



Institut de Neurociències
UNIVERSITAT DE BARCELONA



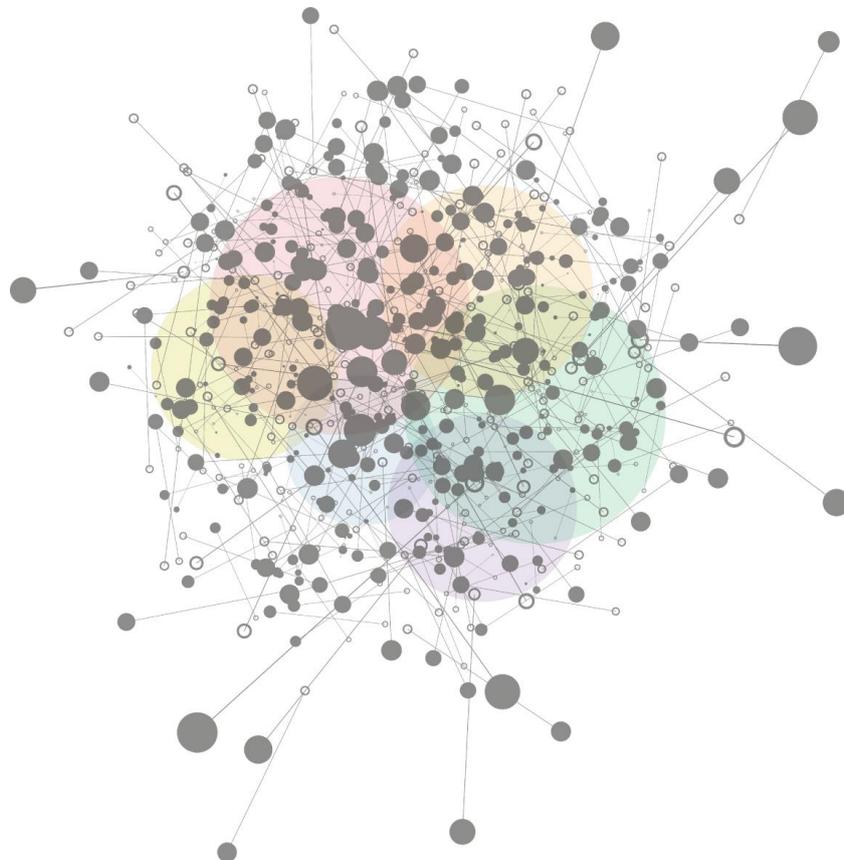
**EXCELENCIA
MARÍA
DE MAEZTU**

IV PhD Workshop, Institute of Neurosciences

University of Barcelona

29 November 2019

Faculty of Medicine and Health Sciences
Campus Bellvitge, Hospitalet de Llobregat



**UNIVERSITAT DE
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Index

Index.....	3
Schedule	6
Plenary speaker	7
Future opportunities	9
Workshop	10
Oral presentations.....	11
Immunological findings of the anti-IgLON5 disease.....	11
Analysis of the role of GABAB receptor in oligodendrocyte differentiation and myelination in vivo	12
Differences in reported rates of mind wandering are associated with divergent exploitation of environmental information in creative problem solving.....	13
The relationship between appearance-focused social network sites use and body image concerns	14
An invisible reality or an ignored minority? Victimization and poly-victimization experiences among people with mental illness in Spain	15
Effects of actions on encoding and retrieval of sounds: Physiological mechanisms	16
Identification of altered specific neuronal subpopulations in stress-induced major depression	17
Repeated optogenetic stimulation of corticostriatal pathway ameliorates huntington’s disease symptoms: from synaptic efficacy to network dynamics.....	18
Order of poster presentations	19
Poster presentations Group 1 (10:45h-11:30h).....	22
1) Factors secreted by astroglia modulate local protein synthesis in neurites.....	22
2) A β oligomers regulate the transcriptional and post-transcriptional control of oligodendrocyte differentiation.....	23
3) NMDA receptor antibodies in autoimmune encephalopathy alter oligodendrocyte function	24
4) How to move to catch flying balls with updating predictions	25
5) The psychological model of Binge Eating Disorder: an structural equation modelling ..	26
6) Cell cycle dysregulation as a novel mechanism of striatal vulnerability in Huntington's disease.....	27
7) Loss of TRESK enhances acute and chronic itch in mice	28
8) Huntington’s disease brain-derived small RNAs trigger motor dysfunction and striatal damage in mice	29
9) Validation of the Spanish version of the Maternal Attachment Inventory	30



10) Cognitive and electrophysiological recovery in a mice model of Alzheimer's disease accumulating both amyloid- β peptide and hyperphosphorylated Tau	31
11) Oscillatory networks underling reward processing of familiar and unfamiliar music ..	33
12) Static and Dynamic Functional Connectivity in Down Syndrome	34
13) Resting-state dinamic connectivity in people with major depressive disoreder in remission	35
14) The frequency-following response (FFR): a useful clinical tool to assess cognitive impairments during the first days of life	36
15) Executive function training as intervention for childhood obesity: Preliminary results	38
16) Math anxiety and the shifting executive function	39
36) Modeling the radial glial niche: mechanical-driven changes in 2D biomimetic materials	40
Poster presentations Group 2 (13:45h-15:30h)	41
17) Local protein synthesis in microglia cells in the healthy and diseased conditions	41
18) Microglial activation prevents A β -induced synaptic dysfunction and reduces extracellular A β in Alzheimer's disease	42
19) Multimodal hierarchical cluster analysis based on grey and white matter measures identifies different patterns in Parkinson's disease	43
20) Quality of life in cerebral palsy: the importance of visuospatial abilities	44
21) c-Jun N-terminal Kinase 1: A key element for the protection against cognitive deficits derived of metabolic alterations	45
22) The Spanish version of the Internet Gaming Disorder Scale-Short Form (IGDS9-SF): An item response theory approach	46
23) How body image is affected by body weight discrimination	47
24) Improving opioid pain treatment: light-activated morphine	48
25) Hippocampal PYK2 modulates impaired social behavious in schizophrenia via regulation of mitochondria dynamics	49
26) Epigenetic changes after unpredictable chronic mild stress in female SAMR1 and SAMP8: Effects on Behavior	50
27) I2-Imidazoline ligand, LSL60101, improves cognition in the 5XFAD mouse model	51
28) Network Analysis of the Brief ICF Core set for schizophrenia	52
29) The role of school personnel knowledge in detecting and reporting children and youth victimization	53
30) Role of the JNK3 isoform in the development of metabolic disorders and their relationship with cognitive alterations	54
31) A new NMDA receptor antagonist improves learning and memory reducing β -amyloid accumulation and preserving synaptic markers in 5XFAD mice	55



32) Corpora amylacea of human brain are intracellular bodies that exhibit a homogeneous distribution of neo-epitopes	56
33) F-actin reorganization and synapse elimination activate intersynaptic homeostatic plasticity	57
34) Extensive in vitro and in vivo characterization of promising NMDA channel blockers	58
35) Role of TRESK potassium channel in the modulation of pain sensitivity by tacrolimus	59
37) Human hierarchical auditory prediction error	60
38) Neurophysiological signals supporting the online formation of life-like episodic sequence of events	61
39) Effect of External Representations on Rhythm Learning	62
40) Human hippocampal neurophysiological signals supporting the formation and retrieval of memories for episodic events	63
41) The Psychoacoustics of Rock Art Landscapes. Relating auditory-evoked emotions to acoustic parameters perception	64
42) What memories are affected in children with cerebral palsy?	65
43) Encoding of fundamental frequency and fine structure of speech sounds: A comparative between adults and newborns	66
44) Neurophysiology of epilepsy	67
45) Pseudoscience Endorsement Scale	68
46) Maternal resveratrol diet regulates Endoplasmic Reticulum Stress in SAMP8 mice model: cognitive and epigenetic changes across generations	69



Schedule

Location: [Faculty of Medicine and Health Sciences](#), Campus Bellvitge, Feixa Llarga s/n, Hospitalet de Llobregat.

9:00 Registration and poster reception [Former concierge, 1st floor, Aulari]

Opening ceremony [Sala de Graus, 1st floor, Aulari]

9:20 Dr. José Luis Rosa López, Research Vice-Dean of the Faculty of Medicine and Health Sciences, UB.

Dr. Raúl Estévez Povedano, Board of Directors of the Institut of Neurosciences, UB.

Oral presentations [Sala de Graus, 1st floor, Aulari]

- 09:30
- Jon Landa Medrano – “*Immunological findings of the anti-IgLON5 disease*”.
 - Laura Bayón Cordero – “*Analysis of the role of GABA_B receptor in oligodendrocyte differentiation and myelination in vivo*”.
 - Diana C. Díaz Cruz – “*Differences in reported rates of mind wandering are associated with divergent exploitation of environmental information in creative problem solving*”.
 - Helena Vall Roqué – “*The relationship between appearance-focused social network sites use and body image concerns*”.

10:30 **3' Poster presentation** (group 1)

10:45 Poster session (group 1) + Midmorning breakfast [Corridor Sala de Graus, 1st floor, Aulari]

Oral presentations [Sala de Graus, 1st floor, Aulari]

- 11:30
- Marina Bartolomé Valenzuela – “*An invisible reality or an ignored minority? Victimization and poly-victimization experiences among people with mental illness in Spain*”.
 - Nadia Paraskevoudi – “*Effects of actions on encoding and retrieval of sounds: Physiological mechanisms*”.
 - Anna Sancho Balsells – “*Identification of altered specific neuronal subpopulations in stress-induced major depression*”.
 - Sara Conde Berriozabal – “*Repeated optogenetic stimulation of corticostriatal pathway ameliorates Huntington's disease symptoms: from synaptic efficacy to network*”.

12:30 **3' Poster presentation** (group 2) [Sala de Graus, 1st floor, Aulari]

12:45 **Plenary lecture: Local translation: the whats and whys of decentralized regulation of gene expression.... and what-nots** - Dr. [Jimena Baleriola](#), Ikerbasque Research Fellow, Achucarro - Basque Center for Neuroscience [Sala de Graus, 1st floor, Aulari]

13:45 Poster session (group 2) + Lunch [Behind restaurant, Governance Pavilion]

15:30 **Life Beyond Post-Graduate** - Jordi Naval, CEO BioCat [Sala de Graus, 1st floor, Aulari]

16:15 **Workshop: Body Language for Scientists** - Brian McCarthy, Executive coach [Sala de Graus, 1st floor, Aulari]

18:15 **Awards** [Sala de Graus, 1st floor, Aulari]

18:30 **Socialization** Life Music with The Rayberis [Entrance Faculty of Medicine and Health Sciences]

Sponsors





Plenary speaker

Jimena Baleriola Gómez de Pablos

Group Leader- Ramón y Cajal Fellow (Ikerbasque Research Fellow in leave of absence)

Laboratory of Local Translation in Neurons and Glia (former Axon-Glia Interactions)

Achucarro Basque Center for Neuroscience

I graduated in Biochemistry at the Universidad Complutense de Madrid (2003) and started my career as a neuroscientist when at Center for Biological Research (Madrid, 2004). From 2004 to 2008 I conducted research on the molecular alterations that affect DNA integrity and impact on programmed cell death during central nervous system development. On 2008 I obtained my Ph.D. from the Department of Biochemistry and Molecular Biology at Universidad Complutense. I continued my research on DNA repair and programmed cell death as a postdoctoral researcher until 2010.

To further my career in neuroscience research, in 2010 I joined the laboratory of Dr. Ulrich Hengst at the Taub Institute for Research on Alzheimer's Disease and the Aging Brain, Columbia University Medical Center (New York, USA). My research projects aimed to unravel a possible role for intra-axonal protein synthesis in amyloid pathology, a central feature of Alzheimer's disease. When I joined the



Taub Institute there was no evidence in the literature that local translation in axons could play a role in the adult central nervous system (CNS) in the context of a neurodegenerative disease. I defined a novel unexpected molecular pathway that mediates axon-to-soma spread of amyloid pathology that requires local protein translation in axons (Baleriola et al. 2014, Cell). My work as a postdoctoral researcher was featured in AlzForum by its scientific advisory board, as well as in scientific journals such as Science Signaling (Editor's Choice) or CNS & Neurological Disorders-Drug Targets. I was also one of the only twelve candidates that Columbia University nominated for the 2015 Blavatnik Awards for Young Scientists.

Throughout these years I've gained extensive expertise, not only in the basic mechanisms that lead to cell death during neural development and neurodegeneration, but more importantly, in mRNA localization and local translation. The study of local protein synthesis is far from trivial, since it requires the use of challenging techniques.

