FUNDACIÓN REINA SOFÍA

MINISTERIO DE ECONOMÍA Y COMPETITIVIDAD

Instituto de Salud Carlos III

cien Fundación Centro Investigación Enfermedades Neurológicas

ciberned Centro Investigación Biomédica en Red Enfermedades Neurodegenerativas

III CONGRESO INTERNACIONAL DE INVESTIGACIÓN E INNOVACIÓN EN ENFERMEDADES NEURODEGENERATIVAS

III International Congress on Research and Innovation in Neurodegenerative Diseases

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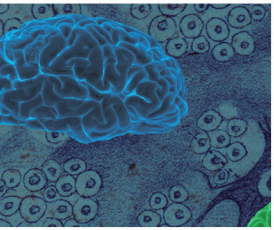
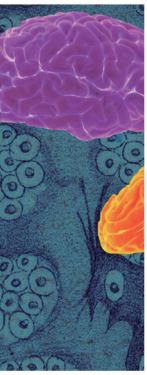


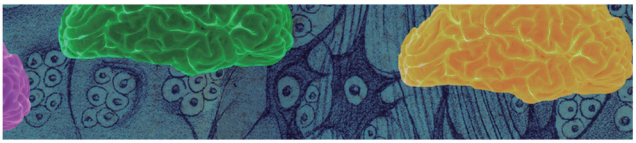
XI SIMPOSIO INTERNACIONAL:

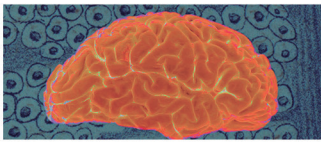
Avances en la Enfermedad de Alzheimer

XI INTERNATIONAL SYMPOSIUM:

Advances in Alzheimer´s Diseases

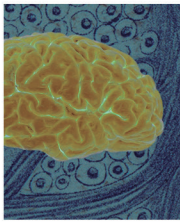


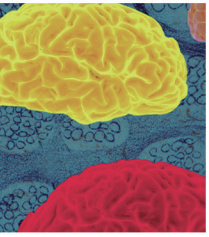


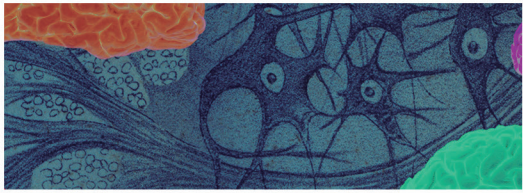


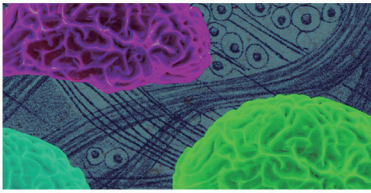
9º Foro Científico CIBERNED

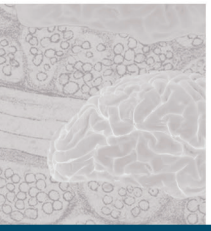
9th CIBERNED Scientific Forum

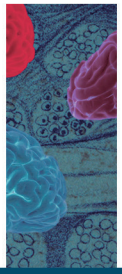


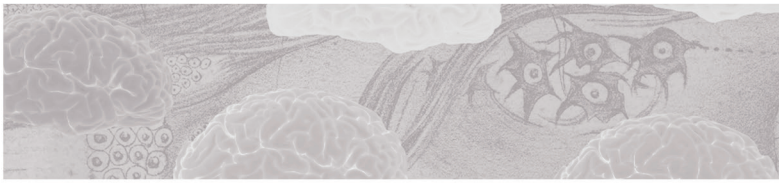












21-23 SEPTIEMBRE · MÁLAGA 2015 · SEPTEMBER 21-23

COVER PHOTO: “Florituras Cerebrales”

Artistic interpretation that combines an idea of multiple neurotransmitters (colored brains) with these neurotransmitters action through the brain cells.

(J. De Felipe)

III International Congress on Research and Innovation in Neurodegenerative Diseases

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Introduction

This report summarizes the activities carried out around the Third International Congress on Innovation and Research in Neurodegenerative Diseases (CIIIEN). CIIIEN is organized annually by the Queen Sofia Foundation, the Center for Research in Neurological Diseases (CIEN) Foundation and the Center for Networked Biomedical Research in Neurodegenerative Diseases (CIBERNED). The Conference took place in Málaga between 21st and 23rd of September, 2015 and attracted more than 200 researchers, clinicians and scientists involved in the field of neurodegeneration research.

Under the Presidency of H. M. the Queen Sofia, the Congress discussed the main recent research advances in neurodegenerative disorders, particularly Alzheimer's, Parkinson's and Huntington's diseases, and marked for the thrid consecutive year, the merger of the XI International Symposium on Advances in Alzheimer's Disease and the IX Scientific Annual CIBERNED Forum.

This annual meeting offers a forum to discuss a range of areas of interest related to basic, clinical and translational aspects of the research in neurodegenerative diseases. It provides opportunities to researchers to discuss and entertain topics that stretch into the future and will be vital to procure the advancement of cooperative research. The CiiiEN will continue to be a meeting point for the world's leading experts in neurodegenerative diseases, allowing sharing of knowledge, working methods, new developments and discoveries in a field in which international cooperation between institutions is becoming increasingly important for obtaining optimal results in research.

Participating Institutions

Public Institutions

- **H.E. Ms. Carmen Vela Olmo,** State Secretary for Research, Development and Innovation.
- **Dr. Jesús Fernández Crespo,** General Director, Carlos III Institute of Health.
- **Ms. Margarita Blázquez,** Deputy General Director of Networks and Cooperative Research Centers, Carlos III Institute of Health.
- **Mr. José Luis Beotas,** Legal Advisor, State General Legal Office.
- **H.E. Mr. Elías Bendodo Benasayag,** President of the delegation of Málaga.
- **H.E. Mr. José Ángel de la Torre Prados,** Mayor of the city hall of Málaga.
- **Ms. Adelaida de la Calle Martín,** Counselor for Education, Government of Andalucía.
- **Dr. José Becerra Ratia,** director of Cell Biology, Genetics and Physiology Department, University of Málaga.
- **Ms. Francisca Marín Pérez,** Technical Management Unit Cabinet Rector of the University of Málaga.
- **Dr. Herminia Peraita Adrados,** Professor of Psychology, Spanish National Distance Education University (UNED).
- **Dr. Francisca Sánchez Jiménez,** Professor of Biochemistry and Molecular Biology, University of Málaga.
- **Dr. Natalia García Casares**, Department of Medicine Professor, University of Málaga.

Private Institutions

- **Ms. Leonor Beleza,** President, Champalimaud Foundation.
- **Mr. José Luis Nogueira**, Secretary of the Queen Sofia Foundation.
- **Dr. Agustín Ruiz**, Research Director, ACE Foundation.

Scientific Conference

Scientific Organizing Committee

- **Dr. Jesús Ávila. –** Scientific Director
- **Dr. Isidro Ferrer**
- **Dr. Antonia Gutiérrez. -** Chairman
- **Dr. Alberto Lleó**
- **Dr. Adolfo López de Munain**
- **Dr. José J. Lucas**
- **Dr. Miguel Medina. -** Deputy Scientific Director
- **Dr. Eduardo Soriano**
- **Dr. Eduardo Tolosa**

CIBERNED Steering Committee

- **Dr. Jesús Ávila** - Scientific Director
- **Ms. Mª Ángeles Pérez** - Managing Director
- **Dr. Miguel Medina** - Deputy Scientific Director
- **Dr. Isidro Ferrer** (until September 2015)
- **Dr. Alberto Lleó**
- **Dr. Adolfo López de Munain**
- **Dr. José J. Lucas**
- **Dr. Eduardo Soriano** (until September 2015)
- **Dr. Eduardo Tolosa**
- **Dr. Rafael Fernández** (since september 2015)
- **Dr. Teresa Iglesias** (since september 2015)

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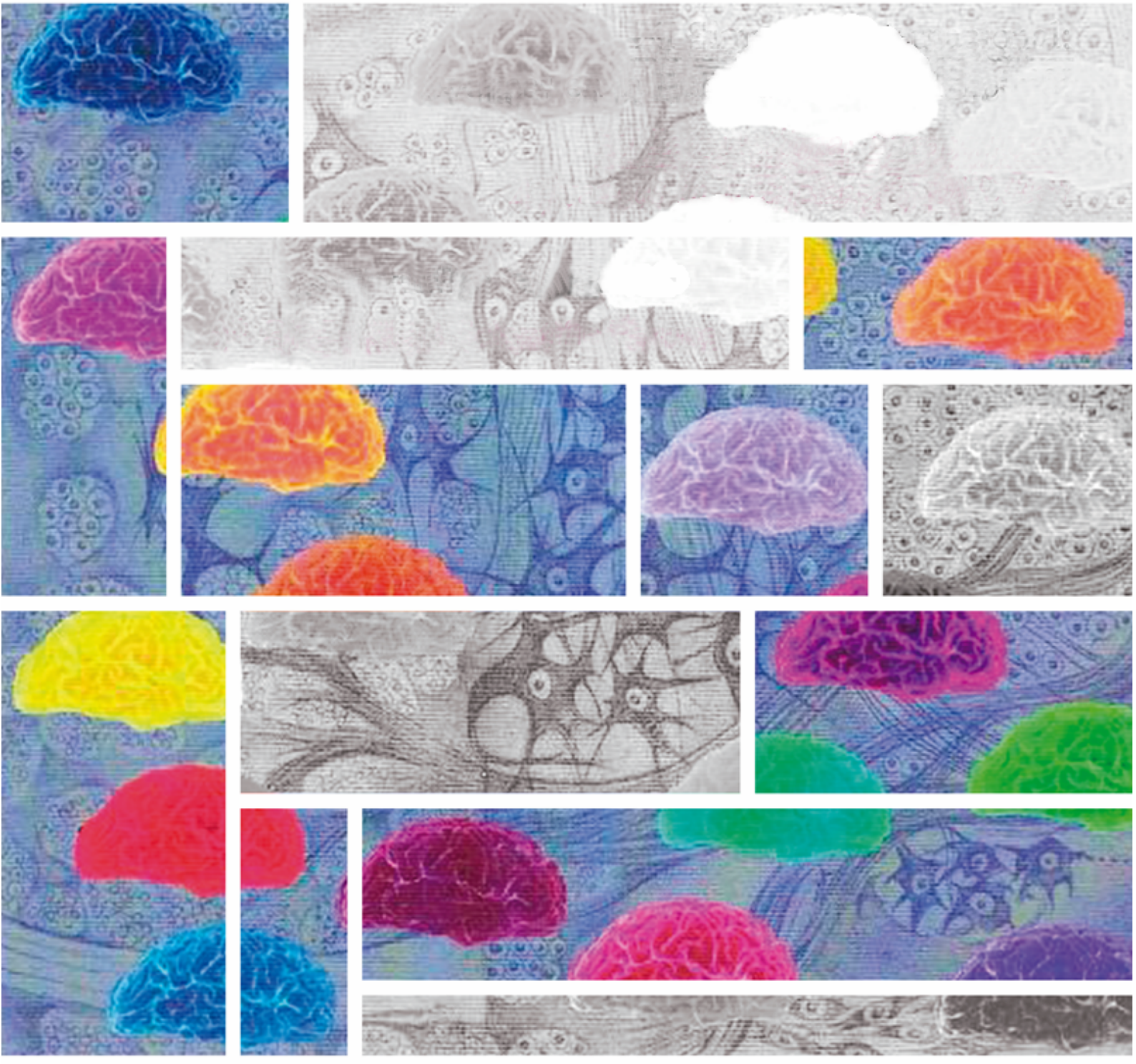

MONDAY, SEPTEMBER 21

10:00 – 15:00 h

WELCOME AND REGISTRATION

13:00 - 13:15 h

OPENING SESSIONS

With the Presidency of Her Majesty Queen Sofia

13:15 - 14:00 h

PLENARY SESSION I:

Guidelines for novel conceptual models of dementia: essential features of an "ideal theory" on dementia

Zaven Khachaturian (Introduced by Jesús Ávila)

The Campaign to Prevent Alzheimer´s Disease 2020, Potomac, Maryland

14:00 – 15:00 h

LUNCH AND POSTER SETUP

Zaven Khachaturian

Zaven Khachaturian, PhD, is the President of the Campaign to Prevent Alzheimer's Disease by 2020 [PAS2020] Inc. www.pad2020.org. He is also a Senior Science Advisor to the Alzheimer's Association; the Editor-in-Chief of Alzheimer's & Dementia: Journal of the Alzheimer's Association. His career spans several major high-level positions requiring strategic decisions regarding research policies and program development. He is generally acknowledged as the 'Founder - Chief Architect' of the extramural research programs on Neurobiology of Aging and Alzheimer supported by the National Institution on Aging (NIA) / National Institutes of Health [NIH]. Formerly he served the dual role of Director, Office of Alzheimer's Disease, responsible for coordinating all Alzheimer's disease related activities NIH-wide; as well as the Associate Director for the Neuroscience and Neuropsychology of Aging Program (NNA) at the NIA/NIH. His academic training includes: BA Yale 1961 / PhD Case-Western Reserve 1967 / Post-doctoral College of Physicians & Surgeons, Columbia 1967-1968.

15:00 - 16:40 h

PLENARY SESSION II:

Chairperson: Jesús Ávila

CIBERNED, Center for Molecular Biology "Severo Ochoa", CSIC-UAM, Madrid

15:00 - 15:50 h

Responding to the dementia challenge – Is there a window of opportunity with early intervention?

Martín Rossor

NIHR Queen Square Dementia BRU, UCL, London

15:50 - 16:40 h

Autophagy and other therapeutic strategies for neurodegenerative Diseases

David Rubinsztein

Cambridge Institute for Medical Research

16:40 - 17:10 h

COFFEE BREAK

Martin Rossor

Martin Rossor trained in Neurology at the National Hospital, Queen Square and undertook research into the neurochemistry of degenerative dementia at the MRC Neurochemical Pharmacology Unit, Cambridge.

He is Professor of Clinical Neurology at the National Hospital for Neurology and Neurosurgery, and established a specialist cognitive disorders clinic which acts as a tertiary referral service for young onset and rare dementias. Clinical research interests are in the degenerative dementias and particularly in familial disease. He was editor of the Journal of Neurology, Neurosurgery & Psychiatry, and President of the Association of British Neurologists. Martin is the NIHR National Director for Dementia Research, Director of the NIHR Queen Square Dementia Biomedical Research Unit and a NIHR Senior Investigator.

David Rubinsztein

David Rubinsztein did a BSc(Med) Hons and PhD at the University of Cape Town after his basic medical training and housejobs. He came to Cambridge in 1993 as a senior registrar in Genetic Pathology. He was awarded a Glaxo Wellcome Fellowship in 1997, a Wellcome Trust Senior Clinical Fellowship (2001, renewed in 2006) and a Wellcome Trust Principal Research Fellowship in 2011. Rubinsztein was elected as a Fellow of the Academy of Medical Sciences (2004), Professor of Molecular Neurogenetics (University of Cambridge, personal chair (2005)) and Spinoza Visiting Professorship (University of Amsterdam (2009)). He was awarded the Graham Bull Prize for Clinical Science (Royal College of Physicians) in 2007 and was elected as a member of EMBO in 2011. In 2014, he was selected as one of Thomson Reuters' Highly Cited Researchers in the categories Biology and Biochemistry and Molecular Biology and Genetics (http://highlycited.com/). He is also deputy director of the Cambridge Institute for Medical Research and Academic Lead of the Alzheimer's Research UK Cambridge Drug Discovery Institute.

David Rubinsztein has focussed on understanding the biology of autophagy in mammalian systems, particularly in the context of neurodegenerative diseases. His laboratory were the first to suggest the strategy of autophagy upregulation as a possible therapeutic approach in various neurodegenerative diseases and have identified drugs and novel pathways that may be exploited for this objective. He has shown how autophagy defects may contribute to various diseases and has contributed to the understanding of the basic cell biology of this important catabolic process. His laboratory has also identified druggable pathways independent of autophagy that may be relevant to diseases caused by aggregate-prone proteins.

17:10 - 17:40 h

SCIENTIFIC SESSION I:
Chairperson: Teresa Iglesias
CIBERNED, Biomedical Research Institute "Alberto Sols" (CSIC-UAM), Madrid, Spain

17:10 - 17:40 h

The effect of GSK3β overexpression in adult neurogenesis
Jesús Ávila
CIBERNED, Center for Molecular Biology "Severo Ochoa", CSIC-UAM, Madrid

17:40 - 18:10 h

Contribution of glial cells to neurodegenerative diseases
Carlos Matute
CIBERNED, University of Basque Country (UPV), Bilbao

18:10 - 18:40 h

Neuronal Plasticity in Huntington´s disease: New (and old) molecules that modulate endogenous BDNF and p75 imbalance
Jordi Alberch
CIBERNED, IDIBAPS, University of Barcelona

19:30 h

TRANSFER BUS TO RECEPTION AT THE RUSSIAN MUSEUM
(Sponsored by the City Hall of Málaga)

20:00 – 20:45 h

RECEPTION AT THE RUSSIAN MUSEUM

Jesús Ávila

Jesús Avila is Professor and former Director of the Center of Molecular Biology, Madrid, Spain and actually Scientific Director of CIBERNED. During the last thirty years have been working in neuron cytoskeleton. Now, he studies the role of tau protein in neurodegenerative disorders (tauopathies) like Alzheimer disease. He is member of different Organizations like EMBO, European Academy and the Spanish Royal Academy of Sciences; he is member of different Editorial Boards and has more than 400 publications, most of them related to Alzheimer disease.

Carlos Matute

Dr. Matute is a full professor at the University of Basque Country, School of Medicine (Spain) and Director of the Achucarro Basque Center for Neuroscience.

He graduated and received his PhD at the University of Zaragoza (Spain) in 1982. He has worked as a postdoctoral fellow in CNS glial cells under the supervision of Drs. M. Cuénod and P. Streit (Brain Research Institute in Zurich) and Dr. R. Miledi (University of California in Irvine). His laboratory has focused on the study of novel mechanisms of neurodegeneration and neuroprotection as well as on the contribution of glial cells to neurodegenerative diseases.

Jordi Alberch

Jordi Alberch is currently Vicerrector of Research, Innovation and Transfer of the University of Barcelona. He is Professor in the Department of Cell Biology, Immunology and Neuroscience in the Medical School of the University of Barcelona. He received his MD (1983) and PhD (1986) degrees from the University of Barcelona. He was visiting researcher in Georgetown University (1988-1989), University of Medicine and Dentistry of New Jersey (UMDNJ)/Robert Wood Johnson Medical School (1994-1995) and Karolinska Institute (1997). His main research topic is the study of the pathophysiology of the neurodegenerative disorders and he has published more than 120 papers in peer-review journals. He is member of the editorial board of several journals. He is the President of the Spanish Society for Neuroscience.

TUESDAY, SEPTEMBER 22

08:30 - 09:30 h

MEETINGS OF COOPERATIVE PROJECTS

09:30 - 11:00 h

SCIENTIFIC SESSION II:

Chairperson: Isabel Fariñas

CIBERNED, Department of Cell Biology UV, Valencia, Spain

09:30 - 10:00 h

Glial activation on Alzheimer disease: transgenic models vs patiens

Javier Vitorica

CIBERNED, IBIS, University of Seville

10:00 - 10:30 h

Targeting non-neuronal cells for the treatment of motorneuron diseases

Xavier Navarro

CIBERNED, Institute of Neurosciences UAB, Barcelona

10:30 - 11:00 h

Pharmacologic targeting of transcription factor Nrf2 in Parkinson´s disease

Antonio Cuadrado

CIBERNED, Medical School UAM, Madrid

11:00 – 11:30 h

COFFEE BREAK

Javier Vitorica

BSc Degree in Biology from the Faculty of Sciences, Autonomous University of Madrid. I received my PhD at the Center of Molecular Biology “Severo Ochoa”, Autonomous University of Madrid. The topic of my PhD focused on the study of calcium homeostasis in rat brain and its variations with aging.

I did a postdoctoral stay at New York University working on the molecular characterization of GABAa ionotropic receptors.

At the end of this period, I got a position as Associate Professor in the Department of Biochemistry and Molecular Biology at the University of Seville. I am currently Professor in that Department.

As senior scientist, one of my main interests has been to identify molecular-cellular changes associated with the aging process in hippocampus and cerebral cortex. Given that aging is one of the main risk factors for Alzheimer's disease, we began studying the potential vulnerability of the GABAergic system in hippocampus and cerebral cortex in transgenic models of Alzheimer's disease. From this moment, our main scientific objectives are the following: 1) studying the cellular/molecular mechanisms involved in neurodegenerative changes occurring in this pathology in regions such as the hippocampus and entorhinal cortex; 2) searching for potential molecular markers that allow for detecting the progression of pathology in the transgenic models; 3) identifying new therapeutic targets for drug development; 4) studying in the transgenic models the potential preventive/curative usefulness of new therapeutic strategies.

I currently have 83 articles published in peer-review journals and my H index is 29.

Xavier Navarro

Xavier Navarro received the MD degree in 1978 and the PhD degree in 1985 from the Unversitat Autonoma de Barcelona (UAB). He completed his speciality training in Neurology at the University of Barcelona, and in Neurophysiology at the University of Minnesota. He was Assistant Porfessor of the Department of Neurology of the University of Minnesota (1986-1988). He returned in 1988 to the UAB as Associate Professor in the Department of Cell Biology and Physiology, where he is currently full Professor of Physiology. He has been a founder of the Institute of Neurosciences of the UAB, and the director of the Department since 2010.

Since 1989 he is heading the research Group on Neuroplasticity and Regeneration. His research interests are focused on axonal regeneration, functional restitution after nerve injuries, cell and molecular therapies for spinal cord injuries, neuroprostheses, peripheral neuropathies, neuropathic pain and motoneuron diseases. He has published more than 300 papers in refereed journals and books in these areas of the neurosciences, and directed 22 PhD theses. He also serves as scientific advisor of the Institut Guttmann of Neurorehabilitation. He has been member of the editorial boards of the journals: Restorative Neurology and Neuroscience, Journal of the Peripheral Nervous System, Muscle and Nerve, Frontiers in Neuroengineering. He has received awards “Ciutat de Barcelona” in 1995, “Josep Trueta” in 2000, ASPAYM in 2009 for his scientific research activities.

Antonio Cuadrado

Antonio Cuadrado, obtained his PhD degree in 1985 and enjoyed several postdoctoral stays in the National Cancer Institute-NIH with the help of Fulbright and Fogarty fellowships. He established his independent laboratory as Professor of Biochemistry in 1997 at the Department of Biochemistry, Faculty of Medicine of Autonomous University of Madrid. His main interest is the study of molecular mechanisms involved in initiation and progression of neurodegenerative diseases. For the past 10 years his main lane of research has been the validation of transcription factor Nrf2, master regulator of cell homeostasis, in protection against oxidative, inflammatory and proteopatic stress in Parkinson's and Alzheimer's disease. He is full professor of Biochemistry and Deputy Director of the Institute of Biomedical Research "Alberto Sols" UAM-CSIC. He has published over 100 peer reviewed articles, several book chapters and reviews.

TUESDAY, SEPTEMBER 22

11:30 - 13:20 h

SCIENTIFIC SESSION II:

Chairperson: Miguel Medina

CIBERNED-CIEN Foundation, Madrid, Spain

11:30 - 12:10 h

Generating and Shaping Novel Actions in Health and Disease?

Rui Costa

Champalimaud Center for the Unknown, Lisbon

12:10 - 12:50 h

Towards a mechanistic understanding of risk factors for Alzheimer´s disease

Ángel Cedazo-Mínguez

Center for Alzheimer Research, Karolinska Institutet, Stockholm

12:50 - 13:20 h

NEFL E396K mutation is associated with a novel dominant intermediate Charcot-Marie-Tooth disease phenotype

José Berciano

CIBERNED, Marqués de Valdecilla University Hospital (IDIVAL), Santander

13:20 – 15:50 h

LUNCH AND POSTER SESSION

13:30 – 15:00 h

CIBERNED STEERING COMMITTEE

Rui Costa

Investigator, Champalimaud Neuroscience Programme, Champalimaud Center for the Unknown, Lisbon , Portugal

EDUCATION/TRAINING

Institution and Location	Degree	Year(s)	Field of Study
Technical University of Lisbon, Portugal	DVM	1996	Veterinary Medicine
UCLA/University of Porto, Portugal	PhD	2002	Neuroscience

A. Main domain of research

Action generation, sequence and skill learning, goal-directed actions versus habits, PD, OCD, autism. Major Tools: Gene targeting in mice, Neuronal ensemble electrophysiology in behaving mice, Slice electrophysiology in mice, Optogenetics and molecular imaging in mice.

B. Positions, honours and scientific activities

Employment/Experience

2002 to 2005 Postdoctoral Fellow, Dr. M. Nicolelis, Duke University, USA

2006 to 2009 Chief, Section of In-Vivo Neural Function, NIAAA, NIH, USA.

2009 to present Investigator, Champalimaud Neuroscience Programme, Portugal.

Honours, Awards and Scholarships

2001 to 2002 Young Investigator Award, National Neurofibromatosis Found., NY, USA.

2009 to 2014 ERC Starting Grant, European Research Council, Brussels, Belgium.

2010 Seeds of Science Prize for Life Sciences 2010, Portugal.

2012 to 2017 International Early Career Scientist, HHMI, MD, USA

2012 Young Investigator Award, Society for Neuroscience, USA.

2014 to 2019 ERC Consolidator Grant, European Research Council, Brussels, Belgium.

2014 Silver Medal Services in Medical Research, Ministry of Health, Portugal.

2014 Elected Member of EMBO

2014 Order of Sant'Iago da Espada, Presidency of the Republic of Portugal.

2014 The Louis-Jeantet Young Investigator Career Award, Switzerland.

Ángel Cedazo-Mínguez

Angel Cedazo-Minguez is Associate Professor and co-director of Center for Alzheimer Research at Karolinska Institutet (Sweden) from 2006.

