



SAMI

Annual Report

2016

*cibersam*

Centro de Investigación Biomédica en Red  
Salud Mental

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**Eduard Vieta**, Scientific Director

## Scientific Director's Presentation

True to our annual appointment to render accounts of the work done by the CIBERSAM, and as its new scientific director, I am very pleased to be presenting the 2016 report, which compiles the results of the hard work done in research and innovation at our centre, leading translational biomedical research into mental health in Spain. I am not going to use this space to highlight the large number of scientific publications, the percentage of cooperative projects, the bibliometric impact or any of the excellence indicators given in the document. What really matters and justifies the social effort of assigning public funds, and what motivates the members of CIBERSAM is to attain tangible progress in the understanding, the diagnosis and the treatment of mental disorders. So, without any wish to understate the many pieces of scientific work produced over 2016, I would like to stress certain clear scientific progress with direct application at the patient's bedside. For example, CIBERSAM and the international ConLiGen consortium have identified a zone of the genome which is associated with a good response to treatment with lithium in bipolar disorder. This discovery, published in *The Lancet*, opens a gateway to personalised medicine for this illness and identifies a possible therapeutic target for new treatments. Another possible therapeutic target, in this case for schizophrenia, could be protein C4, which may be involved in the loss of synapses observed in these patients, as is also indicated by CIBERSAM researchers in *Nature*. Our centre has also led the development of innovative strategies using RNA interference for studying the physiopathology of major depressive disorder, which could result in new mechanisms for action of anti-depression treatments. And, also in depression, CIBERSAM has carried out a pioneering clinical trial in psychosocial prevention of this disorder in primary care. Young people are also a population of special interest for our centre, as we are committed to early intervention and prevention, and we have for this reason analysed the effects of antipsychotic medication on weight gain and hormones in children and adolescents. CIBERSAM has also led significant progress in such pathologies as autism, attention deficit disorder with hyperactivity, obsessive-compulsive disorder and personality disorders. The strategic plan for the coming years (2017-2019) puts special stress on placing the patient at the centre of CIBERSAM's work. One example of this is that in 2016 an international consensus document led by CIBERSAM researchers was published, which commits all the world's Biological Psychiatric Societies to a more human and evidence-based approach of the episodes of agitation, with the ultimate aim of saving lives and preventing involuntary mechanical restraint as far as possible. Lastly, European projects focussing on personalised mental health medicine such as PRISM and RADAR have been obtained which, along with the project for cohorts of first psychotic episodes and projects financed by North American agencies, guarantee a bright future for the coming years. Our platforms and our exclusive inter-university master course will unquestionably make a contribution to consolidating the opportunities offered us by the new strategic plan and the determined wish to contribute to better mental health for our citizens, by means of excellence in translational and collaborative research.



A hand in a white glove points to a whiteboard displaying several axial MRI scans of the brain. The scans are arranged in a grid. Technical data is overlaid on the scans, including parameters like TR, TE, SL, TA, BW, MND, Tra-Cor, W, and C. A large white number '2' is positioned in the upper right quadrant of the image. The background is a solid yellow color.

# 2

## Organisation

# Organisational Structure

CIBERSAM is one of the thematic areas which form the Centro de Investigación Biomédica en Red (CIBER), a Spanish research consortium in the field of biomedical research with enormous scientific potential, set up under the Instituto de Salud Carlos III (ISCIII) – Ministry of the Economy and Competitiveness. In 2016 this was made up of 8 thematic areas, which were extended to 11 in 2017.

The CIBERSAM consists of 24 research groups belonging to institutions of different kinds: university hospitals, universities, Public Research Bodies (OPI), such as the Instituto de Salud Carlos III (ISCIII) itself and the Consejo Superior de Investigaciones Científicas (CSIC), and research centres of Spain's regional "autonomous communities".

CIBERSAM has a large human resources team consisting of over 350 people, including a considerable staff of its own researchers and members of groups as personnel attached to the CIBERSAM. This large team is made up of basic and clinical biomedical researchers, research technicians and management staff.

As a thematic area of the CIBER, the CIBERSAM belongs to this public consortium and is thus governed by a Governing Body and a Permanent Committee (its governing and management bodies) in which the institutions in the consortium take part. The organisational structure is made up of Scientific Management, under Dr Celso Arango, which along with the Management Committee coordinates the work done by the 6 Scientific Programmes into which CIBERSAM groups are divided. The CIBER Technical Unit provides the administrative support required for the Institution to run.

## Members of the Management Committee

The Management Committee is presided over by the Scientific Director and made up of the coordinators of the programmes and manager of the CIBER.

| Name                               | Post   |
|------------------------------------|--|
| Celso Arango López                 | Scientific Director  |
| Eduard Vieta Pascual               | Scientific Assistant Director / Coordinator of the Bipolar Disorder Programme    |
| Victor Pérez Sola                  | Coordinator of the Depression Programme  |
| Julio Sanjuán Arias                | Coordinator of the Schizophrenia Programme and Data Base Common                  |
| Francesc Artigas Pérez             | Coordinator of the Therapeutic Innovation Programme                              |
| Josefina Castro Fornieles          | Coordinator of the Child and Adolescent Psychiatry Programme                     |
| Ángel Pazos Carro                  | Coordinator of Training and Mobility   |
| Ana María González-Pinto Arrillaga | Quality Coordinator  |
| José Javier Meana Martínez         | Coordinator of the CIBERSAM Platforms and the Brain Samples Platform             |
| José Manuel Menchón Magriña        | Coordinator of the Psychosomatic, Anxiety and Impulse Control Disorder Programme |
| Manuel Sánchez Delgado             | Manager  |

Attached to Scientific Director: Pura Morán

Contact: <http://www.cibersam.es/en/about-us/contact>

## External Advisory Scientific Committee

The External Advisory Scientific Committee is a scientific assessment and support body made up of relevant personalities in the world of health sciences who are well-known for their professional or scientific careers in line with the objectives of the centre. This is the body which carries out the annual evaluation of the work done by CIBERSAM and its research groups.

| Name           | Post   |
|----------------|--|
| Jim Van Os     | President of the External Scientific Committee. University of Maastricht, The Netherlands                                  |
| Guy Goodwin    | Member. Department of Psychiatry, University of Oxford, Warneford Hospital, Oxford, United Kingdom                         |
| Michael Hamon  | Vice-president. Institut National de la Santé et de la Recherche Médicale/ Université Pierre et Marie Curie. Paris, France |
| María Ron      | Secretary. Institute of Neurology, University College London, Queen Square, London, United Kingdom                         |
| Marion Leboyer | Member. Groupe Henri Mondor-Albert Chenevier, Pôle de Psychiatrie, Créteil, Paris, France                                  |

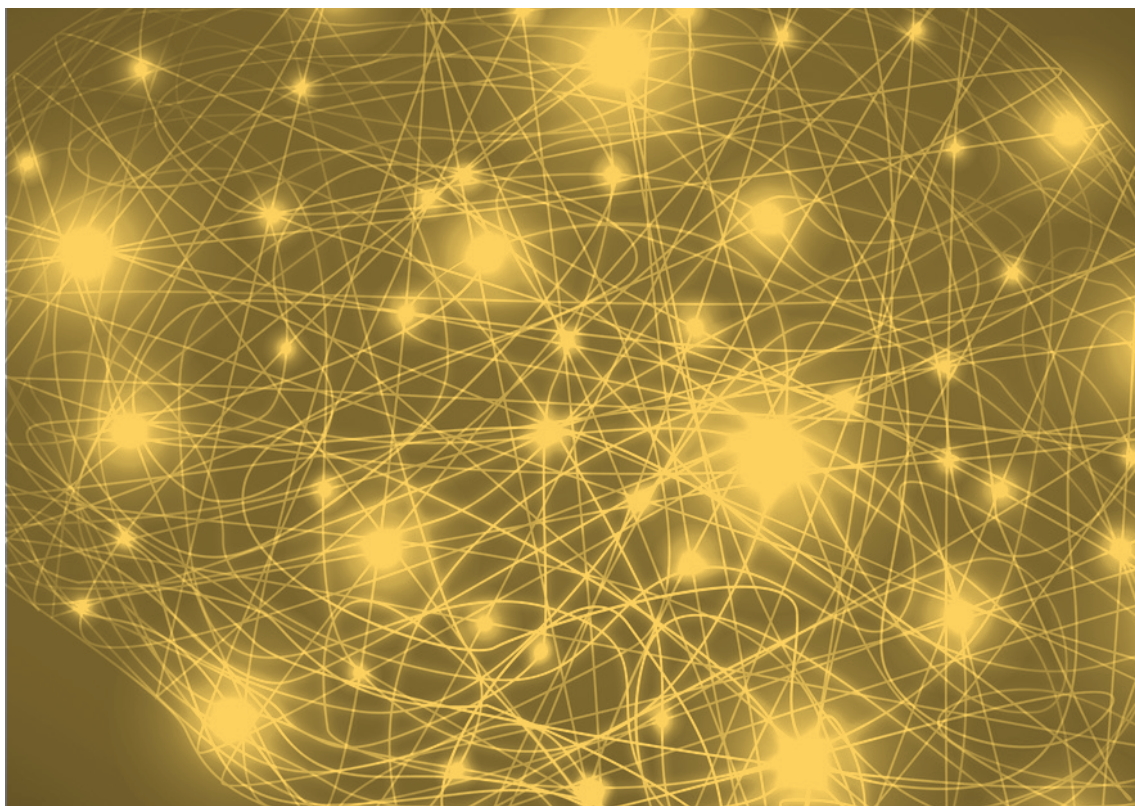
## Technical Unit

See list of personnel: <http://www.cibersam.es/en/about-us/structure/head-office>

## Directory of groups and institutions

| Group Leader                        | Institution   | Centre   | Prov. Centre |
|-------------------------------------|---|--|--------------|
| Arango López, Celso                 | Servicio Madrileño de Salud   | Hospital Gregorio Marañón                            | Madrid       |
| Artigas Pérez, Francesc             | Agencia Estatal Consejo Superior de Investigaciones Científicas             | Instituto de Investigaciones Biomédicas de Barcelona | Barcelona    |
| Ayuso Mateos, José Luis             | Servicio Madrileño de Salud   | Hospital Universitario La Princesa                   | Madrid       |
| Bernardo Arroyo, Miguel             | Hospital Clínico y Provincial de Barcelona                                  | Hospital Clínico y Provincial de Barcelona           | Barcelona    |
| Bobes García, Julio                 | Universidad de Oviedo   | Facultad de Medicina                                 | Asturias     |
| Casas Brugué, Miguel                | Fundación Hospital Universitario Vall d'Hebron - Institut de Recerca (VHIR) | Hospital Vall d'Hebron                               | Barcelona    |
| Cervilla Ballesteros, Jorge Antonio | Universidad de Granada  | Parque Tecnológico de Ciencias de la Salud           | Granada      |
| Crespo Facorro, Benedicto           | Instituto de Investigación Marqués de Valdecilla                            | Hospital Universitario Marqués de Valdecilla         | Cantabria    |
| Desco Menéndez, Manuel              | Servicio Madrileño de Salud   | Hospital Gregorio Marañón                            | Madrid       |
| Fañanas Saura, Lourdes              | Universidad de Barcelona  | Facultad de Biología. Universidad de Barcelona       | Barcelona    |
| González-Pinto Arrillaga, Ana       | Fundación Vasca de Innovación e Investigación Sanitarias                    | Hospital Universitario de Álava - Sede Santiago      | Álava        |
| Haro Abad, Josep María              | Fundación para la Investigación y Docencia Sant Joan de Déu                 | Parc Sanitari Sant Joan de Déu                       | Barcelona    |
| Leza Cerro, Juan Carlos             | Universidad Complutense de Madrid   | Facultad de Medicina                                 | Madrid       |

| Group Leader                 | Institution   | Centre                                       | Prov. Centre |
|------------------------------|---|--|--------------|
| Mckenna, Peter.J             | Fundación para la Investigación y Docencia María Angustias Giménez (FIDMAG) | Hospital Hermanas Hospitalarias Benito Menni | Barcelona    |
| Meana Martínez, José Javier  | Universidad del País Vasco  | Facultad de Medicina y Odontología           | Vizcaya      |
| Menchón Magriña, José Manuel | Fundación IDIBELL   | Hospital Universitario de Bellvitge          | Barcelona    |
| Micó Segura, Juan Antonio    | Universidad de Cádiz  | Facultad de Medicina                         | Cádiz        |
| Palomo Álvarez, Tomás        | Universidad Complutense de Madrid   | Facultad de Medicina                         | Madrid       |
| Pazos Carro, Ángel Armando   | Universidad de Cantabria  | Facultad de Medicina                         | Cantabria    |
| Pérez Sola, Víctor           | Consorti Mar Parc Salut de Barcelona  | Consortio Mar Parc de Salut de Barcelona     | Barcelona    |
| Sáiz Ruiz, Jerónimo          | Servicio Madrileño de Salud   | Hospital Ramon y Cajal                       | Madrid       |
| Sanjuán Arias, Julio         | Universidad de Valencia   | Facultad de Medicina de Valencia             | Valencia     |
| Tabarés-Seisdedos, Rafael    | Universidad de Valencia   | Facultad de Medicina de Valencia             | Valencia     |
| Vieta Pascual, Eduard        | Hospital Clínico y Provincial de Barcelona                                  | Hospital Clínico y Provincial de Barcelona   | Barcelona    |
| Vilella Cuadrada, Elisabet   | Fundación Instituto de Investigación Sanitaria Pere Virgili                 | Universidad Rovira y Virgili                 | Tarragona    |





# Budget

| INCOME            |                 |                   |              |            |              |
|-------------------|-----------------|-------------------|--------------|------------|--------------|
| ISCI III TRANSFER | GRANTS PROJECTS | SERVICES RENDERED | OTHER INCOME | CARRYOVERS | TOTAL        |
| 2.199.190,00      | 295.275,47      | 340.024,81        | 44.453,25    | 359.107,40 | 3.238.050,93 |

| EXPENDITURE  |                   |                                      |                     |                     |
|--|-------------------|--------------------------------------|---------------------|---------------------|
| Project  | Inventoriable     | Supplies and other activity expenses | Personnel           | TOTAL               |
| Scientific Management, Scientific Secretariat, Communication | 747,78            | 24.215,01                            | 55.543,54           | 80.506,33           |
| Groups   | 172.845,94        | 412.071,18                           | 1.406.364,68        | 1.991.281,80        |
| Training   | 0,00              | 35.817,98                            | 12.153,81           | 47.971,79           |
| Programmes   | 6.321,45          | 9.272,23                             | 0,00                | 15.593,68           |
| Platforms  | 47.495,45         | 67.144,26                            | 0,00                | 114.639,71          |
| Intramural Projects  | 7.317,51          | 53.387,74                            | 8.363,76            | 69.069,01           |
| External Projects  | 15.546,37         | 424.548,75                           | 478.893,49          | 918.988,61          |
| <b>TOTAL</b>   | <b>250.274,50</b> | <b>1.026.457,15</b>                  | <b>1.961.319,28</b> | <b>3.238.050,93</b> |

# Personnel

Personnel contracted during the year as of 31 December, classified by categories:

|                 | MEN       | WOMEN     | Overall Total |
|-----------------|-----------|-----------|---------------|
| Diploma holders | -         | 4         | 4             |
| Doctors         | 5         | 20        | 25            |
| Graduates       | 6         | 32        | 38            |
| Technical       | 1         | 10        | 11            |
| <b>TOTAL</b>    | <b>12</b> | <b>66</b> | <b>78</b>     |

# Significant activities

## Projects

### NATIONAL

#### Financing agency: Instituto de Salud Carlos III

Analysis of the alterations of brain connectivity in schizophrenia and their relationship with genetic variants involved in the development and function of excitatory and inhibitory neurons.

10PAFIP neuroimaging: Long-term (10-year) longitudinal study of structural cerebral changes in patients with schizophrenia spectrum psychosis.

Monitoring symptoms and signs of patients with first psychotic or affective episodes by means of a mobile phone app.

Neuropsychological function and inflammatory profile in suicidal conduct. Implication of variants of the DDR1 gene in the integrity of myelin and in the speed of cognitive processing in patients with bipolar disorder in the euthymic phase.

CIBERSAM cohort of cases with first psychotic episode and controls.

#### Financing agency: Ministry of the Economy and Competitiveness

Cannabidiol as an accelerator of the antidepressant pharmacological response: a channel towards identifying the cell mechanisms involved in depression.

The cerebral basis of language disorders in schizophrenia in the relationship with formal thought disorder (FTD) and auditory and verbal hallucinations (AVHS).

#### Other financing entities:

Implication of the Locus Coeruleus in depression and chronic pain comorbidity.

### INTERNATIONAL PROJECTS EU

Mental Health Training through Research Network in Europe (MARATONE).

Translating neuroimaging findings from research into clinical practice (PSYSCAN).

Refactoring Parallel Heterogeneous Resource-Aware Applications - a Software Engineering Approach (REPHRASE).

Psychiatric Ratings using Intermediate Stratified Markers (PRISM).

Remote Assessment of Disease and Relapse in Central Nervous System Disorders (RADAR-CNS).

### OTHER INTERNATIONAL PROJECTS

Efficacy of an Innovative E-neurocognitive Module as and Adjunct to Functional Remediation for Bipolar Disorder.

Genomic risk and resilience in 22Q11 deletion syndrome: a window into the genetic architecture of mental disorders.

Trehalose as add-on therapy in bipolar depression.

## Transfer

One of the CIBER's main objectives is to transfer the knowledge generated by its researchers in order to ensure that its research results can be developed in protocols, services and products for improving clinical practice and people's quality of life. The CIBER Technology Transfer department thus acts as a liaison between its researchers and companies, private institutions, public research centres and other innovation agents to make sure that cooperation with them is effective and that the results of research are actually implemented. Work is done in several approaches in order to achieve this aim:

- Continuous contact with our researchers in order to monitor their results and train them in managing innovation.  
A Technology Transfer Session was arranged for this purpose on 29 and 30 November 2016 as part of the 30th anniversary of ISCIII. At this event experts in different areas shared their knowledge on industrial property, company creation, licencing processes, venture capital, grants for internationalisation, etc.  
So, during the year in 2016 eleven new patent applications and a registration of software were submitted at the CIBER. Seven inventions are furthermore in the patentability study and one in the drafting stage. These are expected to be submitted in early 2017.
- Eight licence contracts have also been signed and in 2016 different negotiations were also got under way, expected to reach successful completion in the first quarter of 2017.  
Presentation of the results of research and technological capacities of our groups in technology transfer sessions. Just as an example of one of its many other measures, CIBER had a stand attended by members of institutions at BIOSPAIN 2016 (28-30 September, Bilbao).
- Support for creating technology-based companies resulting from CIBER groups.
- Other activities involving innovation, public-private cooperation and industrial and intellectual property.

## Dissemination

In 2016 the CIBER'S Communication Department carried out different dissemination and disclosure measures in order to boost the Centre's visibility, as well as to spread knowledge about the research work done by the groups in its eight thematic areas.

The main highlights of the Communication work done by CIBERSAM in 2016 are:

- **The CIBERSAM in the media:**  
67 CIBER press releases were issued this year, 11 of these from the CIBERSAM and 4 in cooperation between several CIBER areas.

| Date       | Thematic area | Holder  |
|------------|---------------|---|
| 26/01/2016 | CIBERSAM      | Identifican las zonas del genoma implicadas en la respuesta al litio en Bipolar disorder  |
| 02/02/2016 | CIBERSAM      | El riesgo genético de la Schizophreniapodría no estar relacionado con las estructuras subcorticales del cerebro   |
| 08/03/2016 | CIBERSAM      | Un proyecto europeo diseñará una herramienta de evaluación neurocognitiva que tendrá en cuenta las variables culturales                                 |
| 13/04/2016 | CIBERSAM      | Un ambicioso proyecto europeo de salud mental buscará las causas que subyacen al aislamiento social   |
| 09/06/2016 | CIBERSAM      | Proponen la realización de ejercicio físico para mejorar los síntomas de trastornos mentales graves   |
| 28/06/2016 | VARIAS ÁREAS  | Los teléfonos inteligentes y la tecnología 'wearable' pueden revolucionar la asistencia médica y la calidad de vida de personas con trastornos mentales |
| 23/09/2016 | CIBERSAM      | Celso Arango, elegido presidente del Colegio Europeo de Neuropsicofarmacología  |
| 14/10/2016 | CIBERSAM      | Identificados nuevos genes asociados al volumen del cerebro humano  |
| 16/11/2016 | VARIAS ÁREAS  | El CIBER acerca su investigación a la sociedad de la mano de la improvisación teatral en #ImproCiencia  |
| 30/11/2016 | CIBERSAM      | "Una mayor inversión en investigación reduciría sustancialmente la carga de las enfermedades mentales"  |
| 01/12/2016 | CIBERSAM      | Eduard Vieta, nombrado nuevo director científico del CIBERSAM   |

There were also 1076 appearances in the media:

| 2016     | News items | Audience   |
|----------|------------|------------|
| CIBERSAM | 1.076      | 98.875.900 |

- **CIBER Newsletter**

This year 5 CIBER newsletters were published and disseminated, including relevant content about the CIBERSAM and other thematic areas. Digital newsletters were sent to roughly 4000 subscribers.

<http://www.ciberisciii.es/en/press/newsletter>

- **CIBERSAM Newsletter**

In 2016 the CIBERSAM was got under way as a new tool for communication in this area. Every month, the newsletter contains an interview of a researcher and gives the news on the CIBERSAM for that period <http://www.cibersam.es/en/press/cibersam-newsletter>. The newsletters are currently sent to all the members of the area via e-mail.

- **CIBERSAM Web page**

In 2016 the CIBERSAM web page published 73 news items and 63 events on the agenda.

| Statistics on visits to the web site 2016 |                       |           |        |                 |                             |             |                |
|---|-----------------------|-----------|--------|-----------------|-----------------------------|-------------|----------------|
|   | No. of visits to page | Sessions* | Users  | Pages / session | Average duration of session | % rebound** | % new sessions |
| CIBERSAM                                  | 106.274               | 40.117    | 24.591 | 2,65            | 2:02                        | 61,64       | 59,78          |

(\*) Sessions: a session is a set of interactions taking place on this website in a certain period. For example, a single session may involve several pages being viewed.

(\*\*) Rebound: the rebound percentage is the percentage of sessions of a single page, i.e. the sessions in which the user has left the site on the entry page without interacting with this.

- **Social Networks**

Main indicators of the presence of the CIBERSAM on Twitter:

|          | Followers |          | Updates |          | Klout (Influence) |          |
|----------|-----------|----------|---------|----------|-------------------|----------|
|          | January   | December | January | December | January           | December |
| CIBERSAM | 909       | 1202     | 1141    | 1546     | 48                | 47       |

- **CIBERSAM Annual Report**

The CIBER Communication area coordinated the content of the CIBERSAM Report 2015 in Spanish/ English in cooperation with the CIBERSAM, drawing up and disseminating 2 reports in interactive (flipbook) format and pdf. These reports have been distributed over the web page and through the Twitter account: <http://www.ciberisciii.es/en/press/annual-report>

- **CIBER Science Week #ImproCiencia**

The #ImproCiencia dissemination event, held on 16 November in Madrid, combined science and theatre improvisation to give a light-hearted explanation of the biomedical research work done by the CIBER in its eight thematic areas. CIBERSAM presented the project: e-teaching and development of a psycho-educational programme based on the evidence of the first psychotic episodes coordinated by Dr Ana González-Pinto from Hospital Santiago Apóstol in Vitoria.