In 2015 I was awarded with an Ikerbasque Research Fellow contract from the Basque Foundation for Science. This 5-year tenure-track style position allowed me to conduct my research at the Achucarro Basque Center for Neuroscience as group leader of the Laboratory of Local Translation in Neurons and Glia. In 2018 I was appointed Ramón y Cajal Fellow. My lab focuses on two main research lines: 1) to decipher the contribution of glial cells to intra-axonal protein synthesis through horizontal transfer of extracellular vesicles in physiological and pathological conditions (e.g experimental models of Alzheimer's disease) and 2) to unravel the role of local protein synthesis in glia (e.g oligodendrocytes, microglia...) in the healthy and the diseased brain.



Local translation: the whats and whys of decentralized regulation of gene expression.... and what-nots

According to text books, most RNA translation in eukaryotic cells occurs in the rough endoplasmic reticulum (RER) after the mRNAs are transcribed and exit the nucleus. Once the proteins are generated and become mature, many of them are targeted to different subcellular compartments. Subcellular protein delivery is typically achieved by localization signals within the protein sequence and it enables functional compartmentalization, which is especially important in signal transduction and cell behavior. However, protein delivery to distinct cellular compartments can rely, not only on the transport of the protein itself but on the transport of the mRNA that is then translated at target sites. Although once considered heretical, the mechanism of localizing RNAs rather than proteins has proven to be highly prevalent and conserved in eukaryotes.

RNA localization and local translation are especially relevant in highly polarized cells, such as neurons, where the tip of an axon for instance can be located more than a meter away from the cell soma. Local translation confers some major advantages to axons over transporting “already made” proteins: 1) localizing the transcript ensures the cell that the protein is generated in a “just in time, just in place” manner; 2) RNAs are tightly packaged in granules and thus the “message” does not diffuse during transport, and 3) one single RNA copy produces several protein copies by undergoing multiple rounds of translation, thus local protein synthesis might be more “economic” for protein subcellular delivery in polarized cells. For the last years, our lab has been committed to better understand localized translation in axons and to demonstrate the contribution of glia to this phenomenon in the physiology and the pathology of the central nervous system (CNS). More recently we became interested in the contribution of local translation in glia itself to brain function and dysfunction.

Even if the existence of localized translation is finally acknowledged by the scientific community there are still fundamental questions that remain unanswered, especially in neurons. Here I will summarize the state-of-the-art of this exciting field of research and discuss about the technical and conceptual challenges we still have ahead of us.



Future opportunities

Life Beyond Post-Graduate: Keys for Entrepreneurship in Life Sciences

Jordi Naval

CEO of BioCat

Jordi Naval is currently director of Biocat, the organization that drives the health and life sciences ecosystem in Catalonia and works to transform science and technology into regional economic growth and social impact.

We'll review the biotech business model, and how academic science at the origin of the development of new medicines, therapies and technologies, and scientific entrepreneurship as one of the major drivers of innovation and social impact, and how specialized positions are in high demand.



Workshop

Body Language for Scientists

Brian McCarthy

Executive coach

Description of Workshop:

This workshop explores the complex world of body language in a professional context. It helps participants understand their own body language and that of others. It consists of interesting and fun exercises by the entire group, followed by a personal analysis of the body language of each participant, all carried out in a supportive and relaxed atmosphere.

Who is this for?

This workshop is for anyone who has to regularly perform as a leader – in presentations, negotiations, interviews or crucial conversations.

Topics Covered (depending on participants' needs):

- What happens to your body language when you are under stress
- Gesturing
- Posture – sitting and standing with confidence
- Voice
- Movement
- Greetings and meeting people for the first time
- Body language when negotiating and presenting



Oral presentations

Immunological findings of the anti-IgLON5 disease

J. Landa¹, J. Planagumà¹, F. Graus¹, J. Dalmau¹, L. Sabater¹

¹IDIBAPS, Hospital Clinic, Barcelona

Objective: To report novel immunological findings in the IgLON5 disease.

Background: IgLON5 disease is an immune-mediated sleep and brainstem disorder that occurs in association with antibodies against IgLON5 and pathological evidence of deposits of tau in neurons of the brainstem.

Methods: HEK293 cells expressing deletion constructs of IgLON5 were used to determine the epitopes. IgG subclasses were quantified by flow cytometry, and dissociated hippocampal neuronal cultures were used to examine the effects of IgG subclasses of IgLON5 antibodies.

Results: Patients' antibodies reacted with the immunoglobulin-like domain 2 of IgLON5. The predominant IgG subclass was IgG4 but all patients also had IgG1. The mean percentage of specific IgLON5 IgG4 and IgG1 antibodies was 64 and 33 % respectively. Patients' antibodies caused an irreversible decrease of neuronal cell surface IgLON5 clusters. These effects were mediated by IgG1 but not IgG4 IgLON5 autoantibodies.

Conclusions: (1) The main epitopes of IgLON5 disease are in the immunoglobulin-like domain 2 of the protein. (2) Patients' IgLON5 autoantibodies cause an irreversible internalization of surface IgLON5. (3) These effects are mediated by specific IgLON5 IgG1, but not IgG4, antibodies, and suggest a pathogenic role of the antibodies.



Analysis of the role of GABAB receptor in oligodendrocyte differentiation and myelination in vivo

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Oligodendrocytes are the myelinating cells of the central nervous system (CNS), and to perform their function they must differentiate from oligodendrocyte progenitor cells, a critical event highly regulated by neuron-oligodendrocyte communication. Among the molecules involved in these interactions are neurotransmitters, including γ -aminobutyric acid (GABA). Our previous work has demonstrated that activation of oligodendroglial GABAB receptors (GABABR) in vitro enhanced oligodendrocyte differentiation and the expression of the myelin basic protein (MBP).

In the present study, the role of GABABR in oligodendrocyte functionality was examined in vivo. First, GABABR expression was verified in oligodendrocytes in white matter tracts of murine CNS.

Then, myelination was studied during development of rats after the administration of GABABR agonist baclofen or the antagonist CGP35348, from P6 to P21. Corpus callosum, a relevant white matter region in the brain, was analyzed at early (P12) and advanced stages (P34-42), and significant increases in oligodendrocyte differentiation in P12 baclofen-treated rats were observed, together with higher MBP expression at advanced ages.

Moreover, electrophysiological records of the compound action potentials in these animals indicated that baclofen enhanced the conduction velocity of the fastest fibers in the corpus callosum. However, in these cases no significant effects were observed after CGP35348 treatment. The effect of baclofen was further investigated in a murine model of primary demyelination induced by the intraspinal injection of lysolecithin. After lesion, mice were injected for seven days with vehicle or baclofen, and baclofen seemed to induce a stronger oligodendrocyte maturation rate. Together, these observations support the relevance of GABABR in oligodendrocyte differentiation and myelination in vivo.



Differences in reported rates of mind wandering are associated with divergent exploitation of environmental information in creative problem solving

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Previous research shows discrepant results regarding the role of inhibition in creativity. Individuals with low inhibition tend to get higher scores in creative achievement questionnaires, presumably because they are prone to notice information that may seem irrelevant and take advantage of it. On the other hand, it has been proposed that an improved inhibitory capacity poses an advantage to overcome adherence to fixed unoriginal ideas in creativity tasks. We asked a group of 161 volunteers to design a method to prevent an egg from breaking when thrown 4 meters above the ground (the egg task). Half of the participants performed the task while listening to auditory stimuli including hints and distractor words unrelated to the task. All the participants also rated their inhibition using a mind wandering questionnaire. We hypothesized that the results of the egg task would be affected by differential exploitation of environmental resources by low and high inhibition individuals. Individuals who reported low inhibition benefited more of the hints mixed within auditory distractors. Accordingly, individual inhibitory capacity should be taken into account to develop optimal conditions for creative problem solving.



The relationship between appearance-focused social network sites use and body image concerns

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¹Department of Clinical Psychology and Psychobiology, University of Barcelona

Objective: The present study aimed to examine if using social network sites (SNS) for appearance-related purposes was associated with a negative body image. This study also explored whether following appearance-focused accounts on Instagram was related to body image disturbances.

Method: A total of 599 participants -both males and females- aged 16-65 years completed questionnaire measures of SNS use and body image concerns.

Results: It was found that those participants that reported using SNS for appearance-related reasons showed significantly higher levels of body dissatisfaction, drive for thinness, internalization of the thin-ideal, social comparison and appearance comparison, compared to those who reported using SNS for other purposes. Similarly, following appearance-focused accounts on Instagram was associated with significantly higher levels of body dissatisfaction, internalization of the thin-ideal, social comparison and physical appearance comparison.

Conclusions: An appearance-focused use of SNS might contribute to body image disturbances. This could have implications for eating disorder prevention programs. However, causality cannot be demonstrated from this cross-sectional study.



An invisible reality or an ignored minority? Victimization and poly-victimization experiences among people with mental illness in Spain

M. Bartolomé¹, M. Codina¹, N. Pereda¹, G. Guilera¹

¹Institute of Neurosciences

Mental illness has often been related to violence and aggressive behaviour. However, contrary to conventional thought, many studies have shown that there is a stronger association between mental illness and victimization than between mental illness violent behaviour.

This research explores the association between different forms of victimization and poly-victimization during the lifetime of a sample of 70 people diagnosed with mental illness. The results show a high prevalence in all types of victimization studied, especially during childhood, as well as a high prevalence of poly-victims within the group of people with mental disorders when comparing to similar investigations done with community samples. This study opens the door to further research in the field of victimization and disability and seeks to change the stigma of the mental illness in order to show a reality that is often unknown or ignored.



Effects of actions on encoding and retrieval of sounds: Physiological mechanisms

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Motor activity has been shown to modulate sensory processing, as evident by the attenuated physiological responses for self- compared to externally-generated stimuli. Although these effects have been traditionally attributed to motor-related predictive signals, they are observed in non-predictive contexts as well, i.e., with mere coincidence between the sound and the motor act. Meanwhile, some evidence also shows memory enhancements for self-generated stimuli (e.g., spoken words), known as the production effect. Yet, to-date, no attempts have been made to link the production effect with the self-generation effects. Here, we aimed to elucidate these possible links from the angles of basic physiology, low-level sensory processing, and memory processes, by examining whether and how motor actions affect the memory encoding of concurrent sounds. We recorded the behavioral and brain responses during a recognition task with both externally- and self-generated, albeit not predictable, sounds. While no memory enhancements were found for the self-generated sounds, our preliminary findings show attenuated evoked activity to sounds coinciding with a motor act, which was, nevertheless, absent when the same sounds were passively presented at a later retrieval phase. Collectively, different mechanisms may underlie the self-generation and production effects, thus pointing to dissociable effects of self-generation on low-level sensory processing and memory.



Identification of altered specific neuronal subpopulations in stress-induced major depression

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Major depression (MD) is a common, relapsing mental illness that affects millions of people worldwide. One of the most studied environmental risk factor associated with MD is chronic stress. Current treatment is ineffective in approximately 30% of patients so there is a need to fully understand the pathophysiology of MD to design more effective therapeutic approaches.

Therefore, our objective was to identify specific neuronal subtypes playing crucial roles in the genesis of stress-induced MD. In order to determine which cells were activated upon chronic unpredictable mild stress (CUMS), we used the Zif268:CreERT2 mice x Floxed-Stop-GFP. These mice allowed us to permanently label the activated cells upon CUMS in a tamoxifen-dependent manner. After CUMS, depressive-like behavior was evaluated and then the brains were analyzed. Results showed that the CA1 of the hippocampus is one of the main brain regions sensitive to chronic stress. Additionally, we found a reduction in spine density in the activated CA1 pyramidal neurons after CUMS. Regarding the identity of the activated engram cells, we observed that the cells inside the engram were Calbindin+ (Calb) pyramidal neurons and that there was a shift from Calb- to Calb+ upon CUMS.

In summary, our works suggest the presence of a hippocampal engram activated due to chronic stress the modulation of which will allow us to better understand the contribution of these cells in the pathophysiology of MD.