He received a Ph.D. in Medicine from Karolinska Institutet (Sweden) in 2002 and a Senior Lecturer Degree in 2010. Cedazo-Minguez was Vice Head (2008 to 2012) and Head (2012-14) of the Department of Neurobiology, Care Sciences and Society at Karolinska Institutet. In 2013, he was appointed Co-director the Swedish Brain Power, a National Network of Centers of Excellence to combat Neurodegenerative Disorders.

Dr. Cedazo-Minguez is currently acting as external advisor of several National and European research programs, including CIBERNED (Spain), INSERN (France), FP7 IDEA, ERA-NET and JPND (EU).

The focus of Dr. Cedazo-Minguez's research involves investigating the pathological mechanisms behind some known risk factors for Alzheimer's disease. Current projects are directed towards fundamental alterations in antioxidant systems and homeostatic dysregulations of cholesterol and glucose metabolisms.

José Ángel Berciano

Chair and Head of Neurology, “Marqués de Valdecilla” University Hospital, University of Cantabria, Santander, Spain.

My main line of investigation has been focused on epidemiologic, genetic, clinico-pathological and electrophysiological studies of peripheral neuropathies and ataxias. Under my tutelage, 17 doctoral thesis have been performed. I have participated in 21 competitive research projects (PI in 9 of them). I was Editor-in-Chief of Neurología between 1997 and 2004. I was Scientific Director of CIBERNED in 2010 and 2011.

Author or co-author of 404 papers indexed in PubMed (accessed, June 26, 2015) with an “h” index of 40 (Web of Knowledge). Ten outstanding papers in the last decade.

15:30 - 17:10 h

SCIENTIFIC SESSION III:

Chairperson: José Luis Cantero

CIBERNED, Laboratory functional neuroscience UPO, Sevilla, Spain.

11:30 - 12:10 h

Quantitative analysis of brain MRI studies: possibilities and difficulties

Manuel Desco

Gregorio Marañón University Hospital, Madrid

16:00 - 16:30 h

MRI in the healthy elderly predicts subsequent development of Mild Cognitive Impairment

Bryan Strange

CIEN Foundation, Center of Biomedical Technology, Technical University, Madrid

16:30 - 16:50 h

Huntington´s disease is a four-repeat tauopathy with tau nuclear rods

Marta Fernández-Nogales. **2014 Young Investigator Award**

CIBERNED, Center for Molecular Biology "Severo Ochoa", CSIC-UAM, Madrid

16:50 - 17:10 h

Cerebrospinal fluid b-Amyloid and Phospho-Tau biomarker interactions affecting brain structure in preclinical Alzheimer disease

Juan Fortea. 2013-2014 Young Clinical Investigator Award

CIBERNED, Sant Pau Hospital, Barcelona

17:10 - 17:45 h
COFFEE BREAK

CLAUSTRO CIBERNED

17:45 - 18:05 h
SCIENTIFIC DIRECTOR REPORT

18:05 - 18:25 h
MANAGER REPORT

18:25 - 18:45 h
DEPUTY SCIENTIFIC DIRECTOR REPORT

20:00 - 21:00 h
MÁLAGA WALKING TOUR

21:00 h
DINNER IN A TYPICAL TAPAS RESTAURANT

Manuel Desco

Manuel Desco reached the degrees of MD, MSEng and PhD, and is specialist in Nuclear Medicine. He is Head of Service of the Experimental Medicine and Surgery Department of the Hospital General Universitario Gregorio Marañón in Madrid and lecturer at the Bioengineering and Aerospace Engineering Dept. of the Universidad Carlos III de Madrid. Presently he also chairs the Spanish Excellence Network on Technological Innovation in Hospitals (ITEMAS) of the Instituto de Salud Carlos III, which brings together more than 100 institutions, health and business .

He has previously worked in various sectors, through the care medicine, as an entrepreneur and finally in research, mainly on medical imaging, in advanced techniques for obtaining image (MRI, positron emission tomography, etc.) and in the subsequent analysis of it, either for better quantitative information or to develop different systems for the diagnosis. A significant amount of work has been devoted to the development of high-performance devices for small-animal molecular imaging, useful in experimental biomedical research.

He has published more than 500 scientific papers and has participated or coordinated more than 85 national and international research projects and technology transfer, excellence networks (for instance, “Molecular and Multimodality Medical Imaging, IM3, with 29 groups from all over the country).

Some relevant awards were the UNICEM prize to technological innovation (2004), Galien prize to best research trajectory (2008) and FEI prize as best innovative researcher (2013). In 2014 he has been named full member by Academia Médico-Quirúrgica Española.

He has directed 20 doctoral theses of physicists, engineers and doctors and more than 25 final projects.

Several technological developments made by his team have been patented and transferred to the industry, reaching a market internationally.

Bryan Strange

Bryan A. Strange completed the M.B.–Ph.D. programme at University College London (UK) in 2004. His Ph.D., conducted at the Functional Imaging Laboratory, Institute of Neurology, London, under the supervision of Ray Dolan and Karl Friston, argued for a functional dissociation between the anterior and posterior hippocampus in humans.

Subsequently, alongside clinical work in general medicine and neurology, he continued to study memory in humans, with particular focus on the effects of emotion on memory formation. He started his own laboratory in 2011, the Laboratory for Clinical Neuroscience, CTB-UPM, and in 2014 became Director of the Department of Neuroimaging, Reina Sofia Foundation Centre for Alzheimer's Research, Madrid, Spain. His recent research has provided evidence for episodic memory reconsolidation in humans. His laboratory uses a multimodal approach to studying human medial temporal lobe function in healthy people and in patients with neurological and psychiatric diseases.

Marta Fernández-Nogales

Marta Fernández-Nogales was graduated in Biology at the University of Valencia (Spain). During this time, she participated as student collaborator in the laboratory of Genetics of Development and Biomedical Models. In 2010, she moved to Madrid where she obtained a Master in Molecular Biomedicine by the Universidad Autónoma de Madrid (Spain). Simultaneously, she started her PhD at the Centro de Biología Molecular Severo Ochoa (CSIC-UAM) (Spain) in the laboratory of Molecular basis of Huntington´s disease and other central nervous system disorders under the direction of the Professor Jose Javier Lucas Lozano. During this time, she worked about the role of Glycogen Synthase Kinase 3 and its substrate Tau in Huntington´s Disease. She made a short stay in the Department of Pathology of at the VU Medical Center in Amsterdan (The Netherlands). As a result of her investigation, she described that the decrease of Glycogen Synthase Kinase 3 contributes to Huntington´s Disease (Fernández-Nogales M, et al. Decreased Glycogen Synthase Kinase-3 levels and activity contribute to Huntington's Disease. Human Molecular Genetics, 2015) and also, she discovered that in Huntington´s Disease there is a disbalance in Tau isoforms like in other tauopathies and, the presence of a new Tau-histopathological hallmark called Tau nuclear rods in patients´ brain (Fernandez-Nogales M, et al. Huntington's disease is a four-repeat tauopathy with tau nuclear rods. Nature medicine, 2014). As a consequence of this paper, she received the award for the best original work published as first author on the Centro de Biología Molecular Severo Ochoa in 2014. She participated in different international conferences included the Society for Neuroscience 2014 Annual Meeting in Washington (EEUU) and in the European Huntington´s Disease Network Plenary Meeting 2014 in Barcelona (Spain). Marta was recently awarded with the Young Investigator Award 2014 in the III International Congress on Research and Innovation in Neurodegenerative Diseases by the CIBERNED (Biomedical Research Network in Neurodegenerative Diseases, Spain). She defended her PhD thesis with distinction of Extraordinary Doctoral Award by the Universidad Autónoma de Madrid (Spain). In June 2015, she moved to Alicante where she started her postdoc at the Instituto de Neurociencias de Alicante (CSIC-UMH) (Spain) in the laboratory Development and assembly of bilateral neural circuits under the direction of Eloisa Herrera Gónzalez de Molina.

Juan Fortea

Dr. Juan Fortea is a behavioral neurologist and a dementia expert. He combines his research and clinical activities between the Memory Unit of the Hospital de la Santa Creu i Sant Pau (HSP) where he leads the neuroimaging unit and his work as Adult Medical Director at Down Medical Center of the Catalan Foundation for Down Syndrome (FCSD), both in Barcelona.

Both his clinical and research activities have been focused on the treatment and study of neurodegenerative diseases. Specifically, Dr. Fortea has specialized in the study of Alzheimer's disease biomarkers, describing the experimental uses of CT, PET, and MRI in characterizing human degenerative brain diseases, a field in which he has co-authored more than 60 publications in international journals.

His main line of research is preclinical AD both in the general population and infamilial AD and Down Syndrome. He has led several multimodal studies that have enabled the description of a 2-phase phenomenon of pathological cortical thickening associated with brain amyloidosis, followed by atrophy once CSF p-tau becomes abnormal.

08:30 - 09:30 h

MEETINGS OF COOPERATIVE PROJECTS

09:30 - 11:00 h

SCIENTIFIC SESSION IV:

Late-breaking news / Poster Highlights

Chairperson: Antonia Gutiérrez

CIBERNED, Santa Creu i Sant Pau Hospital, Barcelona, Spain.

9:30-9:40 h

Irene López-González. IDIBELL, University Hopsital of Bellvitge- University of Barcelona, Spain

Neuroinflammatory gene regulation, tau oligomers and oxidative stress with disease progression in tau P301S transgenic mice as a model of FTLD-tau

Irene López-González, Ester Aso, Margarita Carmona, Mercedes Armand-Ugon, Rosi Blanco, Isidre Ferrer

9:40-9:50 h

Fernando Bartolomé. 12 de Octubre Hospital Research Institute, Spain

p62/SQSTM1 deficiency is associated to mitochondrial disturbances

Fernando Bartolomé, Eva Carro, John Hardy, Helene Plun-Favreau and Andrey Y Abramov

9:50-10:00 h

Marta Pascual. University of Barcelona Spain

Impairment of the Gabaergic Septhohippocampal conecction in a mouse model of Tauopathy

H. Soler, M. González, J. Dorca, D. E. Parruca da Cruz, S. E. Rubio, J. Avila, E. Soriano and M. Pascual

10:00-10:10 h

José Luis Cantero Lorente. University Pablo Olavide of Seville, Spain

Regional hippocampal atrophy and increased plasma amyloid-beta are associated with subjective memory complaints in non-demented elderly subjects

Mercedes Atienza, Juan E. Iglesias, Koen Van Leemput, Jose L. Cantero

10:10-10:20 h
Olivia Belbín. Hospital de la Santa Creu y Sant Pau, Barcelona, Spain
Identification of synaptic proteins detectable in the cerebrospinal fluid in the search for biomarkers of preclinical Alzheimer's Disease
Olivia Belbin, Gemma Gomez-Giro, Laia Muñoz, Daniel Alcolea, Martí Colom-Cadena, María Carmona-Iragui, Juan Fortea, Jordi Clarimon, Àlex Bayés, Alberto Lleó

10:20-10:30 h
Raquel Sánchez-Varo. University of Málaga
Microtubule stabilizing therapy protects cognitive function and ameliorates alzheimer's disease pathology
Fernandez-Valenzuela JJ., Sánchez-Varo R., De Castro V., Moyano FJ, Vizuete M, Davila JC, Vitorica J. and Gutiérrez A

10:30-10:40 h
Eva Díaz Guerra. CSIC, Cajal Institute, Madrid, Spain
Generation of iPSCs and iNSCs from patients having alzheimer's disease with the ?4 and ?3 alleles of the apoe gene
Eva Díaz-Guerra, Eva Rodríguez-Traver, Patricia García-Sanz, Lorena Orgaz, Isabel Hernández, Mercè Boada, Agustín Ruiz, Rosario Moratalla, and Carlos Vicario-Abejón

10:40-10:50 h
Laura Genis. CSIC, Cajal Institute, Madrid, Spain
Dual role of IGF-IR in response to oxidative stress: neurons versus astrocytes
Genís, L; Torres-Alemán, I

11:00 – 11:30 h
COFFEE BREAK AND POSTER SESSION

11:30 - 13:00 h

SCIENTIFIC SESSION V:

Chairperson: Adolfo López de Munaín

CIBERNED, Biodonostia research institute, San Sebastián, Spain

11:30 - 12:00 h

Apathy and Cognitive Impairment in Parkinson´s Disease

Jaime Kulisevsky

CIBERNED, Sant Pau Hospital Research Institute, Barcelona

12:00 - 12:30 h

Parkinson´s disease in advanced stages

Mª Cruz Rodríguez Oroz

CIBERNED, BioDonostia Research Institute, San Sebastián

12:30 - 13:00 h

FACEHBI. Fundació ACE Healthy Brain Initiative

Mercé Boada

Fundació ACE, Barcelona Alzheimer Treatment and Research Center

13:00 - 13:15 h

CONCLUDING REMARKS

Jesús Ávila

13:15 h

END OF MEETING

Jaime Kulisevsky

Dr. Kulisevsky is Associate Professor of Neurology at the Autonomous University of Barcelona, Research Professor of de Open University of Catalonia and Director of the Movement Disorders Unit of the Sant Pau Hospital in Barcelona, Spain. He is also the Director of the Research Institute of this Hospital.

He conducts clinical research in Parkinson´s disease and other movement disorders. His main research interest has been the cognitive and behavioral consequences of basal ganglia dysfunction in Movement Disorders and the impact of antiparkinsonian treatment on cognition and behavior in Parkinson´s disease.

He has been member of the International Movement Disorders Society Task Force for Developing Rating Scales in Parkinson´s Disease (Subcomitee for Cognitive Evaluation) and of the Task Force for Mild cognitive Impairment in Parkinson´s Disease. He acts as the Spanish Coordinator of the European Huntington´s Disease Network and the ENROLL study (CHDI).

He has been awarded with the Research Prize of the Spanish Society of Neurology, has been Principal Investigator of the Spanish Biomedical Network Research Centre for Neurodegenerative Diseases (CIBERNED-Instituto de Salud Carlos III).

Mª Cruz Rodríguez

Professor Rodriguez Oroz completed her medical education at the University of Navarra in 1991 and her training in Neurology at the University Clinic of Navarra (1992-1995). Afterwards she performed a fellowship in Movement Disorders under the supervision of Prof. Obeso. In 1999 she obtained a PhD in Neuroscience from the University of La Laguna with the highest distinction Cum Laude. The topic of her PhD thesis was neurophysiologic characterization and therapeutic involvement of subthalamic nucleus in Parkinson´s disease. She previously worked (2000-2011) at the University Clinic of Navarra as Consultant Neurologist, Neuroscience researcher and Associate Professor of Neurology. Since 2013 she is Tenured Professor of Neurology accredited by the ANECA (National Agency for the Quality Assessment and Accreditation of Spain). Since 2011 she is Ikerbasque Research Professor, Head of Neurodegenerative and Parkinson´s disease Research Program at Biodonostia Health Research Institute, Head of the Neurodegenerative Disease Research Program at Basque Center on Cognition, Brain and Language (BCBL) and Honorary Consultant Neurologist at University Hospital Donostia, in San Sebastian. She is also Associated Professor of Physiology in Biomedical Engineering and Medicine Degrees at the University of Navarra and Professor of Neuroscience Master at University of Navarra and Basque Country University. In the team of Professor Obeso, she pioneered the treatment with deep brain stimulation for Parkinson's disease in Spain. Her former research was centered on this topic and in the neurophysiological study of pathophysiology of Parkinson´s disease and dyskinesias both in patients and in animal models of parkinsonism. Later on, she has developed other lines of research focused on cognitive impairment and Impulse Control Disorders in Parkinson´s disease. During her career she has taken part in a lot of national and international research projects and has produced multiple publications in international and national journals, as well as book chapters. As result of this prolific activity she has an H-index of 37 (Web of Science). Moreover, she is member of the Scientific and Education Committee of the Movement Disorders Society and takes part in several Task Forces of this society. She is also reviewer for several national and international neurology and neuroscience journals, associated editor of Movement Disorders Journal and member of the international editorial board of Movement Disorders Clinical Practice. Finally, she received the Federico Oloriz Neuroscience Institute Award to the best young researcher in neuroscience in 2002, granted from the Royal Academy of Medicine of Granada, Spain.

Merçè Boada

Neurologist, born in Barcelona, Dr. Mercè Boada is founder and medical director of Fundació ACE. Institut Català de Neurociències Aplicades. Until 2013 she was responsible for Neurodegenerative Diseases Unit at the Neurology Service, University Hospital Vall d'Hebron, and Head of the research group "Alzheimer" at the Vall d'Hebron – Research Institute (VHIR), Barcelona, Spain.

Its activity is focused on the treatment of Alzheimer's disease and related dementias. Especially interested in research on the factors involved in the degenerative process of AD and vascular dementia; genome and phenome of common diseases; neuroimaging biomarkers for the diagnosis of prodromal AD, and design of new pharmacological and non-pharmacological treatments.

She is the co-director of «Documento Sitges» on the ability and rights to decision making in the process of dementia. She leads the Observatory on Cognitive Health, Autonomy and competence, «OBSCAC», since 2011.

She was the coordinator of the care model design for people with dementia within the public health system of Catalonia («Model d'atenció per les persones amb deteriorament cognitiu i demència de Catalunya») (1991), She has been Technical Secretary of the Psychogeriatric Council of Catalonia (1996-2001), president of the Pharmacological Treatment for Alzheimer's Disease Advisory Board (1996-2001), member of the Bioethics Committee of Catalonia, and member of the Ministry of Health of the Catalan Government Advisory Board.

She has served on the National Expert Group for the development of the «Standards and recommendations for quality and safety in health centers and services» of the Spanish Ministry of Health, Social Policy and Equality (2011).

He has published more than 125 articles with an impact factor 128,58 (h index, 29) in 2014, 25 book chapters and 12 books of medical outreach.

Winner of the Award for Professional Excellence by the Medical Council of Catalonia (2008), the Josep Trueta Medal for health merit, by the Generalitat de Catalunya (2012) and recently the 2015 "Eduard Beltran Rubió" award for the best professional and academic career by Catalan Neurology Association.

Abstract Book

Libro de Abstract

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2015

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POSTER 1

Presented by the researcher: Lastres Becker, Isabel.

Principal investigator of the group: Cuadrado Pastor, Antonio. (Cod: 101).

Title: New therapeutic strategies in Parkinson's disease: the transcription factor NRF2 as a target for dimethyl fumarate.

Authors: Lastres-Becker, I., García-Yagüe, A.J., Kügler, S., Rábano, A. and Cuadrado, A.

Abstract: Parkinson's disease (PD) is one of the most common disabling neurodegenerative disorders with treatments based on the clinical symptomatic aspects. Therefore it is very important to find a preventive or disease modifying therapy for PD. Dimethylfumarate (DMF), the main ingredient of an oral formulation of fumaric acid esters, has been found to have therapeutic efficacy in relapsing-remitting multiple sclerosis and psoriasis, diseases where inflammation has an essential role. DMF targets the transcription factor NRF2, a master regulator of antioxidant response and inflammation, which are two mayor hallmarks of PD. Therefore, in this study we investigated whether DMF administration could prevent or ameliorate the neurodegeneration/neuroinflammation caused by overexpression of ?-synuclein (?-SYN) and thus provide a new therapeutic strategy for PD. Treatment of microglial BV2 cells with DMF showed a time-dependent increased in mRNA and protein levels of phase II detoxificantion enzymes like heme oxygenase 1 (HO-1), NAD(P)H quinone oxidoreductase 1 (NQO1) and Osgin-1 as well as autophagy related protein p62. Interestingly, DMF treatment decreased the mRNA and protein levels of IL-1? and iNOS induced by ?-SYN, indicating that DMF could modulate the inflammatory response produced by ?-SYN. To further investigate the effect of DMF in a preclinical setting, we used recombinant viral vectors to overexpress human ?-SYN protein in the substantia nigra of Nrf2+/+ and Nrf2-/-mice, which provides a relevant model that recapitulates many cardinal features of the human disease. We found that, in Nrf2+/+ mice, daily oral gavage of 100 mg/kg DMF provided a very significant protection of nigral dopaminergic neurons against ?-SYN toxicity after 3 and 8 weeks following injection with AAV6-?-SYN and at the same time reduced astrogliosis and microgliosis. This protective effect was not observed in the Nrf2-/- mice. These experiments provide a significant support to determine if pharmacological targeting of NRF2 with DMF might be a therapeutic strategy in synucleinopathies.

POSTER 2

Presented by the researcher: Fuentes Rodriguez, Jose Manuel.

Principal investigator of the group: Fuentes Rodriguez, Jose Manuel. (Cod: 103).

Title: PINK1 deficiency enhances autophagy and mitophagy induction

Authors: Rubén Gómez-Sánchez1, Sokhna M.S Yakhine-Diop1, Jose M Bravo-San Pedro1, Elisa Pizarro-Estrella1, Mario Rodríguez-Arribas1, Vicente Climent2, Maria E Gonzalez-Soltero3, Rosa A González-Polo1, Jose M Fuentes1 1 Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Departamento de Bioquímica y Biología Molecular y Genética, Universidad de Extremadura, Facultad de Enfermería y Terapia Ocupacional, 10003 Cáceres, Spain 2 Departamento de Anatomía y Embriología Humana, Facultad de Medicina, Universidad de Extremadura, 06071 Badajoz, Spain 3 Sección de Neurología, Hospital Virgen del Puerto, 10600 Plasencia, Spain

Abstract: Parkinson's disease (PD) is a neurodegenerative disorder with poorly understood etiology. However, growing evidence suggests that compromised maintenance of mitochondrial function in an age-dependent manner is a key risk factor. Several proteins, codified by PD-related genes, are associated with mitochondria, including PTEN-induced putative kinase 1 (PINK1). This gene was firstly identified to be upregulated by PTEN. Loss-of-function PINK1 mutations induce mitochondrial dysfunction and, in last term, neuronal cell death. To mitigate the negative effects of altered cellular functions, cells present a degradative mechanism, called autophagy, for recycling damaged components. Specifically, selective elimination of dysfunctional mitochondria by autophagy is named mitophagy. Our study indicates that autophagy and mitophagy are upregulated in PINK1-deficient cells, being the first report to demonstrate efficient fluxes by one-step analysis. Therefore, we propose that autophagy is induced to maintain cellular homeostasis under non-regulated mitochondrial quality control conditions This work was supported by Instituto de Salud Carlos III (PI12/02280, PI14/00170 (co-financed by European Union FEDER funds) and CB06/05/0041).

POSTER 3

Presented by the researcher: Sánchez Lanzas, Raúl.

Principal investigator of the group: Gonzalez Castaño, Jose. (Cod: 104).

Title: Protein degradation in Lamp2 deficient B-lymphoblastoid cells from a patient with Danon disease

Authors: Raul Sánchez-Lanzas1,2, Beatriz Alvarez-Castelao1,2, Teresa Bermejo1,2,, Teresa Ayuso3, Teresa Tuñón4 and José G. Castaño1,2 1Departamento de Bioquímica, Instituto de Investigaciones Biomédicas "Alberto Sols", UAM-CSIC y 2 Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED). Facultad de Medicina UAM. 28029 Madrid, 3Anatomía Patológica. Complejo Hospitalario de Navarra y Biobanco de Tejidos Neurológicos, 3Neurología, Complejo Hospitalario de Navarra y Biobanco de Tejidos Neurológicos. 31008 Pamplona. Spain

Abstract: Protein degradation is critical for cell proteostasis, and is mainly achieved by the ubiquitin proteasome system (UPS) and the autophagic pathway that includes: chaperone-mediated autophagy (CMA) and macroautophagy. Lamp2A protein, generated by alternative splicing from the Lamp2 pre-mRNA, has been identified as the lysosomal membrane receptor required for protein translocation into the lysosome lumen, being an essential component of the CMA pathway. Danon disease, a condition characterized by cardiomyopathy, myopathy and intellectual disability, is caused by mutations in the LAMP2 gene. A lymphoblastoid cell line was obtained by EBV transformation of B-cells from a Danon patient. The derived cell line showed no significant expression of Lamp2 protein. Degradation of alpha-synuclein (Snca), I?B?, Rcan1 and glyceraldehyde-3-phosphate dehydrogenase (Gapdh), four proteins reported to be direct substrates of CMA were analyzed in control and Lamp2 deficient lympboblastoid cells. The steady-state levels of those proteins and their respective mRNAs were similar in control and Lamp2 deficient cells, indicating that Lamp2 deficiency did not affect the overall turn-over of those proteins. Treatment of cells with cycloheximide showed that the half-life of those proteins was similar in control and Lamp2 deficient cells, and its degradation prevented by proteasome inhibitors. Serum and aminoacid starvation of cells for 8h, to induce CMA and macroautophagy, produced a significant decrease of I?B? and Rcan1 protein levels (Snca and Gapdh levels did not change) and to a similar extent in both control and Lamp2-deficient cells. Treatment of starved cells with 3-methyl adenine (macroautophagy inhibitor), chloroquine, leupeptin, and NH4Cl (CMA inhibitor) showed no differential effect on control and Lamp2 deficient cells. These results showed that the lack of Lamp2 expression did not alter the steady-state levels or the degradation of protein substrates described as specific for the CMA pathway in human lymphoblastoid cells. Our results are in agreement with previously reported data showing that mouse embryo fibroblasts derived from LAMP2, LAMP1 and double LAMP2 and LAMP1 knock-out mice show no defect on the degradation of long-lived protein including degradation by the CMA pathway.

POSTER 4

Presented by the researcher: Pose Utrilla, Julia.

Principal investigator of the group: Iglesias Vacas, Teresa. (Cod: 111).