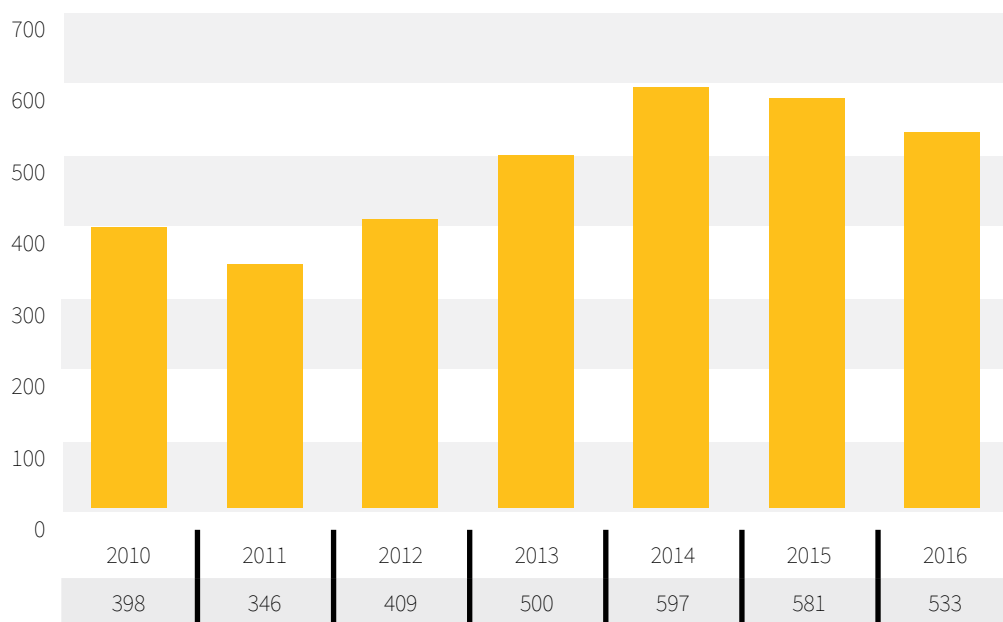
# Scientific production

## Publications

Nº OF AFFILIATED PUBLICATIONS

| Nº of affiliated publications | 2015 | 2016 |
|-------------------------------|------|------|
| Total Publications            | 581  | 533  |
| Q1                            | 355  | 326  |
| D1                            | 145  | 128  |

### EVOLUTION OF PUBLICATIONS PER GROUP FROM 2010-2016



### Most relevant publications of the CIBERSAM in 2016 by impact factor

| Publication  | Impact Factor |
|--|---------------|
| Hou L, Heilbronner U, Degenhardt F, Adli M, Akiyama K, Akula N, et al. Genetic variants associated with response to lithium treatment in bipolar disorder: a genome-wide association study. <i>Lancet</i> . 2016;387(10023):1085-93.   | 44,0020       |
| GBD 2015 SDG Collaborators. Measuring the health-related Sustainable Development Goals in 188 countries: a baseline analysis from the Global Burden of Disease Study 2015. <i>Lancet</i> . 2016;388(10053):1813-50.  | 44,0020       |
| Sekar A, Bialas AR, de Rivera H, Davis A, Hammond TR, Kamitaki N, et al. Schizophrenia risk from complex variation of complement component 4. <i>Nature</i> . 2016;530(7589):177-83.   | 38,1380       |
| De la Torre R, de Sola S, Hernandez G, Farre M, Pujol J, Rodriguez J, et al. Safety and efficacy of cognitive training plus epigallocatechin-3-gallate in young adults with Down's syndrome (TESDAD): a double-blind, randomised, placebo-controlled, phase 2 trial. <i>Lancet Neurol</i> . 2016;15(8):801-10. | 23,4680       |

| Publication   | Impact Factor |
|---|---------------|
| Franke B, Stein JL, Ripke S, Anttila V, Hibar DP, van Hulzen KJ, et al. Genetic influences on schizophrenia and subcortical brain volumes: large-scale proof of concept. <i>Nat Neurosci.</i> 2016;19(3):420-31.  | 16,7240       |
| Adams HH, Hibar DP, Chouraki V, Stein JL, Nyquist PA, Renteria ME, et al. Novel genetic loci underlying human intracranial volume identified through genome-wide association. <i>Nat Neurosci.</i> 2016;19(12):1569-82.   | 16,7240       |
| Bellon JA, Conejo-Ceron S, Moreno-Peral P, King M, Nazareth I, Martin-Perez C, et al. Intervention to Prevent Major Depression in Primary Care: A Cluster Randomized Trial. <i>Ann Intern Med.</i> 2016;164(10):656-65.   | 16,4400       |
| Mehta D, Tropf FC, Gratten J, Bakshi A, Zhu Z, Bacanu SA, et al. Evidence for Genetic Overlap Between Schizophrenia and Age at First Birth in Women. <i>JAMA Psychiatry.</i> 2016;73(5):497-505.  | 14,4170       |
| Norman LJ, Carlisi C, Lukito S, Hart H, Mataix-Cols D, Radua J, et al. Structural and Functional Brain Abnormalities in Attention-Deficit/Hyperactivity Disorder and Obsessive-Compulsive Disorder: A Comparative Meta-analysis. <i>JAMA Psychiatry.</i> 2016;73(8):815-25. | 14,4170       |
| Galling B, Roldán A, Nielsen RE, Nielsen J, Gerhard T, Carbon M, et al. Type 2 Diabetes Mellitus in Youth Exposed to Antipsychotics: A Systematic Review and Meta-analysis. <i>JAMA Psychiatry.</i> 2016;73(3):247-59.  | 14,4170       |

## Nº. of publications per group 2016

| IP                                 | TOTAL PUBLICATIONS | Q1 | D1 |
|------------------------------------|--------------------|----|----|
| Celso Arango López                 | 29                 | 21 | 11 |
| Francesc Artigas Pérez             | 12                 | 11 | 9  |
| José Luis Ayuso Mateos             | 18                 | 16 | 6  |
| Miquel Bernardo Arroyo             | 50                 | 29 | 6  |
| Julio Bobes García                 | 27                 | 11 | 7  |
| Jorge Antonio Cervilla Ballesteros | 15                 | 8  | 4  |
| Manuel Desco Martínez              | 12                 | 6  | 2  |
| Lourdes Fañanás Saura              | 14                 | 12 | 3  |
| Ana González-Pinto Arrillaga       | 30                 | 12 | 3  |
| Josep Maria Haro Abad              | 70                 | 38 | 18 |
| Juan Carlos Leza Cerro             | 12                 | 9  | 5  |
| Peter J. McKenna                   | 32                 | 24 | 14 |
| José Javier Meana Martínez         | 16                 | 13 | 2  |
| José Manuel Menchón Magriñá        | 54                 | 45 | 15 |
| Juan Antonio Micó Segura           | 9                  | 7  | 1  |
| Tomás Palomo Álvarez               | 22                 | 17 | 8  |
| Ángel Pazos Carro                  | 6                  | 6  | 6  |
| Víctor Pérez Sola                  | 51                 | 37 | 16 |
| Jerónimo Saiz Ruiz                 | 22                 | 14 | 3  |
| Julio Sanjuán Arias                | 14                 | 8  | 1  |
| Rafael Tabarés Seisdedos           | 28                 | 18 | 7  |

| IP                        | TOTAL PUBLICATIONS | Q1 | D1 |
|---------------------------|--------------------|----|----|
| Eduard Vieta Pascual      | 56                 | 43 | 21 |
| Benedicto Crespo Facorro  | 22                 | 19 | 8  |
| Miguel Casas Brugué       | 33                 | 12 | 1  |
| Elisabet Vilella Cuadrada | 11                 | 6  | 1  |

## COLLABORATIVE WORK

| Collaborative work      | 2015 | 2016 |
|-------------------------|------|------|
| IntraCIBER publications | 166  | 107  |
| InterCIBER publications | 93   | 94   |

## Clinical Guides

- *Assessment and management of agitation in psychiatry: Expert consensus.*
- *Clinical guideline for the treatment of dual pathology in the adult population.*
- *Criterios de calidad en psiquiatría Schizophrenia Depression Bipolar disorder.*
- *EPA guidance on mental health and economic crises in Europe.*
- *European Psychiatric Association Guidance on psychotherapy in chronic depression across Europe.*
- *Evidence-based guidelines for treating bipolar disorder: Revised third edition recommendations from the British Association for Psychopharmacology.*
- *From Linkage Studies to Epigenetics: What We Know and What We Need to Know in the Neurobiology of Schizophrenia.*
- *Guía de práctica clínica para el tratamiento de la patología dual en población adulta.*
- *mhGAP Intervention Guide - Version 2.0*
- *Mild cognitive decline. A position statement of the Cognitive Decline Group of the European Innovation Partnership for Active and Healthy Ageing (EIPAHG).*
- *Mood stabilizers and antipsychotics during breastfeeding: Focus on bipolar disorder.*
- *Patterns of Comorbidity of Suicide Attempters: An Update*
- *Progress in pharmacogenetics: consortiums and new strategies.*
- *Regulating gambling to prevent addiction: More necessary now than ever*
- *Spanish consensus on the risks and detection of antipsychotic drug-related hyperprolactinaemia.*
- *Standards of care for obsessive-compulsive disorder centres.*
- *Switching long acting antipsychotic medications to aripiprazole long acting once-a-month: expert consensus by a panel of Italian and Spanish psychiatrists.*
- *The International College of Neuropsychopharmacology (CINP) treatment guidelines for bipolar disorder in adults (CINP-BD-2017), part 4: Unmet needs in the treatment of Bipolar disorder and recommendations for future research.*
- *How to ensure that the diet is not a problem?: Guide for prevention of Eating Disorders in adolescents.*
- *Assessment and management of agitation in psychiatry: Expert consensus.*
- *Psychoeducation Manual for working with relatives of patients with bipolar disorder. Clinical Guides for the health system.*







# 3

## Scientific Programmes

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# Depression

Coordinator: **Víctor Pérez Sola** (Hospital de la Santa Creu i Sant Pau)

The CIBERSAM depression programme aims to carry out collaborative projects with basic and clinical researchers: from the animal model to the patient, from genetics to clinical practice, including neurochemistry and molecular biology. To this end it has integrated clinical and basic groups with extensive experience in translational research. In 2016 the different groups in the programme cooperated in publications culminating different intra and extramural projects focussing on basic research, new therapeutic targets and gene-environment interaction, neuroimaging studies and clinical assays which have enabled evaluating pharmacological and physical therapies in refractory depression. A line of research has been consolidated focussing on suicide-risk factors and on the consolidation-evaluation of specific programmes for prevention of suicidal conduct.

The research programmes are structured around three main thematic lines: epidemiology and prevention of depressive illness and suicide; neurobiological bases of mood disorders; efficacy, resistance and new therapeutic targets in depression.

The specific achievements of the programme are as follows:

Depression is one of the illnesses most connected with suicide, currently one of the main causes of death among young people. CIBERSAM researchers have published a systematic review on the effectiveness of suicide prevention strategies. The reference scale in the evaluation of suicidal conduct has been validated into Spanish as well as other evaluation instruments, including scales for evaluation of depressive and cognitive symptomatology.

On the epidemiological level, several pieces of international collaboration work were published over 2016, focussing on evaluation and risks of not performing a proper treatment in depressive patients and on the possible consequences of the economic crisis in the prevalence of depression. Different groups in the programme form part of international consortiums which this year published some important findings stemming from GWAS in patients with major depressive disorder, recurrent depression and obesity.

One of the most active lines in the programme is the one studying the relationship between inflammatory processes and depressive symptomatology, as well as its relationship with different drugs inducing depressive symptomatology such as interferon and the use of anti-inflammatory drugs as possible therapeutic targets in the treatment of this illness. The CIBERSAM groups investigating the neuroanatomical and functional basis of mental illness by means of neuroanatomical and/or neuroimaging methods have published relevant findings as studies relating structural and functional neuroimaging with vulnerability/resilience, cognition or evolution of medium-long-term depressive illness and a review which will become a benchmark in the area on the cerebral circuits implicated in mental illness.

If any of the different lines of research of the programme constitute its core this is doubtlessly the one studying new therapeutic targets and the evaluation of efficacy and safety of treatments. In 2016 different groups published results of several international clinical trials and studies focussing on the neurobiological bases of treatment such as deep brain stimulation or ECT, and put into practice therapeutic proposals such as the use of ayahuasca, cannabidiol or low-intensity psychotherapies. In 2016, the analysis of the DEPRES study was also completed - one of the most ambitious intramural projects of the CIBERSAM - in which a controlled Clinical Trial was used to find out which is the best therapeutic option in a sample of 250 patients resistant to anti-depressive treatment. As regards functionality and quality of life, we went on with the line of research centring on interventions to improve psychosocial difficulties in depression.

# Schizophrenia

Coordinator: **Julio Sanjuán Arias** (Universidad de Valencia)

Some of the most notable results of the programme in 2016 that we could mention are the publication of 116 scientific articles, most of these (n=68; 59%) published in first quartile journals according to the Journal Citation Reports (JCR). It should be mentioned that 28 articles (23%) were published in first decile journals, mostly in the categories of Neurosciences and Psychiatry, and including Nature, Nature Neuroscience, JAMA Psychiatry, American Journal of Psychiatry, Cerebral Cortex, Neuroscience and Biobehavioral Reviews, and Schizophrenia Bulletin.

As regards projects carried out by the members of the programme, we should give special mention to the participation of several CIBERSAM groups in European projects including: METSY, PSYSCAN, PRISM, m-RESIST; as well as obtaining financing in national competitive public calls (ISCIII and MINECO) and other regional ones. Over this year the Cohorts-CIBERSAM project financed by the ISCIII was got under way, with the participation of 13 CIBERSAM groups. We should also stress the proper development of both the CIBERSAM first episodes project (PEPs PI 080208), currently in the stage of exploiting the data and publishing this, and of the Integrated Projects of Excellence (ISCIII) (PIE14/0003) in the stage of completing the collection of samples and preliminary analyses.

Mention should also be given to obtaining Human Resources contracts: researchers in SNS Miguel Servet I (1; G11), Miguel Servet II (1; G15), Sara Borrell (1; G15), predoctoral training contract in research (ISCIII) (1; G15), Juan de la Cierva (1; G15), Juan Rodés contract (1; G01), Ramon y Cajal (1; G19) and Río Hortega Post Specialised Healthcare Training Contracts (1; G26).

The granting of 1 patent on nationwide level should also be mentioned.

The great presence of CIBERSAM groups in major international consortiums engaged in the investigation of genetic aspects (Psychiatric Genetic Consortium) and Neuroimaging-Genetics (ENIGMA) in schizophrenia is also an aspect to be stressed.

In 2016 we can highlight the development of impact research in the following lines:

- The development of clinical trials intended to display the effectiveness of non-pharmacological treatments in schizophrenia.
- Clinical research tackling clinical issues of relevance in the treatment and care of patients with schizophrenia.
- The study of the effects of antipsychotic medication on the physical health of patients.
- Cognition and schizophrenia: biological markers and therapeutic strategies.
- Study of the importance of inflammatory processes in schizophrenia and cognitive aspects.
- The study of metabotropic glutamate receptors and of the mGLu2/5-HT2A complex as potential objectives of new antipsychotic drugs.
- The search for (genetic and neuroimaging) biomarkers associated with the illness and specific clinical aspects from the initial stages of the illness.

# Bipolar Disorder

Coordinator: **Eduard Vieta Pascual** (Hospital Clínico y Provincial de Barcelona)

Some of the most relevant results of the groups forming this programme are the 28 articles in the first decile. The findings of these studies have been published in journals of the greatest reputation such as The Lancet, Molecular Psychiatry, Biological Psychiatry, British Journal of Psychiatry, Psychological, Medicine, Schizophrenia Bulletin and Acta Psychiatrica Scandinavica, amongst others.

The bipolar disorder programme works with a high degree of internationalisation and scientific productivity. In 2016 we should stress the cooperation work between CIBERSAM groups and other CIBERS, as well as national and international collaboration.

The groups in the bipolar programme have furthermore carried out 16 projects in 2016 with competitive financing from public bodies (MINECO- Instituto de Salud Carlos III, Basque Authority, Universidad del País Vasco, Generalitat Valenciana).

Some of the awards and distinctions received by members of the programme are detailed below:

- 1st prize for the best international articles at the Jornadas de Investigación 2016 of the Hospital Universitario Araba: Efficacy and safety of ketamine in bipolar depression: a systematic review Susana Alberich, Mónica Martínez-Cengotitabengoa, Purificación López, Iñaki Zorrilla, Nuria Núñez, Eduard Vieta and Ana González-Pinto. Revista de Psiquiatría y Salud Mental 2016 Jul 4.
- Award for the best poster presentation in Neuropsicofarmacología of the SEPB. XIX Congreso Nacional de Psiquiatría. Is lithium able to prevent depressive/mixed episodes in real life? Results after 10 years' follow-up. Dr Mónica Martínez-Cengotitabengoa.
- Dr Ana González-Pinto was appointed president of the Sociedad Española de Psiquiatría Biológica (SEPB) and head of the bipolar disorder area of the CIBERSAM.
- Prize for Accredited Young Investigator, Sociedad Española de Psiquiatría Biológica going to Dr Iñaki Zorrilla.
- Prize for Accredited Young Investigator, Sociedad Española de Psiquiatría Biológica going to Dr Iria Grande.
- Dr Eduard Vieta, new scientific director of the CIBERSAM.
- Early career psychiatrists Scholarship Programme, European Psychiatric Association going to Dr Iria Grande.
- Honoris Causa award from the Universitat de Valencia going to Dr Eduard Vieta.
- Eduard Vieta appears in the list of researchers in the biomedical world most cited in scientific publications (Highly Cited Researchers 2016), which is drawn up by international agency Thomson Reuters, 2016.
- In 2016, the Acadèmia de Ciències Mèdiques de Catalunya i Balears awarded the Josep Trueta Prize for Scientific Research 2016 for scientific development and leadership to the Fundació FIDMAG Hermanas Hospitalarias.

Some of the more significant scientific achievements by the different groups in the programme are:

- Validation of the psychometric instrument (Strauss-Carpenter) for its use in bipolar disorder.
- Follow-up of patients with first bipolar episode: study of the prognosis, functionality and inflammatory factors.
- Diagnostic discrimination between Alzheimer's disease and late-onset Bipolar Disorder.
- Participation in the publication of the clinical guide of the WHO mhGAP versión 2.0: This is an update of the WHO guide for treatment of mental and neurological disorders and substances in non-specialised care ([http://www.who.int/mental\\_health/mhgap/en/](http://www.who.int/mental_health/mhgap/en/)).
- Activation of the web page [www.bipogent.cat](http://www.bipogent.cat) intended to give information and recruit patients and controls for the study financed by the ISCIII and CIBERSAM.
- Holding the II Intensive Course on Neurocognitive and Functional Evaluation of Patients with Serious

Mental Disorders of the CIBERSAM.

- Demonstration of how functional rehabilitation improves the autonomy and general functions of patients with bipolar disorder in the long term.
- International collaborative study in which genetic variants associated with the response to treatment with lithium in bipolar disorder are found.
- Preparation and publication of several international clinical guides on treatment for bipolar disorder.
- Preparation and publication of an international consensus document for evaluation and handling of agitation in psychiatry.
- Participation in the publication of results of the 2015 edition of the Global Burden of Disease Study in such prestigious journals as The Lancet.
- Preparation of a guide/consensus with the European Psychiatric Association (EPA) - Working Group on Mental Health Consequences of Economic Crises of the EPA Council of National Psychiatric Associations. EPA guidance on mental health and economic crises in Europe”.
- Continuation of the project on “Comorbidity between Cancer and Central Nervous System Disorders. This is a collaborative meta-analysis in 5 countries (Spain, Canada, Australia, United Kingdom and the United States).
- Effectiveness and safety of tobacco withdrawal by means of transdermal nicotine patches and varenicline in patients with schizophrenia and bipolar disorder.



# Therapeutic Innovation

Coordinator: **Francesc Artigas Pérez** (Agencia Estatal Consejo Superior de Investigaciones Científicas)

As some of the most relevant results in 2016 achieved by the groups in the programme we could highlight: the publication of one patent (WO2016/020573: Method for monitoring anti-psychotic treatment) and the publication of around 35 articles in 1st decile journals. Some of these were publications in diverse journals of the Nature group such as Nature Reviews Drug Discovery (FI:47.12), Nature (FI:38.138), Nature Neuroscience (FI:16.724) and Nature Communications (FI:11.329). Different articles have also been published in other leading journals in the field, such as JAMA Psychiatry (FI:14.417), Molecular Psychiatry (FI:13.314), Cerebral Cortex (FI:8.285) and Neuroscience & Biobehavioral Reviews (FI:8.58). A large percentage of these publications are multi-centre, due to the existence of intra-CIBER cooperation (CIBERSAM and other CIBERs), as well as national and international cooperation. Apart from this, some prior articles of the groups in the programme are considered as being highly cited papers according to the Web of Science.

Apart from this, the groups in the programme continue to be particularly active in recruiting resources, having obtained 21 competitive projects in 2016 from public bodies (MINECO/FEDER: SAF2015-67457-R, SAF2015-68346-P, SAF2015-68436-R, SAF2015-68647-R, SAF 2016/75500-R, SAF2016-75797-R, SAF2016-76046-R and DPI2016-79075-R; FIS/ISCIII: PI15/00283, PI15/00330, PI15/01246 and CM16/00034; UCM: PR26/16-11B2 and PR26/16-20278) and from different national foundations (FIPSE, Fundación Mapfre and Fundación Alicia Koplowitz) and international bodies (Brain & Behavior Research Foundation).

Some of the awards and distinctions received by members of the team were:

- Prize for Accredited Young Investigator (SEPB) and Early career psychiatrists Scholarship Programme (EPA), going to Dr Iria Grande.
- Appointment of Dr Eduard Vieta as new scientific director of the CIBERSAM.
- Dr Eduard Vieta appears in the list of researchers in the biomedical world most cited in scientific publications (Highly Cited Researchers 2016), drawn up by international agency Thomson Reuters.

Some of the scientific achievements obtained by the different groups in the programme that we could highlight are, amongst others:

- International collaborative study in which genetic variants associated with the response to treatment with lithium in bipolar disorder are found.
- Drawing up and publishing several international clinical guides on treatment for bipolar disorder and an international consensus document for evaluation and handling of agitation in psychiatry.
- Development of novel strategies using RNA interference for studying the physiopathology and treatment of neuropsychiatric affections, including major depressive disorder and Parkinson's disease.
- The study of the action mechanism of fast-acting anti-depressants, including glutamatergic drugs, such as ketamine.
- Identification of neuronal networks after deep brain stimulation in an animal model of schizophrenia.
- Description of mechanisms for stimulation of innate immunity in schizophrenia in animal and human models and its modulation by antipsychotics.
- Identification of the effects of chronic administration of benzodiazepines and D2 dopamine receptor agonists on the structure of prefrontal cortex neurons.
- Discovery of the implication of the expression of neurexin-2 of prefrontal cortex on the attention deficits induced by peripubertal stress.
- Identification of genetic markers of schizophrenia and of the volume of subcortical structures.

# Mental Disorders of the Child and Adolescent

Coordinator: **Josefina Castro Fornieles** (Hospital Clínic de Barcelona)

The programme for mental disorders of the child and adolescent set up in 2010, it is made up of six CIBERSAM groups (G01, G04, G07, G08, G24 and G27) and has the aim of studying mental disorders with onset in childhood and adolescence.

Some of the most noteworthy outcomes of the programme's work in 2016 are a number of 79 publications mostly in journals indexed in the first quartile according to the JCR, including the British Journal of Psychiatry, Acta Psychiatrica Scandinavica, Psychological Medicine or Human Brain Mapping. This represents a 17% increase in respect of the previous year. It should be highlighted that 19 of these works were published in first decile journals mostly in the categories of psychiatry (37%) and paediatrics (26%).