Repeated optogenetic stimulation of corticostriatal pathway ameliorates huntington's disease symptoms: from synaptic efficacy to network dynamics

S. Conde-Berriozabal^{1,2,3}, S. Fernández-García^{1,2,3}, E. García-García^{1,2,3}, C. Gort-Paniello^{1,2,3}, D. Bernal-Casas⁶, G. García-Díaz Barriga^{1,2,3}, J. López-Gil², E. Muñoz², G. Sòria², L. Campa^{2,4,5}, F. Artigas^{2,4,5}, J.M. Rodríguez^{1,2,3}, J. Alberch^{1,2,3}, M. Masana^{1,2,3}

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Huntington's Disease (HD) is a rare and devastating inherited neurological disorder characterized by motor disturbances including chorea. Brain HD pathology is most prominent in the striatum, the main hub of the basal ganglia circuitry, with a selective degeneration of GABAergic medium spiny neurons. Its main afference is the cortex and indeed, HD is characterized by a progressive disconnection between cortex and striatum manifested as a reduction in striatal synaptic activity. Thus, we aimed to restore motor symptoms by modulating corticostriatal function in the R6/1 HD mice.

Using *in vivo* MRI, optogenetics and microdialysis and *ex vivo* multielectrode arrays, we characterized corticostriatal dysfunction in HD. Then, we applied repeated optogenetic stimulation in symptomatic R6/1 HD mice and evaluated motor learning, coordination. We also measure spine density using Golgi staining and synaptic markers by immunofluorescence and Western-blot.

Structural and functional MRI showed loss of corticostriatal function in R6/1 HD mice. Also, we measured a reduction of striatal glutamate levels (GluCEST and MRS) and corticostriatal release (optogenetics coupled to microdialysis). The electrophysiological response of striatal neurons to optogenetically-induced corticostriatal function was also reduced in HD mice (MEA). Finally, repeated corticostriatal optogenetic stimulation in symptomatic HD mice (R6/1-ChR2) improved motor learning (accelerating rotarod), coordination (balance beam test), exploratory activity (rearings) and stereotypic behavior (grooming), compared to control R6/1-YFP mice, almost reaching WT levels. This improvement was accompanied by a restoration of spine density.

Thus, we demonstrate for the first time an *in vivo* effective optogenetic-induced recovery of HD motor symptoms. Further investigations will help to understand the mechanisms involved and to design novel therapeutic strategies aiming to restore network dysfunction in HD.



Order of poster presentations

	SURNAME/S	NAME	TITLE	NUMBER
10.45 - 11.30h	Gamarra Garcia-Bermejo	María	Factors secreted by astroglia modulate local protein synthesis in neurites	P1
	Gaminde Blasco	Adhara	A β oligomers regulate the transcriptional and post-transcriptional control of oligodendrocyte differentiation	P2
	Maudes	Estibaliz	NMDA receptor antibodies in autoimmune encephalopathy alter oligodendrocyte function	P3
	Aguado Ramirez	Borja	How to move to catch flying balls with updating predictions	P4
	Varela Vázquez	Carmen	The psychological model of Binge Eating Disorder: an structural equation modelling	P5
	Espina Cortes	Marc	Cell cycle dysregulation as a novel mechanism of striatal vulnerability in Huntington's disease.	P6
	Andrés Bilbé	Alba	Loss of TRESK enhances acute and chronic itch in mice.	P7
	Guisado Corcoll	Anna	Huntington's disease brain-derived small RNAs trigger motor dysfunction and striatal damage in mice	P8
	López Fernández	Gemma	Validation of the Spanish version of the Maternal Attachment Inventory	P9
	Dávila Bouziguet	Eva	Cognitive and electrophysiological recovery in a mice model of Alzheimer's disease accumulating both amyloid- β peptide and hyperphosphorylated Tau	P10
	Ara	Alberto	Oscillatory networks underling reward processing of familiar and unfamiliar music	P11
	Cañete Massé	Cristina	Static and Dynamic Functional Connectivity in Down Syndrome	P12
	Duarte Rosas	Patricia	Resting-state dinamic connectivity in people with major depressive disoreder in remission	P13
	Ribas-Prats	Teresa	The frequency-following response (FFR): a useful clinical tool to assess cognitive impairments during the first days of life	P14
	Luis Ruiz	Sandra	Executive function training as intervention for childhood obesity: Preliminary results	P15
	González Gómez	Belén	Math anxiety and the shifting executive function	P16
Soriano Esqué	José Pablo Esqué	Modeling the radial glial niche: mechanical-driven changes in 2D biomimetic materials	P36	



	SURNAME/S	NAME	TITLE	NUMBER
13.45 - 15.30	Blanco Urrejola	Maite	Local protein synthesis in microglia cells in the healthy and diseased conditions	P17
	Zuazo Ibarra	Jone	Microglial activation prevents A β -induced synaptic dysfunction and reduces extracellular A β in Alzheimer's disease	P18
	Inguanzo Pons	Anna	Multimodal hierarchical cluster analysis based on grey and white matter measures identifies different patterns in Parkinson's disease	P19
	Blasco	Montse	Quality of life in cerebral palsy: the importance of visuospatial abilities.	P20
	Busquets Figueras	Oriol	c-Jun N-terminal Kinase 1: A key element for the protection against cognitive deficits derived of metabolic alterations	P21
	Maldonado-Murciano	Laura	The Spanish version of the Internet Gaming Disorder Scale-Short Form (IGDS9-SF): An item response theory approach	P22
	Macho García	Sergio	How body image is affected by body weight discrimination	P23
	López Cano	Marc	Improving opioid pain treatment: light-activated morphine.	P24
	López Molina	Laura	Hippocampal PYK2 modulates impaired social behaviour in schizophrenia via regulation of mitochondria dynamics	P25
	Puigoriol Illamola	Dolors	Epigenetic changes after unpredictable chronic mild stress in female SAMR1 and SAMP8: Effects on Behavior	P26
	Vasilopoulou	Foteini	I2-Imidazoline ligand, LSL60101, improves cognition in the 5XFAD mouse model	P27
	Abdelhamid	Gomaa Said Mohamed	Network Analysis of the Brief ICF Core set for schizophrenia	P28
	Greco	Ana Martina	The role of school personnel knowledge in detecting and reporting children and youth victimization	P29
	Espinosa Jiménez	Triana	Role of the JNK3 isoform in the development of metabolic disorders and their relationship with cognitive alterations	P30
	Comanys Alemany	Júlia	A new NMDA receptor antagonist improves learning and memory reducing β -amyloid accumulation and preserving synaptic markers in 5XFAD mice.	P31
Riba	Marta	Corpora amylacea of human brain are intracellular bodies that exhibit a homogeneous distribution of neo-epitopes	P32	



	SURNAME/S	NAME	TITLE	NUMBER
13.45 - 15.30	Velasco Dominguez	Cecilia	F-actin reorganization and synapse elimination activate intersynaptic homeostatic plasticity	P33
	Turcu	Andreea Larisa	Extensive in vitro and in vivo characterization of promising NMDA channel blockers	P34
	Pujol Coma	Anna	Role of TRESK potassium channel in the modulation of pain sensitivity by tacrolimus.	P35
	Font Alaminos	Marta	Human hierarchical auditory prediction error	P37
	Wu	Xiongbo	Neurophysiological signals supporting the online formation of life-like episodic sequence of events	P38
	Deosdad Díez	Marc	Effect of External Representations on Rhythm Learning	P39
	Saint Amour di Chanaz	Ludovico	Human hippocampal neurophysiological signals supporting the formation and retrieval of memories for episodic events	P40
	Valenzuela Ruiz	Jose	The Psychoacoustics of Rock Art Landscapes. Relating auditory-evoked emotions to acoustic parameters perception	P41
	García-Galant	María	What memories are affected in children with cerebral palsy?	P42
	Arenillas-Alcón	Sonia	Encoding of fundamental frequency and fine structure of speech sounds: A comparative between adults and newborns	P43
	Fuertes Silva	Paula Maria	Neurophysiology of epilepsy	P44
	Torres Domínguez	Marta Natalia	Pseudoscience Endorsement Scale	P45
Izquierdo	Vanessa	Maternal resveratrol diet regulates Endoplasmic Reticulum Stress in SAMP8 mice model: cognitive and epigenetic changes across generations	P46	



Poster presentations Group 1 (10:45h-11:30h)

1) Factors secreted by astroglia modulate local protein synthesis in neurites

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Local protein synthesis is an essential mechanism in neurons, so that neurites can rapidly react to environmental stimuli. Recently, studies have shown that local protein synthesis has a key role not only in Nervous System development but also in cell death due to neurodegenerative signals such as β -amyloid1-42 (A β 1-42) oligomers. Our laboratory analysed the contribution of astroglia to local translation and results showed that neurites increase the number of translational hotspots in the presence of astrocytes in physiological conditions while in amyloid-induced conditions, translation is blocked in the presence of glia. These effects were seen at neurites distant from astrocytes which suggests this regulation could be mediated by secreted factors. Thus, we aim to determine if astrocytes modulate the local proteome in hippocampal neurons. We have used conditioned medium from primary neurons cultures with or without astrocytes and treated or not with A β 1-42 oligomers. We show that conditioned medium from neuron-astroglia cultures is able to increase local protein synthesis in naïve neurons, as the presence of astroglia does in co-cultures. Moreover, we analysed this astroglia effect using cultures in modified-Boyden chambers where there is no direct contact between cells type. By western blot, we confirm previous results, suggesting that glial-secreted factors regulate local translation in neurites. Together, this work suggests an important role for astroglia in local protein synthesis, what could be relevant for therapeutic strategies for neurodegenerative diseases.



2) A β oligomers regulate the transcriptional and post-transcriptional control of oligodendrocyte differentiation

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Oligodendrocytes are a type of neuroglia responsible for the synthesis and maintenance of myelin. Myelin basic protein (MBP), one of the major myelin proteins, is confined to the myelin sheaths in the myelinating oligodendrocytes, where it is essential for the compactation of myelin sheath. MBP mRNA is transported in specialized granules to oligodendroglial processes where the participation of ribonucleoproteins (hnRNPs) is determinant for the transport and the initiation of MBP translation, and MBP mRNA has been speculate to be translated under local regulation.

Maintaining protein homeostasis within myelin is essential, since alterations lead to aberrant myelin, driving the loss of neuronal connectivity and thus leading to cognitive decline, a feature of Alzheimer's disease (AD). AD is an age-related neurodegenerative disorder, with extracellular deposits of amyloid- β (A β) peptide as one of the main hallmarks of the disease. Likewise, the oligomeric form of A β is considered the cause of synaptic loss and neuronal toxicity seen in the disease.

Recently, it has been observed that A β oligomers interfere directly with oligodendrocytes, modifying MBP levels and promoting their differentiation via Fyn-mediated signalling pathways. Nevertheless, the regulatory mechanisms that ensure the tight temporal and spatial control of localized translation of MBP mRNA are poorly defined. Here, we report an A β -induced increase at protein and mRNA levels of MBP, as well as of hnRNPA2 and hnRNPF, the latter responsible for mRNA transport. By contrast, hnRNPE1, arepressor of MBP translation, was downregulated. Furthermore, we observed an increase at the translational level of myelin proteolipid protein (PLP) and myelin oligodendrocyte glycoprotein (MOG). In addition, Myelin Regulatory Factor (MYRF), a membrane-associated transcription factor that regulates MOG and MBP transcription, was cleaved by A β oligomers enhancing the release of the N-terminal active domain with transcriptional activity.

These results suggest that A β oligomers may deregulate myelin-related proteins and the MBP mRNA transport machinery which could have an impact in the oligodendroglial lineage and in the normal growth and extension of myelin the sheath.



3) NMDA receptor antibodies in autoimmune encephalopathy alter oligodendrocyte function

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Objective: High levels of antibodies against neuronal N-methyl-D-aspartate receptors (NMDARs) are observed in patients with anti-NMDAR encephalitis, but their impact in other cells of the central nervous system is unknown.

Methods: We used a functional assay based on cytosolic Ca²⁺ imaging and immunocytochemistry to evaluate the activity of oligodendrocyte NMDARs in vitro after exposure to GluN1 subunit antibodies present in the cerebrospinal fluid (CSF) of patients with anti-NMDAR encephalitis.

Results: Agonists responses were robustly reduced after pre-incubation of oligodendrocytes with patients' CSF but remained largely unaltered with control CSF. These effects were specific as patients' CSFs did not alter responses to AMPA receptor and were abrogated by pre-absorption of CSF in HEK cells expressing GluN1 subunit. Notably, patients' CSF reduced the peripheral expression of glucose transporter GLUT1 induced by NMDAR activity.

Conclusions: Because expression of GLUT1 in oligodendrocytes and myelin is relevant to shuttle energy substrates for axonal function, these findings suggest a novel pathogenic mechanism beyond the reported antibody effects on neuronal synaptic receptors and plasticity. Indeed, the presence of autoantibodies to oligodendrocyte NMDAR may underlie the MRI alterations observed in tractography studies of patients with anti-NMDAR encephalitis.