Title: PKD1 potentiates detoxification pathways and promotes neuroprotection

Authors: Julia Pose-Utrilla, Lucía García-Guerra, Noelia S. De León-Reyes, Jerónimo Jurado-Arjona, Ana Del Puerto, Andrea Gamir-Morralla, Christofer Ireson, Mª José Pérez-Álvarez, Félix Hernández, Jesús Ávila and T. Iglesias

Abstract: Multiple neurodegenerative diseases share a common pathologic pathway for neuronal death known as excitotoxicity. This process is linked to an excessive synaptic release of glutamate, which in turn activates postsynaptic glutamate receptors and overexcites neurons, leading to neuronal death. Among glutamate receptors, both NMDA and AMPA/KA subtypes contribute to excitotoxic neuronal loss in a broad range of neurodegenerative conditions. Their overstimulation triggers primarily an excessive influx of Ca2+ followed by endoplasmic reticulum stress, mitochondria dysfunction and generation of reactive oxygen species (ROS), resulting in neuronal apoptosis and necrosis. Protein kinase D (PKD) is a family of diacylglycerol-stimulated Ser/Thr kinases known to regulate multiple biological processes. Because PKD1 has been implicated in ROS-detoxification and survival in cancer cells we hypothesized that this isoform could confer neuroprotection under excitotoxic conditions. To address this issue we first investigated the possible regulation of PKD in response to overstimulation of NMDA and AMPA/KA receptors. We found a fast PKC- and Src-dependent activation of the kinase followed by a rapid PP1- and STEP-dependent inactivation during excitotoxicity. We also found that pharmacological inhibition or silencing of PKD1 decreased neuronal survival, supporting the fact that PKD inactivation is linked to neuronal death. To analyse the possible neuroprotective effects of PKD1 we generated a constitutively active mutant and cloned it in a lentiviral vector under the control of the synapsin promoter for its neurospecific expression. Transduction with this virus strongly protected neurons from excitotoxic insults by molecular mechanisms that involve potentiation of IKK/NFkB-pathway that in turn increased MnSOD levels and decreased ROS production. Our results indicate that selective and neurospecific PKD1 activators could constitute potent tools to induce neuroprotection in neurodegenerative diseases.

POSTER 5

Presented by the researcher: Del Rio Fernandez, Jose Antonio.

Principal investigator of the group: Del Rio Fernandez, Jose Antonio. (Cod: 114).

Title: Involvement of PrP(C) in kainate-induced excitotoxicity in several mouse strains.

Authors: Carulla P, Llorens F, Matamoros-Angles A, Aguilar-Calvo P, Espinosa JC, Gavín R, Ferrer I, Legname G, Torres JM, Del Río JA.

Abstract: The cellular prion protein (PrP(C)) has been associated with a plethora of cellular functions ranging from cell cycle to neuroprotection. Mice lacking PrP(C) show an increased susceptibility to epileptic seizures; the protein, then, is neuroprotective. However, lack of experimental reproducibility has led to considering the possibility that other factors besides PrP(C) deletion, such as the genetic background of mice or the presence of so-called "Prnp flanking genes", might contribute to the reported susceptibility. Here, we performed a comparative analysis of seizure-susceptibility using characterized Prnp(+/+) and Prnp(0/0) mice of B6129, B6.129, 129/Ola or FVB/N genetic backgrounds. Our study indicates that PrP(C) plays a role in neuroprotection in KA-treated cells and mice. For this function, PrP(C) should contain the aa32-93 region and needs to be linked to the membrane. In addition, some unidentified "Prnp-flanking genes" play a role parallel to PrP(C) in the KA-mediated responses in B6129 and B6.129 Prnp(0/0) mice.

POSTER 6

Presented by the researcher: GENIS MARTIN, LAURA.

Principal investigator of the group: Torres Aleman, Ignacio. (Cod: 409).

Title: Dual role of IGF-IR in response to oxidative stress: neurons versus astrocytes

Authors: Genís, L; Torres-Alemán, I.

Abstract: The brain is highly vulnerable to oxidative damage which is an important contributing factor in the etiology of neurological disorders that are accompanied with neuronal death. Among brain cells, neurons are the most sensitive to oxidative stress due to their high production of ROS and low antioxidant enzymes expression. On the contrary, astrocytes present a wide antioxidant system that contributes to make them important candidates for their role in neuroprotection. Among the neurotrophic factors produced by reactive glial cells, IGF-I is one of the most pleiotropic protective signals in the brain. Astrocyte IGF-I/IGF-IR signaling is implicated in their neuroprotective role as downregulation of IGF-IR in astrocytes blocks their neuroprotective capacity against oxidative stress. However, the functions of the IGF-IR may be cell and context-dependent as its response to oxidative stress is controversial. In relation to this, downregulation of IGF-IR in astrocytes makes them less effective regarding their neuroprotective role against oxidative insults but confers them more resistance to death induced by oxidative stress. According to this, downregulation of IGF-IR increases basal ROS level in astrocytes that may activate alternative antioxidant systems, such as Nrf2, able to completely block ROS under oxidative stress exposure. However, the astrocytary resistance to oxidative stress conferred by the downregulation of IGF-IR does not correlate with astrocyte-mediated neuronal protection against acute oxidative stress in vivo, as astrocyte IGF-IR knock out mice (FIRKO) subjected to brain stroke show higher ischemic damage. Deciphering the different roles of IGF-I/IGF-IR signaling in both astrocytes and neurons under oxidative stress may be crucial to understanding the endogenous neuroprotective mechanisms.

POSTER 7

Presented by the researcher: Bartolome Robledo, Fernando.

Principal investigator of the group: Carro Diaz, Eva Maria. (Cod: 502).

Title: p62/SQSTM1 deficiency is associated to mitochondrial disturbances

Authors: Fernando Bartolome, Eva Carro, John Hardy, Helene Plun-Favreau and Andrey Y Abramov

Abstract: A growing body of published experimental evidences is showing abnormal mitochondrial function related to patients with frontotemporal dementia and amyotrophic lateral sclerosis (FTD/ALS). Mutations in the same disease-causing genes in both disorders have been reported and they support the idea of a FTD-ALS continuum. Interestingly, VCP and p62/SQSTM1 mutations which have been found causing FTD/ALS are also identified causing Paget's Disease of the Bone. We have recently demonstrated that VCP (Valosin Containing Protein) deficiency is associated with profound mitochondrial uncoupling, resulting a significant reduction of cellular ATP production. Decreased ATP levels in VCP deficient cells lower their energy capacity, making them more vulnerable to high energy demanding processes. In this work the mitochondrial pathophysiology associated to p62/SQSTM1 (p62) deficiency will be studied using dynamic live-cell imaging techniques to explore the mitochondrial pathophysiology in a p62-knock-down (p62 KD) human dopaminergic neuroblastoma cell line (SH-SY5Y) and fibroblasts from patients carrying two independent pathogenic mutations in the p62/SQSTM1 gene. We confirm that p62 deficiency is associated to mitochondrial depolarisation and inhibition in the cell respiration process through complex I. This inhibition resulted in higher ROS production, compelling the cells to switch from glycolysis to the pentose phosphate pathway as reflects the elevated NADPH and GSH levels. These findings highlight the pathophysiological events that may occur in FTD/ALS associated with p62 deficiency.

POSTER 8

Presented by the researcher: Robledinos Antón, Natalia.

Principal investigator of the group: Cuadrado Pastor, Antonio. (Cod: 101).

Title: Role of transcription factor NRF2 in self-renewal and multipotency of neural stem cells

Authors: Natalia Robledinos Antón, Ángel Juan García Yagüe, Antonio Cuadrado

Abstract: Neurodegenerative disorders, such as Alzheimer's disease (AD), involve a gradual loss of well-defined neuronal populations and specific alterations in the neurogenic areas of adult brain. In adult brain, neurogenesis persists in two germinal zones: subventricular zone (SVZ) of lateral wall of ventricle and subgranular zone (SGZ) in the dentate gyrus of hippocampus. Alterations in the microenvironment of neurogenic niches, like oxidative stress, have been related with the onset and progression of neurodegenerative diseases. One of the mechanisms to face these processes is the transcription factor Nrf2, master regulator of anti-oxidant and anti-inflammatory response. Here, we report the role of Nrf2 in the maintenance of neurogenic niches, because of its possible link with Wnt signaling, which has a vital role in the modulation of neurogenesis and neuroprotection. We have developed animal models with the main anatomopathological and cognitive hallmarks of AD, expressing TAU(P301L) and APP(V717I) in combination with presence or absence of NRF2. Our data show that lack of NRF2 affects the proliferative capacity of neural stem cells and the cellular composition of the neurogenic niche of the dentate gyrus as well as the response of neuroespheres to WNT signaling.

POSTER 9

Presented by the researcher: González Rodríguez, Patricia.

Investigador principal grupo López Barneo, José. (Cod: 105).

Title: Electrophysiological characterization of iPS cells and iPS-derived neurons differentiated from control, idiopathic and LRRK2 Parkinson patients

Authors: P. González-Rodríguez1,2, K. Levitsky1, H. Sarmiento-Soto1, R. Torrent3, Y. Richaud-Patin4, R. Fernandez5, M. Ezquerra5, J. Canals5, J. Alberch2,5, E. Tolosa2,5, A. Raya4, A. Consiglio3, J. López-Barneo1,2, José A. Rodríguez-Gómez1 1Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla 2CIBERNED, Spain 3Instituto de Biomedicina de la Universidad de Barcelona (IBUB). 4Centro de Medicina Regenerativa de Barcelona (CMRB), CIBER-BBN 5Instituto de Investigaciones Biomédicas Augusto Pi y Sunyer, Universidad de Barcelona

Abstract: Induced pluripotent stem (iPS) cells constitute a powerful tool to develop in vitro models of neurological diseases such as Parkinson (PD). Ion channels play a fundamental role in pathological processes. We show that voltage-dependent outward (K+) and inward (Na+ and Ca2+) currents were present in iPS representing control age-matched, idiopathic and LRRK2-mutant PD patients. Based on electrophysiological and pharmacological properties we found that Ca2+ channels correspond to the T-subtype and were similar in kinetics and level of expression among the different lines. We also have studied dopaminergic neurons of control SP11 cell line using a differentiation method based on dual SMAD inhibition and floor plate induction followed by co-culture with human astrocytic cell line. This differentiation only achieved 11% of dopaminergic neurons from total cells and 55% of neurons at day 30. Levels of neurotransmitters such as noradrenaline, dopamine and DOPAC, were measured by HPLC-ED technique at day 50 of differentiation. We also carried out dopaminergic differentiation using embryoid bodies co-cultured with mouse cortical astrocytes. Electrophysiological properties were analyzed using patch clamp technique to determine whether these cells are capable of generating mature and electrically active neurons forming neuronal networks with functional chemical synapses. In current-clamp conditions, application of depolarizing current pulses evoked repetitive firing of action potentials in mature neurons (>day 50). In contrast only a single action potential was generated in immature neurons (<day 30). These observations fit well with the high level of expression of voltage-dependent Na+ and K+ channels in mature neurons in comparison with immature cells. These results demonstrate that iPS cells obtained from parkinsonian patients have normal ion channels and are capable of generating electrophysiologically functional and synaptically connected neurons in vitro. This work was supported by the Botín Foundation, the Spanish Ministry of Science and Innovation, the Ministry of Health and the European Union.

POSTER 10

Presented by the researcher: Díaz Guerra, Eva.

Principal investigator of the group: Vicario Abejón, Carlos. (Cod: 108).

Title: Generation of iPSCs and iNSCs from patients having alzheimer's disease with the ?4 and ?3 alleles of the apoe gene.

Authors: Eva Díaz-Guerra, Eva Rodríguez-Traver1,2, Patricia García-Sanz1,2, Lorena Orgaz1,2, Isabel Hernández3, Mercè Boada3, Agustín Ruiz3, Rosario Moratalla1,2, and Carlos Vicario-Abejón1,2. 1Instituto Cajal, Consejo Superior de Investigaciones Científicas (CSIC), Madrid; 2CIBERNED, Instituto de Salud Carlos III (ISCIII), Madrid; 3Fundació ACE-Barcelona Alzheimer Treatment and Research Center, Barcelona.

Abstract: The ?4 allele of the APOE gene, which encodes the apolipoprotein E4 (ApoE4), is a strong genetic risk factor for Alzheimer´s disease (AD), the most common form of dementia. In contrast, it is not completely known whether the ?3 allele represents a risk factor for AD. It was recently shown that induced pluripotent stem cell (iPSC)-derived cholinergic neurons from AD patients carrying the ?4 and ?3 alleles (in heterozygosis) were more vulnerable to glutamate-induced excitotoxicity than neurons derived from healthy controls (Duan et al., 2014). Although the neocortex and hippocampus are two brain regions where neuronal damage is associated with impaired cognitive and memory functions in AD, the impact of the ?4 and ?3 alleles (in homozygosis) on iPSC-derived neocortical and hippocampal neurons is not known. Similarly, it remains to be determined whether ApoE4 (and ApoE3) affect astrocyte metabolism. To address these questions, we have derived iPSCs and induced neural stem cells (iNSCs) from AD patients carrying the ?4 or ?3 alleles and from 2 healthy controls. The cell colonies obtained presented the typical iPSC morphology, expressed the pluripotency markers Nanog, TRA-1-60, and SSEA-4, and up to this time, they were passaged 4-5 times in cell culture. Differentiation of embryoid bodies and cytogenetic studies are in progress to confirm the pluripotent capacity and the genetic stability of the ApoE-derived iPSCs. Then, the iPSCs will be converted into iNSCs and these cells differentiated to cortical and hippocampal neurons and to astrocytes with the aim of studying the effects of ApoE4 and ApoE3 on neuronal survival and growth, synaptic integrity and activity as well as on astrocyte metabolism and mitochondrial function. Supported by grants from CIBERNED (ISCIII, MINECO, Spain).

POSTER 11

Presented by the researcher: Morales García, Jose Angel.

Principal investigator of the group: Pérez Castillo, Ana Mª. (Cod: 110).

Title: Phosphodiesterase 7 Inhibition Induces Neurogenesis in vitro and in vivo.

Authors: Morales-García, JA; Alonso-Gil, S; Gil, C; Martinez, A; Santos, A; Pérez-Castillo, A.

Abstract: Parkinson's disease (PD) is characterized by a loss of dopaminergic neurons in a specific brain region, the ventral midbrain. PD is diagnosed when about 50% of the dopaminergic neurons of the substantia nigra pars compacta (SNpc) have degenerated and the others are already affected by the disease. Thus, it is conceivable that all therapeutic strategies, aimed at neuroprotection, start too late. Therefore there is an urgent medical need to discover new pharmacological targets and novel drugs with disease-modifying properties. In this regard, modulation of endogenous adult neurogenesis may provide a new strategy to target PD. The phosphodiesterase 7 (PDE7) enzyme is one of the enzymes responsible for controlling specifically the intracellular levels of cyclic adenosine 3',5'-monophosphate in the immune and central nervous system. We have previously shown that PDE7inhibition exerts potent neuroprotective and anti-inflammatory effects in different rodent models of PD indicating that this target could represent a novel therapeutic agent to stop the dopaminergic cell loss that takes place during the progression of the disease. The aim of the present study was to investigate the effects of the PDE7 inhibition on adult neurogenesis. Here, we show that PDE7 inhibiton controls stem cell expansion in the subventricular zone (SVZ) and the subgranular zone of the dentate gyrus of the hippocampus (SGZ) in the adult rat brain. Our data clearly demonstrate that PDE7 inhibitors promote neurogenesis in vitro and in vivo. In addition, we show that PDE7 inhibition is also able to stimulate adult neurogenesis in the 6-OHDA model of PD, mimicking a severe dopaminergic striatal deficit, promoting endogenous neuroregenerative processes toward a dopaminergic phenotype. Next, using PDE7 inhibitors, we could potentially contribute to upregulate endogenous neurogenesis and/or favor integration of new dopaminergic neurons to stimulate neurorepair in PD.

POSTER 12

Presented by the researcher: Rojo Sanchis, Ana Isabel.

Principal investigator of the group: Cuadrado Pastor, Antonio. (Cod: 101).

Title: NRF2: promising therapeutic target for Alzheimer disease.

Authors: Natalia Robledinos Antón, Ángel Juan García Yagüe, Antonio Cuadrado

Rojo Ana I, Pajares Marta, Rada Patricia, García-Yagüe Angel J y Cuadrado Antonio

Abstract: Despite intensive research in preclinical models and in clinical trials, all pipelines have consistently failed to develop a disease modifying therapy for AD. It is therefore evident that a new innovative focus is needed. NRF2, considered the master regulator of redox homeostasis, regulates the expression of more than 100 anti-oxidant and anti-inflammatory genes. We have generated a new AD model consisting in APP V717I/TAU P301L (AT-NRF2-WT) and APP V717I/TAU P301L NRF2-deficient mice (AT-NRF2-KO). Largely neuronal transgene expression pattern, similar in both genotypes, was demonstrated. We observed strongest signals in brain regions related with learning and memory and in other brain areas involved in motor coordination. Mice exhibited cognitive impairment and died precocious with a marked spinal deformity accompanied with motor problems and strong weight loss. We evidenced that NRF2 deficiency aggravates tauopathy and Aβ oligomer formation compromising motor function, cognitive and learning capacity and accelerates precocious death. These animals will be an excellent tool to study AD due to: The possibility to analyze the role of oxidative stress, proteinopathy, neurodegeneration and neuroinflammation in the evolution of AD and the comparison of AT-NRF2-WT vs. AT-NRF2-KO allows to determine the relevance of NRF2, drug design and analysis of off-target effects.

POSTER 13

Presented by the researcher: Casadó Burillo, Vicent.

Principal investigator of the group: Canela Campos, Enric I. (Cod: 201).

Title: Allosteric interactions between ligands within the adenosine A2A receptor - dopamine D2 receptor heteromer support the use of adenosine receptor antagonists in treating Parkinson's disease

Authors: Vicent Casadó1, Verònica Casadó-Anguera1, Jordi Bonaventura1,2, Gemma Navarro1, Estefania Moreno1, William Rea2, Karima Azdad3, Marc Brugarolas1, Nora D. Volkow4, Josefa Mallol1, Carme Lluís1, Serge N. Schiffmann3, Sergi Ferré2, Antoni Cortés1 and Enric I. Canela1 1Laboratory of Molecular Neurobiology, Department of Biochemistry and Molecular Biology, Faculty of Biology, University of Barcelona, Centro de Investigación Biomédica en Red Sobre Enfermedades Neurodegenerativas (CIBERNED) and Institute of Biomedicine of the University of Barcelona (IBUB), Barcelona, Spain. 2Integrative Neurobiology Section, National Institute on Drug Abuse, Intramural Research Program, National Institutes of Health, Baltimore, MD, USA. 3Laboratory of Neurophysiology, Universite Libre de Bruxelles-Neuroscience Institute, Brussels, Belgium. 4National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health, Bethesda, MD, USA

Abstract: Adenosine A2A receptor (A2AR)-dopamine D2 receptor (D2R) heteromers are key modulators of striatal neuronal function. It has been suggested that the psychostimulant effects of A2AR antagonists depend on their ability to block an allosteric modulation within the A2AR-D2R heteromer, by which adenosine decreases the affinity and intrinsic efficacy of dopamine at the D2R. As demonstrated by radioligand binding and ERK1/2 phosphorylation assays, we describe novel and unexpected allosteric mechanisms within the heteromer, by which not only A2AR agonists but also A2AR antagonists decrease the affinity and intrinsic efficacy of D2R agonists and the affinity of D2R antagonists. Surprisingly, these allosteric modulations disappear upon agonist and antagonist co-administration, also demonstrated by electrophysiological and locomotor activity experiments. This can be explained by a model that considers A2AR-D2R heteromers as heterotetramers, constituted by A2AR and D2R homodimers. As predicted by this model, high concentrations of A2AR antagonists behaved as A2AR agonists and decreased D2R function in the brain. Our model still provides support for the use of A2AR antagonists in treating patients with Parkinson's disease.

POSTER 14

Presented by the researcher: Rodriguez Diaz, Manuel.

Principal investigator of the group: Rodriguez Diaz, Manuel. (Cod: 206).

Title: Respuesta de los astrocitos a la denervación dopaminergica del estriado.

Authors: Ingrid Morales, Alberto Sanchez, Clara Rodríguez Sabaté, Magdalena Sabaté y Manuel Rodríguez

Abstract: Increasing evidence suggests that the dopaminergic degeneration which characterizes Parkinson's disease starts in the striatal dopamine terminals and progresses retrogradely to the body of dopamine cells in the substantia nigra. The role of striatal astrocytes in the striatal initiation of the dopaminergic degeneration is little known. This work was aimed at studying the astrocytic response to the dopaminergic denervation of the striatum. The injection of 6-hydroxydopamine in the lateral ventricle of adult Sprague-Dawley rats induced a fast (4 hours) and selective (not accompanied by unspecific lesions of striatal tissue or microgliosis) degeneration of the dopaminergic innervation of the striatum which was followed by astrocytosis. This astrocytosis was severe and had a specific profile which included some (e.g. upregulation of GFAP, GS, S100β, NDRG2, vimentin) but not all (e.g. astrocytic proliferation or differentiation from NG2 cells, astrocytic scars, microgliosis) the characteristics observed after the non-selective lesion of the striatum. Taken together, present data suggest a complex role of astrocytes in the dopaminergic denervated striatum, where they could keep a delicate balance between the protection of and the damaging of dopamine neurons. The balance between these opposing actions could be critical in PD, and the knowledge of mechanisms involved in the selective profile of the astrogliotic response to DA-denervation could improve the understanding of the role of striatal astrocytes in this illness.

POSTER 15

Presented by the researcher: García García, Mª Concepción.

Principal investigator of the group: Fernández Ruiz, Javier. (Cod: 303).

Title: Potential of the cannabinoid CB2 receptor as a pharmacological target against inflammation in Parkinson's disease

Authors: Concepción García, Yolanda Gómez-Gálvez, Cristina Palomo-Garo, Javier Fernández-Ruiz

Abstract: Inflammation is an important pathogenic factor in Parkinson's disease (PD), so that it can contribute to kill dopaminergic neurons of the substantia nigra and to enhance the dopaminergic denervation of the striatum. The cannabinoid type-2 (CB2) receptor has been investigated as a potential anti-inflammatory and neuroprotective target in different neurodegenerative disorders, but still limited evidence has been collected in PD. Here, we show for the first time that CB2 receptors are elevated in microglial cells recruited and activated at lesioned sites in the substantia nigra of PD patients compared to control subjects. Parkinsonian inflammation can be reproduced experimentally in rodents by intrastriatal injections of lipopolysaccharide (LPS) which, through an intense activation of glial elements and peripheral infiltration, provokes a rapid deterioration of the striatum that may extend to the substantia nigra too. Using this experimental model, we recently described a much more intense deterioration of tyrosine hydroxylase (TH)-containing nigral neurons in CB2 receptor-deficient mice compared to wild-type animals, supporting a potential neuroprotective role for this receptor. In the present study, we further explored this issue. First, we found elevated levels of the CB2 receptor measured by qRT-PCR in the striatum and substantia nigra of LPS-lesioned mice, as well as an increase in the immunostaining for this receptor in the LPS-lesioned striatum. Second, we found a significant increase in CD68 immunostaining, which serve to identify activated microglia and also infiltrated peripheral macrophages, in these brain structures in response to LPS insult, which was much more intense in CB2 receptor-deficient mice in the case of the substantia nigra. Next, we observed that the activation of CB2 receptors with a selective agonist (HU-308) reversed LPS-induced elevation of CD68 immunostaining in the striatum and the parallel reduction in TH immunostaining. Lastly, we found that LPS elevated the gene expression of different pro-inflammatory mediators in both the striatum and the substantia nigra, whereas the selective activation of CB2 receptors reduced a part of these mediators, e.g. inducible nitric oxide synthase, although exclusively in the striatum. In conclusion, we have provided the first evidence on the up-regulation of CB2 receptors in glial elements in postmortem tissues of PD patients, which has been confirmed in an inflammatory model of this disease. In addition, we have provided evidence on the benefits derived from their activation in relation with the activation of microglial cells, the infiltration of macrophages and also certain capability of these cells to generate proinflammatory factors. Supported by MINECO (SAF2009-22847), CIBERNED (CB06/05/0089), The Michael J. Fox Foundation (USA) and GW Pharmaceuticals Ltd (UK). Authors are indebted to Yolanda García-Movellán for administrative support.

POSTER 16

Presented by the researcher: Hernández Hernández, Ivó.

Principal investigator of the group: Lucas Lozano, José Javier. (Cod: 306).

Title: Generation of a new transgenic mouse line for conditional overexpression of the transcription factor ATF5 in adult brain.

Authors: I. Hernández Hernández, José J. Lucas

Abstract: Activating transcription factor 5 (ATF5) is a basic-leucine-zipper transcription factor of the ATF/CREB family. The Atf5 gene generates two transcripts, Atf5? and Atf5?, of which Atf5? is known to be selectively translated in response to different stresses like aminoacid limitation, oxidative stress and endoplasmic reticulum (ER) stress in non-neuronal cells. ATF5 has been implicated in tumor cell survival, apoptosis and cell differentiation among other processes. This transcription factor is widely expressed during development and in the adult. In the developing brain neuroprogenitor cells must have ATF5 levels downregulated to undergo differentiation into mature neurons and glial cells. This has led to the extended notion that differentiated neural cells do not express ATF5 unless they suffer tumorigenic transformation. However, our group recently described a wide, neuronal-patterned ATF5 expression in mouse adult encephalon that can be further induced upon ER stress as a pro-survival mechanism in status epilepticus. Interestingly ER stress condition is believed to contribute to the pathogenesis of many neurodegenerative diseases, like Alzheimer's disease, Parkinson's disease and Huntington's disease. These pieces of evidence suggest that ATF5 holds important roles in the physiology of adult brain. However, little is known about ATF5 transcriptional targets in the nervous tissue. To study neuronal ATF5-responsive genes in vivo we generated a novel tetracycline-responsive, conditional transgenic mouse line overexpressing mouse ATF5 and the reporter ?-galactosidase, designated TREmATF5. To achieve specific induction of ATF5 overexpression in adult neurons we used transgenic mice with a tetracycline-regulated transcriptional transactivator linked to the CamKII? promoter (CamKII?-tTA). As expected, the reporter was induced in adult neurons of the double transgenic animals (CamKII?-tTA; TREmATF5) and we are currently exploring the levels of overexpression of ATF5. These mice will open a new field for neuroprotective strategies focused on ATF5 modulation.

POSTER 17

Presented by the researcher: Furcila, Diana

Principal investigator of the group: De Felipe, Javier (Cod: 403).