As regards the projects carried out by the members of the programme, we should mention the groups' participation in nine European projects, including: METSY, PSYSCAN, PRECIOUS, MATRICS, AGGRESSOTYPE, PreDICT-TB or APUS-eCig, as well as obtaining regional and national financing. The Instituto de Salud Carlos III (ISCIII) issued grants for carrying out a total number of 25 projects connected with psychotic disorders with onset in childhood and adolescence, bipolar disorder, the risk of psychosis, obsessive-compulsive disorder, autism spectrum disorder, child abuse or early onset depression.

Some of the scientific achievements accomplished in 2016 are:

- The clinical, neuropsychological, neuroimaging and genetic characterisation of children and adolescents with a high genetic risk of schizophrenia or bipolar disorder.
- The study of the role of genetic and epigenetic variants in the clinical improvement of children treated with fluoxetine.
- The creation of a predictive model of the severity of obsessive-compulsive disorder based on genetic, cognitive and neuroimaging variables.
- Study on the role of cognitive variables in high-functioning autism.
- The study of the effects of anti-psychotic medication in weight gain and hormones in children and adolescents, as well as the study of the extrapyramidal symptoms which these could cause.
- The development and validation of specific scales for the child and juvenile population valuing obsessive-compulsive symptomatology and the risk of suicide.
- The study of pharmacogenetics of methylphenidate in treatment of Attention Deficit Disorder.
- The study of the role of the childhood trauma in different psychiatric pathologies.

# Psychosomatic, Anxiety and Impulse Control Disorders

Coordinator: **José Manuel Menchón Magriña** (Fundación IDIBELL, Hospital Universitario de Bellvitge)

This programme has the characteristic feature of covering different lines of research representing the activities of one or several of the groups in the programme. Some of the most significant activities are detailed below.

In the field of new physical therapies, specifically in deep brain stimulation, studies have been published on their application in different disorders, molecular and cell mechanisms have been studied, a project has been granted for their study in nervous anorexia and an international clinical test has been concluded in obsessive-compulsive disorder.

Apart from this, new therapeutic strategies have been explored such as mindfulness in impulsiveness of Borderline Personality Disorder (BPD) or in fibromyalgia. Another therapeutic strategy examined in BPD by several groups in the programme was cognitive rehabilitation and the use of long-lasting injectable drugs.

From a transdiagnosis perspective, impulsiveness has been studied in different disorders, such as the pathological game, addictions to substances, borderline personality disorder or attention deficit disorder. These last two disorders were also covered by studies of their association with a record of child abuse.

The study line of neuroinflammation in mental disorders has examined its alterations and modulation in different disorders. We should stress the study on modulation of anti-inflammatory drugs in deep brain stimulation as well as immunological aspects of the innate immune response in neuropsychiatric diseases.

In the area of the relationship between mental disorders and chronic pain noradrenergic mechanisms have been studied, particularly the role of locus coeruleus as a key factor in this comorbidity. On a more clinical level the use, satisfaction and impact of mental health-chronic pain comorbidity in the health system has been studied.

As regards the line of neurocognitive disorders and in particular, mild cognitive impairment, studies have continued for analysing conversion into dementia according to DSM-5 criteria or according to Petersen criteria, epidemiological studies on prevalence in this country and the associated factors, as well as the study of the apathy symptom on both clinical level and as regards structural imaging with magnetic resonance.

The neuroimaging field has performed a large number of studies and has taken part in international consortiums such as ENIGMA and TOC as well as in the International OCD Brain Imaging Consortium.

The epidemiological studies line has been highly active, with numerous studies covering not only European but also Asiatic and Latin-American countries. Some of the more noteworthy studies and projects carried out are on factors associated with suicidal conduct such as solitude, studies on determining factors of the quality of life and subjective well-being, factors associated with mental health, patterns of multi-morbidity, mortality, disability and social stigma in different countries. This angle has enable the group most involved in these studies to make proposals and discuss the priorities of research into mental health in Europe in a publication. Financing has recently been obtained for a project for analysing big data on mortality and comorbidity in mental disorders.





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Transversal  
Programmes

# European Programmes and International Relations

Coordinator: **José Luis Ayuso Mateos** (Hospital Universitario La Princesa)

## Main accomplishments in 2016:

- The two projects obtained in the Innovative Medicines Initiative of H2020 in which CIBERSAM is taking part have started to be implemented. These are the PRISM (Psychiatric Ratings using Intermediate Stratified Markers) and RADAR-CNS (Remote Assessment of Disease and Relapse in Central Nervous System Disorders) projects.
- In September the CIBERSAM organised the meeting for completion of the MARATONE (Mental Health Training through Research Network in Europe) project at the Escuela Nacional de Sanidad, which was attended by researchers from the 14 institutions belonging to this specific Marie Curie network on mental health.
- 260 articles were published in cooperation with international teams and researchers. This figure represents 48.96% of the total number of 531 articles published in 2016 with CIBERSAM affiliation.
- Recruitment of international researchers for stays at CIBERSAM groups.
- Carrying out doctorate courses with European mention by researchers contracted by and attached to the CIBERSAM.
- Participation of CIBERSAM in advisory committees and assessment committees.

## Active European/international projects in which CIBERSAM took part during 2016:

- *MARATONE | Mental Health Training through Research Network in Europe. G03, G11 (IPs Ayuso y Haro).*
- *PSYSCAN| Translating neuroimaging findings from research into clinical practice G01, G26 (IPs Arango y Crespo).*
- *RFA-MH-120 | Genomic Risk and Resilience in 22q11 Deletion Syndrome: A Window into the Genetic Architecture of Mental Disorders. (Collaborative RO1-NIH). G01- IP C. Arango.*
- *RePhrase - REfactoring Parallel Heterogeneous Resource-Aware Applications - a Software Engineering. G07- IP M. Desco.*
- *IMI2 – PRISM – Psychiatric Ratings using intermediate Stratified Markers: providing quantitative biological measures to facilitate the discovery and development of new treatments for social and cognitive deficits in Alzheimer Disease, Schizophrenia, and Major Depression. G01, G25 (IPs Arango y Vieta).*
- *IMI2 – RADAR-CNS – Remote Assessment of disease and Relapse in Central Nervous System Disorders. G11- IP Haro.*
- *Predicting Response to Depression Treatment obtenido en convocatoria de H2020-SMEINST- 1-2014. G21- IP Pérez.*

## European projects in which CIBERSAM is taking part which were granted in 2016:

- *TREATMENT: Training European Network: Metabolic Dysfunctions associated with Pharmacological Treatment of Schizophrenia.*
- *ITN MARIE CURIE - H2020-MSCA-ITN-2016 (P López, G03).*

# Quality Programme and Internal Assessment

Coordinator: **Dr. Rafael Tabarés-Seisdedos** (Universidad de Valencia)

The CIBER is accredited and complies with the requisites contained in ISO 9001:2008 standard in administrative procedures and Biobanks. In this improvement context, assessment becomes necessary and CIBERSAM'S structure, processes and scientific production were evaluated in 2016.

Structure. This takes into account the qualification, technological capacity, infrastructure, economic-administrative organisation, management of material and human resources.

Processes. This stresses accomplishing the mission of the CIBER, the relevance of the work done on national and international scales and consistency in planning, dissemination and disclosure of the results.

Scientific production. Production is appraised in relation with the resources available, the number of publications, patents and evolution over time.

## Indicators for 2016

|   | Situation Indic. 2015           | Objective for 2016 | Situation in 2016             | Observations   |
|---|---------------------------------|--------------------|-------------------------------|--|
| Number of improvement areas detected.   | 3                               | 3                  | 3                             | "Santiago Reig" award for incentives for CIBERSAM contracted staff (best publication as first signatory).  |
|   |                                 |                    |                               | New CIBERSAM training courses: "Critical reading course" and "I Meta-Analysis Course".   |
|   |                                 |                    |                               | Performance of improvements on the GRIDSAM database.   |
| Number of preventive actions implemented.   | 2                               | 2                  | 1                             | Design of an application for performing psychopathological exploration.  |
| Number of internal satisfaction surveys performed *.                                      | 1                               | 1                  | 1                             | Satisfaction survey on Attached CIBERSAM staff.  |
| Number of external satisfaction surveys performed.  | 1                               | 1                  | -                             | The survey on laboratories is not taken because it is decided to eliminate this as an objective for the new Strategic Plan 2017-2019, due to problems in change of human resources of laboratories and impossibility of carrying these out properly. |
| Number of analyses of surveys.  | 2                               | 2                  | 1                             | Satisfaction survey on Attached Staff. The Satisfaction surveys of pharmaceutical laboratories were not analysed as there was no participation (this survey is eliminated in the new Strategic Plan).  |
| Percentage of surveys on internal users out of the total number of surveys performed      | Contracted staff surveys<br>46% | (+5%)              | Contracted staff surveys<br>- | Calculation of the increase in percentage is not applicable because the survey on contracted staff was not issued in 2016.   |
|   | Attached staff surveys<br>-     | (+5%)              | Attached staff surveys<br>21% | Calculation of the increase in percentage is not applicable through being the first year in which the attached staff survey is issued.   |
| Percentage of surveys on external users answered out of total number of surveys performed | 40%                             | >80%               | -                             | It is decided to remove the laboratory survey as an objective for the new Strategic Plan 2017-2019, due to problems in change of human resources of laboratories and impossibility of carrying these out properly.                                   |

\* Survey on contracted CIBERSAM staff in 2015 and a survey on attached CIBERSAM members in 2016.

# Institutional Relations and Communication Programme

Coordinator: **Julio Bobes García** (Universidad de Oviedo)

**V Foro Internacional en Esquizofrenia.** On 24 and 25 November 2016 the International Schizophrenia Forum was held at the Ateneo de Madrid, arranged by CIBERSAM. 174 persons attended this edition of the Forum, including twenty-four Spanish and international neuroscience leaders, as well as representatives of patients and relatives.

Some of the guests reported their information in debate form, giving priority to thematic areas in research into psychosis, with the participation of a representative of patients' groups, relatives, epidemiologists, basic and clinical researchers. There were three plenary lectures, given by guests from Dublin, Rotterdam and Utrecht who spoke on What occurs 15 years before the first psychotic episode? (Mary Cannon); Studies of cohorts, what information can these give that is not answered by other studies? (Henning Tiemeier) and Optimising the treatment of the first episode of schizophrenia (Renè Kahn).

Apart from this, three round tables were held on research into schizophrenia at the CIBER de Salud Mental (CIBERSAM), on the white substance and psychosis and the third on biomarkers in psychosis and personalised medicine.

The balance obtained was also highly positive this year, for which reason the Forum continues to become consolidated as one of the annual events of greatest interest for Spanish neuroscientists. The Annual Meeting of CIBERSAM Principal Investigators was held in the evening on Friday 25.

At the end of November there was also the **Encuentro entre Investigadores en Salud Mental, Pacientes y Familiares**, jointly arranged by the Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM), the Fundación Española de Psiquiatría y Salud Mental (FEPSM), Mundo Bipolar and the Confederación Salud Mental España.

At this encounter, sponsored by Lundbeck and held at the Escuela Nacional de Sanidad del Instituto de Salud Carlos III in Madrid, an open debate was set up in which CIBERSAM researchers gave an informative explanation on the current situation in mental health research to patients and the people around them, at the same time as taking note of their suggestions for the research to be practical and provide them with real improvements in their quality of life.



# Training and Mobility Programme

Coordinator: **Ángel Pazos Carro** (Universidad de Cantabria)

The CIBERSAM has since its beginnings given a Training Programme which sets out to be a reference in the training in mental health in this country.

The backbone of this Programme is the **Official Master Course on Initiation to Mental Health**, which started to be given in academic year 2013-2014. As well as the Master course, the possibility of financing is considered for attendance at other courses connected with different areas of work, preferably the ones offered by the CIBERSAM. Research stays are also financed at other CIBERSAM Units, at other CIBERs, or abroad.

The Master Course on Initiation to Mental Health is an inter-university programme offered by the Complutense, Barcelona, Autónoma de Barcelona, Cadiz and Cantabria Universities and is coordinated by the latter. 11 CIBERSAM groups officially participate in the teaching and a further 6 are indirectly involved.

The Master Programme (worth 60 credits) is characterised by having a major virtual component as well as through the required practical stays, of both clinical and basic nature. It tackles both aspects of research foundations and the neurobiological bases and diagnostic, clinical and therapeutic approaches.

In 2016 all the courses for the second four-month term of the third edition (2015-2016) were given. In the last quarter of the year the first subjects of **the fourth edition also started to be taught**, in-class and online teaching.

There are 37 students enrolled for this fourth edition, currently under way. They come from all over Spain, with 3 students from abroad, all with different training profiles (medicine, psychology, biology, etc.).

As regards financing from the Programme, CIBERSAM has agreed to reserve a significant part of its Training budget for partial financing of researchers' participation in the Master. In its third edition, a total number of 3 groups benefitted from the partial grant for the enrolment fee, while in the fourth edition 4 groups were beneficiaries.

Aside from the Master, the Training Programme has financed 20 attendances at a total number of 14 training activities and courses for members of the CIBERSAM. 18 of these took place in Spain (9 at courses directed by its groups) and 2 abroad. The large numbers attending Intensive Courses on Introduction to Neurosciences and the Ideas Laboratory should be stressed.

4 stays were furthermore financed for CIBERSAM members, 3 in Spain (at other CIBER groups) and the rest abroad.





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Platforms

# Common Database

Platform Committee: **Julio San Juan** (coordinator), **Celso Arango**, **Elisabeth Vilella** y **Benedicto**

**Crespo-Facorro**. In cooperation with the Universidad Politécnica de Valencia.

- The common data platform continues to advance with an increment of 2443 new cases and 23,409 new forms in 2016. The total number of cases stored is 29,078 and these represent 135,177 forms.
- 2 new cooperation projects have been completed (iFightDepresion and MARIDE) and a further 2 projects are in the development and negotiation stages. At the present time there are 18 visible subprojects with different levels of development. A total of 15 CIBERSAM groups have provided data for the platform.
- New functions have been validated, such as the possibility of sending links for the patients to be able to fill in forms, and the new projects have been developed with a new technology (bootstraps) providing a more updated visual appearance. We continued with support for users, having received a large number of suggestions and updates for the forms implemented.
- On the operative level, the uninterruptible power supply has been changed, thus managing to keep the application active throughout the year.





# Mental Health Instruments Library

Platform Committee: **Josep Maria Haro** (coordinator), **Ana González-Pinto**, **Eduard Vieta**,

**José Luis Ayuso**, **Julio Bobes** y **Celso Arango**

The Platform of the Instruments Bank provides information and service for researchers on questionnaires and instruments for assessment in mental health. The Bank currently has 320 instruments in different fields of interest.

Some of the activities carried out in 2016 are:

- **Dissemination:**

After completion of the cooperation agreement established with pharmaceutical company Otsuka in 2015, the instruments bank currently receives no financing whatsoever. In 2016 several contacts were started with the pharmaceutical industry and other companies and institutions in order to go on fostering the development and dissemination of this platform.

- **Methodological advice:**

External and also CIBER network researchers interested in designing studies, validating instruments, using questionnaires or analysing derived data have requested this service. In all, 19 enquiries were dealt with in 2016.

- **Instrument repository:**

Incorporation of 22 new instruments and updating of 100 of the datasheets previously included.

- **Ongoing updating of the web page:**

Incorporation of information on statistics about its activity on the web page: visits counter, origin, average time the session lasts, etc. Since early 2016, the web page has had 6606 visits from 4353 users in Spain, Mexico, the United States, Russia, United Kingdom and several Latin-American countries, amongst others.

The different sections of the web page were updated, including publications stemming from projects financed in the different calls for projects from the Instruments Bank, checks made on instruments, updating of search filters, ongoing updating of news items, amongst others.

- **Holding the VII Workshop formativo del Banco de Instrumentos (14-15 June 2016):**

These sessions focussed on learning techniques for developing and validating instruments, as well as on training and application of scales of mental health in the clinical domain. They also provided a chance to swap and pool the developments and initiatives of other researchers from the network and their groups about procedures for validating instruments. At this event the contributions made by projects financed by the Instruments Bank should be stressed.

- **Projects completed and scientific work stemming from the VI Convocatoria intramural de ayudas para proyectos de investigación:**

Half of the projects financed in the last call successfully completed their validation study. The five remaining ones are developing or extending their work until June 2017.

Up to now, 68 publications have resulted from the successive calls. In 2016 4 scientific articles were published and 4 pieces of work were presented at Congresses and Workshops as a result of the projects financed by the Instruments Bank.

# DNA Collection

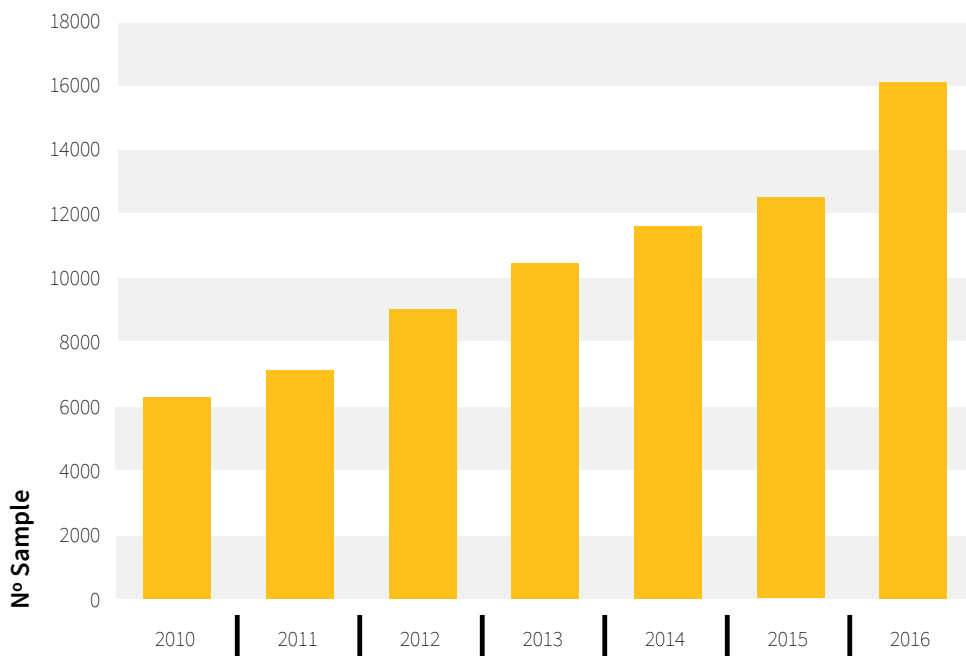
Platform Committee: **Celso Arango** (Coordinator), **Lourdes Fañanás**, **Julio Sanjuán**, **Jorge Cervilla** and **Javier Meana**

- At the end of 2016 a volume of 16,213 samples had been deposited at the repository for collections of samples. These are mainly from patients with schizophrenia, affective disorders, autism spectrum disorders, bipolar disorder and controls.
- Over the year 2016, a total of 3601 samples were deposited, 1961 of which are new samples of patients and controls, while the remaining 1640 are samples that were already deposited at the platform but which were sent and processed again to obtain further stock, so as to be able to guarantee sufficient availability of DNA for future projects. This last year's samples were supplied by 3 CIBERSAM groups. The following table sums up the collection activity over the year in 2016:

| Group | PI depository     | No. of samples |
|-------|-------------------|----------------|
| G01   | Celso Arango      | 2043           |
| G04   | Miguel Bernardo   | 300            |
| G28   | Elisabeth Vilella | 1258           |
|       | Total             | 3601           |

- As in previous years, the number of samples has grown, continuing to develop positively, as can be seen from the table:

## ACCUMULATIVE TABLE OF SAMPLES



- In 2016 samples from the collection were assigned to be part of different genetic research studies. The most noteworthy of these is the cooperation with the Psychiatric Genomics Consortium (PGC), to which around 3000 samples of patients diagnosed with schizophrenia and healthy controls were sent. 9 groups belonging to the CIBERSAM took part in this project and contributed samples to this.

# Brain Samples

Platform Committee: **Javier Meana** (coordinator), **Josep Maria Haro** and **Ángel Pazos**

Over the year 2016, the Platform defined its status as an external platform. At the current time the organisations linked with the CIBERSAM with repositories for brain samples are:

- Banco de Tejidos Neurológicos | Fundación Sant Joan de Dèu, Barcelona
- Biobanco Valdecilla | Instituto de Investigación Sanitaria IDIVAL, Santander
- Colección de muestras cerebrales | Universidad del País Vasco UPV/EHU, Leioa, Bizkaia

Its standard activities for obtaining, storing and assigning samples have also resumed.

- Samples from several regions of the brain have been incorporated (prefrontal cortex, hippocampus, cerebellum, basal ganglia) from 42 subjects with prior psychiatric diagnosis or controls.
- The total number of different subjects whose samples were stored in late 2016 was 1072, mainly from cases of schizophrenia, depression, bipolar disorder, opioid or alcohol use disorder as well as controls. The controls represent roughly 45% of the subjects.
- Samples were assigned to three CIBERSAM groups and a further three groups have made enquiries about the availability of samples.
- The platform assigned samples to five international groups outside the CIBERSAM.
- 7 international publications have been generated in Q1 journals with studies which used samples from the Platform.
- The platform took part in the Jornada de Plataformas CIBERSAM (June 2016) intended for preparing the Strategic Plan.

# Neuroimaging Platform

Platform Committee: **Manuel Desco** (coordinator), **Joost Janssen**, **N. Bargalló**, **Josep Maria Haro**, **Raymond Salvador**, **Julio Sanjuan** and **Benedicto Crespo-Facorro**

At the present time over 30 national and international projects are making use of the Neuroimaging Platform. The fixed resources are located at the Medical Imaging Laboratory, Experimental Medicine and Surgery Unit of the Hospital General Universitario Gregorio Marañón in Madrid. This neuroimaging bank manages around 18 users from different centres and cooperates with around ten groups.

- In 2016 images of 265 new subjects were added to the database of this scientific structure, extending this to a total number of 3305 subjects stored. The total number of images which the Neuroimaging Bank has available comes to 14,3698 (64% more than in 2013).
- In spite of the processing of the images stored being dissociated from this platform, the platform processed a total number of 378 studies over the year in 2016 (25% more than in 2013), belonging to longitudinal projects under way.

As well as the work done for maintenance and optimisation of the present image server (Dicomserver), one of the main measures to be carried out in this platform this year was to develop a new tool for management and storage of neuroimages. The software infrastructure of the platform is based on the XNAT programme, which has the following features:

- Open code allowing personalisation.
- Full DICOM integration.
- Security with control of access privileges and anonymization of images.

- Associated database to facilitate searching for and obtaining data.
- Modular extendibility enabling new functions to be incorporated.

The fixed hardware resources are currently located at the Medical Imaging Laboratory, Experimental Medicine and Surgery Unit of the Hospital General Universitario Gregorio Marañón in Madrid. Along with the change in the tool for management of the platform over this year the architecture required to move the physical resources of the platform to a cloud environment, specifically Amazon Web Services, was implemented. This change will mean greater control over the maintenance costs of the server, an increase in security in both access to the resources and in control of the premises and a minimisation of expenses for updating equipment. The simple scalability of the instances, depending on the requisites of the platform, is another of the major advantages that will be obtained with this change of resources to the cloud.

In 2016 work was done on developing better monitoring of the resources in the new platform. This is going to enable using new indicators to more efficiently reflect the use that can be made of this platform at CIBERSAM. The new indicators will be:

- Number of sequences (total number of images stored).
- Number of applications for use.
- Number of groups (CIBERSAM or others) providing images.
- Number of groups making use of the images stored.

