analysis, Bioinformatics, Semiochemicals

Animals perceive chemical signals in their environment, known as semiochemicals, which are involved in chemical communication. These signals induce behavioural or physiological changes and range from small molecules to larger proteins. Semiochemicals are perceived by different chemoreceptors (CRs), including vomeronasal type-2 receptors (V2Rs) in the vomeronasal organ (OVN), which is the focus of this study. V2Rs are thought to be specialized for the detection of non-volatile peptides and proteins. Despite their role in semiochemical communication, only a few studies have been conducted on the V2Rs of various animal species, and no study has been conducted to examine the structure of V2Rs. This study presents the preliminary results of the analysis and annotation of V2R sequences from 10 animal species, including mammals and a separate outgroup of salmonids. Using computational tools, V2R sequences were analysed for phylogeny, family, and subfamily classification, and sequence conservation. V2R protein and gene sequences were collected on the NCBI server and examined. No sequences have been found for cats, and only some pseudogenes have been identified for dogs and humans. V2R proteins show low conservation between families reaching 25% between murine A and C families and conservation of around 60% between mammalian homologs. Transmembrane helices are well conserved, and some motifs can be identified in the N-terminal loop. Subfamilies were also assigned to different V2Rs according to phylogenetic results and by comparison with the known murine subfamilies. These results are part of a modelling study protocol that aims to investigate the interactions of V2Rs.

Unlocking the Mystery of Odor Recognition: Recent Advances in Understanding Odorant-Receptor Interactions

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Identifier: 16
Type of communication: ABSTRACT SUBMISSION

A central challenge in olfaction is understanding how the olfactory system detects and distinguishes odorants with diverse physicochemical properties and molecular configurations. In humans, ~400 ORs represent the repertoire of receptors responsible for our sense of smell by responding to even a wider pool of odorant molecules in a combinatorial activation pattern. How ORs recognize chemically diverse odorants remains poorly understood. A fundamental bottleneck is the inability to visualize odorant binding to ORs. Only in the last year, we have been able to solve the first structure of a human OR with an odorant bound to it [1]. Using a consensus protein design strategy, three additional consORs have been released, uncovering fundamental molecular properties of odorant-OR interactions [2]. Here, I present the recently revealed structures which provide greatly valuable insight on how this large family of G protein-coupled receptors copes with the immense chemical diversity of odorant molecules enabling our sense of olfaction.

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Unraveling Natural Variations in Olfactory Receptors: Steps Toward an Emerging Sensegenomics Field

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Identifier: 1
Type of communication: ABSTRACT SUBMISSION
Keywords: Olfactory Receptors, Mutation, Natural Variant, GPCR, Sensegenomics

The sense of smell plays a crucial role in human perception, influencing behaviors, emotions, and revealing pathological conditions. Detecting and discriminating among a wide range of odor molecules is a task carried out by olfactory receptors (ORs), encoded by the largest sensory gene family in the human genome. By leveraging large-scale genomic datasets and advanced bioinformatics tools, it is possible to identify and study numerous single nucleotide polymorphisms (SNPs) and structural variants within OR genes across diverse human populations, shedding light on the potential impact of these variations on olfactory perception. Here, we present findings from a study investigating the number and distribution of more than one hundred thousand OR genetic variations in seven human populations, contributing to inter-individual differences in olfactory sensitivity and odor perception. Drawing inspiration from the Pharmacogenomics and Nutrigenomics fields, the investigation through the analysis of genomic data of the elements involved in sensory signal transduction pathways could shape an emerging Sensegenomics field of research, aiming to identify genetic markers associated with sensory traits and to develop personalized approaches for modulating and enhancing sensory genes and proteins. By integrating genomics, sensory physiology, and behavioral studies, researchers can gain valuable insights into the complex interplay between genetics, environment, and olfactory function, ultimately advancing our understanding of human smell perception and its implications for health and well-being.

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Making a new model - Olfactory neuroecology in the migratory locust

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Identifier: 10
Type of communication: ABSTRACT SUBMISSION
Keywords: insect, olfaction, glomerulus, swarming, locust

The locusts differ from many other insects both in ecology, and in olfactory function and anatomy. We have spent the recent five years developing tools to investigate the olfactory ecology of these swarming insects in detail using state-of-the-art technology. I will describe our results from investigations of both the peripheral and the central nervous system, as well as from studies of a specific interaction involving an anti cannibalistic pheromone.