Title: Interactive exploratory data analysis tool in Alzheimer's disease

Authors: Diana Furcila, Juan Morales, Ángel Rodríguez, Javier De Felipe and Lidia Alonso-Nanclares,

Abstract: Alzheimer's disease (AD) is a neurodegenerative disorder characterized by a progressive cognitive impairment, and a variety of neuropathological changes, which are not homogenous between different brain regions within a given patient or between patients. The availability of techniques to explore the brain provides neuroscientists a wealth of data that is difficult to analyze, as a result of both its volume and its complexity.

In order to overcome this problem, we propose to apply a new interactive exploratory data analysis tool, MorExAn (Morphology Exploratory Analyzer), which has been specifically designed to facilitate the study of complex neuroscientific data.

In the present study, we used brain tissue from 10 patients with AD (age range 76 - 90 years old). We included quantitative stereological data of several histological features (e.g., neuron and plaques density) obtained from different hippocampal regions, as well as neuropsychological data and common clinical variables.

Simultaneous analysis of data using MorExAn allows researchers to immediately detect possible differences between regions and relationships between different types of data. Thus, MorExAn provide us the possibility to relate histopathological data with neuropsychological and clinical variables. The aid of this interactive visualization tool brings us the possibility to find unexpected conclusions beyond the insight provided by simple statistics analysis, as well as to improve neuroscientists' productivity.

POSTER 18

Presented by the researcher: D´Anglemont De Tassiony , Xavier.

Principal investigator of the group: López Barneo, José. (Cod: 105).

Title: Effects of chronic hypoxemia on the subventricular neurogenic niche, neuronal and oligodendrocyte survival in the mouse brain

Authors: d'Anglemont de Tassigny X1, Sirerol-Piquer MS2,3, Gomez-Pinedo U4, Pardal R1, Bonilla V1, Capilla-Gonzalez V1, Garcia-Verdugo JM2,3, Lopez-Barneo J1,3. 1 Instituto de Biomedicina de Sevilla (IBIS), Departamento de Fisiología Médica y Biofísica. Hospital Universitario Virgen del Rocío/ CSIC/Universidad de Sevilla. Sevilla, Spain. 2 Instituto Cavanilles de Biodiversidad y Biología Evolutiva, Universidad de Valencia, Spain. 3 Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Spain. 4 Laboratorio de Medicina Regenerativa, Instituto de Investigación Sanitaria San Carlos (IdSS), Madrid, Spain

Abstract: Chronic hypoxemia is a common medical condition that can produce serious longtime neurological alterations and cognitive impairments. However, the pathogenesis of this phenomenon is poorly known. We developed an animal model of chronic hypoxia whereby adult male mice are exposed to low concentration of oxygen (between 14 and 8%) during 12 to 23 days. These animals present arterial oxygen tension similar to that of chronically hypoxemic patients. They manifest a partially irreversible structural disarrangement of the subventricular neurogenic niche (SVZ) characterized by displacement of neurons and myelinated axons, flattening of the ependymal cell layer, and thinning of capillary walls. Despite these abnormalities, the proliferative activity in the SVZ, assessed by several criteria, remained unaffected by chronic hypoxia. On the other hand, in vivo and in vitro experiments indicate that severe chronic hypoxia decreases the survival of newly generated neurons and oligodendrocytes ; with damage of myelin sheaths. These findings show a high resistance of the SVZ progenitor cells to chronic hypoxemia, but matured neural cells (neurons and oligodendrocytes) suffer from low oxygen tension. This work provides new perspectives on brain responsiveness to persistent hypoxemia.

POSTER 19

Presented by the researcher: Lopez de Munain Arregui, Adolfo.

Principal investigator of the group: Lopez de Munain Arregui, Adolfo. (Cod: 609).

Title: Evaluación del potencial terapéutico de la proteína quimérica BD15 en el modelo de encefalomielitis autoinmune experimental

Authors: Mónica Zufiría García, Iñaki Osorio Querejeta, Adolfo López de Munáin, David Otaegi Bichot, Francisco Gil-Bea

Abstract: La desmielinización es un proceso patológico que acontece en muchas enfermedades neurodegenerativas. Independientemente de si es un evento primario o secundario a la enfermedad, la desmielinización afecta la integridad funcional del axón neuronal, y por ello contribuye de forma significativa al agravamiento clínico de la enfermedad. El organismo posee mecanismos reparadores, conocidos como procesos de remielinización, que pueden experimentar agotamiento debido al envejecimiento o a condiciones patológicas. Este estudio trata de analizar el efecto de proteína quimérica BD15 en los procesos de remielinización. Para ello, se generó un modelo de desmielinización por ataque autoinmune, conocido como encefalopatía autoinmune experimental (EAE). La proteína BD15 fue administrada de forma sub-crónica y su efecto en la progresión clínica fue evaluado. Los datos recogidos muestran que la proteína quimérica BD15 disminuye el agravamiento clínico en el modelo de EAE, y proponen una nueva estrategia terapéutica para enfermedades neurodegenerativas con procesos desmielinizantes, como la esclerosis múltiple.

POSTER 20

Presented by the researcher: López Vales, Rubèn.

Principal investigator of the group: Navarro Acebes, Xavier. (Cod: 607).

Title: Combinatory effects of bone marrow cell transplant and molecular therapy in amyotrophic lateral sclerosis

Authors: Anna Martínez-Muriana, Diego Pastor, Renzo Mancuso, Rosario Osta, Salvador Martínez, Rubèn López-Vales, Xavier Navarro

Abstract: Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disorder of adult onset that affects motoneurons (MNs) in brain and spinal cord, causing skeletal muscle weakness and eventual paralysis leading to the death of patients by respiratory failure 3 to 5 years after diagnosis. ALS has a complex pathophysiology involving glutamate-induce cytotoxicity, protein aggregation, cytoskeletal abnormalities and glial cell activation. Due to the complex interplay of several processes, multi-target therapies are needed. Resveratrol (RSV, trans-3,4',5-trihydroxystilbene) is a natural polyphenol with promising neuroprotective effects. Bone marrow cells (BMCs) have been widely used for neuroprotection exerted by releasing neurotrophic factors. In the present work, we assessed the combination of a BMC graft into hindlimb muscles and an enriched-diet with RSV in SOD1-G93A mice, a well estabiehd model of ALS. We found that the combination of both treatments preserved motor function in ALS mice but it was not correlated with MNs preservation in the spinal cord. In order to enhance MNs preservation, BMCs were further transplanted into lumbar spinal cord of ALS mice. Interestingly, electrophysiological assessment revealed that BMCs preserved motor function and locomotor performance. Moreover, intraspinal BMCs preserved spinal lumbar MNs and attenuated microglial reactivity. Overall, our findings show evidence that BMCs transplantation in both muscles and spinal cord plus a diet enriched with RSV provides a novel combined therapy for ameliorating motoneuron diseases.

POSTER 21

Presented by the researcher: Gómez Gutiérrez, Ruben.

Principal investigator of the group: Gutiérrez Pérez, Antonia. (Cod: 415).

Title: Increased alzheimer's disease-like pathology in immunosuppressed APP/PS1 transgenic mice

Authors: R. Gomez-Gutierrez1, R. Sanchez-Varo1, S. Jimenez2, Navarro V, Vizuete M2, JC Davila1, J. Vitorica2 and A. Gutierrez1 1Dept. Cell Biology, Faculty of Sciences, University of Malaga. CIBERNED. IBIMA, Malaga, Spain 2Dept. Biochemistry&Molecular Biology, Faculty of Pharmacy, University of Seville. CIBERNED. IBIS., Seville, Spain

Abstract: OBJECTIVES: Initial cognitive and memory decline in Alzheimer's disease (AD) is highly likely caused by synaptic dysfunction prior to neuronal loss. Previous works have shown that neuroinflammatory response could be implicated in the AD progression. Microglial cells are the main cell type of the innate immune system in the brain. In fact, patients and animal models display abundant microglial activation; however, it is still unknown whether it is a cause or a consequence of the pathology. An inefficient immunologic response could be involved in the increase of amyloid-beta levels with disease progression in aged patients, so we aimed to investigate the effect of immunosuppression over the pathological progression in the hippocampus of APP/PS1dE9 transgenic mouse model. METHODS: Cyclosporine (15 mg/kg) and prednisone (20 mg/kg) were intraperitoneally administered to 9 month-old APP/PS1dE9 mice for 3 months. Untreated mice were used as controls. Hippocampal amyloid burden and glial cells (GFAP, Iba-1) were investigated by immunohistochemistry over free-floating sections and quantified by image analysis. Moreover, Abeta levels, glial activation, cytokines production and GABAergic neurodegeneration were assessed by molecular techniques (Western-blot and RT-PCR). RESULTS: A strong decrease in the microglial marker Iba1 and some proinflammatory cytokines was detected by RT-PCR in the immunosuppressed mice compared to controls. Conversely, a significant increase in Abeta levels and astroglial marker (GFAP) was found. Moreover, SOM and NPY subpopulations were also negatively affected due to the treatment. CONCLUSIONS: Immunosuppression treatment downregulated microglial population activity and accelerated amyloid pathology and neuronal degeneration in this APP/PS1 model. Deficiencies in the innate immune system with age could promote AD pathology and cognitive decline in patients. Therefore, regulating microglial activation signalling pathways in the brain might have therapeutic benefits for AD. This work was supported by FIS PI12/01431 and PI12/01439 grants.

POSTER 22

Presented by the researcher: Bermejo Pareja, Felíx.

Principal investigator of the group: Carro Diaz, Eva Maria. (Cod: 502).

Title: Prognostic significance of MCI subtypes for dementia and mortality: Data from the NEDICES cohort:

Authors: Álvaro Sanchez-Ferro, Félix Bermejo Pareja, Israel Contador, Rocío Trincado, David Lora, Alex J Mitchell, Jesús Hernández-Gallego, Sara Llamas, Alberto Villarejo Galande, Julián Benito León

Abstract: Objective: To analyze the mortality of mild cognitive impairment (MCI) incident subtypes in the NEDICES (Neurological Disorders in Central Spain) cohort.

Background: There is scarce information on long term mortality in MCI subtypes. Recently, we published (Eur J Neurol, 2013) the causes of death and mortality in prevalent MCI subtypes and we review the subject.

Population/Methods: The NEDICES cohort is a census population-based survey of elderly (65 and more years) from three sites of Central Spain. The cohort had a basal survey (1994-5) and its evolution and mortality have been follow-up until 2008, with a link with the National Death Spanish Registry.

Main Results: We obtained 2,328 participants in the second follow-up (1997-8), without dementia or MCI cases. These entire subjects were adequately studied with a MMSE-37 and a normal FAQ of Pfeffer (IADL scale). The majority of them had an extended psychometric evaluation, but the MCI subtypes were performed according to a MMSE-37 paradigm, used in the prevalence study, and they were classified as, non-amnestic (n=428); amnestic-single domain (n=170), amnestic-multiple domain (n=148), and cognitively unimpaired elders (n=1,582). With a mean follow-up of 8.9 years (from 1997-8 until 2008), the mortality of MCI subtypes were respectively: 34.1%, 42.4%, and 55.4%; in the cognitively unimpaired was 34.2%. In a Cox regression adjusted by age, sex, education and co-morbidity, only the amnestic-multiple domain subtype obtained a statistical significant mortality risk, HR(CI95%)=1.61 (1.27-2.05); p<.001.

Conclusions: The long term mortality of MCI subtypes is clearly different, as it was found in other studies, including our previous MCI prevalence mortality. In this cohort, only the amnestic-multiple domain MCI subtype has an increased risk of mortality.

POSTER 23

Presented by the researcher: Lopez Gonzalez, Irene.

Principal investigator of the group: Ferrer Abizanda, Isidro. (Cod: 503).

Title: Neuroinflammatory gene regulation, tau oligomers and oxidative stress with disease progression in tau P301S transgenic mice as a model of FTLD-tau

Authors: Irene López-González, Ester Aso, Margarita Carmona, Mercedes Armand-Ugon, Rosi Blanco, Isidre Ferrer.

Abstract: Tau P301S transgenic mice (PS19 line) are used as a model of FTLD-tau to analyze molecular changes related to disease progression in brain because such changes cannot be satisfactorily assessed in human cases. Behavioral alterations start at about the age of four months in P301S mice and they are characterized by disinhibition, anxiety, increased locomotion, impaired memory, altered nociception and terminal severe motor decline. Hyper-phosphorylated 4Rtau increases from the age of one month in neurons from the entorhinal and piriform cortices to the neocortex, diencephalic nuclei, midbrain, cerebellum and spinal cord. Only at the age of 9/10 months, a small percentage of neurons have, in addition, abnormal tau conformation, tau truncation and ubiquitination. Astrocytosis and microgliosis appear late in the course of the disease and are accompanied by increased expression of cytokines and mediators of the immune response by the age of 9/10 months which are subjected to regional differences, with the hippocampus being the most importantly affected. Tau oligomers are only present in P301S mice and they can be visualized in the somatosensory cortex and hippocampus at the age of 3 months; they increase with disease progression in the somatosensory cortex but are already higher and sustained in the hippocampus. Finally, apoptosis only occurs at advanced stages of the disease in restricted regions such as hippocampus and rarely in ventral spinal cord. Alterations at advanced stages of the disease in P301S mice are similar to those seen in terminal stages of human cases of FTLD-tau. The present observations help to increase understanding of how complex tau pathology (in addition to hyper-phosphorylated tau), mitochondrial alterations, oxidative stress damage, astroglial and microglial reactions, neuroinflammation and cell death in P301S, and probably in human FTLD-tau with only neuronal involvement, occur at advanced stages of the disease.

POSTER 24

Presented by the researcher: Folch Lopez, Jaime.

Principal investigator of the group: Camins Espuny, Antonio. (Cod: 402).

Title: Leptin suppresses nitric oxide production in murine primary glial cultures, by exposure to pro-inflammatory cytokines, through p38 MAPK pathway inhibition

Authors: Iván Patraca1,3, Nohora Martínez1,3, Aleix Martí1, Francesc Sureda1,3, Carme Auladell4, Antoni Camins2,3 and Jaume Folch1,3 1Unitats de Bioquímica i Farmacologia, Facultat de Medicina i Ciències de la Salut, Universitat Rovira i Virgili, C./ St. Llorenç 21 43201 Reus (Tarragona), Spain. 2Unitat de Farmacologia i Farmacognòsia Facultat de Farmàcia, Institut de Biomedicina (IBUB), Universitat de Barcelona, Barcelona, Spain. 3Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (CIBERNED). Instituto de Salud Carlos Tercero. Madrid, Spain. 4 Departament de Biologia Cel•lular, Facultat de Biologia, Universitat de Barcelona, Barcelona, Spain. Joseivan.patraca@urv.cat

Abstract: Leptin (Lep) is a pleiotropic cytokine encoded by the Ob gene. It was identified and cloned from rodent adipose tissue in 1994, and plays a central role in the control of body weight and energy homeostasis. Leptin has been shown to down-regulate inflammatory responses and provide neuroprotection. However, the mechanisms underlying the anti-inflammatory properties of Lep in brain are controversial and poorly understood. In the present work, we studied the modulatory effect of Lep against proinflammatory cytokines in glial cell cultures. Treatment with pro-inflammatory cytokines mainly, tumor necrosis factor-alpha (TNF??, interleukin 1-beta (IL1???and interferongamma (IFN?) induces an increase in inducible nitric oxide synthase (iNOS) expression and nitric oxide production. Results shown that pre-treatment with 500nM Lep produced an inhibitory effect on iNOS expression and NO production, accompanied by a decrease in p38 MAP Kinase (MAPK) pathway activity. Treatment with Lep also reduced the activation of apoptosis though cytochrome c (Cyt-c) release and caspase-3 inhibition. Then, Lep would act as an anti-inflammatory factor in glial cells exposed to pro-inflammatory cytoquines, exerting its function at different levels: acting on p38 MAPK pathway and reducing its activity and NO production; acting on mitochondrial drivers of apoptosis and reducing their content, like for Cyt-c, and activity as in the case of the executioner caspase-3.

POSTER 25

Presented by the researcher: Gutiérrez Pérez, Antonia.

Principal investigator of the group: Gutiérrez Pérez, Antonia. (Cod: 415).

Title: Interactions between amiloid plaques and glial cells: an ultrastructural study in the hippocampus of APP/PS1 mice

Authors: A. Gomez-Arboledas1, L. Trujillo-Estrada1, E. Sanchez-Mejias1, R. Sanchez-Varo1, J. Vitorica2, A. Gutierrez1 and J.C. Davila1. 1 Dpto. Biología Celular, Genética y Fisiología. Facultad de Ciencias, Universidad de Málaga. IBIMA. CIBERNED. Málaga. 2 Dpto Bioquímica y Biología Molecular, Facultad de Farmacia, Universidad de Sevilla. IBIS. CIBERNED. Sevilla

Abstract: The accumulation of amyloid-beta (A?) into diffuse and compact plaques is a major histopathological feature of Alzheimer's disease (AD). Activated glia (microglia and astroglia) surround and infiltrate compact A? plaques in AD patients and APP-based transgenic models, however whether these reactive glial cells are actively contributing to ongoing neurodegenerative processes or play a neuroprotective role is highly debated. Here, we examined the plaque-glia interactions in the hippocampus of PS1M146L/APP751SL transgenic mouse by immunohistochemistry at both light and electron microscopy. This AD model develops A? plaques at early ages (3-4 months), and these plaques are typically surrounded by axonal/synaptic dystrophies intermixed with astroglial and microglial processes. Activated microglial processes completely surrounded all examined A? plaques, independently of their size or location. Ultrastructural analysis revealed that the microglial cell membrane was in intimate contact with the A? fibrils, and that their processes showed frequently numerous cisternae of endoplasmic reticulum in the contact area. Reactive astrocytes also associated with the A? plaques, especially the larger ones. The astrocytic processes contacting the A? plaques were characterized by a virtual lack of glial filaments and other organelles; however these processes were immunoreactive for typical astrocytic markers as ALDH1L1 or AQP4. Near the A? plaques, astrocytic processes were observed contacting microglial cells, and also surrounding dystrophic neurites. Our results highlight the close relationship of the activated glial cells with A? plaques, and suggest a major contribution of these cells in the dynamic of amyloid plaque development/degradation and/or forming a protective barrier around amyloid plaques and therefore modulating plaque toxicity. Supported by FIS PI12/01431, FIS PI12/01439, CIBERNED and La Marató TV3.

POSTER 26

Presented by the researcher: Sabate Bel, Magdalena.

Principal investigator of the group: Rodriguez Diaz, Manuel. (Cod: 206).

Title: Estudio del circuito motor de los ganglios basales mediante resonancia magnética funcional.

Authors: Clara Rodríguez-Sabaté, Ingrid Morales, Alberto Sanchez, Manuel Rodríguez y Magdalena Sabaté

Abstract: Basal ganglia interact in a complex way which is still not completely understood. The model generally used to explain basal ganglia interactions is based on experimental data in animals, but its validation in humans has been hampered by methodological restrictions. The time-relationship (partial correlation) of the fluctuations of the blood-oxygen-level-dependent signals recorded in the main basal ganglia was used here (32 healthy volunteers; 18-72 years of age; 16 males and 16 females) to test whether the interaction of the main basal ganglia in humans follows the pattern of functional connectivity in animals. Data showed that most basal ganglia have a functional connectivity which is compatible with that of the established closed-loop model. The strength of the connectivity of some basal ganglia changed with finger motion, suggesting that the functional interactions between basal ganglia are quickly restructured by the motor tasks. The present study with the motor cortico-BG loop centers supports the circling dynamic of the basal ganglia model in humans, showing that motor tasks may change the functional connectivity of these centers.

POSTER 27

Presented by the researcher: Matute Almau, Carlos.

Principal investigator of the group: Matute Almau, Carlos. (Cod: 404).

Title: Integrin b1 triggers amyloid b-induced astrocyte reactivity through NOX2 activation in Alzheimer disease models

Authors: A Wyssenbach, F. Llavero, JL. Zugaza, C. Matute and E. AlberdiDepartamento de Neurociencias, Achucarro Basque Center for Neuroscience, Universidad del País Vasco (UPV/EHU), and Centro de Investigación Biomédica en Red en Enfermedades Neurodegenerativas (CIBERNED), 48940-Leioa, Spain.

Abstract: Astrocyte reactivity is a hallmark of Alzheimer disease (AD) and can constitute a primary pathogenic element of the disease. Elucidation of the signaling cascades inducing reactivity in astrocytes during AD would help characterizing the function of these cells and identify novel molecular targets to modulate disease progression.Here, we described novel mechanism by which the toxic soluble amyloid beta (Ab) modulates integrin beta 1activity and triggers a reactive oxygen species (ROS)-dependent astrogliosis in vitro and in vivo. First, we observed that Ab oligomers induce ROS production which is prevented by NADPH oxidase (NOX) inhibitors, and that oligomers differentially regulate NOX2 and NOX1 mRNA and protein levels, in a ROS dependent manner. To further investigate the pathway underlying Ab-mediated ROS generation, we analyzed the activation of NOX-interacting protein Rac by Rac-GTP affinity precipitation and PAK1 phosphorylation assay. We found that Ab oligomers produce a sustained Rac activation that is blocked by inhibitors of the classic but not by the novel PKC activities and also by wortmannin, a PI3K inhibitor. Moreover, Ab-induced ROS generation is reduced by an antibody against integrin beta 1, suggesting that this protein is upstream of PI3K/PKC/Rac/NOX pathway activation. Importantly, Ab oligomers induce GFAP, integrin b1 and NOX2 overexpression mediated by integrinb1 activation and NOX-dependent signaling in cultured astrocytes. These findings were confirmed using in vivo models. Intrahippocampal injection of amyloid b oligomers overexpressed astrogliotic and oxidative stress markers (GFAP, S100, grp78 and NOX2) that were reduced by coinjection of Ab-oligomers with the antibody against integrin b1. These data were validated in a triple-transgenic mouse model of AD and in postmortem brains of individuals with AD. Biochemical analysis showed that dysregulation of GFAP, NOX2 and integrin b1 levels correlated with Ab oligomers accumulation in vivo. Furthermore, we found that integrin b1 and NOX2 levels were significantly higher in reactive astrocytes in triple-transgenic mice than in wild type mice, as well as in AD brains as compared to controls. These data suggest that Ab oligomers may directly cause and exacerbate astrocyte reactivity in AD by enhancing integrin b1 and NOX2 activity via ROS-dependent mechanisms. These observations may be relevant to AD pathophysiology. Supported by CIBERNED, Gobierno Vasco and MINECO. AW is a recipient of a fellowship from the University of País Vasco.

POSTER 28

Presented by the researcher: Fernandez Chacon, Rafael.

Principal investigator of the group: Fernandez Chacon, Rafael. (Cod: 606).

Title: CSP-ALFA maintains the quiescence of radial-glia like stem cells in postnatal neurogenesis

Authors: J.L. Nieto-González, L. Gómez-Sánchez, F. Mavillard, P. Linares-Clemente, R. Pardal and R. Fernández-Chacón Instituto de Biomedicina de Sevilla (IBiS) HUVR/CSIC/Universidad de Sevilla, Dpto. de Fisiología Médica y Biofísica and CIBERNED, Seville, Spain

Abstract: Cysteine String Protein-alpha (CSP-alpha) is a synaptic co-chaperone that prevents activity-dependent degeneration of nerve terminals. Mutations in the human CSP-alpha gene cause neuronal ceroid lipofuscinosis characterized by progressive dementia and seizures. Synapses formed onto granule cells by parvalbumin (PV)-expressing basket cells progressively degenerate in CSP-alpha KO mice. On the other hand, adult quiescent neural stem-cell fate decision is regulated by PV+ basket cells. It is, however, unknown if adult neurogenesis is deregulated in the absence of CSP-alpha. Here, we have used BrdU injections to find a significant increased in neuronal proliferation at the hippocampus of CSP-alpha KO mice. We have observed a dramatic loss of quiescence in radial-glial like cells occurring within the two first post-natal weeks that turned into a dramatic depletion of the radial-glial like cell pool at postnatal age P30. In the absence of CSP-alpha, neural stem cells in culture undergo a very high proliferation rate that leads to stem cell depletion. Such an unanticipated finding unveils a novel and direct role for CSP-alpha in the control of neural stem cell proliferation that is not secondary to GABAergic dysfunction. Support: MINECO BFU2013-47493, Junta de Andalucía P12-CTS-2232, ISCIII and FEDER. We are grateful to A. Arroyo and M. C. Rivero for excellent technical assistance.

POSTER 29

Presented by the researcher: Moreno Guillén, Estefanía.

Principal investigator of the group: Canela Campos, Enric I. (Cod: 201).

Title: Cognitive impairment induced by delta9-tetrahydrocannabinol occurs through heteromers between cannabinoid CB1 and serotonin 5-HT2A receptors.