This change in indicators is another of the major accomplishments that were attained in 2016 and will start to be used as soon as the new tool is implemented.

The migration from the old platform to the new one is expected to take place in the first quarter of 2017.




# 6


## Research Groups



LEAD RESEARCHER

**Arango López, Celso**

 **Servicio Madrileño de Salud**  
Hospital Gregorio Marañón  
Pab. del Instituto de  
Investigación Sanitaria (IISGM).  
Ent. C/Maiquez, Nº 9,  
Mod. Prefabricado a la drcha.  
del Edif. de Medicina y Cirugía  
Experimental  
28009 Madrid

 (+34) 91 426 50 17  
(+34) 91 586 81 33

 carango@hggm.es

 [Group website](#)

PROGRAMMES

**Child and Adolescent Psychiatry**  
**Schizophrenia**



## GROUP MEMBERS

**Staff members:** Barcenilla González, Miguel Angel | Del Rey Mejías, Ángel Luis | Hernández Álvarez, Fabián | Merchán Naranjo, Jessica | Morán Moya, Purificación | Rapado Castro, Marta | Recio Lamparero, Sandra | Rodríguez Latorre, Pamela | Tapia Casellas, Cecilia

**Associated members:** Boada Muñoz, Leticia | De Portugal Fernández, Enrique | Espliego Felipe, Ana | Fraguas Herráez, David | Graell Berna, Montserrat | Janssen Jeucken, Joost | Llorente Sarabia, Cloe | Martínez Díaz Caneja, Covadonga | Mayoral Aragón, María | Moreno Pardillo, Dolores María | Moreno Ruiz, Carmen | Parellada Redondo, María José | Penzol Alonso, María José | Pina Camacho, Laura | Rodríguez Martínez, Kenia | Romo Villa, José

**Contributors:** Corral Zarapuz, Azucena

## Main lines of research

- First episode psychosis.
- Autism Spectrum Disorders.
- Neurodevelopmental neuropsychopharmacology.
- Neuroimaging in psychiatric disorders.
- Cognition in psychiatric disorders.
- High risk population studies.
- Schizophrenia.
- Bipolar Disorder.

## Most relevant scientific articles

- FUSAR-POLI P., DIAZ-CANEJA C.M., PATEL R., VALMAGGIA L., BYRNE M., GARETY P. ET AL. Services for people at high risk improve outcomes in patients with first episode psychosis. *Acta Psychiatrica Scandinavica*. 2016;133(1):76-85.
- ARANGO C, FRAGUAS D. Should psychiatry deal only with mental disorders without an identified medical aetiology? *World psychiatry: official journal of the World Psychiatric Association (WPA)*. 2016;15(1):22-3.
- BONNIN C.M., TORRENT C., ARANGO C., AMANN B.L., SOLE B., GONZALEZ-PINTO A. ET AL. Functional remediation in bipolar disorder: 1-year follow-up of neurocognitive and functional Outcome. *British Journal of Psychiatry*. 2016;208(1):87-93.
- GALLING B, ROLDÁN A, NIELSEN RE, NIELSEN J, GERHARD T, CARBON M ET AL. Type 2 Diabetes Mellitus in Youth Exposed to Antipsychotics: A Systematic Review and Meta-analysis. *JAMA psychiatry*. 2016.
- RAPADO-CASTRO M., DODD S., BUSH A.I., MALHI G.S., SKVARC D.R., ON Z.X. ET AL. Cognitive effects of adjunctive N-acetyl cysteine in psychosis. *Psychological Medicine*. 2016;1-11.

## Highlights

During 2016 the research team of the Department of Psychiatry at Hospital General Universitario Gregorio Marañón (CIBERSAM group 1, G01) has obtained competitive funding for new international projects that add to the previous projects funded by international institutions (EU, NIH) that remain active. In the past few years, the group has become an international reference in the study of first episodes of early onset psychosis. More recently, it has developed a growing interest in primary prevention as manifested by the development of novel research projects focused on the prevention of risk factors in healthy populations. Emphasis should be laid on the incorporation of the group to large international scientific consortia such as PGC, ENIGMA or ASC, often hand in hand with other CIBERSAM groups. In 2016, G01 has also described potential mechanisms of action to prevent progression after a first episode of psychosis with psychopharmacological and psychosocial interventions. Several members of the group participate in the development of clinical and therapeutic guidelines through their involvement in expert groups and scientific societies. The quality of the research, teaching, and clinical activity of G01 has been recognized in 2016 with the “AEVAL Management Excellence Award”.



LEAD RESEARCHER

**Artigas Pérez, Francesc**

📍 Agencia Estatal Consejo Superior de Investigaciones Científicas

Instituto de Investigaciones Biomédicas de Barcelona  
C/ Rosselló 161, 6ª Pl.  
08036 Barcelona

☎ (+34) 93 363 83 15

✉ francisc.artigas@iibb.csic.es

🌐 [Group website](#)

PROGRAMMES

**Therapeutic Innovation  
Depression**



### GROUP MEMBERS

**Staff members:** Jaramillo Muñumer, María | Paz Silva, Verónica | Santana Ramos, Noemí

**Associated members:** Bortolozzi BIASONI, Analia | Campa Montobbio, Leticia | Castañe Forn, Anna | Celada Pedrosa, María Paz | Ferrés Coy, Albert | Fullana Llinas, María Neus | Gasull Camós, Júlia | Riga, Maurizio | Ruiz Bronchal, Esther

## Main lines of research

- Neurobiological basis and treatment for severe psychiatric disorders: study of neurotransmitters, receptors and brain circuits involved.
- Mechanism of action of antidepressant and antipsychotic drugs: Identification of new targets and brain circuits involved.
- Study on the brain circuits involved in the psychotropic action of non-competitive NMDA receptor antagonists and serotonergic hallucinogens.
- Neurobiological basis of fast-acting antidepressant strategies (RNAi, glutamatergic agents, including ketamine).
- Study of transgenic mouse models of schizophrenia.
- Neurochemistry and neuropharmacology of brain neurotransmitters.



## Most relevant scientific articles

- ARTIGAS F., SCHENKER E., CELADA P., SPEDDING M. Defining the brain circuits involved in psychiatric disorders: IMI-NEWMEDS. *Nature Reviews Drug Discovery*. 2016;16(1):1-2.
- FERRES-COY A., GALOFRE M., PILAR-CUELLAR F., VIDAL R., PAZ V., RUIZ-BRONCHAL E. ET AL. Therapeutic antidepressant potential of a conjugated siRNA silencing the serotonin transporter after intranasal administration. *Molecular Psychiatry*. 2016;21(3):328-338.
- SANTANA N, ARTIGAS F. Expression of Serotonin2C Receptors in Pyramidal and GABAergic Neurons of Rat Prefrontal Cortex: A Comparison with Striatum. *Cerebral cortex (New York, N.Y.: 1991)*. 2016;.
- JIMENEZ-SANCHEZ L., LINGE R., CAMPA L., VALDIZAN E.M., PAZOS A., DIAZ A. ET AL. Behavioral, neurochemical and molecular changes after acute deep brain stimulation of the infralimbic prefrontal cortex. *Neuropharmacology*. 2016; 108:91-102.
- RIGA M.S., SANCHEZ C., CELADA P., ARTIGAS F.. Involvement of 5-HT3 receptors in the action of vortioxetine in rat brain: Focus on glutamatergic and GABAergic neurotransmission. *Neuropharmacology*. 2016; 108:73-81.

## Highlights

The group has led a total of 10 grants during 2016, including 5 Spanish competitive grants (SAF2015-68346-P, SAF2016-75797-R, PI12/00156, PI13/01390 y RTC-2014-2812), 1 Catalan grant (2014SGR798), 3 contracts with pharmaceutical companies (H. Lundbeck A/S; nLife Therapeutics) and 1 grant from the Alicia Koplowitz Foundation.

From the studies carried out during 2016, we highlight a) the development of novel strategies using RNAi for the study of the pathophysiology and treatment of neuropsychiatric conditions, including major depressive disorder and Parkinson's disease, b) the study of the mechanism of action of fast acting antidepressant strategies, including glutamatergic agents such as ketamine, c) study of the mechanism of action of novel antidepressant drugs, such as vortioxetine, d) development of preclinical models of schizophrenia, and e) identification of the infralimbic prefrontal cortex as a key area in the pathophysiology and treatment of major depression.

The group keeps having a solid international reputation in Neuropsychopharmacology as indicated by the large number of citations (the PI of G02 has an h index of 60, one of the highest in Spanish Neuroscience). Currently, 3 articles published over the last 5 years are considered as "Highly Cited Papers" by the Web of Science, one of them also being a "Popular paper".


Among the papers published during 2016, we highlight i) an original article published in *Molecular Psychiatry* on the use of novel antidepressant RNAi strategies, in collaboration with groups G12 and G20 from CIBERSAM., ii) a paper in *Nat Commun* on the role of the 5-HT system in anxiety epigenetics, in collaboration with a group from Cornell Univ (NY, USA), and iii) a commentary in *Nat Rev Drug Discov*, in collaboration with the former members of the IMI-NEWMEDS EU project.




LEAD RESEARCHER

**Ayuso Mateos, José Luis**

 Servicio Madrileño de Salud  
Hospital Universitario La Princesa  
C/ Diego de León 62, pl. 1ª  
28006 Madrid

 (+34) 91 497 17 05

 cc.oms@uam.es

 [Group website](#)

PROGRAMMES

**Depression**

**Bipolar disorder**



GROUP MEMBERS

**Staff members:** Cabello Salmerón, María

**Associated members:** Caballero Díaz, Francisco Félix | Carvalho de Avila E Pereira, Carolina | Kamenov, Kalouyan | Leal Leturia, Itziar | López García, Pilar | Martín María, Natalia | Martorell Cafranga, Almudena | Miret García, Marta | Moreno Agostino, Darío | Rico Uribe, Laura Alejandra | Rivas Rodríguez, María del Mar

## Main lines of research

- Epidemiology of mental disorders in general population.
- Nosology of mental disorders.
- Assessment of the efficacy of different therapeutical interventions in patients with major depression and bipolar disorders.
- Evaluation of health status, quality of life and well-being in the general population.
- Analysis and prevention of suicide behaviour.
- Strategies for improvement mental health service coverage in low and middle income countries.
- Analyses of factors associated with the onset of first psychotic episodes.
- To identify patterns of healthy ageing, their determinants and the critical points in time when changes in trajectories are produced, and to propose public health interventions to optimise healthy ageing.
- To enhance current strategies for employment integration and reintegration of people with chronic conditions (including mental disorders).
- To identify biomarkers in patients with major depression.

## Most relevant scientific articles

- ANAYA C., TORRENT C., CABALLERO F.F., VIETA E., DEL MAR BONNIN C., AYUSO-MATEOS J.L. ET AL. Cognitive reserve in bipolar disorder: Relation to cognition, psychosocial functioning and quality of life. *Acta Psychiatrica Scandinavica*. 2016.
- KAMENOV K., TWOMEY C., CABELLO M., PRINA A.M., AYUSO-MATEOS J.L.. The efficacy of psychotherapy, pharmacotherapy and their combination on functioning and quality of life in depression: a meta-analysis. *Psychological Medicine*. 2016;1-12.
- MARTIN-MARIA N., MIRET M., CABALLERO F.F., RICO-URIBE L.A., STEPTOE A., CHATTERJI S. ET AL. The Impact of Subjective Well-Being on Mortality: A Meta-Analysis of Longitudinal Studies in the General Population. *Psychosomatic Medicine*. 2016-
- TYROVOLAS S., KOYANAGI A., OLAYA B., AYUSO-MATEOS J.L., MIRET M., CHATTERJI S. ET AL. Factors associated with skeletal muscle mass, sarcopenia, and sarcopenic obesity in older adults: a multi-continent study. *Journal of Cachexia, Sarcopenia and Muscle*. 2016;312-321.
- BONNIN C.M., TORRENT C., ARANGO C., AMANN B.L., SOLE B., GONZALEZ-PINTO A. ET AL. Functional remediation in bipolar disorder: 1-year follow-up of neurocognitive and functional Outcome. *British Journal of Psychiatry*. 2016;208(1):87-93.

## Highlights

In 2016, our group started working on five new research projects in collaboration with other CIBERSAM centres. The Project “*Trajectories on mental health, physical health and functioning: Third wave survey of a Spanish cohort of the adult population*”, which is aimed to carry out a third time point assessment to know trajectories of health in ageing people as well as recruiting new people to make generational comparisons. On the other hand, we have also started the project “*CIBERSAM cohorts about FEP cases and controls*”, which is aimed to create a common cohort from different existing cohorts with first episode patients and controls, and follow-up the common cohort at 5, 10 and 15 years. Furthermore, we have started the project “*Emotional fluctuation in daily life. Ecological analysis of depressive symptomatology in the general population*” which is aimed to analyse the mood fluctuations throughout the day in a general population sample using mobile Apps. Moreover, the Study “*European Welfare Models and Mental Wellbeing in Final Years of Life*”, which is addressed to gather information on the components of wellbeing and welfare in people older than 80 years. In addition, the project “*Peripheral oxidative stress and inflammatory markers in Major Depressive Disorder*”, focuses on finding biological markers in Major Depressive Disorder. Finally, the group has participated in the elaboration of “*mhGAP Intervention Guide for mental, neurological and substance use disorders in non-specialized health setting*”. This work has been led by World Health Organization inside the WHO Mental Health Gap Action Programme.



LEAD RESEARCHER

**Bernardo Arroyo, Miguel**

- Hospital Clínico y Provincial de Barcelona  
Villarroel, 170  
08036 Barcelona
- (+34) 93 227 54 00 ext 3142
- [bernardo@clinic.ub.es](mailto:bernardo@clinic.ub.es)
- [Group website](#)

PROGRAMMES

**Schizophrenia**  
**Child and Adolescent Psychiatry**



## GROUP MEMBERS

**Staff members:** Amoretti Guadall, Silvia | Cabrera Llorca, Bibiana | De la Serna Gómez, Elena | Folch Espada, Anna

**Associated members:** Andrés Perpiña, Susana | Baeza Pertegaz, María Inmaculada | Bioque Alcazar, Miguel | Calvo Escalona, Rosa | Castro Fornieles, Josefina | Catalán Campos, Rosa | Fernández Egea, Emilio | Flamarique Valencia, Itziar | García Rizo, Clemente | Lafuente Flo, Amalia | Lázaro García, Luisa | Lomeña Caballero, Francisco | Mane Santacana, Anna | Más Herrero, Sergio | Massana Montejo, Guillem | Morer Liñan, Astrid | Parellada Rodón, Eduardo | Penades Rubio, Rafael | Pons Villanueva, Alexandre | Puig Navarro, Olga | Romero Cela, Soledad | Sánchez Gistau, Vanesa | Sugranyes Ernest, Gisela

## Main lines of research

- Physical health in Schizophrenia.
- Neuroimaging, Genetics, Neurobiology and Molecular Psychiatry.
- Neuropsychology, Psychoeducation and Psychometric evaluation.
- Neuropsychopharmacology.
- High Risk Population, early-onset and first and second episodes of psychosis.
- Child and adolescent mental health.

## Most relevant scientific articles

- BIOQUE M., CABRERA B., GARCIA-BUENO B., MAC-DOWELL K.S., TORRENT C., SAIZ P.A. ET AL. Dysregulated peripheral endocannabinoid system signaling is associated with cognitive deficits in first-episode psychosis. *Journal of Psychiatric Research*. 2016; 75:14-21.
- CABRERA B., BIOQUE M., PENADES R., GONZALEZ-PINTO A., PARELLADA M., BOBES J. ET AL. Cognition and psychopathology in first-episode psychosis: are they related to inflammation? *Psychological Medicine*. 2016;1-12.
- GARRIGA M, PACCHIAROTTI I, KASPER S, ZELLER SL, ALLEN MH, VÁZQUEZ G ET AL. Assessment and management of agitation in psychiatry: Expert consensus. *The world journal of biological psychiatry : the official journal of the World Federation of Societies of Biological Psychiatry*. 2016;17(2):86-128.
- DE LA SERNA E., VILA M., SANCHEZ-GISTAU V., MORENO D., ROMERO S., SUGRANYES G. ET AL. Neuropsychological characteristics of child and adolescent offspring of patients with bipolar disorder. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*. 2016; 65:54-59.
- ORTIZ AE, MORER A, MORENO E, PLANA MT, CORDOVILLA C, LÁZARO L. Clinical significance of psychiatric comorbidity in children and adolescents with obsessive-compulsive disorder: subtyping a complex disorder. *European archives of psychiatry and clinical neuroscience*. 2016;266(3):199-208.

## Highlights

Our objectives are: to expand theoretical-practical knowledge related to schizophrenia; Longitudinal follow-up of patients with chronic schizophrenia; First psychotic episodes; Pharmacological management of the first psychotic episode, development and validation of psychopathological scales. G04 group includes the Child and Adolescent Psychiatry research group whose objective is the study of the main psychiatric disorders children and adolescents.

### PROJECTS:

**International projects:** •European Network of National schizophrenia Networks studying Gene-environment Interactions (EU-GEI) •Optimization of Treatment and Management of Schizophrenia in Europe- OPTiMiSE •European Long-acting Antipsychotics in Schizophrenia Trial- EULAST Foundation European Group for Research in Schizophrenia(EGRIS) •Multidisciplinary Approaches to Translational Research In Conduct Syndromes, MATRICS. : European Comission. CE\_FP7\_HEALTH\_IN1\_13 • Epigenetic Regulation of BDNF Expression According to Response to Cognitive Remediation in Schizophrenia” NARSAD NIH •European Multicentre Tics in Children Study. FP7\_ 278367

**Principal National Projects(ISCIII):** • Determinantes clínicos y neurobiológicos de segundos episodios de esquizofrenia. Estudio longitudinal de primeros episodios psicóticos. FIS (ISCIII) PI11/00325 • Estudio de aplicabilidad clínica de un modelo predictivo de recaídas en primeros episodios de esquizofrenia. FIS ISCIII PI14/00612 • Traducción y validación al español del inventario “The Symptom Onset in Schizophrenia (SOS) inventory” BICIBERSAM • Estudio multicéntrico longitudinal sobre el papel de marcadores neurobiológicos de estrés en niños y adolescentes con síndrome de riesgo de psicosis y la transición a psicosis FIS\_ISCIII PI15/00444 • Influencia de la genética y la epigenética en la eficacia del tratamiento del trastorno Obsesivo-Compulsivo con terapia cognitivo-conductual o tratamiento farmacológico. FIS\_ISCIII. PI16/01086

**Principal European- National Projects (ISCIII):** Predictor multigenético para la prevención de los efectos secundarios inducidos por antipsicóticos – APSIDE. MINECO -FEDER.


**PATENTS:** Method for predicting the onset of extrapyramidal symptoms (EPS) induced by an antipsychotic-based treatment. • Método in Vitro y KIT para el Pronóstico o Predicción de la Respuesta al Tratamiento con Agentes Antipsicóticos por parte de Pacientes que han Sufrido un Primer Episodio Psicótico.


**CLINICAL GUIDES:** Assessment and management of agitation in psychiatry: Expert consensus. Garriga M et. All. • Spanish consensus on the risks and detection of antipsychotic drug-related hyperprolactinaemia. Montejo ÁL, et. all.



LEAD RESEARCHER

**Bobes García, Julio**

 **Universidad de Oviedo**  
Facultad de Medicina  
C/ Julián Clavería 6  
33006 Oviedo

 (+34) 98 510 35 53

 bobes@uniovi.es

 [Group website](#)

PROGRAMMES

**Schizophrenia**  
**Bipolar disorder**



## GROUP MEMBERS

**Staff members:** Bascarán Fernández, María Teresa | De la Fuente Tomas, Lorena

**Associated members:** Al-Halabí Díaz, Susana | Bombín González, Igor | Bousoño García, Manuel | Burón Fernández, Patricia | Díaz Mesa, Eva María | Flórez Menéndez, Gerardo | García Álvarez, Leticia | García-Portilla González, Mari Paz | Iglesias García, Celso Angel | Jiménez Treviño, Luis | Muñiz Fernández, José | Sáiz Martínez, Pilar Alejandra | Sarramea Crespo, Fernando

## Main lines of research

- Cross-curricular areas of research (applicable to all mental disorders): Genetics: pharmacogenomics and pharmacogenetics; Clinical: cognitive impairment and psychophysiology (sleep and sexuality); Psychometrics: development / cross-cultural validation / psychometric properties of assessments tools for mental disorders; Treatment: efficacy and tolerability of new CNS drugs / new indications of existing CNS drugs / efficacy of new psychotherapeutic strategies; Impact of mental disorders and their treatment in patients' life: functioning (disability) / quality of life.
- Longitudinal areas of research (specific mental disorders): Severe mental disorders (schizophrenia and bipolar disorder) and their initial manifestations (first psychotic episodes), unipolar depression, suicidal behaviour, obsessive-compulsive disorder (OCD), panic disorder, addictions.

## Most relevant scientific articles

- ZALSMAN G, HAWTON K, WASSERMAN D, VAN HEERINGEN K, ARENSMAN E, SARCHIAPONE M ET AL. Suicide prevention strategies revisited: 10-year systematic review. *The Lancet Psychiatry*. 2016;3(7):646-59.
- GARCIA-PORTILLA M.P., GARCIA-ALVAREZ L., SARRAMEA F., GALVAN G., DIAZ-MESA E., BOBES-BASCARAN T. ET AL. It is feasible and effective to help patients with severe mental disorders to quit smoking: An ecological pragmatic clinical trial with transdermal nicotine patches and varenicline. *Schizophrenia Research*. 2016.
- CABRERA B., BIOQUE M., PENADES R., GONZALEZ-PINTO A., PARELLADA M., BOBES J. ET AL. Cognition and psychopathology in first-episode psychosis: are they related to inflammation? *Psychological Medicine*. 2016;1-12.
- BONNIN C.M., TORRENT C., ARANGO C., AMANN B.L., SOLE B., GONZALEZ-PINTO A. ET AL. Functional remediation in bipolar disorder: 1-year follow-up of neurocognitive and functional Outcome. *British Journal of Psychiatry*. 2016;208(1):87-93.
- MCMAHON E.M., CORCORAN P., O'REGAN G., KEELEY H., CANNON M., CARLI V. ET AL. Physical activity in European adolescents and associations with anxiety, depression and well-being. *European Child and Adolescent Psychiatry*. 2016;1-12.

## Highlights

The G05, in 2016, was involved in several research projects funded by the Institute of Health Carlos III, with members of the group being the PI in three of them: "Differential biomarkers of the negative dimension of schizophrenia", "Neuropsychological functioning and inflammatory profile in suicidal behavior" and "Validation of a clinical staging model for bipolar disorder".

We also participated in three clinical trials: "Interventional, randomized, double-blind, active-controlled, fixed-dose study of Lu AF35700 in patients with Treatment-resistant Schizophrenia", "A 52-week, prospective, open-label, multicentre, international study on the transition to a quarterly formulation of paliperidone palmitate in patients with schizophrenia previously stabilized with a monthly formulation of paliperidone palmitate" and "European Long-acting Antipsychotics in Schizophrenia Trial" (EULAST). A specific multi-component program for smoking cessation in patients with schizophrenia or bipolar disorder has been developed and their efficacy and security has been demonstrated.

Members of the G05 have participated in the elaboration of the Clinical Guideline for the treatment of dual pathology in the adult population.

During 2016 two doctoral thesis have been directed and defended, whose titles are: "Adaptation and validation in Spanish of the sixth version of the Addiction Severity Index (ASI-6)" and "Differential biomarkers of schizophrenia"

The thesis entitled "Monitoring of suicidal behavior in the Sanitary Area IV of Asturias" by Dr. Patricia Burón Fernández, has been awarded to the prize of best Doctoral Thesis of the University of Oviedo (Knowledge Area of Psychology).