4) How to move to catch flying balls with updating predictions

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How does an outfielder catch a ball? The mainstream approaches assume that players' behavior is controlled heuristically by online information obtained from the optic flow (e.g. LOT, McBeath, et al 1995 or OAC, Chapman 1968). These heuristics do not consider any predictive component and consequently can't account for unavoidable visuomotor delays. We propose a model that is a generalization of our previous work allowing the observer – at least theoretically – to predict where and when a parabolic flying ball will land. It proposes a prediction that is updated continually as the observer moves as a navigational strategy. We examine how well the model accounts for catching movements collected in one experiment. Participants had to solve a task similar to that of the outfielder problem in an augmented reality setup: We presented them with a soccer ball describing a parabolic movement starting at $(x = 0, z = -12)$ m, with x and z being lateral and depth positions with respect to the observers' initial position $(0, 0)$. The ball could travel to nine different ending positions that resulted from combining the coordinates $x = (-3, 0, 3)$ and $z = (-3, 0, 3)$ m. The participants used a joystick that allowed them to move in the x - z plane at up to 6 m/s. We showed two different motion durations: 1.5 and 3 s. In both cases, participants used a strategy consistent with the use of a predictive model. Interestingly, when the temporal constraints of the task are more demanding, the predictive strategy produces similar catching movements to those elicited by the heuristics described in the literature. Furthermore, unlike pure online approaches, the interplay of a predictive component allows our model to cope with visuomotor delays.



5) The psychological model of Binge Eating Disorder: an structural equation modelling

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Introduction: The recurrent presence of binge eating episodes is an important symptom of the Binge Eating Disorder (BED). BED has shown associations with unhealthy habits and psychological problems.

Objectives: Analyze the BED prevalence in a community sample. Analyze the relationship between BED and different eating behaviors and psychological problems.

Method: After applying inclusion and exclusion criteria, 610 participants were selected to participate in this study. There was 536 women and 74 men. Through the website SurveyMonkey participants had to answer some questionnaires to assess the presence of BED; mood, anxiety and stress; and, the different eating behaviors. A Structural Equation Modelling (SEM) was conducted to analyze the relationship between BED, eating behaviors and psychological variables.

Results: The BED prevalence in this sample was 5.4%, of which 57.6% were overweight or obesity and 42.4% normal-weight. Goodness-of-fit indices for the present model showed an adequate fit of data ($\chi^2=50.7$, $p < 0.001$; CFI=0.971; TLI=0.973; RMSEA=0.069; SRMR=0.052). The model suggest that psychological problems may lead to maladaptive eating behaviors, which finally would be related with the presence of BED.

Discussion: These results support previous reviews. The model suggest that psychological problems could explain the presence of BED via unhealthy eating behaviors, especially emotional intake, which normally appears to face negative emotions.



6) Cell cycle dysregulation as a novel mechanism of striatal vulnerability in Huntington's disease

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Neurons have been typically described as permanently postmitotic cells with dormant cell cycle machineries. However, recent evidence reveals that failure of cell cycle regulation could trigger the re-expression of cell cycle proteins and eventually DNA replication and cell death in several neurodegenerative diseases including Huntington's disease (HD).

HD is a fatal neurodegenerative disorder caused by an abnormally long polyglutamine expansion in the gene that encodes for the Huntingtin protein (Htt) characterized by a selective degeneration of medium spiny neurons within the striatum. The responsible molecular mechanisms, however, remain poorly understood.

Besides, among the numerous pathological hallmarks implicated in HD, excitotoxicity has also been linked with aberrant expression of cell cycle proteins. Therefore, we hypothesize that cell cycle dysregulation could be playing a crucial role as a novel mechanism underlying striatal vulnerability in HD.

To this aim, we sought to determine the levels and distribution of several cell cycle proteins in different HD mouse models, human brain samples and cultured striatal primary neurons challenged with NMDA.

Our results have revealed a shared and reproducible aberrant expression and distribution of p27, Cdk4 and Cyclin D1 and suggests that dysregulation of the cell cycle vigilance in postmitotic neurons may contribute to striatal vulnerability and eventually cell death in HD.



7) Loss of TRESK enhances acute and chronic itch in mice

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TRESK (K2P18.1) is a background K⁺ channel expressed in sensory neurons, where it modulates the resting membrane potential, action potential firing and neuronal excitability. A subset of these sensory neurons, which express specific TRPs and Mas-related G protein-coupled receptors (Mrgprs), are activated by pruritogens and mediate itch sensations. Because TRESK is involved in somatosensitivity and pain perception, we evaluated the contribution of this channel to pruritic sensitivity and its potential as a target for the treatment of chronic itch pathologies including renal or liver failure, Hodgkin's lymphoma and different types of dermatitis. Different populations of primary cultured sensory neurons from both wild-type and TRESK knockout mice were activated by chloroquine (CQ), β -alanine, BAM8-22 or histamine in calcium imaging experiments. At the behavioral level, subcutaneous injection of chloroquine in the cheek model produced an acute scratching response, which was significantly enhanced in mice lacking TRESK. Interestingly, in mice models of chronic itch such as Allergic Contact Dermatitis, there was a significantly higher scratching response in mice lacking TRESK compared to their wild-type counterparts. In the mouse model of imiquimod-induced psoriatic itch, the absence of TRESK produced a significantly enhanced scratching behavior, which developed earlier and was more robust. In summary, our data indicate that TRESK is involved in regulating the excitability of a subset of sensory neurons that mediate histaminergic-independent itch. Given the prominent role of this neuronal subpopulation in chronic itch diseases, TRESK appears as a new potential candidate for therapeutic intervention.



8) Huntington's disease brain-derived small RNAs trigger motor dysfunction and striatal damage in mice

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Huntington's disease (HD) is a trinucleotide repeat expansion disease (TRED) caused by an expansion of CAG repeats in the coding region of huntingtin (*htt*) gene, leading to an expanded polyglutamine track in the *htt* protein. Classically, HD pathogenesis has been linked to abnormal function of the mutant protein through misfolding and aggregation. However, a detrimental role of the expanded CAG repeats at RNA level is gaining importance. It has been shown that CAG repeat small RNAs of approximately 21 nucleotides (sCAGs) are produced in HD human brains and are neurotoxic *in vitro*. It has also been demonstrated that the specific blockage of CAG repeat RNAs is neuroprotective in a neuronal cell model and in a HD mouse model. Here, we have addressed the potential neurotoxic role of small RNAs (sRNAs), including sCAGs, derived from the putamen of HD patients as pathogenic factors *in vivo*. Our results indicate that HD-sRNAs trigger motor coordination abnormalities, decrease striatal HD-related proteins and induce a global dysregulation of gene expression in naïve mice. Importantly, HD-sRNAs cause selective neuronal death and inflammation, which are major neuropathological hallmarks in HD human brains. The present results suggest that sRNAs, including sCAGs, are causative factors in HD and further indicate that their blockage should be envisioned as a therapeutic strategy.



9) Validation of the Spanish version of the Maternal Attachment Inventory

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Introduction: The Maternal Attachment Inventory (MAI, Müller, 1994) is a 26-item self-report questionnaire developed to measure maternal affectionate attachment. Since the publication of the MAI, in 1994, it has been culturally adapted to many languages (e.g., Korean, Chinese, Portuguese, and Turkish). However, to date, no adaptation of the instrument has been published to be used with the Spanish population.

Objective: The purpose of this study was two-fold: first, to translate and adapt the MAI into Spanish and, second, to assess its psychometric properties. **Methodology:** First, the MAI was translated following a standard forward-back translation process and was tested in a pilot test. Second, the MAI factor structure was studied by exploratory factor analysis (EFA), and the psychometric properties of the questionnaire were studied through internal consistency, test-retest reliability (4-6 weeks) and correlations with mother-infant bonding scale (MIBS) in a sample of 656 Spanish mothers with children between 2 and 7 years.

Results: All the steps followed in the first part of the study ensured semantic, linguistic and contextual equivalence between the original instrument and the final Spanish version. The EFA revealed a four-factor structure, with good internal consistency, and test-retest reliability for all the factors and moderate-strong correlations with MIBS.

Conclusions: The Spanish version of the MAI showed adequate reliability and validity for measuring maternal affectionate attachment in mothers with children between 2 and 7 years.



10) Cognitive and electrophysiological recovery in a mice model of Alzheimer's disease accumulating both amyloid- β peptide and hyperphosphorylated Tau

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The two main histopathological hallmarks of Alzheimer's disease (AD) are the accumulation of amyloid- β peptide (A β) and hyperphosphorylated Tau (P-Tau). It has been described that dysfunction of hippocampal interneurons may be responsible for the abnormalities in hippocampal oscillatory rhythms, imbalance of neuronal activity and cognitive deficits associated to AD. J20 and VLW mice, overexpressing mutated hAPP and accumulating P-Tau, respectively, show an imbalance between excitatory and inhibitory activity, hyperexcitability, and cognitive impairments.

Here we analyze double transgenic mice accumulating simultaneously A β and P-Tau (J20/VLW). J20/VLW mice show an A β plaque load similar to J20 single transgenic animals, and high levels of Tau phosphorylated at Thr231 (pThr231) and pThr205 Tau in CA1 pyramidal cells, as observed in VLW animals. In contrast, the density of hippocampal interneurons accumulating pThr205 and pSer262 Tau is higher in J20/VLW than in VLW mice, pointing out that A β presence seems to modulate the phosphorylation of Tau specifically in interneurons.

Subsequently, we investigate the GABAergic septohippocampal (SH) connection, which specifically innervates hippocampal interneurons modulating their activity and, consequently, hippocampal local field potentials. We have previously described an important reduction of GABAergic SH innervation in J20 and VLW single transgenic mice. Our present data demonstrate that hippocampal interneurons in J20/VLW animals are innervated by GABAergic SH fibers in the same way as in control animals, indicating that simultaneous presence of A β and P-Tau protects against the alterations they produce separately on GABAergic SH innervation. Next, we assess hippocampal electrophysiology and cognitive functions. Our data indicate that hippocampal theta rhythms, markedly diminished in J20 and VLW mice, are partially rescued in J20/VLW animals. Finally, our results demonstrate that the simultaneous presence of A β and P-Tau in J20/VLW mice rescues the recognition memory deficits associated to A β accumulation. All these data suggest that the differential Tau phosphorylation pattern in hippocampal interneurons present in J20/VLW mice seems to protect GABAergic neurons from the loss of GABAergic SH



innervation, preventing alterations in local field potentials and, consequently, avoiding cognitive deficits.



11) Oscillatory networks underling reward processing of familiar and unfamiliar music

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Listening to pleasant music engages reward-related brain areas. These areas, in turn, interact with other structures related to music processing and the mechanisms that support it, such as auditory processing and working memory. However, little is known about the temporal dynamics of these brain interactions. The goal of the present experiment was to study the oscillatory activity associated to music-evoked pleasantness and familiarity. EEG was recorded from 22 healthy subjects while they were listening to both familiar and unfamiliar music and rating the experienced degree of evoked pleasantness in two experimental sessions. By using a multilevel Bayesian approach we found that phase synchronization in the theta band between right temporal and frontal electrodes increased with the degree of pleasure experienced by participants when music was unfamiliar. In turn, this positive relationship emerged in right-temporal to left-parietal connections when music was familiar, while the opposite was true for unfamiliar music. These results show that fronto-temporal loops supporting auditory working memory and prediction error play a key role in reward processing of unknown music, while temporo-parietal loops supporting working memory retrieval is involved in reward processing of known music.



12) Static and Dynamic Functional Connectivity in Down Syndrome

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The prevalence of Alzheimer Disease (AD) in Down Syndrome (DS) has dramatically increased and therefore it is essential to identify the protective factors and their effects in DS population. Our main objective is to estimate functional connectivity networks by using fMRI signal in a resting state paradigm within the DS community. Moreover, we would like to examine Down Syndrome time-varying functional network connectivity states that have been blurred in the static FC analysis. These dynamic methods allow the identification of functional connectivity patterns describing whole-brain connectivity throughout scan duration. The sample was composed by 14 individuals with DS between 16 and 35 years old ($M=27.25$ and $SD=5.119$). A 3 Tesla system was used for the acquisition of a high resolution T2 and T1-weighted structural image and also a 6 minutes resting-state fMRI dataset. For each evaluated subject, the connectivity network between regions of interest (ROIs) was obtained. Each of the connectivity networks was characterized by connectivity segregation and the changing points in the temporal series were calculated through spectral clustering. Three indicators of functional integration and segregation were calculated: Strength, Transitivity and Characteristic Path Length. It is feasible to consider the properties of the connectivity network as a biomarker for an approximation of the cognitive state of persons with DS. Fluctuations of the functional connectivity are found meaning that FC is not static but dynamic with changing points tending to happen at the final part of the registry. Strength and path length indicators show greater variability along the temporal axis than transitivity.