Authors: Estefanía Moreno÷,3,4, Xavier Viñals÷,1,2, Laurence Lanfumey5, Arnau Cordomí6, Antoni Pastor2, Rafael de La Torre2, Paola Gasperini3,4,7, Gemma Navarro3,4, Lesley A Howell7, Leonardo Pardo6, Antoni Cortés3,4, Josefa Mallol3,4, Vicent Casadó3,4, Carme Lluís3,4, Peter J McCormick#,*,3,4,7, Rafael Maldonado#1, Patricia Robledo#,*,1,2, Enric I Canela3,4# 1Neuropharmacology Laboratory, University Pompeu Fabra, Barcelona, Spain. 2Human Pharmacology and Clinical Neurosciences Research Group, IMIM-Hospital del Mar Medical Research Institute, Barcelona, Spain. 3Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas. 4Department of Biochemistry and Molecular Biology, Faculty of Biology, University of Barcelona, Spain. 5CPN, INSERM UMR S894, Université Paris Descartes,France. 6Laboratori de Medicina Computacional, Unitat de Bioestadística, Facultat de Medicina, Universitat Autònoma de Barcelona, Spain. 7 School of Pharmacy, University of East Anglia

Abstract: Activation of cannabinoid CB1 receptors (CB1R) by delta9-tetrahydrocannabinol (THC) produces a variety of negative effects with major consequences in cannabis users that constitute important drawbacks for the use of cannabinoids as therapeutic agents. For this reason there is a tremendous medical interest in harnessing the beneficial effects of THC. Behavioral studies carried out in mice lacking 5-HT2A receptors (5-HT2AR) revealed a remarkable 5-HT2AR-dependent dissociation in the beneficial antinociceptive effects of THC and its detrimental amnesic properties. We found that specific effects of THC, such as memory deficits, anxiolytic-like effects, and social interaction are under the control of 5-HT2AR, but not its acute hypolocomotor, hypothermic, anxiogenic and antinociceptive effects. In biochemical studies, we show that CB1R and 5-HT2AR form heteromers that are expressed and functionally active in specific brain regions involved in memory impairment. Remarkably, our functional data shows that co-stimulation of both receptors by agonists reduces cell signaling, antagonist binding to one receptor blocks signaling of the interacting receptor, and heteromer formation leads to a switch in G-protein coupling for 5-HT2AR from Gq to Gi proteins. Synthetic peptides with the sequence of transmembrane helices 5 and 6 of CB1R, fused to a cell-penetrating peptide, were able to disrupt receptor heteromerization in vivo leading to a selective abrogation of memory impairments caused by exposure to THC. These data reveal a novel molecular mechanism for the functional interaction between CB1R and 5-HT2AR mediating cognitive impairment. CB1R-5-HT2AR heteromers are thus good targets to dissociate the cognitive deficits induced by THC from its beneficial antinociceptive properties.

POSTER 30

Presented by the researcher: GAGO CALDERON, BELEN.

Principal investigator of the group: LOPEZ DE MUNAIN ARREGUI, ADOLFO. (Cod: 609).

Title: A model of increased impulsivity in rats with bilateral parkisnonism treated with Pramipexole

Authors: H. Jiménez-Urbieta, B. Gago, C. Marin, M. Delgado-Alvarado, M.C. Rodríguez-Oroz

Abstract: Impulse control disorders (ICD) is a common side effect of the dopaminergic treatment in patients with Parkinson's disease (PD), which is more associated with dopamine agonists than with levodopa. To understand its pathophysiology, reliable animal models are essential. We have developed a model of increased impulsivity in bilateral parkinsonian rats treated with pramipexole (PPX). Impulsivity was evaluated with the variable delay-to-signal (VDS) paradigm. In this test, rats have to introduce the snout into a nose poke that is signaled by a light (presented at variable delays) triggering the delivery of a food reward when the response is correct. As rats reach a stable baseline performance, a partial bilateral dopaminergic lesion was induced with the injection of 6-OHDA in the dorsolateral region of the striatum (AP: +1mm and L: ±3.4mm from Bregma, V:-4.7 mm). Two weeks after the dopaminergic lesion, rats were acutely treated with two doses of PPX (0,25mg/kg and 3mg/kg; Latin-square design) in two different days. Rats undertook the VDS test under 5 different conditions: basal state, after 6-OHDA injection, under the effect of the two doses of PPX, and the day after the last dose of PPX. Only the acute administration of 3 mg/kg of PPX significantly increased the number of premature responses, indicating an increase of the impulsive behavior, in parkinsonian but not in sham rats. Both doses of PPX significantly decreased the accuracy of responding (correct/total number of responses) and increased the incorrect and perseverative (compulsive behavior) responses in both parkinsonian and sham treated groups when compared with saline-treated groups. In conclusion, PPX induced attention deficit, reflected by the lack of accuracy, as well as compulsive behavior in control and parkinsonian rats, but increased impulsivity only in the parkinsonian animals. This model could constitute a valid tool to investigate the pathophysiology of ICD (DFG11/019, PI11/02109).

POSTER 31

Presented by the researcher: Lleo Bisa , Alberto.

Principal investigator of the group: Lleo Bisa , Alberto. (Cod: 504).

Title: Amyloid precursor protein metabolism and inflammation markers in preclinical Alzheimer disease

Authors: Daniel Alcolea 1; Pablo Martínez-Lage 2; Pascual Sánchez-Juan, 3; Javier Olazarán, 4,8; Carmen Antúnez, 5; Andrea Izagirre, 2; Mirian Ecay-Torres, 2; Ainara Estanga, 2; Montserrat Clerigué, 2; Mª Concepción Guisasola, 6; Domingo Sánchez Ruiz, 4; Juan Marín Muñoz, 5; Miguel Calero, 7,8; Rafael Blesa, 1; Jordi Clarimón, 1; María Carmona-Iragui, 1; Estrella Morenas-Rodríguez, 1; Eloy Rodríguez-Rodríguez, 3; José Luis Vázquez Higuera, 3; Juan Fortea, 1; Alberto Lleó, 1. 1 Department of Neurology, Hospital de Sant Pau. 2 Fundación CITA-alzhéimer Fundazioa, San Sebastián. 3 Servicio de Neurología, Hospital Universitario Marqués de Valdecilla, Santander. 4 Servicio de Neurología, Hospital General Gregorio Marañón, Madrid. 5 Unidad de Demencias, Hospital Clínico Universitario Virgen de la Arrixaca, Murcia. 6 Unidad de Medicina Experimental, Hospital General Gregorio Marañón, Madrid. 7 Instituto de Salud Carlos III, CIBERNED, Madrid. 8 Fundación CIEN - Fundación Reina Sofía, Madrid.

Abstract: Objective: To investigate CSF markers involved in amyloid precursor protein processing, neuronal damage and neuroinflammation in the preclinical stages of Alzheimer's disease (AD) and subjects with suspected non-Alzheimer pathology (SNAP). Methods: We collected CSF from 266 cognitively normal volunteers participating in a cross-sectional multicenter study (the SIGNAL study) to investigate markers involved in amyloid precursor protein processing (A?42, sAPP?, ?-secretase activity), neuronal damage (t-tau, p-tau) and neuroinflammation (YKL-40). We analyzed the relationship between biomarkers, clinical variables and the APOE genotype, and we compared biomarker levels across the preclinical stages of the NIA-AA classification: stage 0, 1, 2, 3, and SNAP. Results: The median age in the whole cohort was 58.8 years (range 39.8 – 81.6). Subjects in stages 2-3 and SNAP had higher levels of YKL-40 than those in stages 0 and 1. Subjects with SNAP had higher levels of sAPP? than subjects in stage 0 and 1. No differences were found between stages 0, 1, 2-3 in sAPP? or ?-secretase activity in CSF. Age correlated with t-tau, p-tau and YKL-40. It also correlated with A?42, but only in APOE?4 carriers. A?42 correlated positively with t-tau, sAPP? and YKL-40 in subjects with normal A?42. Conclusions: Our findings suggest that inflammation in the CNS increases in normal aging and is intimately related to markers of neurodegeneration in the preclinical stages of AD and SNAP. sAPP? and ?-secretase activity are not useful diagnostic or staging markers in preclinical AD.

POSTER 32

Presented by the researcher: López de Ceballos Lafarga, María.

Principal investigator of the group: López de Ceballos Lafarga, María. (Cod: 506).

Title: The GSK-3-inhibitor VP2.51 produces antidepressant effects associated with adult hippocampal neurogenesis

Authors: P. Pérez-Dómper; S.Gradari; V. Palomo; C. Gil; A. Martínez; M.L. de Ceballos; J.L. Trejo. 1Molecular, Cellular and Developmental Neurobiology Department, Cajal Institute; 2Instituto de Química Médica,CSIC; 3Centro de Investigaciones Biológicas, CSIC; 4CIBERNED

Abstract: Glycogen synthase kinase 3 (GSK-3) is a constitutively active serine/threonine kinase that is inhibited in response to specific signaling pathways, indicative of a need for its correct regulation. GSK-3? has been implicated in the mechanism of action of mood stabilizers like valproate and lithium, and studies with GSK-3-specific inhibitors have demonstrated their antidepressant properties in the forced swim test (FST). According to the neurogenic hypothesis of depression, the generation of neurons in the adult dentate gyrus is required for the antidepressant effects of certain agents. Indeed, GSK-3 has been shown to influence adult hippocampal neurogenesis (AHN), although its possible effects on subpopulations of immature neurons or their subsequent influence on behavior remain unclear. We used the small heterocyclic GSK-3 inhibitor called VP2.51 as a pharmacological tool to demonstrate that inhibiting GSK-3 in vivo significantly increases the proliferation of certain cell subpopulations in the adult dentate gyrus. Indeed, there is an increase in the number of cells that acquire a neuronal lineage under these conditions, as well as in the survival and/or maturation of immature cell populations. In addition, GSK-3 inhibition by VP2.51 has a clear antidepressant effect in the FST. Furthermore, GSK-3 inhibition of mice stressed in a modified FST first led to increased proliferation in the ventral sub-region of the dentate gyrus and then, an antidepressant effect was produced that was evident in the tail suspension test. For the first time, these data demonstrate a region-specific proneurogenic effect of GSK-3 inhibition in previously depressed/stressed mice, an effect that is ventral specific. To determine if the proneurogenic action of VP2.51 mediates its antidepressant activity, we administered the drug together with the antimitotic agent temozolomide, which partially blocks the antidepressant effect of VP2.51. Together, our results demonstrate that the GSK-3 inhibitor VP2.51 can induce a concomitant proneurogenic and antidepressant effect in stressed animals. Moreover, while AHN contributes to this antidepressant effect, adding further support to the neurogenic hypothesis of depression, it is not the only pathway involved.

POSTER 33

Presented by the researcher: Cantero Lorente, José Luis.

Principal investigator of the group: Cantero Lorente, José Luis. (Cod: 511).

Title: Increased levels of plasma amyloid-beta are related to cortical thinning and cognitive decline in cognitively normal elderly subjects.

Authors: Sandra Llado-Saz, Mercedes Atienza, Jose L. Cantero

Abstract: Plasma levels of circulating amyloid-beta (A?) peptides are of particular interest in Alzheimer' disease (AD), but little is known about cognitive and cortical correlates of A? levels in normal aging. Here, we compared cognitive functioning, vascular risk factors, and patterns of cortical thickness between cognitively intact elderly subjects with low (N=60) and high (N=60) plasma A? levels (cut-offs: 225 pg/ml and 23 pg/ml for A?1–40 and A?1–42, respectively). Overall, subjects with high A? levels showed lower cognitive performance and thinner cortex than those with low A? levels. More specifically, subjects with high A?1-40 showed bilateral thinning of the prefrontal cortex, poorer objective memory, slower processing speed and lower non-verbal reasoning skills, whereas subjects with high A?1-42 had thinner temporal lobe, poorer everyday memory, and increased levels of homocysteine. Overall, these results suggest that high plasma A? levels in normal elderly subjects are associated with subclinical markers of vulnerable aging, which may be helpful at predicting different trajectories of aging in cognitively intact older adults.

POSTER 34

Presented by the researcher: Rodriguez Alvarez, Jose.

Principal investigator of the group: Rodriguez Alvarez, Jose. (Cod: 406).

Title: Analysis of synaptic-related miRNas expression in experimental models of Alzheimer Disease

Authors: Alfredo J. Miñano Molin, Dolores Siedlecki, Amaia Otxoa de Amezaga, Judith Català, Carlos A. Saura & José Rodríguez-Alvarez

Abstract: MicroRNAs are a group of small non-coding RNAs that regulate gene expression post-transcriptionally. Recent studies have shown that deregulation of specific microRNAs could be involved in the development of Alzheimer's disease (AD). However, few studies exploring the relationship between microRNAs deregulation in AD and synaptic plasticity exist despite the involvement of some microRNAs in synaptic plasticity. Since it is believed that alterations in synaptic function are related to mild cognitive impairment, it is feasible to hypothesize that alterations in plasticity-related microRNAs could underlie AD progression. Here, levels of a small number of microRNAs involved in the regulation of AMPAR function were examined in mice hippocampal cultures, an AD mice model, where we reported previously changes in AMPAR regulation related with early deficits in learning and memory processes, and in human samples. We found increases in miR-181c-5p (?40%), miR-210-3p (>60%) and miR-92a-3p (?25%) expression but not in miR-181a-5p after oA? treatment in primary hippocampal neurons. Similar changes in miR-181c-5p and miR-92a-3p were confirmed in the entorhinal cortex of APPSw,Ind transgenic mice. However no significant changes were observed in the hippocampus in these mice. Moreover, the analysis of hippocampal human samples at different Braak stages, show an increase in miR-181c-5p and miR-92a-3p levels during AD progression. These findings indicate a possible relationship between miR-181c-5p and miR92a-3p and the reported changes in glutamate receptor levels and early learning and memory deficits in the APPSw,Ind transgenic mice. Our results suggest that those microRNAs involved in synaptic plasticity might be important factors that contribute to AD neuropathology progress. Support: This work was supported by grants from Ministerio de Economia y Competitividad (SAF2014-59697-R), CIBERNED (CB06/05/0042), Fundació Marato TV3 (2014-3610) and Generalitat de Catalunya (SGR2009-1231).

POSTER 35

Presented by the researcher: Cavaliere, Fabio.

Principal investigator of the group: Matute Almau, Carlos. (Cod: 404).

Title: Role of Asrocytes in α-synuclein mediated Neuronal Degeneration

Authors: P. Ramos1, B. Dehay2, E. Bezard2, J. Obeso3 and C. Matute 1 and , F. Cavaliere1. 1 Achucarro Basque Centre for Neuroscience/University of the Basque Country, and CIBERNED, Leioa, Spain; 2 University of Bordeaux, Institut des Maladies Neurodégénératives, UMR 5293, F-33000 Bordeaux, France; 3 CINAC HM Hospital Puerta del Sur, Mostoles y CEU-San Pablo University, and CIBERNED, Madrid, Spain

Abstract: Parkinson´s Disease (PD) is a neurodegenerative disorder characterized anatomo-pathologically by the loss of dopaminergic neurons in the substantia nigra pars compacta and the presence of intraneuronal cytoplasmic inclusions called Lewy bodies (LB). The main protein component of the LB is the mysfolded α-synuclein (α-syn). Previous studies suggest that α-syn can self-propagate from cell to cell by a simple mechanism of endocytosis, suggesting a “prion-like” activity of α-syn. To validate the infectious nature of aggregated α-syn and to understand the role of astrocytes in the onset and propagation of α-syn-induced neuropathy, we have observed the bi-directional transmission of α-syn between neurons and astrocytes rat cultures on a microfluidic assay. Astrocytes and neurons are separated by microchannels and treated with purified human LB-derived α-syn assemblies from PD patients whereas transport of α-syn is validated by immunofluorescence. Our results demonstrated that α-syn assemblies are uptaken by all cell type and transported directly through all directions (neurons to neuron, neurons to astrocytes, astrocytes to astrocytes and astrocytes to neurons). In addition, we then studied the mechanism by which the α-syn is uptaken by the cells and its localization once internalized. For that, we infected both astrocyte and neuron cultures with baculovirus which marked lysosomes or endosomes. These experiments showed the colocalization of the α-syn with the early endosomes and with the lysosomes in both neurons and astrocytes, suggesting the phagocytosis as the main mechanism of internalization. Finally, we demonstrated that astrocytes incorporating exogenous α-syn induce apoptosis of neurons that are in contact with astrocytes, suggesting a harmful role of these lasts in the onset and developing of neurodegeneration. By elucidating the role of the astrocytes and their properties could suppose the possibility to consider these cells as new therapeutic targets for PD. Supported by CIBERNED, and Euskampus.

POSTER 36

Presented by the researcher: Camins Espuny, Antonio.

Principal investigator of the group: Camins Espuny, Antonio. (Cod: 402).

Title: Early changes in hippocampus induced by high-fat diet in wild-type and in a transgenic mouse model of alzheimer disease

Authors: Miren Ettcheto1,3, Dmitry Petrov1,3, Ignacio Pedrós*2,3, Carlos Bea-Zarate 5,6 , Merce Pallas1,3, Jaume Folch $2,3 and Antoni Camins $1,3 1Unitat de Farmacologia i Farmacognòsia, Facultat de Farmàcia, Institut de Biomedicina de la UB (IBUB), Universitat de Barcelona, Barcelona, Spain. 2Unitats de Bioquímica i Farmacologia, Facultat de Medicina i Ciències de la Salut, Universitat Rovira i Virgili, Reus (Tarragona), Spain. 3Centros de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (CIBERNED). 5Laboratorio de Neurobiología Celular y Molecular, División de Neurociencias, CIBO, IMSS, México 6Laboratorio de Regeneración y Desarrollo Neural, Instituto de Neurobiología, Departamento de Biología Celular y Molecular, CUCBA, México

Abstract: The present study was focused on the early effects of a high-fat diet (HFD) on hippocampal-dependent memory in 3 month-old C57/Bl6 Wild-type (WT) and APPswe/PS1dE9 (APP/PS1) mice, a well-established mouse model of familial Alzheimer's disease (AD). Our results indicate that the continuous HFD administration starting at the time of weaning is sufficient to produce ?-amyloid-independent, hippocampal-dependent memory loss in mice as early as 3 months of age. Furthermore, the resulting metabolic syndrome appears to have direct effects on brain insulin regulation and mitochondrial function. We have observed pathological changes related to both the mitochondrial and beta amyloid signaling in the brains of HFD-fed WT and APP/PS1 mice. These changes are accompanied by a significantly reduced OXPHOS metabolism, suggesting that mitochondria play an important role in hippocampus-dependent memory formation and retention in both the HFD-treated and AD-like rodents at a relatively young age.

POSTER 37

Presented by the researcher: Pascual Sánchez, Marta.

Principal investigator of the group: Soriano Garcia, Eduardo. (Cod: 408).

Title: Impairment of the gabaergic septohippocampal connection in a mouse model of tauopathy

Authors: H. Soler1, 2, M. González1,2, J. Dorca1,2, D. E. Parruca da Cruz1,2, S. E. Rubio1,2, J. Avila2,3, E. Soriano1,2,4 and M. Pascual1,2 1. Department of Cell Biology, University of Barcelona, Barcelona, Spain. 2 Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED, ISCIII), Spain. 3 Centro de Biología Molecular Severo Ochoa (CSIC-UAM), Madrid, Spain. 4 VHIR, Barcelona, Spain

Abstract: Alzheimer's disease (AD) modifies the functioning of cortical networks, including altered patterns of synchronous activity and deficit in cholinergic septohippocampal (SH) innervation. The GABAergic component of the SH pathway (SHP) regulates synchronous hippocampal rhythms by controlling the activity of interneurons. Recently, we have reported a dramatic decrease in the GABAergic SHP in a mouse model with a considerable accumulation of amyloid-β deposits (Rubio et al., 2012). Another characteristic feature of AD is the hyperphosphorylation and aggregation of the microtubule-associated protein Tau. To evaluate the role of tauopathy in the GABAergic SHP, we analyzed VLW transgenic mice overexpressing human mutated Tau. Our characterization data show that pyramidal neurons and some Parvalbumin (PV)-positive hippocampal interneurons accumulate phosphorylated forms of Tau (P-Tau) in 2- and 8-months-old (mo) VLW mice. In addition, no P-Tau accumulation was present in GABAergic SH neurons. Furthermore, using well-characterized tracing experiments, we demonstrate an early onset of GABAergic SHP deterioration in PV-positive interneurons in 2-mo VLW mice. In 8-mo VLW littermates, this alteration was more severe. No major loss of GABAergic SH neurons or PV-positive hippocampal interneurons was observed, thereby indicating that this decline is not caused by neuronal loss, but by the reduced number and complexity of GABAergic SH axon terminals. We thus conclude that GABAergic SH innervation is specifically reduced on PV-positive interneurons accumulating P-Tau in 2- and 8-mo VLW mice. These data, together with our previous results, indicate that the GABAergic SHP is impaired in response to both amyloid-β and P-Tau accumulation, thereby suggesting that cognitive deficits and altered patterns of synchronous activity in AD patients could be caused by the loss of GABAergic SH axons, which modulate hippocampal rhythmic activities. Our findings identify a new target for therapeutic intervention in AD.

POSTER 38

Presented by the researcher: Navarro Acebes, Xavier.

Principal investigator of the group: Navarro Acebes, Xavier. (Cod: 607).

Title: Effects of the spinal cord injury environment on the differentiation capacity of human neural stem cells derived from induced pluripotent stem cells.

Authors: Clara López-Serrano, Abel Torres-Espín, Joaquim Hernández, Ana B Alvarez-Palomo, Jordi Requena, Xavier Gasull, Michael J. Edel, Xavier Navarro

Abstract: Spinal cord injury (SCI) causes loss of neural functions below the level of the lesion mainly due to interruption of spinal pathways and secondary neurodegenerative processes. The transplant of neural stem sells (NSCs) is a promising approach for the repair of SCI, since NSCs are able to differentiate and integrate within the damaged tissue, inducing regeneration of the neuronal network. Reprogramming of adult somatic cells into induced pluripotent stem cells (iPSC) is expected to provide an autologous source of human induced NSCs (hiNSCs), avoiding the immune response as well as ethical issues concerning the use of stem cells from embryonic and fetal tissue. However, there is still limited information on the behavior and differentiation pattern of transplanted hiNSCs within the damaged tissue. Thus, we transplanted hiNSCs to rats at 0 or 7 days after SCI, and evaluated motor evoked potentials and locomotion of the animals during follow-up. We histologically analyzed engraftment, proliferation and differentiation of the hiNSCs, and the spared tissue in the spinal cords at 7, 21 and 63 days post-transplant. Both hiNSCs transplanted groups showed a late decline in functional recovery compared to vehicle-injected groups. Histological analysis showed proliferation of the transplanted cells within the tissue, forming a cell mass that may explain the decline of motor function with time. Most grafted hiNSCs differentiated to neural and astroglial lineages, whereas no differentiation into oligodendrocytes was observed. Furthermore, some cells remained still undifferentiated and proliferating at the final time point, resulting in uncontrolled expansion of the cells within the injured tissue.

POSTER 39

Presented by the researcher: Gago Calderon, Belen.

Principal investigator of the group: Lopez de Munain Arregui, Adolfo. (Cod: 609).

Title: Apomorphine-induced dyskinesias in parkinsonian rats: pet and histological studies

Authors: B. Gago, D. Garcia-Garcia, C. Marin, H. Jimenez-Urbieta, Oregui A, V. Gómez-Vallejo, J. Llop, G. Mengod, R. Cortés, M. Delgado-Alvarado, M.C. Rodríguez-Oroz

Abstract: Dyskinesias induced by dopaminergic drugs complicate the long-term treatment of Parkinson's disease (PD). Animal models of levodopa-induced dyskinesias have provided evidence supporting a relevant role of dopamine and serotonin receptors as well as opioid peptides in their pathophysiology. We have analyzed whether the induction of dyskinesias by apomorphine (APO) in the unilateral 6-hydroxydopamine (6-OHDA)-lesioned rat model alters the expression of serotonin receptors both postmortem, by in situ hybridization, and in vivo using the [18F]Altanserin binding to 5-HT2A receptor by PET. Besides, we have studied the in vivo cerebral metabolism by [18F]FDG PET and the postmortem striatal levels of mRNA of D1R and D2R dopamine receptors, encephalin and dynorphin. A 15-d dose-increase protocol of APO administration followed by 2 weeks of the highest dose administration was used to induce dyskinesias, which were evaluated with the abnormal involuntary movements (AIMs) scale. APO induced significant rotational behavior, proving its antiparkinsonian effect, and dyskinesias (total AIMs score = 50). No significant changes in the 5-HT1A and 5-HT2A mRNA levels in the prefrontal cortex and striatum in both hemispheres were observed in comparison with control animals. [18F]Altanserin binding was neither different between dyskinetic and control animals in any cerebral region. However, dyskinetic animals showed glucose hypometabolism in the anterior striatum of the non-lesioned hemisphere and hypermetabolism in the posterior striatum and globus pallidum in the lesioned hemisphere. This last finding was also present in hemiparkinsonian rats without APO treatment. No differences in the D1R and D2R mRNA striatal levels were found. However, in the lesioned striatum, the 6-OHDA lesion reduced dynorphine mRNA and increased encephalin mRNA while APO treatment increased both opioid peptides mRNA expression. Thus, we have shown that APO-induced dyskinesias are associated with striatal changes in the glucose metabolism and opioid peptides but not with alterations in serotoninergic and dopaminergic receptors (DFG11/019, PI11/02109).

POSTER 40

Presented by the researcher: Ordoñez Gutierrez, Lara.

Principal investigator of the group: Wandosell Jurado, Francisco. (Cod: 412).

Title: Gender differences in APP/PS1 mouse model

Authors: Lara Ordóñez-Gutiérrez, Iván Fernández, Marta Antón, Francisco Wandosell

Abstract: The accumulation of amyloid-beta peptide is one of the major neuropathological hallmarks of Alzheimer's disease (AD). We have analyzed whether the progression of amyloidosis differentially affects males and females along aging in APP/PS1 transgenic mice. We have analyzed the levels of peripheral amyloid, Aß40 and Aß42, and brain burden in cortex and cerebellum. Other markers (synapsis, autophagy) have been checked separately in both sexes. These findings could be essential to design gender-specific strategies in other in vivo experiments or even in AD treatments.

POSTER 41

Presented by the researcher: Gutiérrez Pérez, Antonia.

Principal investigator of the group: Gutiérrez Pérez, Antonia. (Cod: 415).

Title: Microtubule stabilizing therapy protects cognitive function and ameliorates alzheimer's disease pathology

Authors: Fernandez-Valenzuela JJ.1, Sanchez-Varo R.1, De Castro V.1, Moyano FJ2, Vizuete M2, Davila JC1, Vitorica J.2 and Gutierrez A.1 1Dept. Cell Biology, Genetics and Physiology, Faculty of Sciences, University of Malaga. CIBERNED. IBIMA. Malaga, Spain. 2Dept. Biochemistry&Molecular Biology, Faculty of Pharmacy, University of Seville. CIBERNED. BIS. Seville, Spain.