Two members of the group are Editors in chief of two indexed scientific Journals with impact factor: *Revista de Psiquiatría y Salud Mental* and *Adicciones*.


Members of the G05 actively participated in Boards of European and National Scientific Societies and in Scientific and/or Organizer Committees of National and International Conferences/Congress.



LEAD RESEARCHER

**Casas Brugué, Miguel**

 **Fundación Hospital  
Universitario Vall d'Hebron -  
Institut de Recerca (VHIR)**  
Hospital Vall d'Hebron  
Passeig Vall d'Hebron, 119-129  
08035 Barcelona.

 [mcasas@vhebron.net](mailto:mcasas@vhebron.net)

 [Group website](#)

PROGRAMMES

**Psychosomatic, Anxiety  
and Impulse Control Disorders**



GROUP MEMBERS

**Staff members:** Soler Artigas, Maria

**Associated members:** Bosch Munsó, Rosa María | Bruguera Cortada, Eugeni | Calvo Piñero, Natalia | Collazos Sánchez, Francisco | Corominas Roso, Margarita | Daigre Blanco, Constanza | Ferrer Vinardell, Marc | Gómez Barros, Núria | Grau López, Lara | Ramos Quiroga, José Antonio | Ribases Haro, Marta | Richarte Fernández, Vanesa | Roncero Alonso, Carlos | Sánchez Mora, Cristina | Valero Ventura, Sergi | Vidal Estrada, Raquel

## Main lines of research

- Neurodevelopmental Disorders, mainly Attention Deficit and Hyperactivity Disorder (ADHD), their epidemiology and clinical features along lifespan, including the analysis of functional and structural brain abnormalities through neuroimaging, the identification of psychopathological comorbidity and the evaluation of divers therapeutic approaches. We are also interested in the identification of how these different neurodevelopmental disorders and psychopathological factors influences scholar failure and, later on, in how the influence of adult everyday life.
- Impulsive and Disruptive behaviors. This research line concerns the study of diagnostics procedures for Borderline Personality Disorder (BPD) and its comorbidity with ADHD or Addictive behaviors. The definition of clinical subtypes, the development of new treatments and the evaluation of psychopathologic symptoms related to high-risk driving and traffic accidents, are the main subjects for our studies.
- Addictive behaviors and Dual Disorders. This line of research is focused on different clinical issues and neuroimaging studies to identify risk indicators and treatment modalities for Substance Use Disorders.
- Transcultural Psychiatry, Transcultural Psychiatry, mainly focused on the prevalence of psychopathology in the immigrant population, as well as the impact of cultural and ethnic variables on diagnosis and treatment of mental disorders and substance related disorders.



- Genetic basis of the different psychiatric disorders mentioned above through multiple approaches that include Genome-Wide Association Studies (GWAS), candidate-gene association studies, analyses of transcriptomic profiles with microarray technology and next-generation sequencing as well as animal model approaches. Unraveling the genetic basis of these conditions may help to improve diagnostic procedures, provide clues about predictive risk factors and allow the identification of new targets that may eventually lead to novel and more individualized pharmacological treatments.

## Most relevant scientific articles

- RAMOS-QUIROGA JA, NASILLO V, RICARTE V, CORRALES M, PALMA F, IBÁÑEZ P ET AL. Criteria and Concurrent Validity of DIVA 2.0: A Semi-Structured Diagnostic Interview for Adult ADHD. *Journal of attention disorders*. 2016.
- FERRER M, ANDIÓN Ó, CALVO N, RAMOS-QUIROGA JA, PRAT M, CORRALES M ET AL. Differences in the association between childhood trauma history and borderline personality disorder or attention deficit/hyperactivity disorder diagnoses in adulthood. *European archives of psychiatry and clinical neuroscience*. 2016.
- PAGEROLS M, RICARTE V, SÁNCHEZ-MORA C, GARCIA-MARTÍNEZ I, CORRALES M, COROMINAS M ET AL. Pharmacogenetics of methylphenidate response and tolerability in attention-deficit/hyperactivity disorder. *The pharmacogenomics journal*. 2016.
- STRINGER S, MINICĂ CC, VERWEIJ KJ, MBAREK H, BERNARD M, DERRINGER J ET AL. Genome-wide association study of lifetime cannabis use based on a large meta-analytic sample of 32 330 subjects from the International Cannabis Consortium. *Translational psychiatry*. 2016;6: e769.
- GARCIA-MARTÍNEZ I, SÁNCHEZ-MORA C, PAGEROLS M, RICARTE V, CORRALES M, FADEUILHE C ET AL. Preliminary evidence for association of genetic variants in pri-miR-34b/c and abnormal miR-34c expression with attention deficit and hyperactivity disorder. *Translational psychiatry*. 2016;6(8): e879.

## Highlights

In 2016 the research group has led multiples competitive research projects including five European projects (Agressotype, MiND, CoCA, Eat2bNice and MyHealth),

The Group has focused its research on the etiological, clinical and therapeutic aspects of disorders characterized by a high impulsivity that affects the individual across lifespan, focusing its Interest in Attention Deficit Hyperactivity Disorder (ADHD), Personality Limit Disorder (BPD) and Substance Use Disorders (SUD).

The main lines of research include:

- Genome-wide (GWAS) and candidate gene association studies to identify the genetic basis of the previously mentioned psychiatric disorders.
- To evaluate the impact of polygenic risk for ADHD on neurocognitive functions, learning disorders, academic performance or comorbid disorders such as Substance Use Disorders.
- To explore protein-coding and non-coding RNA expression profiling in medicated-naive ADHD subjects and healthy controls using next-generation sequencing and microarray technology.
- To explore differential epigenome signatures associated with ADHD through DNA-methylation
- Pharmacogenetics of methylphenidate response and tolerability in ADHD.
- Characterization of the intestinal microbiota in patients with ADHD through metagenomic-wide association study (MGWAS) through next generation sequencing of DNA from faecal samples.
- To study how the different neurodevelopmental disorders affect the functionality of patients, including the study of academic performance, traffic accidents and criminal behaviour.
- Validation of new psychometric instruments on ADHD and BPD.
- Application of eHealth programs for the assessment and treatment of mental disorders, as virtual reality.
- Performing neuroimaging studies in disorders such as fetal alcohol syndrome, ADHD and BPD.
- To determine the prevalence of psychopathology in the immigrant population, as well as to develop specific assessment instruments for psychopathology in the immigrant population.



LEAD RESEARCHER

## Cervilla Ballesteros, Jorge Antonio

📍 **Universidad de Granada**  
Parque Tecnológico de  
Ciencias de la Salud, CIBM  
Avda. del Conocimiento, S/N  
18100 Armilla

✉️ [jcervilla@ugr.es](mailto:jcervilla@ugr.es)

PROGRAMMES

**Schizophrenia**  
**Depression**  
**Psychosomatic, Anxiety**  
**and Impulse Control Disorders**



GROUP MEMBERS

**Staff members:** Lozano Gutiérrez, Vanessa

**Associated members:** Gutiérrez Martínez, Blanca | Ibañez Casas, Inmaculada | Lorente Acosta, José Antonio | Pérez García, Miguel | Rivera Sánchez, Margarita | Torres González, Francisco

## Main lines of research

- Redefining Psychotic Phenotypes (J. Cervilla).
- Treatment of Refractory Psychoses (J. Cervilla).
- Gene by environment interaction in Psychiatry (B. Gutiérrez).
- Psychopharmacogenetics (B. Gutiérrez).
- Social Psychiatry (F. Torres).
- Psychogeriatrics (J. Cervilla).
- Medical Issues in Mental Disorder (M. Rivera).

## Most relevant scientific articles

- BUESO-IZQUIERDO N, VERDEJO-ROMÁN J, CONTRERAS-RODRÍGUEZ O, CARMONA-PERERA M, PÉREZ-GARCÍA M, HIDALGO-RUZZANTE N ET AL. Are batterers different from other criminals? An fMRI study. *Social cognitive and affective neuroscience*. 2016;11(5):852-62.
- DIREK N., WILLIAMS S., SMITH J.A., RIPKE S., AIR T., AMARE A.T. ET AL. An Analysis of Two Genome-wide Association Meta-analyses Identifies a New Locus for Broad Depression Phenotype. *Biological Psychiatry*. 2016.
- DE JONG S., NEWHOUSE S.J., PATEL H., LEE S., DEMPSTER D., CURTIS C. ET AL. Immune signatures and disorder-specific patterns in a cross-disorder gene expression analysis. *British Journal of Psychiatry*. 2016;209(3):202-208.
- BANDRES-CIGA S., PRICE T.R., BARRERO F.J., ESCAMILLA-SEVILLA F., PELEGRINA J., AREPALLI S. ET AL. Genome-wide assessment of Parkinson's disease in a Southern Spanish population. *Neurobiology of Aging*. 2016; 45:213.
- BELLON J.A., CONEJO-CERON S., MORENO-PERAL P., KING M., NAZARETH I., MARTIN-PEREZ C. ET AL. Intervention to prevent major depression in primary care: A cluster randomized trial. *Annals of Internal Medicine*. 2016;164(10):656-665.


## Hightlights

During 2016, the group has formalized a service contract with the company Ferrer S.L. to carry out our project's part of observational study titled "Measurement of mechanical restraints performed in patients treated with inhaled loxapine versus patients with conventional treatment in a mental health hospitalization unit". In addition, we have implemented an application to collect data referring to the monitoring of population cohorts. For this, an extension of the PISMA project was requested, and it was called PISMA PHENO-PSYCH. Finally, one of the members of our group participated in several scientific activities, among which we highlight a paper in the workshop held by the CIBERSAM instrument bank in Barcelona. And also in a divulgative activity called "The European Night of Researchers", where she implemented a workshop on mental health and cognition.



LEAD RESEARCHER

## Crespo Facorro, Benedicto

 Instituto de Investigación  
Marques de Valdecilla  
Hospital Universitario Marqués  
de Valdecilla  
Avda. Valdecilla S/N  
39008 Santander

 (+34) 94 220 25 45

 benedicto.crespo@unican.es

 [Group website](#)

PROGRAMMES

### Schizophrenia Therapeutic Innovation



#### GROUP MEMBERS

**Staff members:** Ayesa Arriola, Rosa | Setién Suero, María Esther | Tordesillas Gutiérrez, Diana

**Associated members:** Gaité Pindado, Luis | Gómez Del Barrio, Jose Andrés | Herrán Gómez, José Andrés | Herrera Castañedo, Sara | Mata Pastor, Ignacio | Ortíz-García De La Foz, Víctor | Pelayo Terán, José María | Pérez Iglesias, Rocío | Rodríguez Sánchez, José Manuel | Suárez Pinilla, Paula | Vázquez Barquero, José Luis | Vázquez Bourgon, Javier

## Main lines of research

- First episode non-affective psychosis: clinical and biological aspects.
- Neuroimaging: methods development.
- Genomic studies in schizophrenia.
- First episode of eating disorders.
- Physical health in severe mental disorders .

## Most relevant scientific articles

- SEKAR A., BIALAS A.R., DE RIVERA H., DAVIS A., HAMMOND T.R., KAMITAKI N. ET AL. Schizophrenia risk from complex variation of complement component 4. *Nature*. 2016;530(7589):177-183.
- MAYORAL-VAN SON J., ORTIZ-GARCIA DE LA FOZ V., MARTINEZ-GARCIA O., MORENO T., PARRILLA-ESCOBAR M., VALDIZAN E.M. ET AL. Clinical outcome after antipsychotic treatment discontinuation in functionally recovered first-episode nonaffective psychosis individuals: A 3-year naturalistic follow-up study. *Journal of Clinical Psychiatry*. 2016;77(4):492-500.
- MELLOR-MARSA B., CABALLERO F.F., CABELLO M., AYUSO-MATEOS J.L., SETIEN-SUERO E., VAZQUEZ-BOURGON J. ET AL. Disability multilevel modelling in first episodes of psychosis at 3-year follow-up. *Schizophrenia Research*. 2016.
- MORLÁN-COARASA MJ, ARIAS-LOSTE MT, ORTIZ-GARCÍA DE LA FOZ V, MARTÍNEZ-GARCÍA O, ALONSO-MARTÍN C, CRESPO J ET AL. Incidence of non-alcoholic fatty liver disease and metabolic dysfunction in first episode schizophrenia and related psychotic disorders: a 3-year prospective randomized interventional study. *Psychopharmacology*. 2016.
- ADAMS H.H.H., HIBAR D.P., CHOURAKI V., STEIN J.L., NYQUIST P.A., RENTERIA M.E. ET AL. Novel genetic loci underlying human intracranial volume identified through genome-wide association. *Nature Neuroscience*. 2016;19(12):1569-1582.

## Highlights

Our research group has continued the progress on clinical and basic research projects in usual areas (clinical aspects of non-affective psychosis, cognition, neuroimaging, genomic, metabolomics). In 2016, we highlight our collaboration in the following projects obtained in previous competitive national calls from the Ministry of Economy and Competitiveness (MINECO):

- Exp. PIE15/00079 (PI: Javier Crespo García). ISCIII. Call AES of Integrated Projects of Excellence 2015;
- Exp. SAF2015-71526-REDT (PI: Lourdes Fañanás Saura), within the Framework of the Call for Actions to Stimulate “Networks of Excellence” 2015;
- Exp. PIE14/00031 (PI: José María Mato de la Paz). ISCIII. Call AES of Integrated Projects of Excellence 2014.

We also have got funding to carry out 2 new projects:

- Exp.: SAF2016-76046-R. Title: GEXMOLANT - Towards a stratified treatment in schizophrenia: integrating insights from human and cellular transcriptome into antipsychotic strategies (PI: Benedicto Crespo Facorro). MINECO. Call 2016 de Ayudas del Programa Estatal de Investigación, Desarrollo e Innovación Orientada a los Retos de la Sociedad (Proyectos I+D+i - Retos 2016).
- Exp.: CM16/00034. Title: Ayudas para Contratos post Formación Sanitaria Especializada Río Hortega. MINECO. Instituto de Salud Carlos III. Call AES de Contratos Río Hortega 2016. (PI: Manuel Delgado Alvarado).
- During 2015, it is of note that our group published 8 articles in scientific journals ranked in the first decile in JCR (Web of Science) with an special mention to an article published in *Nature* describing the involvement of gene C4 in schizophrenia.

As part of our major interest in building up solid research and scientific collaborations with international group, we keep up our active involvement in Psychaitric Genomic Consortium –PGC-, ENIGMA, ENPACTSZ, PEIC and also we have established a new and productive collaboration with the *Virginia Commonwealth University* exploring new drug target with clinical impact in schizophrenia (Prof. J. González-Maeso) and *The University of Yale* (Prof. D. Glahn) with the primary aim of investigating longitudinal changes and outcome in first episode patients.

LEAD RESEARCHER

## Desco Menéndez, Manuel

-  Servicio Madrileño de Salud  
Hospital Gregorio Marañón  
C/ Ibiza, 43  
Anexo de psiquiatría, 1ª pl.  
28009 Madrid
-  (+34) 91 586 66 78
-  desco@mce.hggm.es
-  [Group website](#)

PROGRAMMES

### Therapeutic Innovation Child and Adolescent Psychiatry

#### GROUP MEMBERS

**Staff members:** Alemán Gómez, Yasser | Garrido Huerta, Rosa Trajana | Rolin Ferrer, Daniel | Sierra Palomares, Yolanda

**Associated members:** Calvo Manuel, Felipe | Carmona Cañabate, Susana | Cusso Mula, Lorena | Domínguez Montero, Pedro Luis | García Barreno, Pedro | García García, David | Guzmán de Villoria Lebieziejewski, Juan | Lafuente Martínez, Javier | Pascau González-Garzón, Javier | Soto Montenegro, María Luisa

**Contributors:** De Francisco López, Alexandra

## Main lines of research

The research of the group is devoted to investigate medical imaging techniques, developing new image-related technology, innovative processing methodology and their translation into practice. The multidisciplinary character of the group enables fast clinical validation of the results thereby facilitating the transfer of advanced technological solutions to the industry.

The activities of the laboratory are organized in (a) Clinical Research Support (Neuroimaging, Image-guided Surgery; Cardiac imaging), (b) Development of new technology and (c) Preclinical Research.

The available equipment for small animal multimodal molecular imaging (CY, PET, SPECT, CT-PET, MRI, optical fluorescence tomography) is unique at the national scale, and it is accesible for external users.

## Most relevant scientific articles

- NAVAS-SANCHEZ F.J., CARMONA S., ALEMAN-GOMEZ Y., SANCHEZ-GONZALEZ J., GUZMAN-DE-VILLORIA J., FRANCO C. ET AL. Cortical morphometry in frontoparietal and default mode networks in math-gifted adolescents. *Human Brain Mapping*. 2016;37(5):1893-1902.
- COLLANTES M., SERRANO-MENDIORIZ I., BENITO M., MOLINET-DRONDA F., DELGADO M., VINAIXA M. ET AL. Glucose metabolism during fasting is altered in experimental porphobilinogen deaminase deficiency. *Human Molecular Genetics*. 2016;25(7):1318-1327.
- BIKOVSKY L., HADAR R., SOTO-MONTENEGRO M.L., KLEIN J., WEINER I., DESCO M. ET AL. Deep brain stimulation improves behavior and modulates neural circuits in a rodent model of schizophrenia. *Experimental Neurology*. 2016; 283:142-150.
- NEHRHOFF I., BOCANCEA D., VAQUERO J., VAQUERO J.J., RIPOLL J., DESCO M. ET AL. 3D imaging in CUBIC-cleared mouse heart tissue: Going deeper. *Biomedical Optics Express*. 2016;7(9):3716-3720.
- CASQUERO-VEIGA M., HADAR R., PASCAU J., WINTER C., DESCO M., SOTO-MONTENEGRO M.L. Response to deep brain stimulation in three brain targets with implications in mental disorders: A PET study in rats. *PLoS ONE*. 2016;11(12).

## Highlights

In 2016, the G07 group works in 23 research projects. Also, the group coordinates the “Plataforma de Neuroimagen” of “CIBER de Salud Mental, a neuroimaging platform that stores more than 14000 neuroimages, manages 18 usage requests, and collaborates with ten research groups. During 2016, the “Plataforma de Neuroimagen” has processed approximately 500 images.

This year the group has obtained the following projects associated to the “CIBER de Salud Mental”:

1) “Nuevos escenarios de tomografía por rayos X (NEXT)” (DPI2016-79075-R), funded by “Ministerio de Economía, Industria y Competitividad”, and whose IP is Mónica Abella (2016-2019); 2) “Ejercicio físico y N-acetil cisteína como terapias preventivas en la aparición de esquizofrenia durante la adolescencia: estudios preclínicos de imagen molecular y de comportamiento”, funded by “Fundación Alicia Koplowitz”, and whose IP is Marisa Soto (2016-2018); 3) “Estimulación cerebral profunda (DBS) en el tratamiento de la obesidad: estudio experimental en dos modelos animales”, funded by “Fundación Mapfre”, and whose IP is Marisa Soto (2016-2017); y, 4) “Sistema de simulación clínica híbrida (Hybrids)” (06-00001315-15), funded by “Fundación para la Innovación y la Prospectiva en Salud en España (FIPSE)”, and whose IP is Manuel Desco (2016).

In addition, throughout 2016 the group has patented, with the “Carlos III University of Madrid”, the “Celda Centelleadora” (Spanish Patent and Trademark Office, application no.: P201631258, application date: 09/28/2016). The researchers who signed the patent are: Georgios Konstantinou, Juan José Vaquero, Rigoberto Chil and Manuel Desco.

Finally, it should be noted that the group maintains collaboration with the following entities: “Universidad Carlos III de Madrid” (UC3M), “Philips”, “Institut d’Investigacions Biomèdiques August Pi i Sunyer” (IDIBAPS), “Unitat de Recerca en Neurociència Cognitive Center “(URNC),” Center d’Imatge Molecular “(CRC CIM), “Sociedad Española de Electromedicina y Calidad” (SEDECAL).



LEAD RESEARCHER

**Fañanas Saura, Lourdes**

-  **Universidad de Barcelona**  
Facultad de Biología.  
Diagonal, 645  
08028 Barcelona
-  (+34) 93 402 14 61
-  lfananas@ub.edu
-  [Group website](#)

PROGRAMMES

**Schizophrenia  
Child and Adolescent Psychiatry**



## GROUP MEMBERS

**Staff members:** Martín García, María José | Valldeperes Llaberia, Anna

**Associated members:** Arias Sanperiz, Bárbara | Barrantes Vidal, Neus | Cirera Miquel, Flors | Córdova Palomera, Aldo | Fatjó-Vilas Mestre, Mar | Ibañez Ribes, Manuel Ignacio | Marqués Feixa, Laia | Miret Fallada, Salvador | Mitjans Niubo, Marina | Moya Higuera, Jorge | Ortet Fabregat, Generós | Palma Gudiel, Helena | Papiol Miró, Sergi | Prats Balado, Claudia | Rosa de la Cruz, Araceli | Soler García, Jordi

## Main lines of research

- The study of genetic and environmental risk factors in mental disease (SCH, BD and MD), and its relationship with clinical-cognitive and brain phenotypes (fMRI, MRI): case-control designs, family-based studies, and twin-based studies.
- Pharmacogenetics of antidepressants, antipsychotics and mood stabilizers.
- The study of early stress (prenatal stress and childhood and adolescence stress) and its impact on HPA axis dysfunction and the development of externalizing and internalizing psychopathology in early stages of life.
- Recognition of epigenetic changes induced by prenatal psychosocial stressors and childhood abuse, and its association with peripheral biomarkers of immune response and changes in brain neuronal connectivity (connectomics).
- The study of GxE mechanisms present in mental disease and populational intermediate phenotypes, from an etiological continuum hypothesis; with special relevance for the study of: schizotypy, attenuated psychotic symptoms and depression.
- The development of new psychometric and clinical evaluation instruments, especially in child and adolescent population.



Some of these research lines are developed in close collaboration with other national research groups (CIBER: CIBERSAM and CIBERER) and International research groups, under the coordination of G08 researchers and with some new funded projects:

- Maternal prenatal stress and HPA axis sensitization mediated by 11 $\beta$ -HSD2 gene epigenetic signatures and its interplay with childhood psychosocial stress in explaining risk for psychopathology in adolescence. (PINT1512\_IP L. Fañanas (G8)+G1+G4+G5+G22+ Ciberer-U719r+MHI of Manheim.
- Brain development and early stressful conditions in mental Health: the mediating role of epigenetic mechanisms and neuroimaging correlates (ES-EUEpiBrain) SAF2015-71526-REDT\_MINECO Acciones de Dinamización “Redes de Excelencia”\_IP.L.Fañanas (G8)+G4+G24+G25+Ciberer-U719+MHI of Manheim+ U Paris Descartes+ U Medical Center Utrech+U of Milan.

## Most relevant scientific articles

- CORDOVA-PALOMERA A., TORNADOR C., FALCON C., BARGALLO N., BRAMBILLA P., CRESPO-FACORRO B. ET AL. Environmental factors linked to depression vulnerability are associated with altered cerebellar resting-state synchronization. *Scientific Reports*. 2016;6.
- CORDOVA-PALOMERA A., DE REUS M.A., FATJO-VILAS M., FALCON C., BARGALLO N., VAN DEN HEUVEL M.P. ET AL. FKBP5 modulates the hippocampal connectivity deficits in depression: a study in twins. *Brain Imaging and Behavior*. 2016;1-14.
- PERALTA V, GOLDBERG X, RIBEIRO M, SANCHEZ-TORRES AM, FAÑANÁS L, CUESTA MJ. Familiality of Psychotic Disorders: A Polynologic Study in Multiplex Families. *Schizophrenia bulletin*. 2016.
- PRATS C., ARIAS B., MOYA-HIGUERAS J., POMAROL-CLOTET E., PARELLADA M., GONZALEZ-PINTO A. ET AL. Evidence of an epistatic effect between Dysbindin-1 and Neuretin-1 genes on the risk for schizophrenia spectrum disorders. *European Psychiatry*. 2016; 40:60-64.
- SOLER J, MIRET S, LÁZARO L, PARELLADA M, MARTÍN M, LERA-MIGUEL S ET AL. Influence of DAOA and RGS4 genes on the risk for psychotic disorders and their associated executive dysfunctions: A family-based study. *European psychiatry : the journal of the Association of European Psychiatrists*. 2016; 32:42-7.