13) Resting-state dynamic connectivity in people with major depressive disorder in remission

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Background: Functional Magnetic Resonance studies show abnormal functional connectivity in patients with major depressive disorder (MDD). Antidepressant treatment has been associated with changes in brain connectivity with trends toward his normalization. In addition few works studied dynamic connectivity in depressed patients. This approach can provide evidence about the patterns of change during the registration phases. The aim of this study is to identify resting state dynamic brain connectivity networks in MDD patients in remission and to study if they are differences on the connectivity patterns related to clinical and neuropsychological characteristics of the illness.

Material and Methods: The sample is composed of 17 patients with MDD diagnosis in symptomatic remission phase (Hamilton-Depression Rating Scale 17 item version = 3.6 (2.36)) with a mean age of 33.12 (11.09). Functional Magnetic Resonance images were acquired with a 10 minutes duration resting-state paradigm with open eyes.

Results: Each of the connectivity networks was characterized by connectivity segregation. Moreover, the changing points and the temporal series were calculated through spectral clustering. Some indicators were calculated in order to describe this connectivity networks.

Conclusions: The results indicate that there are different patterns of dynamic functional connectivity in this analyzed sample, that may be related with some clinical and neuropsychological characteristics of the MDD patients, proposing some interpretation criteria.



14) The frequency-following response (FFR): a useful clinical tool to assess cognitive impairments during the first days of life

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The frequency-following response (FFR) is an electrophysiological response that reflects how the spectrotemporal features of complex evoking sounds are encoded in a cortico-subcortical auditory network. Recently, an increased number of studies explore the use of FFR as a clinical tool to assess neurodevelopmental disabilities. Disruptions in the FFR are observed in children with learning disabilities, dyslexia or autism. However, with our study we want to investigate if during the first days of life the presence of neurodevelopmental impairments could already be detected with the FFR. To that end, we recorded the FFR from healthy newborns and those affected by fetal growth restriction (FGR). Newborns born with FGR are those who weigh less than 10th percentile for gestational age. Several studies described that being born with FGR entails several cognitive consequences such as lower intelligence levels, poor academic performance and low social competence. These conditions are maximized in a subpopulation of FGR known as intrauterine growth restriction (IUGR) that includes those newborns whose weight is \leq 3rd percentile or between 3rd and 10th percentiles with abnormal placental function. If differences are observed between healthy newborns and those affected by FGR, our findings would reinforce the usefulness to record the FFR during the first days of life giving the possibility to detect earlier neurocognitive disabilities than the tools used nowadays.

A total of 70 term newborns were recruited between May and August 2019, including 38 controls and 32 born with FGR. All of them passed the universal hearing screening. The FFR was recorded to the syllable /da/ (170 ms long; $F_0=113$ Hz; intensity: 60 dB SPL, 4000 sweeps, delivered with alternating polarities) and seven parameters were analyzed. To control gestational age effects, this variable was included in the statistical analysis as a covariable. No significant differences were observed between control and FGR groups. However, once the FGR was split between the two subgroups, significant differences were observed in one of the parameters assessed (Pitch strength; $F(1,29) = 3.161$, $p = 0.049$, $\eta^2 = 0.087$). Although, the differences in the rest of the parameters were not significant, all of them showed similar results pattern. These findings are in line with previous literature in which it is suggested that the several risk to born small for gestational age is confined to the subgroup of FGR babies born with IUGR, showing similar IQ results between FGR not included in the IUGR groups and the control group. Therefore, this study evidences the potential use of FFR as a cognitive biomarker that



makes possible the implementation of early intervention programs whose importance is indisputable in those populations whose neuronal development is restricted, as in IUGR newborns.



15) Executive function training as intervention for childhood obesity: Preliminary results

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Introduction: Cognition-focused interventions addressed to enhance executive functions in obese adults appear to reduce overweight[1]. In children, only a few studies have addressed this question, with inconclusive results[2,3]. Our aim was to examine how executive function training influences weight loss in children with obesity.

Method: Fourteen children with obesity [aged 10-12; Body Mass Index (BMI) $P_c \geq 95$] underwent executive function training (30-45'/day, 5 days/week over 6 weeks; n=6) or an active control training (placebo training with no increasing difficulty; n=8). Both groups had to learn basic healthy habits and send pictures of all the meals. Anthropometric (height and weight) and neuropsychological assessments were carried out both before (T0) and after (T1) the intervention. Baseline differences between groups were assessed with independent T-tests or Fisher's exact test. Differences from baseline to post-training were assessed with paired T-tests, separately for each group.

Results: A trend for significance was found in the training group, showing lower BMI at post-training ($p=.081$). This tendency was not found in the control group. Regarding neuropsychological variables, the experimental group showed higher performance in Spatial Span Forward on Wechsler Nonverbal Scale of Ability (WNV) ($p=.007$), Choosing Subtest ($p=.025$), Inhibition ($p=.037$) and Flexibility Indexes ($p=.036$) on Five Digits Test (FDT) and Total Time on Tower of London (ToL). No significant differences were found in other cognitive tests at post-training. The control group showed better performance in FDT, specifically in Counting ($p=.037$), Choosing ($p=.004$) and Shifting ($p=.001$) subtests and Inhibition and Flexibility Indexes ($p=.042$; $p=.001$). Significant differences were also found in Continuous Performance Test (CPT) commissions ($p=.003$), showing less errors after training. No differences were detected in other tests.

Discussion and conclusion: Our preliminary results suggest that executive function training could be useful to enhance treatment outcomes, as the tendency toward BMI decreases suggests. Both groups improved in inhibition and cognitive flexibility/shifting, whereas only the experimental group showed better performance in attentional span and planning and BMI.



16) Math anxiety and the shifting executive function

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Attentional Control Theory proposes that general anxiety mostly affects two central executive functions related with attentional control: inhibition and shifting. Math anxiety, a feeling of tension and fear that usually impairs math performance, also affects inhibition, but its influence on shifting has not been studied yet. We aimed to investigate whether math-anxiety also affects the shifting function by using a task-switching paradigm. Twenty highly math-anxious (HMA) and 20 low math-anxious (LMA) participants verified additions and subtractions on two two-digit numbers preceded by a transition cue. At the beginning of each trial, the cue indicated whether to repeat or to switch the arithmetical task. HMA individuals were slower than their LMA peers. Subtractions took more time to be verified than additions. More interestingly, there was a Switching x Group interaction. The LMA group showed no significant switch cost when verifying additions and a switch benefit when verifying subtractions. In contrast, the HMA group had a significantly stronger switch cost in additions than their LMA peers and no significant switch benefit in subtractions. These data suggest that the low processing efficiency shown by HMA individuals in arithmetical tasks might be related to difficulties when shifting their focus of attention.



36) Modeling the radial glial niche: mechanical-driven changes in 2D biomimetic materials

J.P. Soriano-Esqué, C. Borau, J. Asín, J. M. García-Aznar, S. Alcántara

Radial glia (RG) is the principal neural stem cell (NSC) in the embryonic central nervous system. Poly (methyl methacrylate) (PMMA) with 2 μ m linear topographies (Ln2PMMA) mimics RG niche, inducing the conversion of primary cultured astrocytes into RG cells phenotype. How mechanical forces in the periphery are translated to the nucleus, inducing changes in nuclear shape, chromatin structure and gene expression is still poorly understood. Modeling the niche in biomimetic materials we want to identify the biophysical and metabolic parameters required for NSC/RG maintenance.

We used astrocyte cultures from neonatal mice grown in control (culture plastic/glass), flat PMMA and Ln2PMMA. We determined nuclear physical parameters (shape, size, orientation) in nuclei stained with Hoechst; and the expression of lineage-specific cell markers (GFAP, NG2, nestin and Sox2) and mechanosensitive transcription factors (YAP/TAZ) by immunofluorescence and confocal imaging. Image analysis was performed with a custom-made MatLab algorithm. Phosphorylation key metabolic enzymes (ej. phosphorylated pyruvate dehydrogenase, pPDH) were also analyzed to determine mechanical-driven changes in oxidative/glycolytic cell metabolism.

Here we found that nuclear physical parameters of glial cells change in response to substrate and topography. In Ln2 PMMA most nuclei were aligned in the direction of the topography and were significantly smaller and more eccentric than nuclei on control substrates; although the smallest nuclei were found on flat PMMA. The substrate also affected YAP/TAZ subcellular distribution in glial cells. In control substrates 77% of positive cells presented nuclear YAP/TAZ in contrast to PMMA where only in 39-48% (flat and Ln2 respectively) of positive cells YAP/TAZ were nuclear. In addition, pPDH decreases in Ln2 PMMA suggesting a reduction in the glycolytic cell metabolism.

Finally, nuclear physical parameters, expression of lineage-specific cell markers and preferential oxidative/glycolytic cell metabolism data will be integrated, and a model for mechanical-driven astrocyte to RG phenotypic transformation will be discussed.



Poster presentations Group 2 (13:45h-15:30h)

17) Local protein synthesis in microglia cells in the healthy and diseased conditions

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One of the most polarized cell in the brain is the neuron, whose axon terminal could be more than a meter away from the cell soma. In this structure, local translation has an important role, since it provides the axon a means of a quick and effective response. Our lab is focused on understanding this local translation in axons and to demonstrate the contribution of surrounding glia cells to this phenomenon in physiological and neurodegenerative conditions. Interestingly, when analysing the effect of microglia on local translation in neurites we realized that microglia itself localizes newly synthesized proteins to their processes. Thus, we propose that local translation in microglia also plays an important role in brain function and dysfunction. Importantly, local protein synthesis in microglia has not been established. So far, our results revealed that in peripheral processes of microglia the novo synthesis of proteins occurs in response to inflammation and to a neurodegenerative stimulus (A β). In order to determine if localized proteins arise from localized transcripts we are performing RNA-protein co-localization assays. If successful, our work will reveal a new molecular mechanism through which microglia respond to their environment by means of local translation in the healthy and diseased brain.



18) Microglial activation prevents A β -induced synaptic dysfunction and reduces extracellular A β in Alzheimer's disease

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Alzheimer's disease (AD) is a neurodegenerative disorder and the most common cause of progressive cognitive decline in the aged population. Accumulation of β -amyloid (A β) peptide and the synaptic dysfunction are the main hallmarks of AD neuropathology. Loss of synapses occurs early in AD and is considered the best pathological correlate of cognitive decline.

The role of microglia, innate immune cells of the brain, in AD remains controversial. In one hand, microglia mediates early synapse loss in AD models. In contrast, activation of microglia by immunotherapy or the cytokine macrophage colony stimulating factor (MCSF) results in a more efficient A β degradation.

To study the role of microglia in A β -related synapse pathology we performed immunofluorescence to measure levels of pre- and post-synaptic markers in neurons cultured alone or together with microglia in the presence or absence of A β oligomers. We also carried out immunofluorescence to detect A β within microglia and immunoprecipitation for A β detection in the culture media.

We observed a significant reduction of both pre-(synaptophysin) and postsynaptic (homer) markers labelling in primary neuron cultures in presence of A β compared to controls. However, we did not observe synapse pruning in our model. In the contrary, we found that microglia decreased extracellular amyloid in microglia-neuron co-cultures in presence of extracellular A β oligomers although this was not enough to restore synapses in control conditions. Notably, microglial activation by MCSF was not only able to reduce extracellular amyloid load but also to prevent synapse damage.

Overall, these results show the A β impact on synaptic loss in neuronal primary culture and that microglia activation is able to reduce extracellular A β and to avoid synaptic damage in vitro. These results strongly suggest that A β oligomers are deleterious to synaptic function by interfering with neurons, and that microglial modulation constitutes an important therapeutic target for the prevention of synapse toxicity.

Supported by Basque Government (PIBA PI-2016-1-0009 and ELKARTEK KK-2017-00067) and CIBERNED. J.Z-I and C.L. are recipients of fellowships from Basque Government and Tatiana Pérez Guzmán el Bueno foundation, respectively.