Abstract: Cognitive and memory decline in Alzheimer's disease (AD) is highly related to synaptic dysfunction and subsequent neuronal loss. In AD patients, the hiperphosphorylation of the microtubule associated protein tau leads to the destabilization of microtubules and axonal transport failure, with the consequent accumulation of autophagic/vesicular material, generation of dystrophic neurites, and thus contributing to synaptic dysfunction. The aim of this study was to analyze the effect of a treatment with a microtubule stabilizing agent in the progression of the disease in the APP751SL/PS1M146L transgenic model of AD. APP/PS1 mice (3 month-old) were treated with a weekly intraperitoneal injection of 2 mg/kg epothilone D (Epo-D) for 3 months. Vehicle-injected animals were used as controls. At the end of treatment mice were tested on the Morris water maze, Y-maze and object recognition task for memory performance. Levels of A?, AT8 (hyperphosphorylated tau), ubiquitin and synaptic markers (PSD95, VGAT) were analyzed by Western-blot. Hippocampal plaque loading and dystrophic area were quantified by image analysis after immunostaining for A?42, APP or ubiquitin. Epo-D treated transgenic mice showed a significant improvement in the performance of hippocampus-associated cognitive tests. The recovery of spatial/episodic-like memory correlated with a reduction in the AD-like hippocampal pathology. The levels of A?, APP and ubiquitin significantly decreased in treated animals at both histological and molecular levels. However, phospho-tau (AT8) levels did not change. Synaptic markers (PSD95 and VGAT) were found to be increased in treated animals compared to controls. Our results indicated that Epo-D treatment promotes synaptic and cognitive recovery in APP/PS1 mice, and reduces the accumulation of extracellular A? and the associated dystrophic pathology in the hippocampus. Therefore, microtubule stabilizing drugs could be considered potential therapeutic agents for Alzheimer's disease. This work was supported by FIS PI12/01431 and PI12/01439 grants.

POSTER 42

Presented by the researcher: López de Ceballos Lafarga, María.

Principal investigator of the group: López de Ceballos Lafarga, María. (Cod: 506).

Title: Arginase enzymatic activity is increased in Alzheimer's disease brain

Authors: C. González-Martínez 1*, N. Wilson1*, and M L de Ceballos1 *These authors contributed equally to the work 1Department of Cellular, Molecular and Developmental Neuroscience and CIBERNED, Cajal Institute, CISC, Madrid, Spain.

Abstract: Alzheimer's disease (AD) is characterized by ongoing neuroinflammation, as a consequence of astrogliosis and microglial activation. Arginase1 expression is considered a feature of M2 alternative microglial activation. L-arginine (Arg) is a semi-essential amino acid with a number of bioactive metabolites. Accumulating evidence suggests the implication of altered Arg metabolism in the pathogenesis of AD. Arginase1 is considered to be beneficial and neuroprotective in many instances, while the reduction Arg brain levels in AD may be detrimental. We have studied arginase activity by means of the colorimetric measurement of ornithine produced by enzymatic hydrolysis of L-Arg in control subjects, devoid of neurological symptoms, and AD patients, clinically diagnosed and histopathologically defined. Another cohort of control brains and Braak-staged AD brains were used for the assessment of Arg1 protein expression by Western blotting. We have found a double-fold increase in arginase activity in cortical samples from AD when compared with control subjects. In contrast, Arg 1 protein levels were unchanged in Braak-staged brains, although there was a trend towards an increase in Braak stage V-VI samples. There was no correlation between Arg1 protein levels and any ante-mortem or post-mortem parameters. These results are in accordance with other works using other methods for Arg metabolism assessment and they may suggest that an increase in Arg2 is responsible for the changes in activity and not Arg1.

POSTER 43

Presented by the researcher: Belbin , Olivia.

Principal investigator of the group: Lleo Bisa , Alberto. (Cod: 504).

Title: Identification of synaptic proteins detectable in the cerebrospinal fluid in the search for biomarkers of preclinical Alzheimer's Disease

Authors: Olivia Belbin, Gemma Gomez-Giro, Laia Muñoz, Daniel Alcolea, Martí Colom-Cadena, María Carmona-Iragui, Juan Fortea, Jordi Clarimon, Àlex Bayés, Alberto Lleó

Abstract: Objectives: To identify and quantify synaptic protein levels in cerebrospinal fluid (CSF) in the search for biomarkers of synaptic loss at the preclinical stage of AD. Methods: The CSF proteome was constructed by performing a proteomic study of the CSF of 50 cognitively healthy controls and 10 age-matched AD patients (mean age=64 years). Samples were pooled, immunodepleted, digested, and analysed by liquid chromatography mass-spectrometry. The synaptic proteome was constructed by retrieving proteins from a systematic literature search of proteomic studies of mouse, rat or human synaptic fractions (n=16) and proteins annotated with a synaptic function in the Gene Ontology, Kegg and SynSysNet databases. Results: In total, CSF proteomic profiling identified 2,482 proteins (1,826 from control pools and 1,705 from the AD pool). Cross-referencing the CSF (n=2,482) and synaptic proteomes (n=3,359), resulted in 817 CSF proteins functionally and/or topographically related to the synapse. Proteins considered to be non-specific to the synapse (expressed at ?moderate/medium levels in glia or neuronal soma and ?moderate/medium levels in the neuropil of the human cortex according to the 'Human Protein Atlas' database) were subsequently removed leaving 192 proteins (8% of the CSF proteome). Quantification of these proteins in CSF from cognitively healthy controls, age-matched AD and preclinical AD cases using targeted mass spectrometry is currently underway. Conclusions: By performing a detailed characterization of the CSF and synaptic proteomes, we have identified 192 synaptic proteins detectable in the CSF, which, if confirmed as biomarkers of synaptic loss, could be invaluable for the diagnosis of preclinical AD.

POSTER 44

Presented by the researcher: Cantero Lorente, José Luis.

Principal investigator of the group: Cantero Lorente, José Luis. (Cod: 511).

Title: Regional hippocampal atrophy and increased plasma amyloid-beta are associated with subjective memory complaints in non-demented elderly subjects.

Authors: Mercedes Atienza, Juan E. Iglesias, Koen Van Leemput, Jose L. Cantero

Abstract: Growing evidence suggests a link between the presence of subjective memory complaints (SMCs) and atrophy of the hippocampus, one of the first regions to show neuropathological lesions in patients with Alzheimer's disease (AD). However, it remains to be investigated whether self-reported memory concerns are associated with volume loss of specific hippocampal subregions, and whether these regional changes are in turn related to memory performance and other indirect markers of AD neuropathology such as plasma levels of circulating amyloid-beta (A?) peptides. In this study, volumes of hippocampal subregions and plasma A? levels were compared between cognitively intact elderly subjects with (N=47) and without SMCs (N=48). Regional hippocampal changes were further correlated with objective memory performance and with plasma A? levels in each group, separately. Results showed that individuals with SMCs showed increased plasma levels of A?1-42 and reduced volume of total hippocampus mainly due to atrophy of CA1, CA4, dentate gyrus (DG), and molecular layer (ML). Regression analyses further showed that volume reduction of the DG was related to both poorer memory performance and increased plasma A?1-42 concentrations in SMC subjects. Together, these results suggest that self-reported memory complaints, combined with regional hippocampal atrophy, may represent one of the first stages on a continuum between normal aging and AD, which may be helpful in offering clinical follow-up to cognitively intact older adults.

POSTER 45

Presented by the researcher: Rodriguez Alvarez, Jose.

Principal investigator of the group: Rodriguez Alvarez, Jose. (Cod: 406).

Title: CRTC1 activates a memory transcriptional program deregulated at early Alzheimer's disease pathological stages.

Authors: Arnaldo J. Parra-Damas1,2, Jorge Valero1, Meng Chen1,2, Judith España1,2, Elsa Martin1,2, José Rodríguez-Alvarez1,2 & Carlos A. Saura1,2

Abstract: Cognitive decline is associated with gene expression changes in the brain, but the transcriptional mechanisms underlying memory impairments in cognitive disorders, such as Alzheimer's disease (AD), remain largely unknown. In this study, we aimed to elucidate relevant mechanisms responsible for transcriptional changes underlying early memory loss in AD by examining pathological, behavioural and transcriptome changes in control and mutant β.amyloid precursor protein (APP Sw,Ind) transgenic mice during raging. Genome-wide transcriptome analysis using mouse microarrays revealed deregulation of a gene network related with neurotransmission, synaptic plasticity and learning/memory in the hippocampus of APP Sw.Ind mice after spatial memory training. APP Sw,Ind mice show changes on a transcriptional program dependent on the CREB-regulated transcription coactivator-1 (CRTC1). Importantly, we found that synaptic activity and spatial memory induces CRTC1 dephospho rylation and activation leading to CRTC1-dependent transcription in the hippocampus, and these events are impaired in APP Sw.Ind mice at early pathological and memory decline stages. Furthermore, CRTC1 oveexprssion in the hippocampus of APP SwInd mice efficiently reverses Aβ-induced spatial learning and memory deficits by restoring a specific subset of CREB/CRTC1 target genes. Our results reveal a critical role for CRTC1-dependent transcriptionn on spatial memory and provide evidence that targeting CRTC1 can ameliorate memory deficits in AD.

POSTER 46

Presented by the researcher: Garcia Esparcia, Paula.

Principal investigator of the group: Ferrer Abizanda, Isidro. (Cod: 503).

Title: Altered machinery of protein synthesis from the nucleolus to the ribosome in Parkinson's disease

Authors: Paula Garcia-Esparcia and Isidre Ferrer

Abstract: Parkinson's disease (PD) is characterized by the accumulation of abnormal ?-synuclein in selected regions of the brain following a gradient of severity with disease progression. Whether this is accompanied by globally altered protein synthesis is poorly documented. The present study was carried out in PD stages 1-6 of Braak and corresponding controls in the substantia nigra, frontal cortex area 8, angular gyrus, precuneus and putamen (122 cases in total). Marked reduction in mRNA expression of nucleolar proteins nucleolin (NCL), nucleophosmin (NPM1) and upstream binding transcription factor (UBTF), and reduced NPM1 and NMP3 proteins in remaining neurons; reduced rRNA 18S, rRNA 28S expression; reduced expression of several mRNAs encoding ribosomal protein subunits including RPL and RPS; and altered protein levels of initiation factor eIF3 and elongation factor eEF2 of protein synthesis was found in the substantia nigra in PD cases which deregulation augmented with disease progression. NPM1 mRNA and rRNA 18S were increased in the frontal cortex area 8 at stage 5-6; modifications were less marked and region-dependent in the angular gyrus and precuneus. Several RPL and RPS were down-regulated at stages 3-4 and up-regulated at stages 5-6 in the frontal cortex area 8 and precuneus, but only one RP in the angular gyrus, in PD cases. Reduction of eIF3 at stages 3-4 and 5-6, increase of eIF1 at stages 5-6, and decrease of eEF1A and eEF2 at stages 3-4, more marked of eEF1A at stages 5-6, was observed in the frontal cortex in PD. Curiously, no modifications were found in the putamen at any time of the study. These changes demonstrate dramatic alterations in the protein synthesis machinery from the nucleolus to the ribosome with marked regional differences and increased involvement with disease progression. Whether these changes are associated with the presence of ?-synuclein oligomers was assessed in total homogenate fractions blotted with anti-?-synuclein oligomer-specific antibody demonstrating altered solubility and ?-synuclein oligomer formation in the substantia nigra and frontal cortex in PD cases. However, the band patterns differed in both regions thus indicating regional differences in ?-synuclein oligomerization in PD. In contrast, ?-synuclein oligomers were barely present in the putamen in PD cases. Observations show close relationship between molecular alteration of pathways of protein synthesis and presence of ?-synuclein oligomers.

POSTER 47

Presented by the researcher: Lavado Roldan, Angela.

Principal investigator of the group: Fernandez Chacon, Rafael. (Cod: 606).

Title: Mouse genetics to study neuronal function in transgenic mice carrying mutated forms of cysteine string protein-alpha (CSP-ALPHA) causing autosomal-dominant neuronal ceroid lipofuscinosis in humans

Authors: Angela Lavado-Roldán, Fabiola Mavillard, Jose Luis Nieto-González and Rafael Fernández-Chacón Instituto de Biomedicina de Sevilla (IBiS) Hosp.Univ. Virgen del Rocío/CSIC/Universidad de Sevilla, Dpto. de Fisiología Médica y Biofísica and CIBERNED, Seville, Spain

Abstract: Mutations in the DNAJC5 gene, that encodes the synaptic vesicle protein CSP-alpha, cause adult-onset autosomal dominant neuronal ceroid lipofuscinosis (NCL-4), a devastating neurodegenerative disease. CSP-alpha is bound to the synaptic vesicle through the palmitoylation of several cysteines and it functions as a co-chaperone for the SNARE protein SNAP25. Interestingly, genetic deletion of CSP-alpha in mice triggers activity-dependent presynaptic degeneration, alterations in the synaptic vesicle cycle and early death. In humans, the two point mutations causing NCL4 (Leu116del and Leu115Arg) render a full length protein with apparently dysfunctional palmitoylation. In any case, the cascade of molecular events underlying the severe neuropathological phenotype in humans is completely unknown. In order to investigate those mechanisms specifically in neurons we have used the neuronal specific promoter Thy1 to drive the transgenic expression of three different versions of CSP-alpha in mice. As expected for Thy1 promoter, we have obtained the typical variegated gene expression that ensures expression in certain neuronal populations surrounded by normal non-expressing neurons allowing a side by side comparison of mutant and control neurons within a common niche. In particular, the expression in hippocampus and cerebellum will be potentially very useful to investigate multiple aspects of biochemical alterations in nerve terminals, dysfunction of synaptic transmission and behavioral abnormalities. Supported by: MINECO (BES-2011-046029, BFU2013-474933), Junta de Andalucía (CTS2012-2232), ISCIII and FEDER. Acknowledgments: We are grateful to M.C.Rivero, A. Arroyo-Saborido and CPYEA (Univ. Sevilla) for excellent technical assistant and to L. Gómez-Sánchez for help and advice.

POSTER 48

Presented by the researcher: Nuñez Díaz, Cristina.

Principal investigator of the group: Gutiérrez Pérez, Antonia. (Cod: 415).

Title: Characterizing beta-amyloid plaque properties in the hippocampus of APP/PS1 alzheimer mice

Authors: C. Nuñez-Diaz1, R. Sanchez-Varo1, L. Trujillo-Estrada1, E. Sanchez-Mejias1, A. Gomez-Arboledas1, J.C. Davila1, J. Vitorica2 and A. Gutierrez1. 1 Dept. Cell Biology, Faculty of Sciences, University of Malaga. IBIMA. CIBERNED. Malaga, Spain. 2 Dept. Biochemistry & Molecular Biology, University of Seville. IBIS. CIBERNED. Seville, Spain.

Abstract: Amyloid plaques, which are composed of beta-amyloid peptides (A?), constitute one of the main pathological hallmarks of Alzheimer's disease (AD). In this disease, A? progressively accumulates and aggregates giving rise to toxic oligomers, fibrillar structures and, eventually, amyloid plaques. In turn, plaques may release soluble oligomeric forms of A?, contributing to the progression of the pathology. Here we aimed to characterize amyloid plaques properties during the pathological progression in the hippocampus of the APP751SL/ PS1M146L mouse model of AD. 4, 6, 12 and 18 month-old APP/PS1 mice were analyzed to determine changes in the number, size and toxicity of plaques during this model aging. Tioflavin-S and immunohistochemical stainings with different anti-A? antibodies were performed in order to identify different amyloid conformations. Afterwards, quantifications were done by densitometry and stereology. Both the number and size of amyloid plaques increased with age in the hippocampus proper and subiculum, especially in the latter. At early ages, amyloid plaques were mainly of non-fibrillar nature, however, as they grew they turned into a fibrillar conformation. On the other hand, the compaction of plaques diminished with the progression of the pathology, which might be related to an increase in their toxicity. Importantly, the ring of oligomeric A? surrounding the plaque core increased in size during the disease progression. Plaques may play a relevant role in the pathological progression of AD by acting as reservoirs of soluble A? oligomers that, as the disease progresses, could release these toxic amyloid species to the brain parenchyma, causing synaptic/neuronal damage. Therefore, regulating plaque quality properties might be a promising therapeutic approach. This work was supported by FIS PI12/01431 (to AG) and PI12/01439 (to JV) grants.

POSTER 49

Presented by the researcher: Carro Diaz, Eva Maria.

Principal investigator of the group: Carro Diaz, Eva Maria. (Cod: 502).

Title: Expression of regulatory proteins in choroid plexus changes in early stages of Alzheimer´s disease

Authors: Agnieszka Krzyzanowska, Inés García-Consuegra, Consuelo Pascual, Desiree Antequera, Isidro Ferrer, Eva Carro

Abstract: The role of choroid plexus in Alzheimer's disease (AD) is being increasingly recognized. Recent studies suggest that the choroid plexus has a more important role in physiological and pathological brain functions than previously appreciated. To obtain additional insight on choroid plexus function, we performed a proteomic analysis of choroid plexus samples from AD stages I-II (n = 16), III–IV (n = 16), and V–VI (n = 11), and 7 age-matched control subjects. We used differential 2D electrophoresis (2-D DIGE) coupled with mass spectrometry to generate a complete picture of changes in choroid plexus protein expression occurring in AD patients. We identified 6 proteins: 14-3-3 ?????14-3-3 ???moesin, proteasome activator complex subunit 1 (PSME1), annexin V, and aldehyde dehydrogenase (ALDH), which are significantly regulated in AD pathology ($p<0.05$, >1.5-fold variation in expression comparing with control samples), with central physiological functions, including mitochondrial dysfunction and apoptosis regulation, and able to model key pathological events. The data presented here contribute additional significance to the emerging importance of molecular and functional changes of choroid plexus function in the development of AD pathology.

POSTER 50

Presented by the researcher: García Sanz, Patricia.

Principal investigator of the group: Moratalla Villalba, Rosario. (Cod: 204).

Title: Compensatory sprouting to methamphetamine-induced dopaminergic degeneration

Authors: Noelia Granado 1,2, Sara Ares-Santos 1,2, Yousef Tizabi 3 and Rosario Moratalla 1,2 . 1Instituto Cajal, Consejo Superior de Investigaciones Científicas, CSIC, Madrid, Spain. 2CIBERNED, ISCIII, Madrid, Spain. 3Department of Pharmacology, Howard University College of Medicine, Washington, DC, USA

Abstract: Methamphetamine (METH), a psychostimulant with high abuse potential, may double the risk of developing Parkinson's disease. Animal studies have shown that this drug produces persistent dopaminergic neurotoxicity in the nigrostriatal pathway. However, some compensatory changes to dopaminergic damage, as observed with other neurotoxins, may also occur following METH treatment. Here, we wanted to confirm such recovery and determine the detailed structural nature as well as possible role of glia. Hence, three established neurotoxic regimens of METH: a single high dose (1x30mg/kg), multiple lower doses (3x5 mg/kg) or (3x10 mg/kg) of METH were applied. As expected, significant degeneration of striatal dopaminergic fibers were observed a day later in all cases. The damage was highest with the 3x10 mg/kg dose followed by 3x5 mg/kg, which was followed by 1x30 mg/kg. Moreover, regimen-dependent partial recovery was also noticed after 3 days. Interestingly, the recovery was also highest in 3x10 mg/kg, followed by 3x5 mg/kg, followed by 1x30 mg/kg. These partial recoveries were associated with a similar pattern of increase in tyrosine hydroxylase immunoreactivity and some fiber sprouting as evidenced by GAP-43 positive fibers. Additionally, METH treatment resulted in an increase in Iba-1 staining (reflective of microglia activation) after one day that was fully recovered by day 3. However, the increase in GFAP staining (reflective of astroglia activation) that was observed after one day was further increased by day 3. These results confirm that partial striatal recovery occurs following METH treatment and that astro- and micro-glia may have some role in this compensatory process. This work was supported by grants from the Spanish Ministry of Sanidad, Servicios Sociales e Igualdad, PNSD #2012/071, Spanish Ministry of Economía y Competitividad grant # BFU2010-20664, CIBERNED #CB06/05/0055 and Comunidad de Madrid ref S2010/BMD-2336.

POSTER 51

Presented by the researcher: Alberdi Alfonso, Elena.

Principal investigator of the group: Matute Almau, Carlos. (Cod: 404).

Title: Src-like tyrosine kinases mediate amyloid -induced myelin dysregulation in Alzheimer´s disease models

Authors: T. Quintela , A. Wyssenbach, C. Matute and E. Alberdi Departamento de Neurociencias, Universidad del País Vasco (UPV/EHU), Leioa, Spain Achucarro Basque Center for Neuroscience, UPV/EHU, Zamudio, Spain Centro de Investigación Biomédica en Red en Enfermedades Neurodegenerativas (CIBERNED)

Abstract: A reduction in the size of corpus callosum as a consequence of myelin loss and oligodendrocyte cell death has been reported to occur in Alzheimer´s disease (AD) and in transgenic mice models. These alterations may slow action potential propagation and contribute to AD progression. Here, we have characterized the effects of oligomeric amyloid b peptide (Ab) in primary oligodendrocyte and cerebellar organotypic cultures. First, we observed that Ab promoted the transition of early oligodendrocyte progenitors to late progenitor stages, and oligodendrocyte maturation. In addition, Ab peptide induced myelin basic protein (MBP) expression and myelination. To further investigate the mechanisms underlying Ab-mediated myelin changes, we analyzed the activation of Src family protein kinase and CREB, two key signalling pathways involved in myelin synthesis. We found that Ab caused a sustained Src and CREB protein phosphorylation in primary cultures of oligodendrocytes, and specific pharmacological inhibition of both pathways reduced Ab-induced MBP upregulation. Moreover, Ab enhanced the expression of other major components of CNS myelin including PLP and CNPase, and favored remyelination after lysolecithin-induced demyelination in cultured cerebellar slices. Importantly, Ab-mediated MBP upregulation in cultured slices was blocked by PP2, a Src family kinase inhibitor that potently inhibits Lck/Fyn proteins which suggests that they play a key role in that process. We next examined whether Ab accumulation in vivo was associated with MBP dysregulation. Western blotting of MBP and Ab oligomers in hippocampus and corpus callosum of 18-month old triple-transgenic mouse model of AD showed an increase of MBP levels in both regions that correlated with Ab oligomer burden. Consistent with those findings, MBP levels in frontal cortex of AD brains were significantly higher than in age-matched non-demented controls. Together, these data support a role of Ab and Src-like kinases in the pathophysiology of myelin in AD though the sequence of events leading to upregulation of MBP levels in this disease remains to be clarified. Supported by CIBERNED, Gobierno Vasco and MINECO. TQ and AW are recipients of a fellowship from the Gobierno Vasco and Universidad del País Vasco (UPV/EHU), respectively.

Dissemination

Press releases

Nota informativa

III Congreso Internacional sobre Investigación e Innovación en Enfermedades Neurodegenerativas

Expertos nacionales e internacionales analizarán en Málaga las principales enfermedades neurodegenerativas

- **S.M. la Reina Doña Sofía inaugurará oficialmente el congreso internacional el próximo lunes en Málaga**
- **Coincidiendo con la conmemoración del Día Mundial del Alzhéimer, el próximo 21 de septiembre, la Fundación Reina Sofía, la Fundación CIEN y CIBERNED, celebran el III Congreso Internacional sobre Investigación e Innovación en Enfermedades Neurodegenerativas**

(Madrid, 17 de septiembre de 2015). **Bajo la Presidencia de S.M. la Reina Doña Sofía**, más de 150 investigadores se darán cita en el III **Congreso Internacional sobre Investigación e Innovación en Enfermedades Neurodegenerativas** (CIIIEN), que tendrá lugar los próximos 21, 22 y 23 de septiembre en Málaga.

El congreso, organizado por La Fundación Reina Sofía, junto con la Fundación Centro de Investigación en Enfermedades Neurológicas (Fundación CIEN) y el Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (CIBERNED), abordará, principalmente, las **enfermedades de Alzheimer, Parkinson y Huntington.**

Miguel Medina, director científico adjunto de CIBERNED y Fundación CIEN, destacó hoy en la presentación del congreso la importancia de que los científicos "trasladen su conocimiento a la sociedad", aprovechando precisamente foros como este congreso, "que queremos consolidar como un **foro de referencia en nuestro país, para todos los investigadores en neurodegeneración**, pertenezcan o no a CIBERNED, con la idea de poner el énfasis en la investigación traslacional, que es la que **traslada el conocimiento generado en el laboratorio por la investigación básica la práctica clínica"**. Aunque coincidente con la conmemoración del Día Mundial del Alzheimer -21 de septiembre-, Medina ha señalado que el congreso "abordará el estudio del **conjunto de las enfermedades neurodegenerativas**", ya que "**aunque cada una de ellas presenta una manifestación clínica distinta, presentan una base con multitud de factores comunes que merecen ser estudiados en su conjunto".**

El congreso se estructura alrededor de tres sesiones plenarias y cinco sesiones científicas, y contará con la presencia de varios expertos internacionales como **Zaven Khachaturian**, presidente de la **Campaña Estadounidense de Prevención de la Enfermedad de Alzheimer para 2020,** "un líder de opinión y referente en el campo del alzhéimer, que dará una **visión general del concepto de demencia** y de nuevos modelos conceptuales para su estudio", explicó Medina. Participarán asimismo los científicos **Martin Rossor,** neurólogo clínico del Instituto de Salud Británico, experto en la **prevención de la aparición de demencias**, y en particular del alzhéimer, área de particular interés, según explicó el director científico adjunto de CIEN y CIBERNED, ya que "los resultados de las investigaciones en los últimos años sugieren que hemos llegado a un **cierto consenso en cuanto a la necesidad de intervención antes de que se**

presenten los síntomas clínicos" (lo que se conoce como prevención secundaria). En este tiempo hemos visto, remarcó, cómo "los tratamientos que estamos empleando podrían no están funcionando porque **llegamos demasiado tarde, cuando ya no es posible revertir los síntomas**".