## Highlights

The most relevant results of our group during 2016 are, on the one hand, the identified relationship between genetic variants in the FKBP5 gene and deficits in hippocampal connectivity in patients with depression. In addition, these patients seem to show alterations in cerebellum synchronization processes in resting state. Our designs, based on informative samples of monozygotic twins, have allowed us to attribute this alteration to non- shared environmental risk factors in pairs.


On the other hand, and with the collaboration of some CIBERSAM groups, different synaptic plasticity genes have been analysed in relation to the risk for psychosis and, especially, the role that some of these most significant variants might have on vulnerability to schizophrenia, its age of onset and altered cognitive functions. In this regard, it has been possible to demonstrate the epistasis between the DTNBP1-1 and NRN1 genes on the risk for schizophrenia and spectrum disorders, and the role of the NRN1 gene on the early onset of these disorders and on the presence of some cognitive deficits.


New research projects focused on the study of neurobiological mechanisms altered by exposure to child maltreatment have been established with the Central Institute of Mental Health in Mannheim. This new project has been linked to the multicenter FIS study PI15 / 00097 “Multicenter study of child maltreatment in children and adolescents with psychiatric disorders: epigenetic modifications and correlates with peripheral markers of innate immunity”, coordinated by our group, in which several CIBERSAM groups are involved.




LEAD RESEARCHER

**González-Pinto Arrillaga,  
Ana**

 **Fundación Vasca de Innovación  
e Investigación Sanitarias**  
Hospital Universitario  
de Álava-Sede Santiago  
C/ Olaguibel 29  
01004 Osakidetza

 (+34) 945 007 769

 [anamaria.gonzalez-  
pintoarrillaga@osakidetza.net](mailto:anamaria.gonzalez-pintoarrillaga@osakidetza.net)

 **Group website**

PROGRAMMES

**Bipolar disorder  
Schizophrenia**



## GROUP MEMBERS

**Staff members:** Alberich Mesa, Susana | García Alocén, Adriana | Martínez Cengotitabengoa, Mónica

**Associated members:** Bermúdez Ampudia, Cristina | De León Molina, José Alfonso | Echeburua Odriozola, Enrique | Echevarría Orella, Enrique | Fernández Hernández, Miryam | García Alocén, Adriana | García Fernández, Saínza | Gil Goikouria, Javier | González Ortega, Itxaso | Irazusta Astiazarán, Jon | López Peña, M<sup>a</sup> Purificación | Martín Carrasco, Manuel | Mosquera Ulloa, Fernando | Vega Pérez, Patricia | Zorrilla Martínez, Iñaki

**Contributors:** Alonso Pinedo, Marta | Besga Basterra, Adriana | Fernández de Corres Aguiriano, Blanca | Hernánz Manrique, Margarita | Karim Haidar, Mahmoud | Ruiz de Azua García, Sonia | Sáenz Herrero, Margarita | Ugarte Ugarte, Amaia

## Main lines of research

- Epidemiology, neurobiology, Bipolar Disorder.
- Epidemiology, neurobiology. First-Episode Psychosis (FEP)
- Etiopathogeny. Genes and environment.
- Cognitive Behavioural Therapy (CBT) for cannabis addiction in FEP.
- Cognitive Therapy in depressive episodes.
- Neuropsychological and neurobiological functioning in suicidal behaviour.
- Psychopathology of severe mental illness.
- Treatment and adherence.
- Telemedicine.

## Most relevant scientific articles

- MARTINEZ-CENGOTITABENGOA M, MACDOWELL KS, ALBERICH S, DIAZ FJ, GARCIA-BUENO B, RODRIGUEZ-JIMENEZ R ET AL. BDNF and NGF Signalling in Early Phases of Psychosis: Relationship With Inflammation and Response to Antipsychotics After 1 Year. *Schizophrenia bulletin*. 2016.
- SANADA K., ZORRILLA I., IWATA Y., BERMUDEZ-AMPUDIA C., GRAFF-GUERRERO A., MARTINEZ-CENGOTITABENGOA M. ET AL. The efficacy of non-pharmacological interventions on brain-derived neurotrophic factor in schizophrenia: A systematic review and meta-analysis. *International Journal of Molecular Sciences*. 2016;17(10).
- GARCIA S., MARTINEZ-CENGOTITABENGOA M., LOPEZ-ZURBANANO S., ZORRILLA I., LOPEZ P., VIETA E. ET AL. Adherence to Antipsychotic Medication in Bipolar Disorder and Schizophrenic Patients: A Systematic Review. *Journal of Clinical Psychopharmacology*. 2016.
- GONZÁLEZ-PINTO A, GONZÁLEZ-ORTEGA I, ALBERICH S, RUIZ DE AZÚA S, BERNARDO M, BIOQUE M ET AL. Opposite Cannabis-Cognition Associations in Psychotic Patients Depending on Family History. *PloS one*. 2016;11(8): e0160949.
- MARTIN-CARRASCO M., EVANS-LACKO S., DOM G., CHRISTODOULOU N.G., SAMOCHOWIEC J., GONZALEZ-FRAILE E. ET AL. EPA guidance on mental health and economic crises in Europe. *European Archives of Psychiatry and Clinical Neuroscience*. 2016;1-36.

## Highlights

The G10 group led by Ana González-Pinto has participated in several projects in 2006, such as the Mastermind project for the treatment of Depression focusing on telemedicine, the implementation of technology to Psychiatry and the improvement of clinical outcomes.

The group has also led 6 competitive national projects (ISCIII), being specially noteworthy the project on therapeutic adherence in First-Episode Psychosis (FEP) within SEPs study, the continuation in the Cognitive Behavioural Therapy for FEP and cannabis abuse, the project for Cognitive Therapy based on mindfulness for Bipolar Disorder and the study about the functioning of patients with suicidal behaviour. Moreover, two projects have been funded by Gobierno Vasco and another one received a grant for research groups from UPV/EHU.

As for collaborative projects, the participation on the study of infant maltreatment led by Dr Fañanas (G8) for the improvement of child mental health should be emphasized. Furthermore, the project led by Dr Molina (G19) which studies brain connectivity alterations in Schizophrenia, and the PEPs study directed by Dr Bernardo (G4) are also remarkable.


Besides, the group set a milestone with the national patent "*In vitro method and kit for the prognosis or prediction of response to treatment with antipsychotic agents in patients who have suffered a FEP*", as well as with the designation of Dr González-Pinto as president of SEPB.


Finally, the incorporation of new talents into research through internship training in the group and the completion of doctoral theses continues to be a priority in this group, having worked with Dr Kenji Sanada from Tokyo and Dr Zorrilla having defended his doctoral thesis on the long-term prognosis of Bipolar Disorder with mixed episodes.




LEAD RESEARCHER

**Haro Abad, Josep Maria**

 **Fundación para la Investigación y Docencia Sant Joan de Deu**  
Parc Sanitari Sant Joan de Deu  
Dr. Antoni Pujadas, 42  
08830 Sant Boi de Llobregat

 (+34) 93 600 26 85

 [jmharo@pssjd.org](mailto:jmharo@pssjd.org)

 [Group website](#)

PROGRAMMES  
**Schizophrenia**



## GROUP MEMBERS

**Staff members:** Mellor Marsa, Blanca | Moneta, Victoria | Obradors Tarragó, Carla | Olaya Guzmán, Beatriz | Siddi, Sara | Stephan Otto Attolini, Christian

**Associated members:** Araya la Rivera, Susana | Arranz Martí, Belén | Brébion, Gildas | Dolz Abadía, Montserrat | Foix Sanjuan, Alexandrina | Fuste Boadella, Montserrat | Garín Escrivá, Noé | Huerta Ramos, María Elena | Koyanagi, Al | Lara Pérez, Elvira | Moreno Bote, Rubén | Navarra Ordoño, Jordi | Ochoa Guerre, Susana | Rubio Abadal, Elena | San Molina, Luis | Tyrovolas, Stefanos | Usall Rodie, Judith

**Contributors:** Iniesta Benedicto, Raquel | López Carillero, Raquel | Roca Casasús, Mercedes

## Main lines of research

- Clinical, cognitive and psychosocial aspects of severe mental disorders.
- Epidemiology of mental disorders and ageing.
- Mental health interventions.
- Molecular psychiatry.
- Mental disorders in childhood and adolescence.

## Most relevant scientific articles

- FUSTE M., MELENDEZ-PEREZ I., VILLALTA-GIL V., PINACHO R., VILLALMANZO N., CARDONER N. ET AL. Specificity proteins 1 and 4, hippocampal volume and first-episode psychosis. *British Journal of Psychiatry*. 2016;208(6):591-592.
- KOYANAGI A., STICKLEY A., HARO J.M.. Psychotic symptoms and smoking in 44 countries. *Acta Psychiatrica Scandinavica*. 2016.
- GARIN N., KOYANAGI A., CHATTERJI S., TYROVOLAS S., OLAYA B., LEONARDI M. ET AL. Global Multimorbidity Patterns: A Cross-Sectional, Population-Based, Multi-Country Study. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences*. 2016;71(2):205-214.
- OLAYA B., MONETA M.V., KOYANAGI A., LARA E., MIRET M., AYUSO-MATEOS J.L. ET AL. The joint association of depression and cognitive function with severe disability among community-dwelling older adults in Finland, Poland and Spain. *Experimental Gerontology*. 2016;76:39-45.
- BRÉBION G., STEPHAN-OTTO C., OCHOA S., ROCA M., NIETO L., USALL J. Impaired Self-Monitoring of Inner Speech in Schizophrenia Patients with Verbal Hallucinations and in Non-clinical Individuals Prone to Hallucinations. *Frontiers in psychology*. 2016;7:1381.

## Highlights

Group 11 is the CIBER's representative in the international collaborative project RADAR-CNS (<http://www.radar-cns.org/>), funded by the IMI2 program to explore the potential of portable devices in the Prevention and treatment Depression, multiple sclerosis and epilepsy, in order to improve the quality of life of patients. Specifically, group 11 participates in the work-package that has explored the needs and viewpoints of patients with depressive disorder in relation to the use of multiparametric remote control technologies and has defined the most appropriate tools for assessing the fluctuation in time of sleep patterns, physical activity level, cognitive functioning, social interactions, and mood and stress so as to make meaningful predictions in these clinical populations.

It also participates as partner in the M-RESIST European project (<http://www.mresist.eu/>), funded by the EU's HORIZON 2020 with the main objective of developing a therapeutic program that draws on the support of mobile devices to actively involve patients with treatment-resistant schizophrenia to make them capable of self-managing their illness, as well as to support their careers.

Moreover, it is important to highlight its coordination of the European project ATHLOS (<http://athloproject.eu/>), funded by the EU's HORIZON 2020 with the aim of identifying healthy ageing trajectories and their determinants in order to achieve a better understanding of the ageing process to provide actionable insights to inform public policies. The consortium has already compiled data from longitudinal European and international studies on ageing to create the harmonized dataset (basis of the project results) and has developed the protocol for the creation of algorithms for the harmonization of variables and evaluated the statistical methodology to create a single metric of health.





LEAD RESEARCHER

**Leza Cerro, Juan Carlos**

 **Universidad Complutense de Madrid**

Facultad de Medicina  
Pza. Ramón y Cajal, s/n.  
Ciudad Universitaria  
28040 Madrid

 (+34) 91 394 14 78

 [jcleza@med.ucm.es](mailto:jcleza@med.ucm.es)

 **Group website**

PROGRAMMES

**Psychosomatic, Anxiety  
and Impulse Control Disorders  
Therapeutic Innovation**



GROUP MEMBERS

**Staff members:** Maccowell Mata, Karina

**Associated members:** Carrasco Perera, José Luis | Díaz Marsa, Marina | García Bueno, Borja | Muñoz Madrigal, José Luis | Rodríguez Maus, Sandra | Sayd, Aline

## Main lines of research

- Search for inflammatory biomarkers in plasma and peripheral blood mononuclear cells from neuropsychiatric diseases (depression, schizophrenia, bipolar disease) in order to identify and develop new therapeutic strategies.
- Potential new mechanisms: role of innate immunity receptors (TLRs) in stress-related processes in experimental models of neuro-psychiatric pathologies and in humans with depression, schizophrenia, autism spectrum disorders and ethanol abuse.
- Identification of possible trait or status biomarkers in eating disorders and in impulse control disorders.
- Regulatory intra and inter cellular mechanisms of noradrenaline and chemokines as anti-inflammatory mediators in experimental models and in patients with Alzheimer disease.
- Study of the mechanisms of brain passing of signaling molecules and the role of some blood brain barrier cells in its regulation.
- Study on protective mechanisms against oxidative and inflammatory cellular damage in experimental models of psychopathologies. Neuroprotective strategies.
- Study on intestinal translocation of bacteria in experimental models and in patients with depression, schizophrenia and autism spectrum disorders.

- Evaluation of the therapeutic potential of the endocannabinoid system in first episode psychosis and other psychiatric diseases.
- Evaluation of the therapeutic potential of the endocannabinoid system in gastrointestinal pathologies related with stress exposure.
- Search for novel antiinflammatory/antioxidant mechanisms of antidepressants and antipsychotics in experimental models (in vivo and in vitro).

## Most relevant scientific articles

- MARTIN-HERNANDEZ D., CASO J.R., BRIS A.G., MAUS S.R., MADRIGAL J.L.M., GARCIA-BUENO B. ET AL. Bacterial translocation affects intracellular neuroinflammatory pathways in a depression-like model in rats. *Neuropharmacology*. 2016; 103:122-133.
- BIOQUE M., CABRERA B., GARCIA-BUENO B., MAC-DOWELL K.S., TORRENT C., SAIZ P.A. ET AL. Dysregulated peripheral endocannabinoid system signaling is associated with cognitive deficits in first-episode psychosis. *Journal of Psychiatric Research*. 2016; 75:14-21.
- GARCÍA-BUENO B, GASSÓ P, MACDOWELL KS, CALLADO LF, MAS S, BERNARDO M ET AL. Evidence of activation of the Toll-like receptor-4 proinflammatory pathway in patients with schizophrenia. *Journal of psychiatry & neuroscience : JPN*. 2016;41(3):150195.
- GARCIA BUENO B., CASO J.R., MADRIGAL J.L.M., LEZA J.C. Innate immune receptor Toll-like receptor 4 signalling in neuropsychiatric diseases. *Neuroscience and Biobehavioral Reviews*. 2016; 64:134-147.
- MACDOWELL K.S., CASO J.R., MARTIN-HERNANDEZ D., MORENO B.M., MADRIGAL J.L.M., MICO J.A. ET AL. The Atypical Antipsychotic Paliperidone Regulates Endogenous Antioxidant/Anti-Inflammatory Pathways in Rat Models of Acute and Chronic Restraint Stress. *Neurotherapeutics*. 2016:1-11.

## Highlights

Dr. Leza leads a stable and consolidated group. During the year 2016, new public and private funds have been granted (MINECO SAF, Fund. Santander-UCM).


This group is also characterized by its active involvement in teaching and training of new researchers, receiving in the last year both national and international undergraduate, master, doctorate and postgraduate students. Leza's group maintains its commitment to the co-organization of the "young scientists' ideas laboratory" annual meeting.

Finally, this group is committed to the diffusion and search of collaborations between the different groups of CIBERSAM and other consortia.



LEAD RESEARCHER

**Mckenna, Peter.J**

 **Fundación para la Investigación y Docencia María Angustias Gimenez (FIDMAG)**  
Hospital Hermanas Hospitalarias Benito Menni  
C/ Dr. Pujadas, 38  
08830 San Boi de Llobregat

 (+34) 93 652 99 99 (Ext 1486)

 pmckenna@fidmag.com

 **Group website**

PROGRAMMES

**Schizophrenia  
Bipolar disorder**



#### GROUP MEMBERS

**Staff members:** Alonso Lana, Silvia | Canales Rodríguez, Erick Jorge | Guardiola Ripoll, María | Moreno Alcazar, Ana | Salgado Pineda, Pilar

**Associated members:** Gomar Soñes, Jesús Joaquín | Martín Subero, Marta | Monte Rubio, Gemma Cristina | Pomarol Clotet, Edith | Radua Castaño, Joaquín | Romaguera Piñol, Anna | Salvador Civil, Raymond | Sarro Maluquer, Salvador | Valiente Gómez, Alicia | Vicens Soler, Víctor

**Contributors:** Ortiz Gil, Jordi

## Main lines of research

The main research areas involve: a) the development and clinical application of multimodal neuroimaging techniques in major psychiatric illnesses such as schizophrenia and bipolar disorder (also combined with clinical and neuropsychological data) in order to study their brain structural and functional correlates, and b) carrying out of clinical trials of novel treatment strategies.

- Neuroimaging in major psychiatric illnesses:
  - Multimodal imaging: Development and use of new methods of image analysis in different pathologies. Design of new studies involving the development and implementation of new cognitive paradigms for use with fMRI.
  - The research team mainly works with schizophrenia, bipolar disorder and first episode psychosis. We currently have several ongoing projects involving novel fMRI paradigms for use in schizophrenia and bipolar disorder, the usefulness of machine learning for establishing diagnosis and predicting outcome in these disorders.
- Development of new MRI analysis methods of analysis. Specifically, we work on the creation of tools applicable to white matter imaging (DTI and tractography), functional connectivity in the resting state and analysis of structural MRI images. In addition, our unit has developed state-of-the-art meta-analytic methods for brain imaging data.
- Genetic studies of psychiatric disorders, especially schizophrenia, as well as the studies of genotype-phenotype relationships (clinical and neuroimaging) in these disorders.



- Development of new therapeutic approaches.
- Studies directed to the brain mechanisms underlying psychotic symptoms such as delusions, hallucinations and formal thought disorder.
- Development and validation of symptom scales.

## Most relevant scientific articles

- VICENS V, RADUA J, SALVADOR R, ANGUERA-CAMÓS M, CANALES-RODRÍGUEZ EJ, SARRÓ S ET AL. Structural and functional brain changes in delusional disorder. *The British journal of psychiatry : the journal of mental science*. 2016;208(2):153-9.
- ALONSO-LANA S., VALENTI M., ROMAGUERA A., SARRI C., SARRO S., RODRIGUEZ-MARTINEZ A. ET AL. Brain functional changes in first-degree relatives of patients with bipolar disorder: evidence for default mode network dysfunction. *Psychological Medicine*. 2016;1-9.
- SALGADO-PINEDA P., LANDIN-ROMERO R., PORTILLO F., BOSQUE C., POMES A., SPANLANG B. ET AL. Examining hippocampal function in schizophrenia using a virtual reality spatial navigation task. *Schizophrenia Research*. 2016;172(1-3):86-93.
- ALONSO-LANA S, GOIKOLEA JM, BONNIN CM, SARRÓ S, SEGURA B, AMANN BL ET AL. Structural and Functional Brain Correlates of Cognitive Impairment in Euthymic Patients with Bipolar Disorder. *PloS one*. 2016;11(7): e0158867.
- LANDIN-ROMERO R, MCKENNA PJ, ROMAGUERA A, ÁLVAREZ-MOYA E, SARRÓ S, AGUIRRE C ET AL. Examining the continuum of psychosis: Frequency and characteristics of psychotic-like symptoms in relatives and non-relatives of patients with schizophrenia. *Schizophrenia research*. 2016.

## Highlights

In 2016 FIDMAG Hermanas Hospitalarias was awarded the Josep Trueta Prize, by the “Acadèmia de Ciències Mèdiques de Catalunya i Balears” for scientific leadership.

We are currently carrying out, in collaboration with a group in Hospital Sant Pau, the first clinical trial of Deep Brain Stimulation (DBS) in treatment-resistant schizophrenia. Six of a projected 8 patients have now been treated and initial results have been published. We have also participated in several multicenter phase III clinical trials, including on esketamine in major depression.

Among our studies published in 2016 is the first modern imaging study of delusional disorder. Although this is a well-validated diagnostic entity, there has been very little examination of its biological basis. In particular, it is not known whether patients show the kinds of structural and functional brain changes seen in schizophrenia, a disorder which it is believed to be closely related to. Vicens et al (2016) collected a sample of 22 patients meeting DSM IV criteria for delusional disorder and compared them to 44 healthy controls using a) whole-brain brain structural imaging, (voxel-based morphometry, VBM), b) functional imaging (fMRI) during performance of a widely used cognitive task, the n-back working memory task, and c) resting state functional connectivity. Evidence was found of structural and functional brain abnormality in the medial frontal cortex and the insula in the patients.


We continue to develop new neuroimaging techniques, including functional imaging paradigms, new methods for processing white matter images, and meta-analytic methods for integrating the results of neuroimaging studies.


In parallel with this, we continue with an active programme of pre- and post-doctoral research training. This year five research students have been awarded PhDs.




LEAD RESEARCHER

**Meana Martínez,  
José Javier**

 **Universidad del País Vasco**  
Facultad de Medicina y  
Odontología.  
Campus de Leioa.  
Barrio Sarriena s/n  
48940 Leioa

 (+34) 94 601 27 57

 javier.meana@ehu.es

 **Group website**

PROGRAMMES

**Schizophrenia  
Therapeutic Innovation**



## GROUP MEMBERS

**Staff members:** Corada Galarreta, Leire | Munarriz Cuezva, Eva

**Associated members:** Ballesteros Rodríguez, Francisco Javier | Barrondo Lakarra, Sergio | Callado Hernando, Luis Felipe | Díez Alarcia, Rebeca | Erdozain Fernández, Amaia Maite | Gabilondo Urquijo, Ane Miren | Gutiérrez Fraile, Miguel | Horrillo Furundarena, Igor | Ibarra Lecue, Inés | López de Jesús, Maider | Mollinedo Gajate, Irene | Ortega Calvo, Jorge Emilio | Peñagarikano Ahedo, Olga | Pérez del Palomar, Blanca | Rivero Calera, Guadalupe | Salles Alvira, Joan | Urigüen Echeverría, Leyre

**Contributors:** Eguiluz Uruchurtu, Iñaki | Elizagarate Zabala, Edorta | Muguruza Millán, Carolina | Palomo Lerchundi, Javier | Querejeta Ayerdi, Imanol | Segarra Echebarría, Rafael

## Main lines of research

- Therapeutic interventions in mental health.
- Neuropsychopharmacology.
- First psychotic episodes: prognosis, diagnosis, and predictive factors in the evolution of the disease.
- Biological markers in psychiatric diseases and their treatment.