19) Multimodal hierarchical cluster analysis based on grey and white matter measures identifies different patterns in Parkinson's disease

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Background. Clinical variability in Parkinson's disease (PD) suggests the existence of disease subtypes. Cluster analysis based on cortical thickness has been used to identify distinct anatomical subgroups (Uribe et al., 2016; 2018).

Objective. We aim to study the potential of a multimodal clustering approach based on grey matter (GM) regional volumes and fractional anisotropy (FA) measures to characterize PD subtypes.

Methods. We included T1 and DWI MRI data from 33 healthy controls (HC) and 62 PD. Individual GM probability and skeletonized FA maps were obtained with FSL. We calculated mean GM within 48 cortical and 17 subcortical regions from the Harvard-Oxford Atlas, and the mean FA of 20 tracts from the JHU atlas. Hierarchical cluster analysis was performed using Ward's linkage method. Whole brain intergroup comparisons were performed using VBM and TBSS. Neuropsychological and demographic statistical analyses were conducted using IBM SPSS Statistics 25.0.

Results. We identified two PD subtypes. PD1 group (N:36) showed widespread atrophy in cortical and subcortical regions compared to HC and PD2 (N:26), and less FA than HC in the left inferior occipital fasciculus (FWE corrected, $p < 0.05$). PD1 also performed cognitively worse than HC and PD2 (FWE corrected, $p < 0.05$). Both PD groups showed the same disease evolution time, although PD2 group had an early disease onset, was significantly younger, and did not show brain atrophy in comparison to HC.

Conclusion. Multimodal clustering analysis was able to detect two PD subtypes, one with widespread GM and white matter atrophy, cognitive decline and late onset, and another one with preserved brain structure and cognition.



20) Quality of life in cerebral palsy: the importance of visuospatial abilities

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Introduction: Cerebral palsy (CP) is a motor function disorder often accompanied by disturbances of communication, cognition and psychological problems that seem to have an impact on quality of life (QOL). This study aims to identify the impact of potentially relevant variables on quality of life in young and middle-aged adults with dyskinetic CP.

Patients and methods: Thirty-seven participants with dyskinetic CP (19 females, mean age 30.11 years, SD 11.87 years) were included in the study. Their caregivers completed the Cerebral Palsy Quality of Life questionnaire (CP QOL). Motor status, communication, intelligence functioning, executive function, visuospatial and visuospatial abilities, anxiety and depression symptomatology, and socioeconomic status were evaluated.

The relationship between CP QOL total score and each one of the other variables was examined using correlations and multiple linear regression models.

Results: Total score of the CP QOL is only predicted by visuospatial abilities. Visuospatial abilities also predict scores in two CP QOL domains (General well-being and participation; and Communication and physical health). Communication ability, goal setting skills, monthly income and fine motor function level predict respectively scores of School well-being, Access to services, Family health and Feelings about functioning. Gross motor functioning, intelligence functioning and psychological problems do not predict any domain of QOL.

Conclusions: These findings highlight the importance of visuospatial abilities in QOL. This study also demonstrates the relationship between communication, executive function, motor status, socioeconomic status and QOL. Results of this study suggest that visuospatial abilities should be considered in intervention programs designed to improve QOL of people with CP.



21) c-Jun N-terminal Kinase 1: A key element for the protection against cognitive deficits derived of metabolic alterations

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The appearance of cognitive affectations has been linked with the development of insulin resistance in the brain, alterations in the oxidative capacity of mitochondria and the induction of neuroinflammatory responses. Due to this situation it is imperative to find molecules that can be used for therapeutic purposes through the regulation of these alterations.

In this study, the effects of the inactivation of the c-Jun N-terminal Kinase 1 (JNK1; *Jnk1*^{-/-}) was evaluated in a model of metabolic alteration induced by the feeding of a high-fat diet (HFD). The results indicate that the *Jnk1*^{-/-} animals are significantly more sensitive to insulin, show lower body weight and higher mitochondrial activity, just like lower cellular reactivity in astrocytes and microglia. Also, these animals were protected against any cognitive affectations derived of metabolic dysregulations as it was demonstrated through the Novel Object Recognition Test, the observation of the state and number of dendritic spines in hippocampal neurons and the detection of proteins like the brain-derived neurotrophic factor (BDNF) or others like spinophilin or ARC.

In conclusion, the results indicate that a reduction in the activity of JNK1 has neuroprotective effects and thus, its modulation could become a promising therapeutic strategy for the treatment of cognitive affectations derived of a metabolic dysregulation.



22) The Spanish version of the Internet Gaming Disorder Scale-Short Form (IGDS9-SF): An item response theory approach

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In 2013, the American Psychiatric Association recognized the Internet Gaming Disorder (IGD) as a tentative disorder in the fifth revision of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). Pontes and Griffiths (2015) developed the Internet Gaming Disorder Scale-Short Form (IGDS9-SF) which assesses IGD behaviors following the nine DSM-5 core criteria. It consists of nine items with a 5-point scale examining gaming activities occurring over the last 12 months. The main objective is to develop and validate the Spanish version of this scale using methods based on classical test theory and item response theory. In a sample of 267 gamers (mean age 24 years, SD = 8.37), we assessed the unidimensionality of the scale using confirmatory factor analysis, reliability of the scores as internal consistency and temporal stability, and the graded response model was fitted to observe the items performance. The one-factor structure was confirmed. Cronbach's alpha and test-retest coefficients were, respectively, .83 and .89. The item fit was acceptable for all the items and the test information function showed that the IGDS9-SF is more informative at higher levels of the trait. In conclusion, the Spanish version of the IGDS9-SF is a suitable tool to assess the severity of IGD.



23) How body image is affected by body weight discrimination

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Weight discrimination is associated with a great variety of psychopathology disorders such as depression or anxiety, as well as medical disorders. Weight discrimination is present in many areas of life and has a high prevalence, similar to race discrimination.

Objective: the aim of this study was to evaluate how body image satisfaction is affected by weight bias.

Method: 198 discriminated and non-discriminated people were recruited through social media. Of them, 99 had suffered weight bias and 99 had not suffered weight bias. The distribution of the body mass index (BMI) of the participants in both groups was similar. Participants answer the Multidimensional Body Self Relations Questionnaire (MBSRQ).

Results: the results show that people who suffer body weight discrimination experience higher body dissatisfaction, in especial on their face, weight, muscle tone and top, medium and lower part of their body compared to non-discriminated people. In the discriminated group, the highest BMI participants experience higher dissatisfaction in face and hair. In addition, the highest BMI people had admitted trying to lose weight by following a fad diet.

Conclusion: this research provides large evidence about how weight discrimination is associated with body dissatisfaction.



24) Improving opioid pain treatment: light-activated morphine

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Opioid-based therapies are widely used for pain-related pathologies. Insomuch, they often are the most effective available therapy for some pain disorders (i.e. chronic pain). Specifically, clinicians world-wide have been relying on μ -opioid receptor agonist (i.e. morphine) for pain management. However, severe side-effects have been well documented since its discovery which often lead to forced drug discontinuation and inadequate pain relief. Those undesirable effects are supported by the fact that opioid receptors are widely distributed through the body, thus determining effectiveness differences upon drug targeting (i.e. central versus peripheral). Subsequently, both analgesic and non-analgesic effects (i.e. adverse effects) depend on the opioid receptor distribution along pain neuraxis.

Interestingly, novel photo-pharmacological approaches provide us promising strategies to control opioid drug effectiveness in a space and time-dependent manner. Those new tools rely mainly on the use of photo-sensitive drugs (i.e. caged-compounds) that can become active with the use of proper light wavelength (i.e. 405nm). Accordingly, a new morphine-derivative compound (morphine-caged; M-C) was synthesized showing in-vitro and in-vivo anti-nociceptive efficacy under light irradiation as opposed to dark condition. Most interestingly, we demonstrated the usefulness of the M-C to avoid and prevent some of the opioid-related side-effects (i.e. gastrointestinal tract inhibition) at effective anti-nociceptive doses (i.e. 10mg/kg) in formalin mice model test.



25) Hippocampal PYK2 modulates impaired social behaviours in schizophrenia via regulation of mitochondria dynamics

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Schizophrenia (SZ) is a chronic neuropsychiatric disorder with positive, negative and cognitive symptoms. Among the different factors, mitochondria have raised as a potential contributor of SZ symptomatology regarding to negative symptoms, particularly in sociability. Sociability alterations in schizophrenia may have its hub in the hippocampal formation. Pyk2 is a non-receptor tyrosine kinase protein enriched in the hippocampus and has been proposed as a genetic risk factor for schizophrenia and it is key in modulating hippocampal function. We tested whether Pyk2 could have a role in mitochondria function and its implication in SZ. First, we observed dysregulated Pyk2 protein levels in the hippocampus of SZ patients correlating with alterations in sociability. Moreover, social interaction induced robust changes in several oxidative phosphorylation complexes in Pyk2 knockout mice. We also challenged mitochondria dynamics in Pyk2^{+/+} and Pyk2^{-/-} hippocampal primary neurons by using OXPHOS complexes inhibitors to identify the specific molecular pathway mediating these alterations.

Taken all together, our results suggest that Pyk2 could be highly relevant in the modulation of hippocampal mitochondria function underlying social behaviors.



26) Epigenetic changes after unpredictable chronic mild stress in female SAMR1 and SAMP8: Effects on Behavior

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Cognitive and behavioral disturbances are growing public healthcare issue for the modern society. It has been shown that the environment is crucial in the development of several diseases, as well as compromising healthy aging. Accumulated evidence suggests that stress is an important risk factor in cognitive decline. Besides, life rhythm has changed becoming increasingly stressful. Therefore it is important to study the effects of stressful lifestyle on cognition and its relationship with aging to unveil what challenges we might have to cope with as a society in a not so far future. Likewise, epigenetic alterations are present in brain disorders and are affected by environmental stress. However, little is known about the interaction of stress, learning-memory and epigenetics. Thus understanding the epigenetic modifications that stressful environment triggers in cognition is essential to develop novel therapeutics for age-related cognitive decline. This study aims to determine the effects of a stressful lifestyle in an animal model with accelerated senescence (SAMP8) and compare it with its control strain (SAMR1). Female SAMR1 and SAMP8 mice (n=48) 5 month-old were divided into four groups: SR1-Ct, SR1-UCMS, SP8-Ct and SP8-UCMS. Unpredictable chronic mild stress (UCMS) groups received for one month an UCMS treatment, which consisted of daily applying different stressors such as food/water deprivation, overnight illumination, sawdust removal, among others. To evaluate the behavior and cognitive performance, several tests as novel object recognition test (NORT) and open field test (OFT) were conducted, followed by molecular analysis of neurodegenerative and epigenetic markers in the hippocampus using Western blot, ELISA, RT-PCR and miRNA assay. Changes in behavioral tests were found leading to reduced recognition and spatial memory in SAMP8, which worsened when UCMS treatment in both strains, as well as a loss of recklessness. Consistent with these results, we found an increased in inflammatory and oxidative stress (OS) markers. Additionally, changes on epigenetic machinery and their epigenetic marks such as DNA methylation (5-mC) and hydroxymethylation (5-hmC) were found. Interestingly, several miRNAs were modified, which were related to neurodegenerative processes. In conclusion, a stressful lifestyle leads to age-related cognitive decline. Besides, UCMS is a feasible intervention to understand the influence of stress on epigenetic mechanisms underlying cognition, opening new avenues for treating cognitive impairment



27) I2-Imidazoline ligand, LSL60101, improves cognition in the 5XFAD mouse model

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Alzheimer's disease (AD) is characterized by β -amyloid (A β) plaques, tau tangles and synaptic dysfunction leading to cognitive impairment. Development of effective therapeutic strategies remains a challenge. I2-Imidazoline receptors (I2-IR) ligands have demonstrated a neuroprotective role in the central nervous system. LSL60101 (2-(2-benzofuranyl)-2-imidazole), a selective I2-IR ligand, has been shown to induce several biological effects associated with I2-IR occupancy. To further investigate the role of I2-IR ligands in the mechanism of AD hallmarks and cognitive impairment, we evaluated the neuroprotective effect of LSL60101 in 5XFAD mice, a transgenic mouse model of early-onset AD.

The intervention was performed on female mice with 7 months of age, divided into control groups (Wild-Type-Ct (n=12), 5XFAD-Ct (n=12)) and LSL60101 treated groups (Wild-Type-LSL (n=12) and 5XFAD-LSL (n=12) 1mg/kg/day, per os, for 4 weeks. Cognitive performance was evaluated by the Novel Object Recognition Test (NORT) and the Morris Water Maze (MWM). A β plaques were analyzed using Thioflavin-S immunostaining as well as β -amyloid, and synaptic markers were determined by Western blot.