David Rubinsztein, Director Adjunto del Instituto de Investigación Médica de Cambridge, será otro de los expertos internacionales presentes la semana próxima en Málaga, que, con un perfil más científico, es pionero en proponer la **regulación positiva de la autofagia** (proceso que parece ayudar a eliminar la proteína tóxica acumuladas de forma anómala en el cerebro de los pacientes) **como posible terapia en enfermedades neurodegenerativas.**

Rui Costa, investigador de la Fundación Champalimaud (Portugal) y **Ángel Cedazo-Mínguez**, del Instituto Karolinska (Suecia) completan la presencia internacional, centrados en el estudio de la **conectividad entre las distintas áreas del cerebro y los efectos de su disfunción**, el primero, y los mecanismos patológicos relacionados con los **factores de riesgo** conocidos.

Además, se tratarán durante el congreso otras enfermedades neurodegenerativas menos comunes como la **enfermedad de Charcot-Marie-Tooth**, y los investigadores nacionales pertenecientes a CIBERNED profundizarán en áreas como las **técnicas de neuroimagen**, la **investigación con células gliales** (células que dan soporte a la función neuronal, interviniendo directamente en el procesamiento de la información cerebral), la **plasticidad neuronal en la enfermedad de Huntington**, o la **señalización neuronal en párkinson**. Asimismo, y respondiendo a la vocación de impulso a la formación de jóvenes investigadores de CIBERNED, se hará entrega durante el congreso del Premio Joven Investigador (básico y clínico) y sus galardonados, Marta Fernández Nogales y Juan Fortea, expondrán durante el mismo las conclusiones de los estudios por los que se les ha otorgado dicho reconocimiento.

Cupón de la ONCE dedicado al alzhéimer

Previamente se ha presentado el cupón de la ONCE del próximo 21 de septiembre, cuya imagen se ha dedicado a la lucha contra el alzhéimer. **José Luis Nogueira**, secretario de la Fundación Reina Sofía, agradeció a la ONCE la emisión de este cupón, que "ayudará a **conocer el alzhéimer y concienciar a la sociedad"** sobre la importancia de esta enfermedad. En la misma línea se pronunció **Alberto Durán**, vicepresidente ejecutivo de Fundación ONCE, que destacó que el cupón pretende "rendir un homenaje" a las personas afectadas por esta enfermedad, a las familias "que soportan gran parte de la atención, cariño y apoyo económico", **a los investigadores y a la Fundación Reina Sofía, por su "apuesta decidida" en la lucha contra el alzhéimer**.

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Convocatoria de prensa

Lunes 21 de septiembre, en el Hotel Barceló Málaga

S.M. la Reina Sofía inaugura en Málaga el III Congreso Internacional sobre Alzheimer

- **El Congreso analizará durante tres días las enfermedades de Alzheimer, Parkinson y Huntington, principalmente.**

(Málaga, 21 de septiembre de 2015). Coincidiendo con el Día Mundial del Alzheimer, **S.M. la Reina Doña Sofía** inaugura hoy lunes 21 de septiembre, acompañada del Alcalde de Málaga, **Francisco de la Torre Prados,** y de la Secretaria de Estado de Investigación, Desarrollo e Innovación, **Carmen Vela**, el **Congreso Internacional sobre Investigación e Innovación en Enfermedades Neurodegenerativas** (CIIIEN), que se celebra en la ciudad andaluza los días 21, 22 y 23 de septiembre.

El Congreso, organizado por la Fundación Reina Sofía, la Fundación Centro de Investigación en Enfermedades Neurológicas (Fundación CIEN) y el Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (CIBERNED), celebra este año su tercera edición, y contará con la presencia de **investigadores nacionales e internacionales** que debatirán sobre los avances en el conocimiento y tratamiento de múltiples enfermedades neurodegenerativas, principalmente **alzhéimer, párkinson y huntington**.

De forma previa a la inauguración oficial, **a las 12,20h,** el director científico de Fundación CIEN y CIBERNED, **Jesús Ávila**, atenderá a los medios acreditados **en rueda de prensa para explicar los principales contenidos** que se tratarán durante el encuentro.

Fecha y hora: **Lunes, 21 de septiembre de 2015. 13,00h. Los medios acreditados deberán estar presentes a las 12,15h.**

Lugar: **Hotel Barceló Málaga** (Calle Héroe de Sostoa, 2, 29002 Málaga)

Contacto: Ida de la Hera 91 545 01 96 / 667 148 353 idelahera@servimedia.net

Nota informativa

III Congreso Internacional sobre Investigación e Innovación en Enfermedades Neurodegenerativas

S.M. la Reina Sofía inaugura en Málaga el III Congreso Internacional sobre Alzheimer

- **El Congreso analizará durante tres días las enfermedades de Alzheimer, Parkinson y Huntington, principalmente.**

(Málaga, 21 de septiembre de 2015). Coincidiendo con el Día Mundial del Alzheimer, **S.M. la Reina Doña Sofía** inauguró hoy lunes 21 de septiembre, acompañada del Alcalde de Málaga, **Francisco de la Torre Prados,** del director general del Instituto de Salud Carlos III, **Jesús Fernández Crespo** y de la Secretaria de Estado de Investigación, Desarrollo e Innovación, **Carmen Vela**, el **Congreso Internacional sobre Investigación e Innovación en Enfermedades Neurodegenerativas** (CIIIEN), que se celebra en la ciudad andaluza los días 21, 22 y 23 de septiembre.

Durante su intervención, el alcalde de Málaga remarcó de que **el alzhéimer es uno de los mayores desafíos a los que se enfrenta la sociedad en el siglo XXI**, ya que "cada 3 segundos se diagnostica en el mundo un nuevo caso de esta enfermedad", y alertó de que dado que nuestra población se articula en base a una pirámide de población cada vez más invertida, puede originarse una situación "difícil de mantener". Por este motivo, agradeció su trabajo a los investigadores participantes en el encuentro que, según recordó, provienen de diversas ciudades tales como Londres, Lisboa, Estocolmo, Madrid, Bilbao y Málaga, entre otras, y les animó a seguir planteando estrategias y compromisos de colaboración público-privada.

La Secretaria de Estado de Investigación, Desarrollo e Innovación, **Carmen Vela**, coincidió con De la Torre Prados en que el alzhéimer es uno de los desafíos más importantes "**no solo para España, sino también para Europa, que además ha sido considerado como reto número uno en el programa 2020**". Vela definió el envejecimiento como un desafío de salud pública, y la enfermedad de alzhéimer como una patología que tiene importantes consecuencias "no solo para el enfermo, sino para el entorno familiar, y por tanto a nivel social y económico". Así, declaró su voluntad de aumentar los recursos porque "**el reto es de tal envergadura que solo trabajando juntos científicos, empresas, médicos, pacientes, familiares, y Administraciones, lo podemos abordar**".

Por su parte, el director general del Instituto de Salud Carlos III, **Jesús Fernández Crespo**, agradeció tanto a S.M. la Reina Doña Sofía, como a la Fundación que lleva su nombre, su dedicación y sensibilidad hacia este gran problema social como es la enfermedad de Alzheimer,

"ya que **ha hecho posible que**, con el apoyo de instituciones estatales, autonómicas y locales, entre ellas, el Instituto de Salud Carlos III, **el complejo proyecto Alzheimer sea un hecho, y esté funcionando en estos momentos a pleno rendimiento** y que junto a Ciberned, haya sido designado **centro de excelencia de investigación en enfermedades neurodegenerativas**".

El Congreso, organizado por la Fundación Reina Sofía, la Fundación Centro de Investigación en Enfermedades Neurológicas (Fundación CIEN) y el Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (CIBERNED), celebra este año su tercera edición, y contará con la presencia de **investigadores nacionales e internacionales** que debatirán sobre los avances en el conocimiento y tratamiento de múltiples enfermedades neurodegenerativas, principalmente **alzhéimer, párkinson y huntington**.

Conferencia inaugural

Zaven Khachaturian, presidente de la Campaña Estadounidense de Prevención de la Enfermedad de Alzheimer para 2020, resaltó durante la ponencia inaugural "la necesidad de trabajar en **una teoría común sobre demencias**", tal y como se está haciendo desde el grupo internacional de trabajo que lidera. Esta "teoría ideal", según el experto, debería abordar cuestiones clave como "ampliar el espectro de dianas terapéuticas; resolver el rompecabezas de patologías presente en el diagnóstico diferencial y en los estudios clínicos sobre tratamiento, y la urgente necesidad de entender las transiciones entre las distintas fases de la enfermedad".

Así, según el científico, la "teoría ideal" del alzhéimer, debería "profundizar entre la **relación entre la biología del envejecimiento normal y la de la patología concreta de alzhéimer**, y relacionar los factores de riesgo conocidos con los mecanismos neurobiológicos y ambientales que los modifican".

Las demencias representan, en opinión de **Khachaturian,** un problema de salud global ya que "el impacto económico y social de los trastornos cerebrales crónicos como la enfermedad de Alzheimer, y otras enfermedades neurodegenerativas, **se convertirá en el principal problema de salud pública en todo el mundo, afectando directamente a 100 millones de personas para el año 2050".**

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Nota informativa

III Congreso Internacional sobre Investigación e Innovación en Enfermedades Neurodegenerativas

Marta Fernández-Nogales y Juan Fortea, Premios Joven Investigador 2014

- **Los investigadores Marta Fernández-Nogales (Centro de Biología Molecular Severo Ochoa, CSIC-UAM) y Juan Fortea (Hospital San Pau) han presentado hoy en Málaga, durante el III Congreso Ciiien, las investigaciones que les han hecho merecedores del Premio Joven Investigador 2014 y Joven Investigador Clínico 2013-2014 que otorga anualmente Ciberned**
- **El Congreso se está celebrando en Málaga bajo la presencia de S.M. la Reina Doña Sofía y analizará hasta mañana miércoles las principales enfermedades neurodegenerativas, haciendo especial hincapié en la traslación del conocimiento de la investigación básica a la práctica clínica y en la base común de las distintas enfermedades neurodegenerativas**

(Málaga, 22 de septiembre de 2015). **Marta Fernández-Nogales**, del Centro de Biología Molecular Severo Ochoa (CSIC-UAM) **y Juan Fortea**, del Hospital San Pau (Barcelona) recibieron hoy, en el Marco del III Congreso Internacional sobre Investigación e Innovación en Enfermedades Neurológicas (Ciiien), el **Premio Joven Investigador 2014** y **Premio Joven Investigador Clínico 2013-2014** que concede anualmente (y bienalmente en el caso de investigador clínico) el Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (CIBERNED). El premio, que reconoce la **labor destacada en la investigación de personas menores de 35 y 40 años respectivamente**, destaca en la presente convocatoria el trabajo de Fernández-Nogales en la enfermedad de Huntington y su vinculación con la proteína tóxica tau y la labor de Fortea en el establecimiento de una relación entre biomarcadores de beta-amiloide y tau en la etapa preclínica de alzhéimer.

Durante la jornada de hoy martes, contó con la **presencia de S.M. la Reina Doña Sofía**, los investigadores **Javier Vitorica, Xavier Navarro, Antonio Cuadrado, Rui Costa y Ángel Cedazo-Mínguez,** presentaron los resultados de sus trabajos sobre posibles estrategias terapéuticas en alzhéimer (activación glial) y enfermedades neuromotoras; así como en relación al avance en dianas terapéuticas en enfermedad de Parkinson y en la identificación de factores de riesgo en enfermedad de Alzheimer. En las sesiones de la tarde, los investigadores **José Berciano, Manuel Desco, y Bryan Strange** centraron sus intervenciones el área de resonancia magnética cerebral y el estudio del comportamiento de las proteínas beta-amiloide y tau en las enfermedades de Alzheimer y Huntington.

Bryan Strange, director del área de neuroimagen de la Fundación CIEN y miembro del Centro de Tecnología Biomédica (CTB) de la UPM, presentó a los asistentes datos avanzados de la investigación longitudinal que están llevando a cabo desde la Fundación CIEN y la Fundación Reina Sofía, el **Proyecto Vallecas,** que está estudiando a una muestra de 1200 sujetos para la identificación de marcadores tempranos de alzhéimer, y en la que están observando que existen cambios significativos en el cerebro antes de la aparición de síntomas clínicos, resultados que esperan puedan ser publicados en los próximos meses.

Otro de los temas tratados en la jornada de hoy ha sido la **enfermedad de Charcot-Marie-Tooth** (CMT), caracterizada por provocar atrofia muscular, pérdida de sensibilidad distal en las extremidades y pie cavo es la neuropatía hereditaria más frecuente, con una **prevalencia en torno a 30 casos por cada 10.000 habitantes**. **José Berciano**, miembro del Hospital Universitario Marqués de Valdecilla e investigador principal de CIBERNED, explicó el reciente avance de su equipo de trabajo en el conocimiento de la enfermedad, con la **asociación de la mutación de un gen** (NEFL E396K) **al nuevo fenotipo intermedio de la enfermedad** de Charcot-Marie-Tooth (CMT). Así, el trabajo reciente del grupo liderado por Berciano ha conseguido identificar como **una de las causas del tipo intermedio dominante de la enfermedad** (la enfermedad puede presentarse en siete categorías distintas), además de demostrar que ésta "puede expresarse por semiología polineuropática y del sistema nervioso central, lo cual está **en concordancia con modelos animales de la enfermedad** en los que la disfunción neuronal ocurre tanto en el sistema nervioso periférico como en el sistema nervioso central". La **asimilación de modelos animales con el funcionamiento cerebral humano es uno de los mayores retos en el conocimiento y tratamiento de las enfermedades neurodegenerativas**, ya que en muchas ocasiones, el mayor escollo en la eficacia de los tratamientos es que, al ser testados en modelos artificiales de la enfermedad (animales modificados transgénicamente), y dado el diferente comportamiento cerebral, la eficacia probada en ratones no es tal en su traslación a humanos. Pese a la aparente simplicidad semiológica de la enfermedad de la enfermedad de CMT, es uno de los síndromes neurológicos genéticamente más complejos, dado que **se han identificado mutaciones en 60 genes diferentes, quedando por descubrir la base molecular de un tercio de los casos.** Esto implica, según el investigador, "la ardua tarea que queda para desenmarañar la patogenia de enfermedad".

El **III Congreso Internacional sobre Investigación e Innovación en Enfermedades Neurológicas**, que se está celebrando en Málaga hasta mañana miércoles, está organizado por la Fundación Reina Sofía, la Fundación Centro de Investigación en Enfermedades Neurológicas (Fundación CIEN) y el Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (CIBERNED), y cuenta con la presencia de más de 140 investigadores nacionales e internacionales que están analizando los principales avances en el conocimiento y tratamiento de múltiples enfermedades neurodegenerativas, fundamentalmente alzhéimer, párkinson y huntington.

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Nota informativa

III Congreso Internacional sobre Investigación e Innovación en Enfermedades Neurodegenerativas

Finaliza el congreso internacional sobre neurodegeneración en Málaga

- **El Congreso, presidido por S.M. la Reina Doña Sofía, ha estado organizado por la Fundación Reina Sofía, la Fundación Centro de Investigación en Enfermedades Neurológicas (Fundación CIEN) y el Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (CIBERNED).**
- **Durante tres días, ha analizado las principales enfermedades neurodegenerativas, haciendo especial hincapié en la traslación del conocimiento de la investigación básica a la práctica clínica y en la base común de las distintas enfermedades neurodegenerativas**

(Málaga, 23 de septiembre de 2015). **Jesus Ávila**, director científico de la Fundación CIEN y CIBERNED, clausuró hoy el III Congreso Internacional sobre Investigación e Innovación en Enfermedades Neurodegenerativas, que ha tenido lugar en Málaga entre el 21 y 23 de septiembre, **bajo la presidencia de S.M. la Reina Doña Sofía**.

Ávila aprovechó su intervención de clausura para agradecer "el **apoyo recibido por parte de la Fundación Reina Sofía, de todas las instituciones públicas y privadas que han formado parte del congreso, y de la ciudad de Málaga**". El director científico de CIEN y CIBERNED remarcó la importancia de este tipo de encuentros, "que mejoran nuestro conocimiento en el campo de las demencias y las enfermedades neurodegenerativas, gracias **al excelente nivel de los ponentes y asistentes**, tanto extranjeros como nacionales", que cada año representan "una altísima contribución" con la puesta en común en este foro de sus investigaciones más recientes.

El **III Congreso Internacional sobre Investigación e Innovación en Enfermedades Neurológicas**, estuvo organizado por la Fundación Reina Sofía, la Fundación Centro de Investigación en Enfermedades Neurológicas (Fundación CIEN) y el Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (CIBERNED), y durante tres días, **más de 140 investigadores nacionales e internacionales** han analizado los principales avances en el conocimiento y tratamiento de múltiples enfermedades neurodegenerativas, haciendo especial hincapié en la **traslación del conocimiento de la investigación básica a la práctica clínica y en la base común que comparten las distintas patologías que forman parte del campo de la neurodegeneración.**

Durante la jornada de hoy, **Jaime Kulisevsky** investigador principal de CIBERNED perteneciente al Instituto de Investigación Hospital San Pau (Barcelona), centró su intervención en la **apatía y**

deterioro cognitivo presente en la enfermedad de Parkinson, patología que constituye la segunda enfermedad neurodegenerativa en prevalencia, por detrás del alzhéimer, y que afecta a un 25% de las personas de entre 85 y 90 años.

Conocida tradicionalmente como una enfermedad puramente motora, existe actualmente un **amplio consenso en cuanto a la consideración de múltiples factores** asociados a la progresión de la enfermedad, como son el deterioro cognitivo (presente en su forma leve casi en la totalidad de los pacientes), la aparición de trastornos psiquiátricos como la apatía, la ansiedad y la depresión, e incluso la aparición de efectos psicóticos como las alucinaciones.

En un porcentaje importante de los casos, los pacientes en estados avanzados de la enfermedad desarrollan demencia, aspecto en que centró su intervención **Mª Cruz Rodríguez Oroz, investigadora de** CIBERNED desde el Instituto de Investigación BioDonostia (San Sebastian). Oroz defendió la hipótesis de que **el hipometabolismo cerebral que caracteriza la enfermedad de Parkinson y la atrofia asociada a las demencias parecen ser "dos partes del mismo proceso"**, por lo que **el** deterioro cognitivo de pacientes en estados avanzados de párkinson se debería a la propia progresión de la enfermedad.

Mercè Boada, directora de la Fundació ACE (Barcelona), cerró el ciclo de ponencias como invitada, compartiendo con los asistentes las principales actividades y líneas de investigación de la entidad que coordina.

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Selection of mentions in mass media

Málaga hoy

PAÍS: España
PÁGINAS: 10
TARIFA: 2250 €
ÁREA: 428 CM² - 59%

FRECUENCIA: Diario
O.J.D.: 7045
E.G.M.: 23000
SECCIÓN: MALAGA

21 Septiembre, 2015

La Reina Sofía inaugura hoy un congreso sobre enfermedades neurodegenerativas

● Más de 150 investigadores internacionales se darán cita hasta el miércoles en el hotel Barceló de la capital

JAVIER ALBIÑANA

La Reina Sofía, junto a De la Torre, en su última visita en 2013.

EP MÁLAGA

Bajo la presidencia de Su Majestad la Reina doña Sofía, más de 150 investigadores se darán cita en el III Congreso Internacional sobre Investigación e Innovación en Enfermedades Neurodegenerativas (Ciiien), que se desarrollará desde hoy y hasta el miércoles en la ciudad de Málaga. La inauguración del Congreso Internacional sobre Investigación e Innovación en Enfermedades Neurodegenerativas, presidida por la Reina Sofía, tendrá lugar en el Hotel Barceló de Málaga, a partir de las 13:00, según informaron desde la organización.

El congreso, organizado por la Fundación Reina Sofía, junto con la Fundación Centro de Investi-

La Junta destaca la labor del SAS contra el Alzheimer

El consejero de Salud destacó ayer, en la víspera del Día Mundial del Alzheimer, la "importante labor asistencial y de investigación" que realiza la sanidad pública y sus profesionales contra una enfermedad que afecta a más de 95.000 personas en la comunidad. Recordó que tanto el Plan Andaluz del Alzheimer como el Proceso Asistencial Integrado de Demencia constituyen dos instrumentos para "mejorar la calidad de vida de las personas afectadas y sus familiares", un

dientes del Ministerio de Economía y Competitividad, a través del Instituto de Salud Carlos III–, abordará, principalmente, las enfermedades de Alzheimer, Parkinson y Huntington.

El congreso, cuya apertura coincide con el Día Mundial del Alzheimer, se estructura alrededor de tres sesiones plenarias y cinco científicas, y contará con la presencia de varios expertos internacionales como Zaven Khachaturian, presidente de la Campaña Estadounidense de Prevención de la Enfermedad de Alzheimer para 2020.

Participarán, asimismo, los científicos Martin Rossor, neurólogo clínico del Instituto de Salud

Además del Alzheimer, se tratará sobre el Parkinson, el Huntington y distintas terapias

Británico, experto en la prevención de la aparición de demencias y, en particular, del Alzheimer. El director adjunto del Instituto de Investigación Médica de Cambridge, David Rubinsztein, será otro de los expertos presentes en Málaga, que, con un perfil más científico, es pionero en proponer la regulación positiva de la autofagia como posible terapia en enfermedades neurodegenerativas.

Rui Costa, investigador de la Fundación Champalimaud (Portugal), y Ángel Cedazo-Mínguez, del Instituto Karolinska (Suecia), completan la presencia internacional, centrados en el estudio de la conectividad entre las distintas áreas del cerebro y los efectos de su disfunción, el primero, y los mecanismos patológicos relacionados con los factores de riesgo conocidos, el segundo.

Además, se tratarán durante el congreso otras dolencias neurodegenerativas menos comunes como la enfermedad de Charcot-Marie-Tooth, y los investigadores nacionales pertenecientes a Ciberned profundizarán en áreas como las técnicas de neuroimagen, la investigación con células gliales, la plasticidad neuronal en la enfermedad de Huntington o la señalización neuronal en párkinson.

Asimismo, Ciberned hará entrega durante el congreso del Premio Joven Investigador y sus

LA VERDAD

PAÍS: España
PÁGINAS: 64
TARIFA: 2344 €
ÁREA: 475 CM² - 50%

FRECUENCIA: Diario
O.J.D.: 15504
E.G.M.: 194000
SECCIÓN: CONTRAPORTADA

22 Septiembre, 2015

Doña Sofía, el día de la proclamación de su hijo Felipe como Rey de España. :: E. COBO / AFP

La voz de los que olvidan

La Reina Sofía ha sido propuesta para el Premio Nobel de la Paz por su lucha contra el alzhéimer

:: ALFONSO R. ALDEYTURRIAGA

Doña Sofía es la única persona sobre la faz de la tierra que es hija de rey, esposa de rey, madre de rey y hermana de rey. Y Reina. Desde bien pequeña, sus padres Pablo y Federica le inculcaron el amor por los demás, la solidaridad. Le hicieron ver que su posición, privilegiada, era un atractivo para desarrollar con éxito causas benéficas. Y en cuanto se asentó en el trono de España, una vez proclamado Juan Carlos I, se puso a ello, en primera fila. Creó en 1977, con dinero propio, de su bolsillo, la Fundación Reina Sofía, que en su vertiente social ha regalado no pocas sonrisas en estas casi cuatro décadas.

Pero es por uno de los proyectos más ambiciosos que impulsó Doña Sofía por lo que hoy es noticia: por la lucha contra el alzhéimer, cuyo principal exponente es el Centro Alzhéimer inaugurado en 2007 en Vallecas, donde se han llevado a cabo en estos años 27 proyectos de investigación, seis de ellos a nivel internacional. También ha generado más de 60 publicaciones científicas y 38 comunicaciones en congresos y reuniones científicas. Además, en la actualidad, está en marcha un proyecto de investigación de diagnóstico precoz, llamado Vallecas, dotado con 1,8 millones de euros y que cuenta con la ayuda de mil voluntarios.

Por prestar su imagen y su voz a los que sufren la enfermedad del olvido, una universidad del sur de EE UU ha propuesto a Doña Sofía para el premio Nobel de la Paz. Así lo anunció ayer Jesús Ávila, director científico de la Fundación Centro de Investigación en Enfermedades Neurológicas, en la presentación de un congreso internacional que estos días se celebra en Málaga. Los méritos, apuntó Ávila, los anteriormente mencionados: «Doña Sofía es muy conocida en el ámbito de la investigación de la enfermedad del alzhéimer por su trabajo y presencia en congresos».

El fallo, el 9 de octubre

Y será en unas semanas, el 9 de octubre para más señas, cuando se desvele si la Reina Sofía se convierte en el primer miembro de la realeza que alcanza tal distinción. Junto a la madre de Felipe VI, en la lista –extraoficial– de finalistas también figuran el Papa Francisco, el diputado noruego Abid Raja, el religioso católico y luchador por los derechos de los migrantes africanos Mussie Zerai y el jurista español Federico Mayor Zaragoza, que preside la Comisión Internacional contra la Pena de Muerte.

No es sin embargo Doña Sofía el primer miembro de la realeza propuesto para el Nobel de la Paz. Con anterioridad también lo fue su marido, el rey Juan Carlos, en los años 1980 y 1981, por la instauración de la democracia y su papel en el 23-F; antes, en 1950, la candidatura de Pablo I Grecia estuvo sobre la mesa, por su labor para poner fin a la Guerra Civil, y mucho antes, en 1917, Alfonso XIII, quien fue uno de los mayores impulsores de la ayuda humanitaria durante la Primera Guerra Mundial. A ellos se suman el zar Nicolás II (1901), el príncipe Carl de Suecia (1919), el rey Alberto de Bélgica (1922) y la princesa Guillermina de los Países Bajos (1951).

La Opinión DE MÁLAGA

PAÍS: España
PÁGINAS: 7
TARIFA: 477 €
ÁREA: 101 CM² - 13%

FRECUENCIA: Diario
O.J.D.: 3064
E.G.M.: 16000
SECCIÓN: MALAGA

21 Septiembre, 2015

La Reina Sofía inaugura hoy un congreso médico en Málaga

▶ Más de 150 investigadores participan en el Congreso sobre Enfermedades Neurodegenerativas

LA OPINIÓN MÁLAGA

■ La Reina doña Sofía presidirá hoy la inauguración del III Congreso Internacional sobre Investigación e Innovación en Enfermedades Neurodegenerativas (Ciiien), que se desarrollará desde este lunes y hasta el miércoles en Málaga con más de 150 investigadores. La inauguración tendrá lugar en el Hotel Barceló de Málaga, a partir de las 13.00 horas, según la organización.