## Most relevant scientific articles

- MORENO J.L., MIRANDA-AZPIAZU P., GARCIA-BEA A., YOUNKIN J., CUI M., KOZLENKOV A. ET AL. Allosteric signaling through an mGlu2 and 5-HT2A heteromeric receptor complex and its potential contribution to schizophrenia. *Science Signaling*. 2016;9(410).
- RIVERO G., MARTIN-GUERRERO I., DE PRADO E., GABILONDO A.M., CALLADO L.F., GARCIA-SEVILLA J.A. ET AL. Alpha2C-adrenoceptor Del322-325 polymorphism and risk of psychiatric disorders: significant association with opiate abuse and dependence. *World Journal of Biological Psychiatry*. 2016;1-8.
- DIEZ-ALARCIA R., IBARRA-LECUE I., LOPEZ-CARDONA A.P., MEANA J., GUTIERREZ-ADAN A., CALLADO L.F. ET AL. Biased agonism of three different cannabinoid receptor agonists in mouse brain cortex. *Frontiers in Pharmacology*. 2016;7(NOV).
- GARCÍA-BUENO B, GASSÓ P, MACDOWELL KS, CALLADO LF, MAS S, BERNARDO M ET AL. Evidence of activation of the Toll-like receptor-4 proinflammatory pathway in patients with schizophrenia. *Journal of psychiatry & neuroscience : JPN*. 2016;41(3):150195.
- GARCIA-PORTILLA M.P., GARCIA-ALVAREZ L., SARRAMEA F., GALVAN G., DIAZ-MESA E., BOBES-BASCARAN T. ET AL. It is feasible and effective to help patients with severe mental disorders to quit smoking: An ecological pragmatic clinical trial with transdermal nicotine patches and varenicline. *Schizophrenia Research*. 2016.

## Highlights


### PROJECT

DM-DX: Desarrollo y validación de un test de diagnóstico molecular in vitro de la Depresión Mayor. Proyecto entre Progenika Biopharma S.A. y Asoc. Instituto de Investigación Sanitaria BioCruces. Programa Retos Colaboración. Ministerio de Economía y Competitividad. Reference Project RTC-2015-3911-1.



LEAD RESEARCHER

**Menchón Magriña,  
José Manuel**

 **Fundación IDIBELL**  
Hospital Universitario  
de Bellvitge  
C/ Freixa Larga s/n  
08907 Hospitalet de Llobregat

 (+34) 93 260 79 22

 [jmenchon@bellvitgehospital.cat](mailto:jmenchon@bellvitgehospital.cat)

 [Group website](#)

PROGRAMMES

**Depression  
Psychosomatic, Anxiety  
and Impulse Control Disorders**



GROUP MEMBERS

**Staff members:** Giménez Navarro, Mónica | Suñol Rodrigo, María

**Associated members:** Albacete Belzunces, Auría | Alonso Ortega, María del Pino | Cano Catalá, Marta | Contreras Fernández, Fernando | Contreras Rodríguez, Oren | Crespo Blanco, José Manuel | Hernández Ribas, Rosa | López Solá, Clara | Real Barrero, Eva | Segalas Cosi, Jacinto | Soria Tomás, Virginia | Soriano Más, Carles | Subira Coromina, Marta | Urretavizcaya Sarachaga, Mikel | Vallejo Ruiloba, Julio

## Main lines of research

- Obsessive-compulsive disorder; compulsivity.
- Neuroimaging.
- Mood disorders.
- Physical therapies.

## Most relevant scientific articles

- BOEDHOE PS, SCHMAAL L, ABE Y, AMEIS SH, ARNOLD PD, BATISTUZZO MC ET AL. Distinct Subcortical Volume Alterations in Pediatric and Adult OCD: A Worldwide Meta- and Mega-Analysis. *The American journal of psychiatry*. 2016; appiajp201616020201.
- COSTAS J, CARRERA N, ALONSO P, GURRIARÁN X, SEGALÀS C, REAL E ET AL. Exon-focused genome-wide association study of obsessive-compulsive disorder and shared polygenic risk with schizophrenia. *Translational psychiatry*. 2016; 6:e768.
- CANO M., CARDONER N., URRETAVIZCAYA M., MARTINEZ-ZALACAIN I., GOLDBERG X., VIA E. ET AL. Modulation of Limbic and Prefrontal Connectivity by Electroconvulsive Therapy in Treatment-resistant Depression: A Preliminary Study. *Brain Stimulation*. 2016;9(1):65-71.
- STEIN D.J., HERMESH H., EILAM D., SEGALAS C., ZOHAR J., MENCHON J. ET AL. Human compulsivity: A perspective from evolutionary medicine. *European Neuropsychopharmacology*. 2016;26(5):869-876.
- MENCHON J.M., VAN AMERINGEN M., DELL'OSSO B., DENYS D., FIGEE M., GRANT J.E. ET AL. Standards of care for obsessive-compulsive disorder centres. *International Journal of Psychiatry in Clinical Practice*. 2016;20(3):204-208.

## Highlights

The group has maintained the development of different research lines in the field of mental disorders and some cross-diagnostic lines such as neuroimaging or genetics.


In the field of obsessive-compulsive disorder (OCD), the group has participated in several international consortiums sharing projects, publications and leading some studies. The group, and particularly the neuroimaging lab, has had a role within the ENIGMA (Enhancing NeuroImaging Genetics through Meta-Analysis) consortium in which our group participates in the OCD working group as well as within the International OCD Brain Imaging Consortium, which is oriented to the research on neuroimaging with groups from four continents. The group has kept the collaboration with other CIBER groups in the study of compulsive behaviors that arise in gambling disorder and in the eating behavior disorders. Further, promoted by the ICOCS, it has been developed and published a proposal of standards of care for OCD units in which groups from the five continents have participated. Regarding deep brain stimulation, the group has contributed to the exploitation and interpretation of the data from the international multicenter trial in which the group has participated.


In the field of mood disorders, it has been kept a significant activity in collaborative projects and studies on bipolar disorder, whereas in unipolar depression the group has continued developing the Integrated Project of Excellence 'Epigenetic and environmental factors bracing cognitive impairment and late-onset depression in elderly and early stages of Alzheimer disease'. The group has also participated in a national consensus on the use of electroconvulsive therapy further to organize an educational course biannually. Lastly, the schizophrenia research line has developed studies on the deficits in contrafactual reasoning in this disorder.



LEAD RESEARCHER

**Micó Segura,  
Juan Antonio**

 **Universidad de Cádiz**  
Facultad de Medicina  
Calle Ancha, 16  
11001 Cadiz

 (+34) 95 601 52 47

 [juanantonio.mico@uca.es](mailto:juanantonio.mico@uca.es)

 [Group website](#)

PROGRAMMES

**Depression | Schizophrenia | Therapeutic  
Innovation | Psychosomatic, Anxiety  
and Impulse Control Disorders**



GROUP MEMBERS

**Staff members:** Díaz Gañete, Antonia | Llorca Torralba, Meritxell | Torres Sánchez, Sonia

**Associated members:** Berrocoso Domínguez, Esther | Bravo García, Lidia | Gibert Rahola, Juan | Pérez Caballero, Laura | Romero Grimaldi, Carmen

**Contributors:** Gallego Gamó, Jesús

## Main lines of research

- Major Area 1: Pain & Depression
- Major Area 2: Mechanisms of action of Deep Brain Stimulation in CNS Disorders.
- Major Area 3: Neurobiology and Treatment of Schizophrenia and related mental disorders.

## Most relevant scientific articles

- TORRES-SANCHEZ S, PEREZ-CABALLERO L, BERROCOSO E. Cellular and molecular mechanisms triggered by Deep Brain Stimulation in depression: A preclinical and clinical approach. *Progress in neuro-psychopharmacology & biological psychiatry*. 2016.
- BRAVO L., MICO J.A., REY-BREA R., CAMARENA-DELGADO C., BERROCOSO E.. Effect of DSP4 and desipramine in the sensorial and affective component of neuropathic pain in rats. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*. 2016; 70:57-67.
- LLORCA-TORRALBA M, BORGES G, NETO F, MICO JA, BERROCOSO E. Noradrenergic Locus Coeruleus pathways in pain modulation. *Neuroscience*. 2016.
- MACDOWELL K.S., CASO J.R., MARTIN-HERNANDEZ D., MORENO B.M., MADRIGAL J.L.M., MICO J.A. ET AL. The Atypical Antipsychotic Paliperidone Regulates Endogenous Antioxidant/Anti-Inflammatory Pathways in Rat Models of Acute and Chronic Restraint Stress. *Neurotherapeutics*. 2016:1-11.
- KOSEK E., COHEN M., BARON R., GEBHART G.F., MICO J.-A., RICE A.S.C. ET AL. Do we need a third mechanistic descriptor for chronic pain states? *Pain*. 2016;157(7):1382-1386.

## Highlights

In 2016, our group has continued focussing on three of its main translational and collaborative lines with other CIBERSAM groups: 1) the molecular mechanisms involved in the mechanism of action of Deep Brain Stimulation (DBS); 2) the biochemical mechanisms involved in the comorbidity of mental disorders and chronic pain and 3) the implication of neuro-inflammatory mechanisms in schizophrenia. The results obtained in these investigations have been published in journals situated in the first decile of JCR (*Schizophrenia Bulletin*, *Cerebral Cortex*, *Pain*). In relation to these investigations, specifically the line 2, we have obtained a Project of the Brain & Behavior Foundation (EEUU) as well as a project of the National Research Plan.

The key milestones may be summarized as follow: In relation to treatment-resistant depressions, we have demonstrated that AMPA receptor activation appears necessary and sufficient to elicit an antidepressant response with DBS.

In the line of schizophrenia, our group in collaboration with several CIBERSAM groups, has investigated whether potential changes in plasma levels of neurotrophins (BDNF and NGF) and their specific receptors, may act as potential biomarkers of risk and protective factors of schizophrenia. In the same vein, we have also participated, in collaboration with other CIBERSAM groups, in the demonstration that the increase of endogenous antioxidant / anti-inflammatory factors may be the basis of the mechanism of action of some of the current antipsychotics.

In the line of comorbidity mental disorders-chronic pain, our group in relation to other international groups, have proposed a new terminology in pain that allows to interpret the emotional symptoms in relation to the physical symptoms presents in patients.

Finally, our group has actively participated in the organization and scientific facts of the Master of Initiation to Research in Mental Health.




LEAD RESEARCHER

**Palomo Álvarez, Tomás**

 **Universidad Complutense de Madrid**

Facultad de Medicina  
Pza. Ramón y Cajal, s/n.  
Ciudad Universitaria  
28040 Madrid

 (+34) 91 394 15 93

 tomas.palomo@gmail.com

 **Group website**

PROGRAMMES

**Schizophrenia  
Psychosomatic, Anxiety  
and Impulse Control Disorders**



## GROUP MEMBERS

**Staff members:** González Guede, Irene | Villar Bogalo, María del Pilar

**Associated members:** Aguera Ortíz, Luis Fernando | Aragües Figuero, María | Caso Fernández, Javier Rubén | Hoenicka Blanco, Janet | Jiménez Arriero, Miguel Ángel | Lobo Satué, Antonio | Molina Rodríguez, Vicente | Moreno Ortega, Marta | Sanz Fuentenebro, Francisco Javier

**Contributors:** Guerra Martín-Polanco, Noelia | Navío Acosta, María Mercedes

## Main lines of research

- Schizophrenia. First psychotic episodes.
- Bipolar disorder.
- Addictive disorders.
- Psychosomatic disorders.
- Personality disorders.
- Depression.
- Dementia.
- Molecular and genetic basis, neurocognition, neurophysiology, neuroinflammation and neuroimaging in psychiatric disorders.



## Most relevant scientific articles

- LANCTÔT KL, AGÜERA-ORTIZ L, BRODATY H, FRANCIS PT, GEDA YE, ISMAIL Z ET AL. Apathy associated with neurocognitive disorders: recent progress and future directions. *Alzheimer's & dementia : the journal of the Alzheimer's Association*. 2016.
- GARCIA BUENO B., CASO J.R., MADRIGAL J.L.M., LEZA J.C. Innate immune receptor Toll-like receptor 4 signalling in neuropsychiatric diseases. *Neuroscience and Biobehavioral Reviews*. 2016; 64:134-147.
- ESPAÑA-SERRANO L, GUERRA MARTÍN-PALANCO N, MONTERO-PEDRAZUELA A, PÉREZ-SANTAMARINA E, VIDAL R, GARCÍA-CONSUEGRA I ET AL. The Addiction-Related Protein ANKK1 is Differentially Expressed During the Cell Cycle in Neural Precursors. *Cerebral cortex (New York, N.Y.: 1991)*. 2016;.
- MARCOS G., SANTABARBARA J., LOPEZ-ANTON R., DE-LA-CAMARA C., GRACIA-GARCIA P., LOBO E. ET AL. Conversion to dementia in mild cognitive impairment diagnosed with DSM-5 criteria and with Petersen's criteria. *Acta Psychiatrica Scandinavica*. 2016;133(5):378-385.
- MARTIN-HERNANDEZ D., CASO J.R., BRIS A.G., MAUS S.R., MADRIGAL J.L.M., GARCIA-BUENO B. ET AL. Bacterial translocation affects intracellular neuroinflammatory pathways in a depression-like model in rats. *Neuropharmacology*. 2016; 103:122-133.

## Highlights

The group G19 scientific activity is focused mainly on the molecular and genetic bases, neurocognition, neurophysiology, neuroinflammation and neuroimaging in psychiatric disorders. All these research lines are being financed through ongoing projects grants.

In 2016 we should highlight the creation of a new laboratory for molecular and genetic studies in psychiatric diseases. The opening of this laboratory will allow us to continue to deepen the functionality of the ANKK1 gene. These studies have resulted in several papers, the most recent being "The Addiction-Related Protein ANKK1 is Differentially Expressed During the Cell Cycle in Neural Precursors" published this year in *Cereb cortex*. This new lab will allow us to continue the molecular studies of the dopaminergic system closely linked to the functionality of the ANKK1 gene.

In 2016, the IP of this G19 Group has established an institutional relationship with the San Carlos Sanitary Research Institute (IdISSC) as IP of the Psychiatric Disorders Group of the Institute. The 2017 Integrated Project of Excellence of Hospital Clínico de San Carlos, "Dysfunction of the coronary microcirculation, small vessel cerebral disease and depression in the patient with ischemic heart disease", coordinated by the Cardiology Service, is a result of this collaboration.

The incorporation of Dr. Lobo to the group in Zaragoza has reinforced Dr. Agüera research in Madrid on dementia and cognition. This has resulted in a noticeable increase in the number of publications in this field by the group.


Our close collaboration with Dr. Leza's group and other CIBERSAM groups is being very fruitful in the field of neuroinflammation with eight collaborative papers published in 2016.


Finally, with regard to teaching and training, we continue to coordinate the groups participating in the Interuniversity Master's Degree in Mental Health Research at the Hospitals of Madrid.




LEAD RESEARCHER

**Pazos Carro,  
Ángel Armando**

 **Universidad de Cantabria**  
Facultad de Medicina.  
Instituto de Biomedicina y  
Biotecnología de Cantabria.  
c/ Albert Einstein, 22  
39011 Santander

 (+34) 94 220 19 85

 pazosa@unican.es

 **Group website**

PROGRAMMES

**Depression  
Therapeutic Innovation**



GROUP MEMBERS

**Staff members:** Luque Jiménez, María del Rocío | Pilar Cuellar, María Fuencisla

**Associated members:** Castro Fernández, Elena | Díaz Martínez, Álvaro Marcelino | Garro Martínez, Emilio | Linge Méndez, Raquel | Marrón Souto, Eva | Vidal Casado, Rebeca

**Contributors:** Vargas, Verónica

## Main lines of research

- New etiopathogenic hypothesis of mental illness.
- Serotonergic system and Cannabinoid system in depression.
- Intracellular signaling pathways involved in psychiatric disorders.
- Involvement of hippocampal neurogenesis in depressive disorders.
- Animal models of depression / anxiety.
- Antidepressants and pain.
- Molecular basis for the development of fast-acting antidepressants.
- siRNA as a novel therapeutic strategies in psychiatry.
- Pharmacogenetics of depression.

## Most relevant scientific articles

- LINGE R, JIMÉNEZ-SÁNCHEZ L, CAMPA L, PILAR-CUÉLLAR F, VIDAL R, PAZOS A ET AL. Cannabidiol induces rapid-acting antidepressant-like effects and enhances cortical 5-HT/glutamate neurotransmission: role of 5-HT<sub>1A</sub> receptors. *Neuropharmacology*. 2016; 103:16-26.
- AMIGÓ J, DÍAZ A, PILAR-CUÉLLAR F, VIDAL R, MARTÍN A, COMPAN V ET AL. The absence of 5-HT<sub>4</sub> receptors modulates depression- and anxiety-like responses and influences the response of fluoxetine in olfactory bulbectomised mice: Adaptive changes in hippocampal neuroplasticity markers and 5-HT<sub>1A</sub> autoreceptor. *Neuropharmacology*. 2016.
- FERRES-COY A., GALOFRE M., PILAR-CUÉLLAR F., VIDAL R., PAZ V., RUIZ-BRONCHAL E. ET AL. Therapeutic antidepressant potential of a conjugated siRNA silencing the serotonin transporter after intranasal administration. *Molecular Psychiatry*. 2016;21(3):328-338.
- JIMENEZ-SANCHEZ L., LINGE R., CAMPA L., VALDIZAN E.M., PAZOS A., DIAZ A. ET AL. Behavioral, neurochemical and molecular changes after acute deep brain stimulation of the infralimbic prefrontal cortex. *Neuropharmacology*. 2016; 108:91-102.
- ESPAÑA-SERRANO L, GUERRA MARTÍN-PALANCO N, MONTERO-PEDRAZUELA A, PÉREZ-SANTAMARINA E, VIDAL R, GARCÍA-CONSUEGRA I ET AL. The Addiction-Related Protein ANKK1 is Differentially Expressed During the Cell Cycle in Neural Precursors. *Cerebral cortex (New York, N.Y.: 1991)*. 2016.

## Highlights

During 2016, our group has focused on: (1) the study of fast acting antidepressants. In this sense, we are working in a nationally financed project (SAF2015-67457-R) for the study of the neuroplastic and neurochemical mechanisms of action involved in the rapid antidepressant effect of the phytocannabinoid compound cannabidiol. This compound exhibits an important anti-inflammatory effect. Therefore, we are evaluating cannabidiol actions in a neuroinflammatory animal model of depression. Additionally, we are involved in a collaborative study on deep brain stimulation as a rapid and effective antidepressant therapy. (2) On the other hand, we are studying novel therapeutic targets for the treatment of depression, specially evaluating mTOR and Wnt/ $\beta$ -catenin pathways, involved in neuroplasticity, to understand their contribution to the neurobiology of depression and antidepressant effects. (3) Finally, another relevant lines are the study of the implication of serotonergic 5-HT<sub>4</sub> in 5-HT<sub>1A</sub> receptors by using animal models of depression.


Our group also has an important dedication to the coordination of the “Máster Interuniversitario de Iniciación a la Investigación en Salud Mental”.



LEAD RESEARCHER

**Pérez Sola, Víctor**

 **Consorci Mar Parc Salut de Barcelona**  
Consorcio Mar Parc de Salut de Barcelona  
Dr. Aiguader, 88, 1ª Pl.  
08003 Barcelona

 (+34) 607 664 285

 [vperezsola@parcdesalutmar.cat](mailto:vperezsola@parcdesalutmar.cat)

 [Group website](#)

PROGRAMMES

**Depression  
Psychosomatic, Anxiety  
and Impulse Control Disorders**



GROUP MEMBERS

**Staff members:** Allende Leal, Saiko | Blanco Hinojo, Laura | Elices, Matilde | Grasa Bello, Eva María | Pujol Nuez, Jesús

**Associated members:** Alonso Solís, Ana | Álvarez Martínez, Enrique | Antonijoan Arbos, Rosa María | Arranz Calderón, María Jesús | Berge Baquero, Daniel | Bulbena Vilarrasa, Antonio | Carceller Sindreu, María del Mar | Clos Batet, Susana | Colom Victoriano, Francesc | Córcoles Martínez, David | Corripio Collado, Iluminada | De Diego Adeliño, Francisco Javier | Durán-Sindreu Terol, Santiago | Fullana Rivas, Miquel Àngel | Giménez Badía, Sandra | Martín Blanco, Ana | Martín López, Luis Miguel | Oller Canet, Sílvia | Pascual Mateos, Juan Carlos | Pérez Blanco, Josefina | Pérez de los Cobos Peris, José | Pérez Egea, Rosario | Portella Moll, María Jesús | Puigdemont Campos, Dolors | Rabella Figueras, Mireia | Ramos Ferraz, Liliana | Riba Serrano, Jordi | Sauras Quetcuti, Rosa Blanca | Serra Blasco, María | Soler Ribaudí, Joaquín | Tiana Sastre, Thais | Toll Privat, Alba | Trujols Albet, Joan | Valle Cano, Marta

**Contributors:** Ballester Verneda, María Rosa | Gich Saladich, Ignacio José | Romero Lafuente, Sergio

## Main lines of research

**Permanent research lines:**

- Affective disorders: new therapeutic strategies in treatment-resistant major depression; Deep Brain Stimulation in Treatment Resistant Major Depression; structural neuroimaging; treatment resistance biological and genetic biomarkers; biological and genetic studies of inflammatory processes in major depression; identification and evaluation of new therapeutic targets and programs; pharmacogenetics; ICT application and new technologies in the prevention and treatment of depression and bipolar disorder; assessment of traumatic processes in affective disorders and treatment using psychotherapeutic techniques, e.g. EMDR; assessment of therapeutic strategies in suicidal behavior.
- Psychotic disorders: efficacy and effectiveness of antipsychotic drugs; first episodes of psychosis; genotype-phenotype and environment interaction; neuroimaging; pharmacogenetics; ICT and Apps in m-health for treatment resistant schizophrenia; Deep Brain Stimulation in Treatment Resistant Schizophrenia; third generation therapies for the treatment of schizophrenia (metacognition and mentalization); assessment of the possible beneficial effect of physical activity and intensive reemployment programs in first psychotic episodes.

- Personality disorders: mixed treatment in patients with Borderline Personality Disorder (BPD), validation of diagnostic instruments; genetic-environment studies; structural and functional neuroimaging studies on mindfulness effects; design and assessment of ICTs in the follow-up of BPD.
- Addictive Disorders: Patient satisfaction concerning maintenance treatment with opioid agonists (methadone and buprenorphine/naloxone); Methadone pharmacogenetics and satisfaction of heroin-dependent patients regarding methadone as a medication; explanatory factors of absence of cocaine craving throughout inpatient detoxification treatment; studies on the human reward circuit in abstinent cocaine-dependent patients.
- Mental health therapeutics: efficacy and resistance to treatment; validation of diagnostic and assessment scales; systematic reviews; neuropsychology; neurophysiology; neuroimaging and response to treatment.

#### **New research lines:**

- Adjuvant use of Ayahuasca in the treatment of Borderline Personality Disorder; Extreme phenotypes of treatment resistance in Depression; Prognostic study on treatment response prediction in Depression using PReDicT test; Analysis of clusters of cognitive performance in Depression and Schizophrenia; assessment of specific treatments in patients with bipolar disorder and history of trauma.

## **Most relevant scientific articles**

- VAQUERO L., CAMARA E., SAMPEDRO F., PEREZ DE LOS COBOS J., BATLLE F., FABREGAS J.M. ET AL. Cocaine addiction is associated with abnormal prefrontal function, increased striatal connectivity and sensitivity to monetary incentives, and decreased connectivity outside the human reward circuit. *Addiction Biology*. 2016.
- SERRA-BLASCO M., DE DIEGO-ADELINO J., VIVES-GILABERT Y., TRUJOLS J., PUIGDEMONT D., CARCELLER-SINDREU M. ET AL. NATURALISTIC COURSE OF MAJOR DEPRESSIVE DISORDER PREDICTED BY CLINICAL AND STRUCTURAL NEUROIMAGING DATA: A 5-YEAR FOLLOW-UP. *Depression and Anxiety*. 2016.
- MARTÍN-BLANCO A, FERRER M, SOLER J, ARRANZ MJ, VEGA D, CALVO N ET AL. The role of hypothalamus-pituitary-adrenal genes and childhood trauma in borderline personality disorder. *European archives of psychiatry and clinical neuroscience*. 2016;266(4):307-16.
- DAVEY C.G., PUJOL J., HARRISON B.J. Mapping the self in the brain's default mode network. *NeuroImage*. 2016; 132:390-397.
- PINHO M., SEHMBI M., CUDNEY L.E., KAUER-SANT'ANNA M., MAGALHAES P.V., REINARES M. ET AL. The association between biological rhythms, depression, and functioning in bipolar disorder: A large multi-center study. *Acta Psychiatrica Scandinavica*. 2016;133(2):102-108.