We found a significant cognitive improvement in the 7-month-old 5XFAD-LSL treated group, as assessed with NORT and MWM. In line with the cognitive results, treatment of 5XFAD mice with LSL60101 had a strong effect, reducing β -amyloid hippocampal levels and increasing levels of α -secretase (ADAM10) when compared to the 5XFAD-Ct group. Furthermore, the number of A β plaques stained with Thioflavin-S revealed that treatment with the I2-IR ligand prevented the amyloid burden in brains of LSL60101 treated 5XFAD mice. Additionally, the attenuation of β -amyloid accumulation was accompanied by a significant increase in synaptic markers levels such as postsynaptic density 95 protein and synaptophysin in the 5XFAD-LSL treated group. Our results suggest that I2-IRs constitute a relevant pharmacological target for the therapeutic strategy against AD.

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28) Network Analysis of the Brief ICF Core set for schizophrenia

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Background: Schizophrenia is a severe mental disorder that is associated with deficits in human functioning. The development of the International Classification of Functioning, Disability and Health (ICF) has been used as a theoretical framework that measures the disability and functionality globally. With that, a subset was introduced known as the Brief ICF Core Set for Schizophrenia which lists the categories of the common problems for those affected with this health condition. This study aims to a) construct the Brief ICF core sets (ICF-CS) network and assess the interactions between the wide range of problems, b) examine the most important categories within the network, c) evaluate the category clusters in patients with schizophrenia.

Methods: The estimation of the network was 25 categories for the Brief ICF-CS. The use of the Delphi data came from 638 professional in different fields of health who serve people with schizophrenia from the six regions of the world health organization.

Results: The network found a strong connection between individual categories within-component of the ICF (i.e., Body functions, Activities and participation, and Environmental factors). Results reported that there are three distinct clusters of categories corresponding to Body functions, Activities and participation, and Environmental factors. The categories e410-Individual attitudes of immediate family members, e450-Individual attitudes of health professionals, d910-Community life, and d175-Solving problems were among the most central categories in the network.

Conclusion: To conclude, the network findings support the importance of analyzing the associations between the ICF categories. Moreover, the identification of the core categories and functioning clusters within the ICF-CS network provides useful indicators for clinical interventions as well as the need for the development of a new instrument for assessing the functioning of patients with schizophrenia.



29) The role of school personnel knowledge in detecting and reporting children and youth victimization

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It is common to assume a relationship between knowledge of child victimisation among school staff and the detection and reporting of potential cases in the school environment. However, contradictory findings in this regard have been published. We tested the statistical significance and size of the link between knowledge of victimisation, confidence in the ability to recognise it and experience in detecting and reporting it in a sample of 169 school staff members from Spain (82.9% females, $M = 43.3$, $SD = 10.5$). Higher levels of knowledge of victimisation and detection than of reporting were found. Only specific knowledge about reporting procedures was significantly linked to reporting experience. These findings suggest that more specific guidelines and ways of recreating experience may improve training programmes for school staff, if we aim to increase early reporting of potential victimisation encountered at school.



30) Role of the JNK3 isoform in the development of metabolic disorders and their relationship with cognitive alterations

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Obesity is defined as a condition in which there is an abnormal or excessive fat accumulation that causes risk to health. It has been described that the appearance of insulin resistance, due to obesity, can be the leading step towards the development of idiopathic Alzheimer's Disease. This situation has been defined as type 3 diabetes.

The c-Jun-N-terminal-kinases (JNK) play an important role in the repair, development and plasticity of the brain, as well as in degeneration, apoptosis and neuroinflammation. JNKs are also one of the most investigated signal transducers in obesity and insulin resistance. In the past, different studies have indicated that normal JNK3 activity has protective effects against excessive adiposity.

This research focused on understanding the role of JNK3 on the regulation of insulin, endoplasmic reticulum (ER) stress, obesity and cognitive disorders. Thus, wild-type (WT) and Jnk3^{-/-} animals fed with control and high-fat diet (HFD) were used. Our observations determined how HFD and the ablation of JNK3 produced an alteration in the insulin receptor pathway, increased ER stress and caused cognitive impairment. Also, interesting observations were made since only WT HFD animals showed inflammatory responses. In conclusion, JNK3 absence causes deleterious alterations in proper cellular function in the hippocampal tissue.



31) A new NMDA receptor antagonist improves learning and memory reducing β -amyloid accumulation and preserving synaptic markers in 5XFAD mice

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Alzheimer's Disease (AD) is an irreversible and progressive neurodegenerative disease characterized by A β depositions, neurofibrillary tangles (NFTs) and cognitive decline with no effective treatment. Although the N-methyl-d-aspartate receptor (NMDAR) is necessary for learning and memory, excessive NMDAR activity causes excitotoxicity and participates in the pathogenesis of AD at the synaptic level. Therefore, drug development aimed at neuroprotection has targeted the NMDAR. Unfortunately, treatment of AD with NMDAR antagonist demonstrated limited success. Despite this, recent mechanistic studies demonstrated new neuroprotective effects of NMDAR antagonist that can be explored. In this study, we carried out the neuropharmacological evaluation of a novel NMDAR antagonist, (UB-EV-19, IC₅₀ = 1.9 μ M) bearing a polycyclic amine scaffold, and Memantine (IC₅₀ = 1.5 μ M), both administered in drinking water during four weeks at a dose 5mpk. The experiment was performed on female 5XFAD mice, which displays a range of cognitive and motor deficits accompanied by A β amyloid plaques, and gliosis as early as 2 months of age.

After the treatment, we found better recognition and spatial memories in 5XFAD treated-mice groups as assessed with Novel object recognition test (NORT) and Morris water maze (MWM). Consistent with cognitive results, the treatment with UB-EV-19 reduced the β -amyloid accumulation revealed by Western blotting and the number of A β plaques by Thioflavin-S immunostaining. Interestingly, significant diminished BACE1 protein levels in 5XFAD treated with UB-EV-19, but not by memantine, were found. Finally, UB-EV-19 increased protein levels of synaptic markers such as PSD95 and SYN in 5XFAD mice.

In sum, our results demonstrate the neuroprotectant role of UB-EV-19, having a potential therapeutic effect in neurodegeneration induced by AD-hallmarks.



32) Corpora amylacea of human brain are intracellular bodies that exhibit a homogeneous distribution of neo-epitopes

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Corpora amylacea (CA) are spherical polyglucosan bodies that accumulate primarily in the periventricular and subpial regions of the human brain during aging process and some neurodegenerative diseases. CA have been associated with degenerative granular structures that appear progressively with age in the mouse brain and which are known as PAS granules. We previously reported that both CA and PAS granules contain neo-epitopes recognized by natural IgMs, revealing a possible link between them and natural immune system. Although the genesis and ultrastructure of the mouse PAS granules have been previously described, little is known about human CA formation. Here, we performed an ultrastructural study complemented with confocal microscopy in order to shed light on the genesis of CA and to precisely localize the neo-epitopes in them. We show that immature CA are intracellular astrocytic structures that contain mitochondria, cellular debris and membranous blebs entrapped in a scattered mass of randomly oriented short linear fibers. In mature CA, the structure becomes a core or compacted mass of fibrillary material. We also determined that the neo-epitopes were uniformly distributed throughout the whole structure. All these findings support the correspondence between human CA and PAS granules and reinforce the hypothesis that CA, as PAS granules, are involved in the entrapment of damaged and non-degradable products and have a role in protective or cleaning mechanisms.



33) F-actin reorganization and synapse elimination activate intersynaptic homeostatic plasticity

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Synapses adapt their strength to a constantly changing environment through homeostatic mechanisms that return synaptic transmission to basal levels. During postnatal development there is a pruning of synapses formed exuberantly during embryonic development. Thus, correct processing of information must concur with a massive synapse loss.

Although neuronal activity drives synapse elimination, there are growing evidences invoking the participation of glial cells. Among the many molecules produced by glial cells, Secreted Protein Acidic and Rich in Cysteine (SPARC) emerges as an important cue capable of decreasing synapse numbers. SPARC is exclusively produced by glial cells and its production peaks postnatally; suggesting the contribution of SPARC to synaptic pruning.

The current work investigates how synapses grown in the constraint environment of an autaptic circuit react to the elimination of synaptic contacts driven by SPARC. Results show that synapse elimination triggered by SPARC is dependent on F-actin reorganization and is compensated by the addition of new release sites and an overall increase of presynaptic calcium influx.

Therefore, neurons have the capacity to sense and correct alterations in their synaptic output by inserting a finite number of presynaptic terminals with customized properties.



34) Extensive in vitro and in vivo characterization of promising NMDA channel blockers

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The absence of an effective therapy for Alzheimer's disease (AD), which is the most common form of dementia, urges the development of new drugs that may change the illness faith. So far only memantine –a voltage dependent and uncompetitive antagonist– has been clinically approved for the treatment of AD.

Having in mind AD as the target, our research group has synthesized and carried out the pharmacological and electrophysiological evaluation of a variety of new NMDA antagonists bearing an amine polycyclic scaffold. On the basis of these studies, we determined the ideal candidates for further in vitro profiling. One compound was selected for in vivo evolution in SAMP8 mice model and demonstrated better cognitive performance and a neuroprotective effect through specific pathways. Hence, a new and promising therapeutic agent for brain disorders and age-related neurodegenerative diseases may have been unveiled.



35) Role of TRESK potassium channel in the modulation of pain sensitivity by tacrolimus

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Noxious thermal, mechanical or chemical stimuli activate specific primary sensory neurons (nociceptors) that convey painful signals towards the spinal cord and the brain. In physiological conditions, these neurons are silent, being activated when a potential damaging stimulus is detected or the tissue has been injured. When persistently activated, nociceptors become hyperexcitable producing hyperalgesia and allodynia (pain elicited by non-noxious stimuli). Therefore, the control of nociceptor excitability is essential to avoid persistent or chronic pain states. TRESK is a background potassium channel expressed in nociceptors, where it acts as a brake to avoid neuronal hyperexcitation and to prevent pain hypersensitivity. Here we show that in addition to sensory ganglia, TRESK is also expressed in other neuronal areas, although at a lower extent. Also, we show that mice lacking TRESK are more sensitive to cold and mechanical stimuli than wild-type mice, while their heat sensitivity is not significantly altered. Interestingly, the role of TRESK in cold sensitivity seems more significant in male than in female mice. Tacrolimus, a calcineurin inhibitor, is widely used as an immunosuppressant and produces an increase in pain sensitivity. Because calcineurin modulates TRESK activity through dephosphorylation, we here explore whether Tacrolimus effects on heat, cold and mechanical sensitivity is mediated by TRESK inhibition. Preliminary results indicate that TRESK might have a role in modulation of mechanical sensitivity but not in heat or cold sensitivity.



37) Human hierarchical auditory prediction error

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Auditory prediction errors have been extensively associated with the mismatch negativity (MMN), a cortical auditory evoked potential that denotes deviance detection. Yet, many studies lacked the appropriate controls to disentangle sensory adaptation from prediction error. Furthermore, subcortical deviance detection has been shown in humans through recordings of the frequency-following response (FFR), an early auditory evoked potential that reflects the neural tracking of the periodic characteristics of a sound, which raises the issue of the origin of prediction error along the auditory pathway. The present study aimed at investigating the emergence of prediction error along the auditory hierarchy in humans through combined recordings of the FFR and the MMN, that come from subcortical and cortical levels, respectively, while disentangling prediction error from sensory adaptation with the use of appropriate controls. “Oddball” sequences of pure tones featuring repeated “standard” stimuli (269 Hz; $p=0.8$) and rare “deviant” stimuli ($p = 0.2$; of 289, 329 and 409 Hz delivered in separated blocks to test “deviance magnitude” effects) were presented to 19 healthy young participants. “Reversed” oddball sequences (where standard and deviant tones swapped their roles) were presented allowing comparison of responses to same physical stimuli as a function of functional role (i.e., standard, deviant). Critically, control sequences featuring five equiprobable tones ($p = 0.2$) allowed to dissociate sensory adaptation from prediction error. Results revealed that the MMN amplitude increased as a function of deviance magnitude yet displayed the same amplitude when retrieved against the control sequences, confirming previous results. FFRs showed a clear sensory adaptation effect across all frequencies repetition, as supported by larger spectral amplitude to standard than to control stimuli, but did not reveal subcortical prediction error, as deviant FFRs were similar to control FFRs. This pattern of results provides insights into the hierarchy of the human prediction error system in audition.