El congreso, organizado por la Fundación Reina Sofía, junto con la Fundación Centro de Investigación en Enfermedades Neurológicas (CIEN) y el Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (Ciberned), abordará las enfermedades de alzheimer, parkinson y huntington.

El congreso, que coincide con el Día Mundial del Alzheimer, se estructura alrededor de tres sesiones plenarias y cinco científicas, y contará con expertos internacionales. Además, se tratarán otras dolencias neurodegenerativas menos comunes.

Diario de Ferrol

PAÍS: España
PÁGINAS: 48
TARIFA: 974 €
ÁREA: 510 CM² - 44%

FRECUENCIA: Diario
O.J.D.:
E.G.M.: 14000
SECCIÓN: CONTRAPORTADA

22 Septiembre, 2015

Doña Sofía, durante la inauguración de un congreso sobre enfermedades neurodegenerativas EFE

Proponen a la reina Sofía, para el Nobel de la Paz

Una universidad del sur de Estados Unidos decidió promover su candidatura por su compromiso en la lucha contra alzhéimer

EP MÁLAGA

La reina Sofía fue propuesta como candidata al Premio Nobel de la Paz por una universidad de Estados Unidos por su compromiso con la investigación del alzhéimer, desveló ayer el director científico de la Fundación Centro de Investigación en Enfermedades Neurológicas (CIEN), Jesús Ávila.

En una rueda de prensa ofrecida durante el Congreso Internacional sobre Investigación e Innovación en Enfermedades Neurodegenerativas (CIIIEN), Ávila afirmó que doña Sofía es "conocida" en el ámbito de la investigación de la enfermedad de Alzheimer por su trabajo y presencia en congresos.

Ávila, que se limitó a señalar que la candidatura parte de una universidad del sur de EEUU cuyo nombre no ha revelado, ha destacado la implicación de la reina en el estudio de esta enfermedad, así como en las actividades sobre discapacidades y en áreas desfavorecidas.

> LA REINA EMÉRITA RETOMÓ AYER SU AGENDA OFICIAL CON LA VISITA A UN CENTRO DE INVESTIGACIÓN

Añadió que suele haber "muchos más candidatos" a este premio, que se dará a conocer en octubre en Noruega.

El anuncio se produjo poco antes de la inauguración del congreso, organizado por la Fundación Reina Sofía junto con la Fundación CIEN y el Centro de Investigación biomédica en Red de Enfermedades Neurodegenerativas (CIBERNED), que ha estado presidida por la reina Sofía.

En el encuentro, que reúne hasta el próximo miércoles en Málaga a más de 150 investigadores, se analizan los últimos avances en investigación, de las enfermedades de Alzheimer , Parkinson y Huntington.

El envejecimiento de la población constituye un factor de riesgo para el desarrollo de este tipo de enfermedades, que tienen un importante impacto económico y social, por lo que el reto pasa por la prevención. ■

LaOpinión DE MÁLAGA
PAÍS: España
PÁGINAS: 1,16-17
TARIFA: 8930 €
ÁREA: 1900 CMP - 243%
FRECUENCIA: Diario
O.J.D.: 3064
E.G.M.: 16000
SECCIÓN: MALAGA
22 Septiembre, 2015

III CONGRESO INTERNACIONAL DE INVESTIGACIÓN E INNOVACIÓN EN ENFERMEDADES NEURODEGENERATIVAS

III International Congress on Research and Innovation in Neurodegenerative Di...

Alzheimer: el olvido temido de guante blanco

Conferencia ▶ El Congreso Internacional sobre Investigación en Enfermedades Neurodegenerativas se inauguró ayer en Málaga con la presencia de la reina Sofía **Esperanza** ▶ Los investigadores aguardan sin euforia la posibilidad de dar con el origen que desencadena el avance de una patología que no conoce retrocesos **Diagnóstico** ▶ Cuando aparecen los primeros síntomas ya es demasiado tarde

Matías Stuber
Málaga
@matias_stb

Un apellido que dibuja rostros de miedo y sufrimiento se ha enclaustrado durante estos días en Málaga: Alzheimer. Como un ladrón de guante blanco se acecha la muerte anunciada. Sin ruido ni olor. Un desfallecimiento celular programado y paulatino que primero roba la memoria y después hurta la independencia. Un proceso imparable e inclemente que no para hasta la aniquilación del propio yo. Una enfermedad sufrida por los que la padecen y llorada por los que los rodean. Ni con un bate químico criado en los departamentos de neurología de las universidades más prestigiosos se ha podido poner freno hasta ahora. Tampoco nadie ha descubierto una pócima mágica. La industria farmacéutica ha naufragado con compuestos revolucionarios. Una sustancia misteriosa que la anterior suspendo categóricamente en los estudios clínicos.

A pesar de todas las retrogresiones la ruda parca ha dejado de dar vueltas. Los tests continúan y, entre los científicos, crece la esperanza de que sus remedios definitivamente pudieran llegar a ser efectivos. Siempre que sean administrados a tiempo. Mucho antes de que se aprecien los primeros síntomas sustanciosos. Sobre las perspectivas de éxito sólo cabe especular porque el misterio elemental de la enfermedad sigue sin resolverse en su origen. ¿Por qué existen personas a las que se les hace de noche a los 70 años y otros que llegan a los 90 años con una memoria a prueba de bombas? En concreto, lo que se busca, también durante estos días en Málaga, es dar con esa especie de mecanismo de ignición que decide si una persona, en algún momento de su vida, va a sufrir una enfermedad neurodegenerativa.

Málaga, capital de la ciencia

¿Sería posible que todas las variables necesarias para crear la fórmula mágica contra el alzheimer ya pudieran estar sobre la mesa? Que sólo sea necesario que llegue alguien capaz de juntarlas todas para ilustrar una teoría concluyente que explique el porqué de una tragedia que afecta cada año a miles de personas en España. En medicina, las explicaciones fáciles pocas veces suelen ser las correctas. En el Tercer Congreso Internacional sobre Alzheimer, que se celebra desde ayer, y hasta el próximo día 23 en la capital malagueña ya que fue inaugurado por la reina Sofía, un centenar de investigadores nacionales e internacionales provenientes de las universidades más prestigiosas del mundo quieren llenar de luz un camino oscuro que les llevaría a tocar todos los sanedrios de la investigación neurológica. Hay algo que sí parece claro y así lo confirmó ayer el director de la Fundación Centro de Investigación en Enfermedades Neurológicas, Jesús Ávila, en su comparecencia durante la primera jornada de este congreso que se celebra en el Hotel Barceló. El principal factor de riesgo es el envejecimiento. «Cuantos más años tengamos, más probabilidad de tener alzheimer», se mostró contundente. Mientras que otras enfermedades se han podido ir controlando con los avances de la ciencia, el alzheimer se está convirtiendo en un factor de riesgo para el futuro de las sociedades occidentales, tan acostumbradas a buscarle contención a todos los elementos de riesgo que amenazan a su población.

Una enfermedad olvidada por los políticos

▶ La enfermedad de alzheimer es la forma de demencia más frecuente entre los mayores. Afecta a unas 600.000 personas en España. En un 80 por ciento de los casos, son las familias las que asumen en solitario el cuidado y los gastos generados por estos enfermos ante el imperante olvido institucional. Con motivo del Día Mundial de la Enfermedad de Alzheimer que se celebró ayer, la Sociedad Española de Neurología (SEN) advirtió de que en los próximos 35 años el número de personas afectadas por esta patología en España podría ascender a más de 1,5 millones debido al envejecimiento de la población. Esta demencia es, además, una de las principales causas de discapacidad y la enfermedad crónica que provoca mayor dependencia. En definitiva, el alzheimer es una enfermedad familiar, ya que el núcleo social cercano es el que tiene que atender a estas personas.

LaOpinión DE MÁLAGA
PÁGINAS: 1,16-17
TARIFA: 8930 €
ÁREA: 1900 CMP - 243%
FRECUENCIA: Diario
O.J.D.: 3064
E.G.M.: 16000
SECCIÓN: MALAGA
22 Septiembre, 2015

GREGORIO TORRES

La reina Sofía, a su llegada al Congreso, junto a la secretaria de Estado de Investigación, el alcalde de Málaga y el presidente de la Diputación

El reto del envejecimiento

▶ La reina Sofía, propuesta para el Nobel de la Paz por una universidad de EEUU, inauguró ayer en Málaga un congreso internacional donde expertos en enfermedades neurodegenerativas abogaron por la prevención y por un envejecimiento saludable 16-17

DIARIO MEDICO
PAÍS: España
PÁGINAS: 6
TARIFA: 1245 €
ÁREA: 186 CM² - 24%
FRECUENCIA: Martes a viernes
O.J.D.: 39315
E.G.M.:
SECCIÓN: PROFESION
23 Septiembre, 2015

Sobrexpresión de GSK3 ß genera pérdida de memoria

MADRID
LAURA PÉREZ TORRES

Los efectos de la sobreexpresión de GSK3beta en la zona del giro dentado han sido uno de los temas analizados en el III Congreso Internacional sobre Investigación e Innovación en Enfermedades Neurodegenerativas (Ciiien), celebrado en Málaga.

Jesús Ávila, director científico de del Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (Ciberned) y de la Fundación Centro de Investigación en Enfermedades Neurológicas (CIEN), ha expuesto la relevancia de esa cinasa: "Se sabe que los enfermos de Alzheimer tienen dos estructuras aberrantes. Una son las placas seniles, que están hechas de amiloide beta; y la otra son los ovillos neurofibrilares, que están compuestos de la proteína tau". Estas dos estructuras podrían estar implicadas en la pérdida de memoria y "el nexo de unión es, precisamente, la GSK3beta, una cinasa implicada en fosforilar las proteínas".

Según los análisis del grupo de Ávila, es la proteína tau fosforilada, no la agregada, la que puede dar lugar a la degeneración que se observa en regiones como el giro dentado, cuando se fosforila por GSK3beta.

Este equipo ha demostrado en ratones que la sobreexpresión de GSK3beta en ratones conduce a una pérdida de memoria. Además, dicho fenómeno produce una neurogénesis aberrante en el giro dentado.


LAURA PÉREZ TORRES

Jesús Ávila, director científico de Ciberned.

Ávila ha descrito la importancia de la neurogénesis adulta, que "cuando tiene lugar en el giro dentado, esas nuevas neuronas están implicadas en la formación de nuevas memorias y nuevos aprendizajes".

La manipulación de la neurogénesis en esa zona del cerebro produce pérdida de memoria. "Si la pérdida es reciente o es un ratón joven, somos capaces de recuperarla; pero si el ratón es muy viejo ya no la recuperamos".

Asociaciones de familiares exigen más celeridad en los diagnósticos del alzhéimer

ÁNGEL ESCALERA
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Las trabas burocráticas retrasan hasta año y medio el dictamen que confirma que los pacientes sufren esa demencia

MÁLAGA. Cuanto antes se diagnostique el alzhéimer, mejor, puesto que así se pueden aplicar tratamientos para frenar el avance de la enfermedad. Sin embargo, el diagnóstico de los pacientes se demora hasta año y medio por culpa la lentitud del sistema y de las trabas burocráticas. «Desde que los familiares sospechan de la presencia alzhéimer hasta que se confirma pasa año y medio. Eso es una barbaridad y supone un perjuicio para los enfermos», manifestó a este periódico la presidenta de la Asociación de Familiares de Pacientes de Alzhéimer y Otras Demencias de Málaga, Paloma Ramos.

Unas 15.000 personas están diagnosticadas de alzhéimer en la provincia de Málaga. El número real de afectados puede todavía ser mayor, ya que son frecuentes los casos en los que la demencia todavía no ha sido detectada. El día mundial de este padecimiento se celebrará este lunes, 21 de septiembre.

El alzhéimer es la demencia senil más frecuente. Aunque no tiene cura, cuanto antes se detecte, más tiempo se puede retrasar el avance del deterioro cognitivo. Sin embargo, la falta de medios y la lentitud del sistema sanitario público hacen que el diagnóstico de la enfermedad se demore hasta un año y medio. Ese hecho provoca que cuando el paciente comienza a recibir un tratamiento farmacológico y una terapia no farmacológica el mal se encuentra en una fase más avanzada, lo que repercute negativamente tanto en él como en su familia.

A ese respecto, Paloma Ramos incidió en la necesidad de agilizar los trámites para la detección del alzhéimer. Asimismo, lamentó que no haya un sistema para realizar un diagnóstico precoz. «Desde que el enfermo va al médico de familia, ese lo deriva al especialista, se le hacen las pruebas y el neurólogo emite el informe definitivo, en algunos casos, transcurre año y medio», puntualizó Ramos.

La presidenta de la Asociación de Familiares de Pacientes de Alzhéimer y Otras Demencias de Málaga explicó que hace falta crear un censo nacional de demencias. Con ese registro se podría saber el número exacto de personas afectadas.

Con motivo de la celebración el lunes del Día Mundial del Alzhéimer, los hospitales que Quirón tiene en Málaga y Marbella se han sumado a la campaña 'Haz que ese deseo se pegue' (#hazqueesedeseosepegue), organizada por la Confederación Española de Asociaciones de Familiares de Personas con Alzhéimer y otras Demencias (CEAFA). La iniciativa pretende sensibilizar a la sociedad acerca de la llamada epidemia del siglo XXI y promover la prevención de este tipo de demencia, que padecen 600.000 personas, aunque la cifra asciende a 3,5 millones de afectados en España si se tienen en cuenta a familiares y cuidadores. Los expertos calculan que esas cifras se duplicará en el año 2050.

El alzhéimer «es el tipo de demencia más prevalente, una enfermedad neurológica degenerativa que debuta como un progresivo deterioro cognitivo y funcional de inicio insidioso al que en el transcurso del tiempo se asocian cambios en el estado de ánimo con alteraciones psicológicas y de conducta», explicó el jefe del servicio de neurología de Hospital Quirón Marbella, Mario von Maravic.

Carpas informativa y de la memoria en la plaza de Félix Sáenz

La Asociación de Familiares de Pacientes de Alzhéimer y Otras Demencias de Málaga, que preside Paloma Ramos, instalará dos carpas en la plaza de Félix Sáenz con motivo de la celebración este lunes del Día Mundial del Alzhéimer. Las carpas permanecerán abiertas al público desde las once de la mañana hasta las ocho de la tarde. En una de ellas se informará a la población sobre esa demencia y se explicarán los síntomas. En la otra se hará de forma gratuita un test de memoria a aquellas personas que lo soliciten. «Esta iniciativa es positiva. Hay personas que cuando sufren un olvido creen que pueden sufrir alzhéimer. Con el test que se hará podrán comprobar que no tienen nada anómalo. No hacemos esa prueba para alarmar, sino por todo lo contrario: para tranquilizar, afirmó Paloma Ramos.

La Asociación de Familiares de Enfermos de Alzhéimer de Málaga ha celebrado este año su 25.º aniversario fundacional. Fue creada el 24 de abril de 1990. Su fundador y primer presidente fue el geriatra Carlos Linares del Río. La asociación se ha convertido en un referente en toda España. Cuenta con un centro en el camino de Los Almendrales que es un modelo a seguir y en el que reciben terapia y cuidados los pacientes.


Miguel Medina, director científico adjunto de CIBERNED y Fundación CIEN. :: SUR

Expertos en enfermedades neurodegenerativas participan en Málaga en un congreso

:: **A. ESCALERA**

MÁLAGA. Más de 150 expertos se darán cita en Málaga en el seno del tercer congreso internacional sobre investigación e innovación en enfermedades neurodegenerativas, que se desarrollará del 21 al 23 de septiembre en el hotel Barceló. El evento será inaugurado el lunes por la Reina Doña Sofía. El congreso lo organizan la Fundación Reina Sofía, la Fundación Centro de Investigación en Enfermedades Neurológicas (Fundación CIEN) y el Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (CIBERNED). Se debatirá sobre las enfermedades de alzhéimer, parkinson y huntington, sobre todo.

El director científico adjunto de CIBERNED y Fundación CIEN, Miguel Medina, en declaraciones realizadas a este periódico, se refirió a la importancia de que los científicos trasladen su conocimiento a la sociedad en foros como los del congreso de Málaga.

Respecto a las investigaciones encaminadas a detectar el alzhéimer 15 o 20 años antes de que se manifieste, Medina dijo que ese asunto está restringido al ámbito de la investigación. Todavía no se ha llegado al punto en el que eso se pueda aplicar de una manera rutinaria en la práctica clínica. «Ya hemos identificado que entre 15 y 20 años antes de aparecer los síntomas clínicos ya hay cambios en el cerebro, que podríamos ver con determinadas técnicas bioquímicas a través de una resonancia magnética. Hay muchos estudios en marcha; estamos avanzando mucho, pero todavía nos queda un recorrido, espero que no sea de muchos años, para que esas investigaciones ayuden a desarrollar nuevos tratamientos», señaló.

Ese experto, al ser preguntado sobre las posibilidades de curación del alzhéimer, respondió: «El consenso general a día de hoy es que a corto o medio plazo, curar, en el sentido estricto de eliminar la enfermedad, va a ser muy complicado, no conocemos lo suficiente. Lo que sería factible en los próximos diez o quince años es conseguir frenar el alzhéimer lo suficiente para que el impacto de la enfermedad sea mucho menor. Si lográsemos frenar la aparición del alzhéimer cinco o diez años supondría, además de una ventaja socioeconómica, que el paciente viviese una mejor calidad de vida».

Recortes por la crisis

Medina se refirió a los problemas que sufren los familiares de los enfermos, dificultades que se han visto agravadas con la crisis. «El alzhéimer es una enfermedad que tiene un impacto terrible en la familia y en los cuidadores, no solo desde un punto de vista de estrés personal, sino también de gasto económico. Con la crisis ha habido unos recortes bestiales. Los recortes en la ley de dependencia han hecho que la situación no sea la ideal».

Sobre el parkinson, manifestó que al menos hay un tratamiento eficaz que mejora parte de los síntomas. Miguel Medina añadió: «Ponemos mucho énfasis en crear las enfermedades neurodegenerativas en su conjunto. Hay muchos factores, desde un punto de vista biológico y celular, que son comunes a todas esas enfermedades».

Málaga hoy

PAÍS: España
PÁGINAS: 10
TARIFA: 3814 €
ÁREA: 726 CM² - 100%

FRECUENCIA: Diario
O.J.D.: 7045
E.G.M.: 23000
SECCIÓN: MALAGA

22 Septiembre, 2015

Carmen Vela inaugura el Congreso acompañada de la reina Sofía, el alcalde de Málaga y el consejero de Salud, ayer.

La reina Sofía es propuesta para recibir el Nobel de la Paz

● La iniciativa parte de una universidad del sur de EEUU ● Entre los candidatos se encuentra el Papa

M. Valverde MÁLAGA

La reina doña Sofía es una de las candidatas al Nobel de la Paz gracias a la propuesta de una prestigiosa universidad del sur de Estados Unidos. Así lo dio a conocer ayer el director científico de la Fundación CIEN y de Ciberned, Jesús Ávila, en una rueda de prensa ofrecida antes del III Congreso Internacional sobre Alzheimer que se celebra en Málaga hasta el próximo miércoles y a cuya inauguración asistió la propia reina. El elecro finalmente será conocido el próximo octubre en Noruega.

Ávila apeló al compromiso de su majestad con la investigación de enfermedades neurodegenerativas, implicación que llevó a esta institución del sur de EEUU cuyo nombre no quiso revelar, a impulsar su candidatura. "Ha estado bastante implicada en todo lo que tiene que ver con las discapacidades y cuando hay un problema de áreas deprimidas, intenta ayudar siempre", manifestó.

Jesús Ávila muestra a la reina algunos avances de las distintas investigaciones, ayer.

"Tiene algún tipo de relevancia lo que ha hecho", explicó Ávila, quien recordó de manera un tanto anecdótica la impresión que le causó, al asistir en Boston (Massachusetts), observar la fotografía de doña Sofía entre las personas aludidas por su gran implicación en la búsqueda o prevención del alzheimer.

Asimismo, el director científico de la Fundación Cien y Ciberned insistió en que "está muy implicada". "En el caso especial de la discapacidad, de la que posiblemente la mayor sea perder la cabeza, que es lo que sucede en el caso del alzheimer, ha participado en varios congresos", apostilló. No obstante, Ávila concretó que no hay nada decidido aún en cuanto al nombramiento final del Nobel de la Paz, pero sí avanzó que, entre los postulantes, también se encuentra el Papa Francisco.

Coincidiendo con el Día Mundial del Alzheimer, ayer se inauguró el III Congreso Internacional sobre esta enfermedad que durará hasta el próximo miércoles y que reunirá a más de 150 expertos en enfermedades neurodegenerativas para analizar los últimos avances en investigación, principalmente de las enfermedades de Alzheimer, Parkinson y Huntington. El evento está organizado por la Fundación Reina Sofía, la Fundación Centro de Investigación en Enfermedades Neurológicas (Fundación CIEN) y el Centro de Investigación Biomédica en Red de Enfermedades Neurodegenerativas (Ciberned).

El caso del alzheimer concretamente, es uno de los principales focos de atención y debate del evento. "Cuando empieza la diagnosis clínica, ya es muy tarde" porque se ha producido un gran deterioro en el sistema nervioso del paciente, y por este motivo los estudios se dirigen a la búsqueda de biomarcadores de la enfermedad, indicó Ávila.

Más de 150 expertos analizarán los avances en el Alzheimer, Parkinson y Huntington

Uno de los principales factores de riesgo para el desarrollo de este tipo de enfermedades es el envejecimiento de la población, por lo que el reto, según indicó Ávila, pasa por la prevención.

A este respecto, si se detecta que una persona en edad de procrear tiene una mutación genética, se podría "evitar que se propague" la enfermedad a través de la fertilización in vitro. De este modo, se escogerían a los embriones que carecen de la mutación mientras se continúa investigando sobre el diagnóstico y el tratamiento.

El congreso se compone de tres sesiones plenarias y cinco sesiones científicas que contarán con ponentes internacionales como Zaven Khachaturian, presidente de la Campaña Estadounidense de Prevención de la Enfermedad de Alzheimer para 2020, que dio comienzo a la jornada de inauguración junto a otros como Martin Rossor, neurólogo clínico del Instituto de Salud Británico y experto en aparición de demencias.

Asimismo, entre los asistentes se encontraron invitados como el alcalde de la ciudad, Francisco de la Torre, los consejeros de Salud y Educación, Aquilino Alonso y Adelaida de la Calle respectivamente, o la secretaria de Estado de Investigación, Desarrollo e Innovación, Carmen Vela, quien apuntó el "desafío enorme" que suponen las enfermedades asociadas al envejecimiento, "el reto número uno al que nos enfrentamos", concluyó.

ABC

PAÍS: España
PÁGINAS: 71
TARIFA: 24866 €
ÁREA: 566 CM² - 77%

FRECUENCIA: Diario
O.J.D.: 123534
E.G.M.: 494000
SECCIÓN: GENTE

26 Septiembre, 2015

El padre de *Doña Sofía* fue nominado al premio Nobel de la Paz en 1950

La Reina emérita sigue los pasos de Pablo de Grecia y aspira este año al codiciado galardón

ANA MELLADO
MADRID

España atesora ocho premios Nobel (seis en Literatura y dos en medicina), pero nunca ha logrado conquistar el de la Paz. El curso de la historia podría cambiar este año si el próximo 9 de octubre el Comité Nobel de Oslo pronunciara el nombre de Doña Sofía como destinataria del galardón. La Reina emérita ha sido propuesta por «una universidad del sur de Estados Unidos» como candidata, según reveló el director científico de la Fundación Centro de Investigación en Enfermedades Neurológicas, Jesús Ávila. «Su Majestad ha estado implicada en actividades solidarias, especialmente en el ámbito de las discapacidades neurodegenerativas», señaló Ávila en la inauguración del III Congreso Internacional sobre Alzhéimer.

A lo largo de la historia del premio Nobel desde 1901, varios reyes han sido nominados. Sin ir más lejos, el padre de Doña Sofía, el Rey Pablo I de Grecia, optó al galardón en 1950, por su contribución para terminar con la guerra civil griega. Su nombre fue propuesto por Michel Dendias, profesor de Derecho de la Universidad de Atenas. El abuelo de Don Juan Carlos, Alfonso XIII, fue nominado en 1917 por el senador Francisco de Lastres (seis años antes de que apoyase el golpe de Estado de Miguel Primo de Rivera). Ninguno de ellos fue proclamado vencedor. En el caso de que Doña Sofía se alzara con el galardón no sólo sería la primera personalidad española en conseguirlo, sino también el primer miembro de una Familia Real.

MIKEL PONCE/ABC

CANDIDATOS
Los nominados por el Comité permanecen en secreto medio siglo

No obstante, conviene ser cautos. En primer lugar porque en la lista de candidatos figuran hasta 276 nombres, entre ellos el del Papa Francisco, que se irán depurando hasta quedar en cinco finalistas. En segundo, porque según los estatutos de la Fundación Nobel los nombres de los candidatos de cada año permanecen en secreto durante medio siglo, así como los nombres de quienes los propusieron. Es decir, todos estos aspirantes sólo integran una lista extraoficial construida en base a filtraciones por quienes los nominaron y en muchos casos, son sólo especulaciones.

La concesión del premio Nobel de la Paz siempre viene envuelto en la polémica. Probablemente más de uno se pregunte cómo Stalin, Adolf Hitler y Benito Mussolini pudieron estar nominados o cómo el indio Mahatma Gandhi, candidato cinco veces, con una larga lista de proezas a sus espaldas, nunca lo consiguió. El Comité también quedó en el punto de mira en 2009 después de proclamar a Barack Obama como ganador, cuando llevaba solamente nueve meses en la Casa Blanca, sin éxitos diplomáticos notables y con dos guerras en curso, en Irak y Afganistán.

Aspirantes reales

El Rey Alfonso XIII (imagen superior) fue nominado al Nobel de la Paz en 1917. El padre de la Reina Sofía, Pablo I de Grecia, también aspiró al galardón, en 1950

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