## **Hightlights**


- Epigenetic study in patients with Borderline Personality Disorder.
- Clinical trial on the effects of mindfulness for the treatment of borderline personality disorder, assessed with fMRI.
- Development and validation of a new technique for the temporal determination of cortisol in hair, as a biomarker of stress and depression.
- Collaborative European project for the implementation of ICT in the prevention and treatment of schizophrenia.
- Collaborative European and Spanish project on treatment response prediction using an algorithm based on negative emotional bias.
- Publication of the first positive results on efficacy of deep brain stimulation in treatment-resistant schizophrenia.
- Assessment of proneurons derived from the olfactory bulb as a model of mental disorders (Schizophrenia and Major Depressive Disorder).
- Funding to conduct a clinical trial on Deep Brain Stimulation in treatment-resistant anorexia nervosa.
- Pilot study with S-Ketamine for treatment-resistant major depression.




LEAD RESEARCHER

**Sáiz Ruiz, Jerónimo**

 **Servicio Madrileño de Salud**  
Hospital Ramón y Cajal  
Carretera de Colmenar, km 9.1  
28034 Madrid

 (+34) 91 336 83 93

 [jsaiz.hrc@salud.madrid.org](mailto:jsaiz.hrc@salud.madrid.org)

 [Group website](#)

PROGRAMMES

**Schizophrenia  
Psychosomatic, Anxiety  
and Impulse Control Disorders**



GROUP MEMBERS

**Staff members:** Almeida Nunes, Rosa María | Anaya Suárez, Celia | Grillo Durán, Beatriz

**Associated members:** Artes Rodríguez, Antonio | Baca García, Enrique | Blasco Fontecilla, Hilario | Ibáñez Cuadrado, Ángela | Lahera Forteza, Guillermo | Llerena Ruíz, Adrián | López Castroman, Jorge | Montes Rodríguez, José Manuel | Pérez Rodríguez, Mercedes

## Main lines of research

- Impulse control disorders and impulsive-compulsive spectrum disorders.
- Genetics and pharmacogenetics of mental disorders.
- Epigenetics of mental disorders.
- First psychotic episodes, risk factors in their development and predictors of relapse.
- Affective disorders, bipolar disorder.

## Most relevant scientific articles

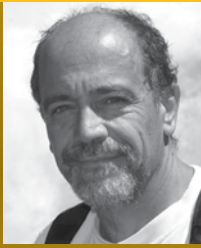
- CARIAGA-MARTINEZ A., SAIZ-RUIZ J., ALELU-PAZ R. From linkage studies to epigenetics: What we know and what we need to know in the neurobiology of schizophrenia. *Frontiers in Neuroscience*. 2016;10(MAY).
- ANAYA C., TORRENT C., CABALLERO F.F., VIETA E., DEL MAR BONNIN C., AYUSO-MATEOS J.L. ET AL. Cognitive reserve in bipolar disorder: Relation to cognition, psychosocial functioning and quality of life. *Acta Psychiatrica Scandinavica*. 2016.
- NARANJO M.E.G., DE ANDRES F., DELGADO A., COBALEDA J., PENAS-LLEDO E.M., LLERENA A. High frequency of CYP2D6 ultrarapid metabolizers in Spain: controversy about their misclassification in worldwide population studies. *Pharmacogenomics Journal*. 2016.
- DELGADO-GOMEZ D., BACA-GARCIA E., AGUADO D., COURTET P., LOPEZ-CASTROMAN J. Computerized Adaptive Test vs. decision trees: Development of a support decision system to identify suicidal behavior. *Journal of Affective Disorders*. 2016; 206:204-209.
- BLASCO-FONTECILLA H., RODRIGO-YANGUAS M., GINER L., LOBATO-RODRIGUEZ M.J., DE LEON J. Patterns of Comorbidity of Suicide Attempters: An Update. *Current Psychiatry Reports*. 2016;18(10).

## Highlights

The research activity of Group 22 of CIBERSAM during the year 2016 has been developed in the lines that we maintain. Among them we highlight:

- Our active participation in the AGES-CM and 2EPS projects, all related to the genetic-environmental interaction and the follow-up of patients with first psychotic episodes, who have given rise to publications and have been able to be part of the Cohort Project.
- Within the T.O.C. Program, we obtained an ISCIII Support for the Project: “Genetic and epigenetic mechanisms in refractory obsessive compulsive disorder: development and validation of a cellular model through reprogramming”. Also, as an activity of the Working Group of the Spanish Society of Psychiatry, we are participating in the elaboration of a Clinical Guide on pharmacological treatment of this pathology.
- In the field of Schizophrenia we have continued the study of factors associated with cognitive disorders and their possible approaches.
- We participated in two Intramural Projects of CIBERSAM, one related to stressors and epigenetics and risk of psychopathology in adolescence and the other with the evaluation of social cognition.

We have also carried out other actions such as the organization of the “II Encounter between Researchers in Mental Health, Patients and Families” that was successfully held and participated in IPs of different groups.



LEAD RESEARCHER

**Sanjuán Arias, Julio**

- Universidad de Valencia**  
Facultad de Medicina  
Avda. V. Blasco Ibáñez, 15  
46010 Valencia
- (+34) 96 398 33 79
- julio.sanjuan@uv.es
- [Group website](#)

PROGRAMMES  
**Therapeutic Innovation  
Schizophrenia**



### GROUP MEMBERS

**Staff members:** García Martí, Gracián | Llacer Iborra, Blanca | Sebastiá Ortega, Noelia

**Associated members:** Aguilar García Iturrospe, Eduardo Jesús | Bobes Bascarán, María Teresa | Carot Sierra, José Miguel | De la Iglesia Vaya, María | Gadea Domenech, Marien | González Piqueras, José Carlos | Herrero Sebastián, Neus | Ivorra Martínez, José Luis | Leal Cercos, Carmen | Moltó Ruíz, M<sup>a</sup> Dolores | Nacher Rosello, Juan Salvador | Olucha Bordonau, Francisco | Rivero Martín, Olga | Tolosa Montero, Amparo

**Contributors:** Brotons Girona, Olga | Escartí Fabra, María José | Jover Martínez, Manuel | Lorente Rovira, Esther

## Main lines of research

- Identification of risk polymorphisms in psychosis and affective disorders.
- Epigenetic Studies (functional expression) of candidate genes in psychosis in mental illness.
- Study of animal models in severe mental illness.
- Study of monogenic mutations in neurodegenerative diseases.
- Identification of genetic factors and environmental risk in affective and psychotic disorders.
- Identification of abnormal patterns in neuroimaging (morphometry, functional, spectroscopy) in psychotic patients .
- Database Design and coordination of clinical, genetic and neuroimaging for conducting multicenter projects data.
- Development of interactive systems for improving therapeutic adherence.
- Study of genetic and environmental factors in the development of language in children.
- Study the effectiveness of techniques of psycho- social intervention in severe mental disorders.



## Most relevant scientific articles

- TZANOULINO S., GARCIA-MOMPO C., RICCIO O., GROSSE J., ZANOLETTI O., DEDOUSIS P. ET AL. Neuroligin-2 Expression in the Prefrontal Cortex is Involved in Attention Deficits Induced by Peripubertal Stress. *Neuropsychopharmacology*. 2016;41(3):751-761.
- GUIRADO R., LA TERRA D., BOURGUIGNON M., CARCELLER H., UMEMORI J., SIPILA P. ET AL. Effects of PSA removal from NCAM on the critical period plasticity triggered by the antidepressant fluoxetine in the visual cortex. *Frontiers in Cellular Neuroscience*. 2016;10(FEB).
- CARCELLER H., ROVIRA-ESTEBAN L., NACHER J., CASTREN E., GUIRADO R. Neurochemical phenotype of Reelin immunoreactive cells in the Piriform cortex layer II. *Frontiers in Cellular Neuroscience*. 2016;10(MAR2016).
- GARCIA-PORTILLA M.P., GARCIA-ALVAREZ L., SARRAMEA F., GALVAN G., DIAZ-MESA E., BOBES-BASCARAN T. ET AL. It is feasible and effective to help patients with severe mental disorders to quit smoking: An ecological pragmatic clinical trial with transdermal nicotine patches and varenicline. *Schizophrenia Research*. 2016.
- MAS S., GASSO P., LAFUENTE A., BIOQUE M., LOBO A., GONZALEZ-PINTO A. ET AL. Pharmacogenetic study of antipsychotic induced acute extrapyramidal symptoms in a first episode psychosis cohort: role of dopamine, serotonin and glutamate candidate genes. *Pharmacogenomics Journal*. 2016.

## Highlights

In this year the group has obtained the Prometeo Scholarship for groups of excellence in Research of the Conselleria of Education of the Valencian Community.

We have participated in the elaboration of the General Strategic Plan of Mental Health and in particular in the area for the implantation of first Psychotic Episodes Units.


We have published the monograph: *Treating the Mind or Treating the Brain? Towards an integration between psychopharmacology and psychotherapy*. Desclee de Brouwer. Bilbao 2016. It has been included in various web pages as one of the essential reading books for psychiatrists and psychologists in training.


We have completed the development of the application for mobile phones to improve adherence to treatment in patients with a first psychotic episode.



LEAD RESEARCHER

**Tabarés-Seisdedos, Rafael**

 **Universidad de Valencia**  
Facultad de Medicina  
Dpto. Medicina.  
Avda. V. Blasco Ibañez, 15, Pl. 2  
46010 Valencia

 (+34) 96 386 47 44

 rafaেল.tabares@uv.es

 [Group website](#)

PROGRAMMES

**Bipolar disorder**  
**Child and Adolescent Psychiatry**



GROUP MEMBERS

**Staff members:** Amezcua García, Cristina | Correa Ghisays, Patricia | Fores Martos, Jaume

**Associated members:** Balanzá Martínez, Vicent | Catalá López, Ferrán | Fuentes Durá, Inmaculada | Geijo Barrientos, Emilio | Girón I Giménez, Manuel | Gómez Beneyto, Manuel | Martínez Pérez, Salvador | Munariz Ferrandis, Mikel | Salazar Fraile, José | Selva Vera, Gabriel

## Main lines of research

- Cognitive endophenotypes and biomarkers in schizophrenia, bipolar Patients and Their relatives of the 1st degree.
- Global Burden of Disease studies.
- Systematic reviews and meta-analysis network.
- Multimorbidity in Patients With complex diseases: such as CNS disorders, cancer or metabolic diseases.
- Neurogenetics and Cell Therapy (stem cells).
- Nutritional Psychiatry.

## Most relevant scientific articles

- BAUER I.E., GALVEZ J.F., HAMILTON J.E., BALANZA-MARTINEZ V., ZUNTA-SOARES G.B., SOARES J.C. ET AL. Lifestyle interventions targeting dietary habits and exercise in bipolar disorder: A systematic review. *Journal of Psychiatric Research*. 2016; 74:1-7.
- CATALA-LOPEZ F., MACIAS SAINT-GERONS D., GONZALEZ-BERMEJO D., ROSANO G.M., DAVIS B.R., RIDAO M. ET AL. Cardiovascular and Renal Outcomes of Renin–Angiotensin System Blockade in Adult Patients with Diabetes Mellitus: A Systematic Review with Network Meta-Analyses. *PLoS Medicine*. 2016;13(3).
- BUENO C., TABARES-SEISDEDOS R., MORALEDA J.M., MARTINEZ S. Rett syndrome mutant neural cells lacks MeCP2 immunoreactive bands. *PLoS ONE*. 2016;11(4).
- TABARES-SEISDEDOS R., BAUDOT A. Editorial: Direct and inverse comorbidities between complex disorders. *Frontiers in Physiology*. 2016;7(MAR).
- GBD 2015 SDG COLLABORATORS, HARO ABAD JOSEP MARÍA, TABARES-SEISDEDOS R, CATALÁ-LÓPEZ, F., KOYANAGI A, TYROVOLAS S. Measuring the health-related Sustainable Development Goals in 188 countries: a baseline analysis from the Global Burden of Disease Study 2015. *Lancet* (London, England). 2016.

## Highlights

The development of consensus with “Asociation European Psychiatric Association (EPA) - Working Group on Mental Health Consequences of Economic Crises of the EPA Council of National Psychiatric Associations EPA guidance on mental health and economic crises in Europe”. Dr. Gómez-Beneyto. We participate, we direct from the G24 by Dr. Balanzá in the project CIBERSAM of Cohortes, an innovative national cohort of cohorts of first episode of psychosis.

From the project “Comorbidity between Cancer and Central Nervous System Disorders”, which aims to synthesize epidemiological evidence and assess the validity of associations between central nervous system disorders and the risk of developing or dying from cancer. We work a collaborative meta-analysis with 5 countries (Spain, Canada, Australia, United Kingdom and the United States) coordinated by the University of Valencia/CIBERSAM (Dr. Catalá-López, Prof. Tabarés-Seisdedos). The study has been prospectively registered in PROSPERO and the protocol article is currently under review.

“The Global Burden of Disease Study” is the largest international collaborative project on the epidemiology of diseases, injuries and risk factors at the global, national and regional levels. During this year, results corresponding to the 2013 (Dr. Catalá-López) and 2015 iterations (Dr. Catalá-López, Prof. Tabarés-Seisdedos) have been published in prestigious journals such as *The Lancet* and *JAMA*.

Projects in advanced methods of systematic reviews and meta-analyses, including the publication of two papers in *PLoS Medicine* (*PLoS Med.* 2016;13(5): e1002028 and *PLoS Med.* 2016;13(3): e1001971).

From the line of Neuroscience, they have granted the Cell Therapy Network Project (TERCEL-ISCIH), with Prof. Martínez the Coordinator of the Neurocell Program. Communications have been presented at two international congresses; the Federation of European Societies of Neuroscience (FENS) and Society for Neuroscience (SfN) 2016.




LEAD RESEARCHER

**Vieta Pascual, Eduard**

 Hospital Clínico y Provincial  
de Barcelona

Escalera 12, planta 0  
C/ Villarroel, 170  
08036 Barcelona

 (+34) 93 227 54 00 ext. 3130

 [evieta@clinic.ub.es](mailto:evieta@clinic.ub.es)

 [Group website](#)

PROGRAMMES

**Bipolar disorder  
Therapeutic Innovation**



## GROUP MEMBERS

**Staff members:** Bonnin Roig, Caterina del Mar | Garriga Carrizosa, Marina | Jiménez Martínez, Esther | Reinares Gagneten, Maria | Sánchez Moreno, José | Sole Roige, Eva | Valls Roig, Elia

**Associated members:** Benabarre Hernández, Antonio | Blanch Andreu, Jordi | De Dios Perrino, Consuelo | Gastó Ferrer, Cristobal | Goikolea Alberdi, Jose Manuel | Grande i Fullana, Iria | Martínez Arán, Anabel | Martín-Santos Laffont, Rocío | Navarro Odriozola, Victor | Navinés de la Cruz, Ricard | Popovic, Dina | Torrent Font, Carla | Undurraga Fourcade, Juan Pablo | Valentí Ribas, Marc

**Contributors:** Comes Forastero, Mercé

## Main lines of research

- Epidemiology and disability associated with bipolar and unipolar disorders.
- Endophenotypes, genetics and biomarkers of affective disorders.
- Clinical trials and innovation in psychopharmacology of bipolar and depressive disorders.
- Observational studies in affective disorders.
- Innovative psychological interventions for bipolar disorder.
- Neurocognition and neuroimaging of bipolar and unipolar disorders.
- First affective and psychotic episodes.
- Psychometrics of bipolar disorders.

## Most relevant scientific articles

- HOU L, HEILBRONNER U, DEGENHARDT F, ADLI M, AKIYAMA K, AKULA N ET AL. Genetic variants associated with response to lithium treatment in bipolar disorder: a genome-wide association study. *Lancet* (London, England). 2016.
- VIETA E., TORRENT C.. Functional remediation: the pathway from remission to recovery in bipolar disorder. *World Psychiatry*. 2016;15(3):288-289.
- KUSWANTO C., CHIN R., SUM M.Y., SENGUPTA S., FAGIOLINI A., MCINTYRE R.S. ET AL. Shared and divergent neurocognitive impairments in adult patients with schizophrenia and bipolar disorder: Whither the evidence? *Neuroscience and Biobehavioral Reviews*. 2016; 61:66-89.
- REINARES M., BONNIN C.M., HIDALGO-MAZZEI D., SANCHEZ-MORENO J., COLOM F., VIETA E. The role of family interventions in bipolar disorder: A systematic review. *Clinical Psychology Review*. 2016; 43:47-57.
- BONNIN C.M., TORRENT C., ARANGO C., AMANN B.L., SOLE B., GONZALEZ-PINTO A. ET AL. Functional remediation in bipolar disorder: 1-year follow-up of neurocognitive and functional Outcome. *British Journal of Psychiatry*. 2016;208(1):87-93.


## Highlights


- Dr. Iria Grande was awarded with Early career psychiatrists Scholarship Programme by the European Psychiatric Association.
- Development and publication of several international clinical guidelines on the treatment of bipolar disorder.
- Development and publication of an international consensus for the assessment and management of agitation in psychiatry.
- Dr. Eduard Vieta, new scientific director of CIBERSAM.
- Eduard Vieta appears in the list of the most cited investigators in scientific publications in the biomedical field (Highly Cited Researchers 2016), elaborated by the international agency Thomson Reuters, 2016.
- International collaborative study were genetic variants associated to lithium response in bipolar disorder have been found.
- Study on the implication of variants of the DDR1 gene in myelin integrity and processing speed in euthymic patients with bipolar disorder.
- Study on the efficacy of an e-neurocognitive module as an adjuvant treatment in functional remediation for patients with bipolar disorder.
- The Sociedad Española de Psiquiatría Biológica “Joven Investigador Acreditado Award”, given to Dr. Iria Grande.
- Dr. Eduard Vieta invested Doctor Honoris Causa by the University of Valencia.
- Collaborative publications demonstrating that functional remediation enhances long-term autonomy and global functioning of patients with bipolar disorder.



LEAD RESEARCHER

**Vilella Cuadrada, Elisabet**

 **Fundación Instituto de Investigación Sanitaria Pere Virgili**  
Universidad Rovira y Virgili  
Facultat de Medicina i Ciències de la Salut, edif. 4, Pb  
C/ Sant Llorenç, 21  
43201 Reus

 (+34) 977 33 33 38

 vilellae@peremata.com

 **Group website**

PROGRAMMES

**Schizophrenia  
Bipolar disorder**



## GROUP MEMBERS

**Staff members:** Díaz Peña, Roberto

**Associated members:** Abasolo Zabalo, Nerea | Aguilera Inés, Francisco | Alonso Pérez, Yolanda | Cabezas Serisa, Ángel | Cortés Ruíz, María José | Franco Vasquez, José Gabriel | Gaviria Gómez, Ana Milena | Gutiérrez Zotes, Alfonso | López Seco, Fernando | Martínez Leal, Rafael | Martorell Bonet, Lourdes | Masara Marín, Adela | Mena Sánchez, Isaias | Ortega Sanz, Laura | Pablo Rabasso, Juan de | Solé Moix, Montserrat | Valero Oyarzabal, Joaquín | Valiente Palleja, Alba

## Main lines of research

- Identification of genetic, molecular and hormonal schizophrenia markers.
- Identification of genetic markers for autism and intellectual disability.
- Stress and HPA axis in mental illness.
- Cognition and neuropsychology of schizophrenia and personality disorders.
- Co-morbidity of psychiatric disorders and intellectual disability.

## Most relevant scientific articles

- CANGA E., PUERTO M., ORTEGA L., SOLE M., VILELLA E., LABAD J. ET AL. Parental antecedents of psychosis are associated with severity of positive and negative symptoms in schizophrenia patients. *Journal of Clinical Psychiatry*. 2016;77(9):1201-1202.
- LABAD J., GUTIERREZ-ZOTES A., CREUS M., MONTALVO I., CABEZAS A., SOLE M. ET AL. Hypothalamic-pituitary-adrenal axis measures and cognitive abilities in early psychosis: Are there sex differences? *Psychoneuroendocrinology*. 2016; 72:54-62.
- LABAD J, MARTORELL L, HUERTA-RAMOS E, COBO J, VILELLA E, RUBIO-ABADAL E ET AL. Pharmacogenetic study of the effects of raloxifene on negative symptoms of postmenopausal women with schizophrenia: A double-blind, randomized, placebo-controlled trial. *European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology*. 2016;
- STOJANOVIC-PEREZ A., MARTORELL L., MONTALVO I., ORTEGA L., SOLE M., MORENO I. ET AL. The relationship between antidepressant treatment and inflammatory markers in early psychosis: preliminary results. *Psychopharmacology*. 2016;1-3.
- GATTERE G., STOJANOVIC-PEREZ A., MONSENY R., MARTORELL L., ORTEGA L., MONTALVO I. ET AL. Gene-environment interaction between the brain-derived neurotrophic factor Val66Met polymorphism, psychosocial stress and dietary intake in early psychosis. *Early Intervention in Psychiatry*. 2016.

## Highlights

### Scientific dissemination

Creation of the website of the project on Bipolar Disorder BIPOGENT ([www.bipogent.cat](http://www.bipogent.cat))

### Projects financed in 2016

- Coordinator: Elisabet Vilella. IPs: Elisabet Vilella, Erick Jorge Canales Rodríguez and Eduard Vieta. Title: Implication of DDR1 gene variants on myelin integrity and cognitive processing speed in euthymic bipolar disorder patients. Acronym: BIPOGENT. Agency: ISCIII. PI15-00852. Budget G28: €111,320.
- Coordinator: Eduard Vieta. IPs: Eduard Vieta, Elisabet Vilella and Edith Pomarol-Clotet. Title: Comparison of DNA methylation patterns on DDR1 gene in euthymic bipolar disorder patients according to exposure to childhood maltreatment. Acronym: EPI-DBIP (Epigenetics DDR1 Bipolar Disorder). Agency: Intramural CIBERSAM. Budget: €28,000.

# Linked group

## Diego José Palao Vidal

### Programme: Depression and Therapeutic Innovation

Corporación Sanitaria Parc Taulí

#### ASSOCIATED MEMBERS:

Andero Galí, Raúl | Armario García, Antonio | Barbero Valverde, Juan David | Cardoner Álvarez, Narcis | Cebria Meca, Ana Isabel | Cobo Gómez, Jesús Vicente | Coronas Borri, Ramón | Duño Ambrós, Roso | Fernández Gonzalo, M. Soledad | Giraldo Arjonilla, Jesús | Jodar Vicente, María Mercedes | Labad Arias, Javier | Martínez Amorós, Erika | Monreal Ortiz, José Antonio | Montalvo Aguirrezabala, Itziar | Nadal Alemany, Roser | Ortiz de Pablo, Jordi | Pàmias Massana, Montserrat | Parra Uribe, Isabel | Vía Virgili, Esther

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Centro de Investigación Biomédica en Red (CIBER)  
Instituto de Salud Carlos III  
C/ Monforte de Lemos 3-5. Pabellón 11  
28029 Madrid  
[www.ciberisciii.es](http://www.ciberisciii.es) | [www.cibersam.es](http://www.cibersam.es)