38) Neurophysiological signals supporting the online formation of life-like episodic sequence of events

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As the stream of experience unfolds, our memory system needs to rapidly transform sequence of events into long-lasting meaningful memories. It is unclear, however, to what extent such transformation depends on the process engaged during online encoding. In the first experiment of current study, we used behavioral and neurophysiological (EEG) measures during the encoding of life-like sequences of events to test the hypothesis that specific brain mechanisms operate during encoding to support the formation of meaningful event memory representations. Our findings revealed a continuous increment of brain activity supporting the ongoing accumulation of event information during online encoding and that this neural response was associated with participants' ability to later recall accurately the encoded events. In the second experiment, we repeated the same paradigm with randomly shuffled stimuli, which impeded the construction of meaningful episode in each sequence of events. The results showed that the brain activity elicited during encoding of sequence of events no longer showed a gradual increment pattern as found in the first experiment and neither did correlate with later memory retrieval performance. These findings reveal the existence of specific brain mechanisms that support the online transformation of real-life sequences of events into a long-term memory representation, and that such brain mechanisms engage in the encoding process only when the sequence of events can be constructed as a meaningful episode.



39) Effect of External Representations on Rhythm Learning

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Representing externally can facilitate the cognitive processing of the information encoded in those objects. This has been studied in the writing domain but has been overlooked in the musical domain. Simultaneously, the effect of visual information in the processing of musical rhythm has not been studied. In order to explore these topics, an experimental setting was designed where healthy subjects (N=33) had to tap rhythms and learn them by means of visual and auditory information. The preliminary behavioural results show that the asynchrony between the tapped rhythms and the ideal pattern was reduced in early stages of learning. Asynchrony was reduced more by a representation that relies in spatial distances rather than categories. The complexity of the stimuli increased the asynchrony values without having an interaction with the kind of representation. These results open the study of the role of predictability of stimuli from different modalities in rhythm learning.



40) Human hippocampal neurophysiological signals supporting the formation and retrieval of memories for episodic events

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The hippocampus has a well-established role in transforming our experience into coherent episodic memories that can be accessed at long term. However, the exact nature of its involvement is still unknown. Here, we sought to investigate this issue by examining hippocampal neurophysiological activity recorded via depth electrodes in drug-resistant epileptic patients while they were encoding and retrieving sequences of life-like episodic events. We found that episodic sequences that were later retrieved elicited a strong hippocampal response during encoding, thereby revealing the hippocampal engagement in memory formation online, as the experience unfolds. In addition, we found that successful episodic encoding was accompanied by a transient hippocampal burst of activity at high frequency range (HFA; 60-160Hz) at the event offset, suggesting the hippocampal involvement in signalling episodic boundaries for discrete event memories. Finally, we also observed that their successful recollection 24 hours after encoding was associated to greater hippocampal HFA during a successful retrieval attempt implemented right after encoding, thereby suggesting the existence of specific hippocampal mechanisms promoting memory consolidation during retrieval practice. The current findings provide evidence of the hippocampal underpinnings that support early stages of how the unfolding experience is shaped into a long-term memory representation in humans.

Key words: episodic memory, human hippocampus, depth electrodes.



41) The Psychoacoustics of Rock Art Landscapes. Relating auditory-evoked emotions to acoustic parameters perception

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Can archaeologists and neuroscientists study the human experience of the sacred among premodern societies? Is the sonic behaviour of landscapes an essential component of religious emotion? In the ARTSOUNDSCAPES project we aim to analyse the peculiarities of soundscapes around rock art sites in the open air and evaluate their potential to induce emotional states and specific patterns of brain activity comparable to those elicited during trance and meditation. We will explore the psychoacoustics of selected rock art landscapes by gathering information from the external world and from the listeners themselves, pioneering in the field of archaeoacoustics by applying both methods. In a purposely-built psychoacoustics lab we will conduct the experimental work and test whether art rock soundscapes induce special emotions in comparison with other control soundscapes. In separate experiments, features such as audibility, reverberation, echolocation and some other more specific parameters will be manipulated to ascertain whether a particular acoustic property identified in the tested rock art soundscape is more powerful in inducing special emotions. As a result, we will hypothesize how sound may have contributed to the understanding of the sacred at rock art sites and to the belief in ensouled landscapes by hunter-gatherer and early agricultural societies around the globe.



42) What memories are affected in children with cerebral palsy?

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The impairment of visual-perception is considered a core disorder in people with Cerebral Palsy (CP). It is suggested that visual-perceptual difficulties negatively influence the formation of visual data-bank, slowing down the development of categorization and the outgrowth of visual memory. However, functions related with verbal skills are more preserved. The aim of this study is to analyze the differences between verbal and visual learning/long term-memory in children with CP. Twenty-one children with spastic CP from 8 to 12 years old (mean age 9.9, SD 1.375, 14 males) were included. Visual and verbal learning and long-term memory were assessed by means of the Memory for Designs (NEPSY-II) and the Word Selective Reminding (TOMAL) tests. Differences between visual and verbal standardized scores were compared using the Wilcoxon Signed Rank Test. There were no differences in learning between visual and verbal tests ($Z = -1.873$, p -value: .06). However, visual learning impairment was present in 60% of participants (median $Z = -1.83$) while verbal learning impairment was present in 35% of participants (median $Z = -0.67$). Significant differences emerged between visual (median $Z = -1.33$, 45% of impairment) and verbal (median $Z = 0.17$, 10% of impaired) long-term memory ($Z = -3.069$, p -value: .02). There is a tendency toward a better verbal than visual long-term memory in children with CP. Taking into account the importance of long-term memory in academic performance and daily activities, the results of our study highlight the importance of considering not only visual-perception but also visual long-term memory in clinical interventions.



43) Encoding of fundamental frequency and fine structure of speech sounds: A comparative between adults and newborns

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The encoding of voice pitch and formant structure changes plays an important role in speech comprehension since birth. However, to the best of our knowledge, no study up to date has investigated the ability to encode both elements in newborns. Moreover, research classically used consonant-vowel stimuli. Our aim was to assess the feasibility of using a short stimulus with a rising pitch to reveal both pitch tracking and low-frequency formant encoding accuracy within the time constraints of a newborn FFR (frequency-following-response) recording setup. We tested the diphthong /oa/ in 14 normal-hearing adults (10 females; mean age 26 years) and 17 healthy term newborns (11 females; gestational age 37-42 weeks) by presenting 4 blocks of 1000 sweeps (alternating polarities, 4000 presentations in total).

FFRs were averaged together to emphasize F0 encoding (from steady to rising segment) and subtracted to isolate the encoding of formant structure (from /o/ to /a/ vowel). Results showed that the encoding of voice pitch is fully functional already at birth but that some aspects of fine structure encoding develop late. Moreover, we demonstrated the feasibility to record pitch and low-frequency formant structure changes with a single stimulus in a short recording time (30 min), which makes the diphthong /oa/ a good candidate for newborn FFR research.



44) Neurophysiology of epilepsy

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A single idiopathic episode -or a chronic epileptic disorder, Abnormal electrical brain activity from a crisis produced during the periictal period is usually associated with - cognitive changes --and psychiatric manifestations: ---confusion --- and altered mood. Interictal abnormalities may also occur. -of cognition -and the mood. Due to the different origins and clinical manifestations of seizures, there is no cognitive profile associated with epilepsy, but there are many investigations that suggest that there are several related cognitive deficits -with this disease - and with your treatment. Vingerhoets, 2006, observed slight impairments in intellectual functioning in children and adults with chronic epilepsy. These global cognitive deficits are not universal, and some factors have been linked to an increased risk of neuropsychological deterioration: -THE TYPE OF CRISIS generalized rather than focal -THE MORE FREQUENCY OF THE CRISIS -THE MOST USE OF ANTIEPILEPTIC -A YEAR OF STARTING EARLY. These impairments of general intelligence have the potential to interfere in -the activities of daily living, including exercise -educational -and work. Memory dysfunction is one of the cognitive problems described most frequently associated with epilepsy, especially in temporal lobe epilepsy. -The verbal memory deficits are associated with epilepsy of the left temporal lobe, -Non-verbal memory deficits have been associated with right temporal lobe epilepsy. Some neurologists have failed to observe this clear lateralization relationship between -the epileptic center -and specific memory deficits depending on the material. There is evidence that memory problems - They are important in adults with epilepsy, -and they can negatively affect your quality of life. Other cognitive deficits associated with epilepsy: -language disorders - executive dysfunction - and attention -and processing speed. As with other cognitive functions, a patient's specific deficits can be determined by numerous factors related to the crisis (age of onset, epileptic centers and duration of antiepileptic use). Psychiatric and behavioral disorders may also be prevalent in epileptic patients. Mood disorders, such as depression, are relatively common in this sample of patients. Similar to cognitive problems, these psychiatric disorders can have significant adverse effects on patients and their families, and in these cases evaluation and possible treatment are warranted. A complicated aspect in the identification of cognitive and behavioral deficits associated with epilepsy is the independent effect that therapeutic approaches, such as antiepileptic and neurosurgery, usually have on neuropsychological functioning. 1-Many studies have described potentially harmful effects of antiepileptics on cognitive function, with lower performance in tests of -motor speed, -Attention, -memory, - perceptual functions -and motor coordination. 2-Although surgical resection of epileptogenic brain tissue may be effective in intractable epilepsy, cognitive decline (decline in verbal memory after resection of the dominant temporal lobe, and visual memory deficit after resection of the non-dominant temporal lobe) may occur. Up to one year after the intervention. Neuropsychological evaluations can help neurosurgeons -in the preoperative location of the crisis center -and in the evaluation of cognitive and functional abilities.



45) Pseudoscience Endorsement Scale

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Previous studies have aimed to identify the cognitive mechanisms underlying unwarranted beliefs, especially those related to paranormal phenomena. However, research aimed to study the cognitive basis of other different types of unwarranted beliefs, such as those related to pseudoscience, has been sparse. We designed the Pseudoscience Endorsement Scale aimed to measure pseudoscientific beliefs. This novel scale consists of 20 items referring to popular pseudoscientific myths and disciplines that the respondent has to rate on a scale from 1 (i.e., “Totally disagree”) to 7 (i.e., “Totally agree”). A group of psychology students from the University of Barcelona responded to the questionnaire along with other measures of paranormal beliefs. Our scale presented good reliability values. The degrees of endorsement of pseudoscientific and paranormal beliefs were significantly correlated. However, the volunteers presented significantly higher levels of pseudoscientific beliefs, underscoring the need to study these specific types of unwarranted beliefs.



46) Maternal resveratrol diet regulates Endoplasmic Reticulum Stress in SAMP8 mice model: cognitive and epigenetic changes across generations

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While the elderly segment of the population continues to grow in size and importance, dementia incidence increases exponentially. Lifestyle factors such as diet, exercise, education, among others, influence ageing progression. In particular, Central Nervous System (CNS) can benefit from a diet strategies to prevent signs of senescence, as cognitive decline or neurodegenerative diseases, like Alzheimer's disease (AD). Recent evidence has shown that epigenetic modifications can occur in response to environmental stimuli, one of the most important of which is diet. The mechanisms by which diet affects epigenetics are not fully understood. Dietary polyphenols such as resveratrol possess anti-oxidant, anti-aging, neuroprotection, anti-inflammatory, anti-diabetic, anti-dementia, and extends lifespan. Resveratrol has pleiotropic effects, demonstrating its activity through several biological pathways, including epigenetics. The aim of the work is to study the influence of an enriched resveratrol diet in maternal offsprings. We evaluated cognitive effects of dietary resveratrol on inheritance in 6-month-old Senescence-accelerated mouse prone 8 (SAMP8) mice. We found a reduction in cognitive impairment by Novel Object Recognition Test (NORT) in F1 and F2. At the molecular level, we observed a reduction antioxidant enzymes gene expression such as Hmox1, Aldh2, as well as hydrogen peroxide levels (H₂O₂) in the hippocampus of both generations. Besides, a reduction of ER stress proteins for example p-PERK, Bip, p-EIF2 α and epigenetic changes in global DNA methylation (5-mC) and hydroxymethylation levels (5-hmC). Likewise, we found changes in the hippocampal gene expression of several chromatin-modifying enzymes, such as Dnmt1, Dnmt3a/b and Tet1. These new findings suggest that the environmental influence by early-diet can modify the risk of cognitive decline and provide a better understanding of the mechanisms involved in neurodegeneration.

