

An abstract, golden, branching structure resembling a tree or a network of fibers, set against a dark background. The structure is composed of thick, textured branches that spread outwards, creating a sense of growth and connectivity. The color transitions from a dark gold at the top to a lighter, more vibrant yellow at the bottom.

# ANNUAL REPORT 2014

The logo for Cibersam, featuring the word "cibersam" in a lowercase, sans-serif font. The "cibers" part is in a dark blue color, and the "sam" part is in a golden-yellow color. Above the "i" in "cibers" are three small blue dots.

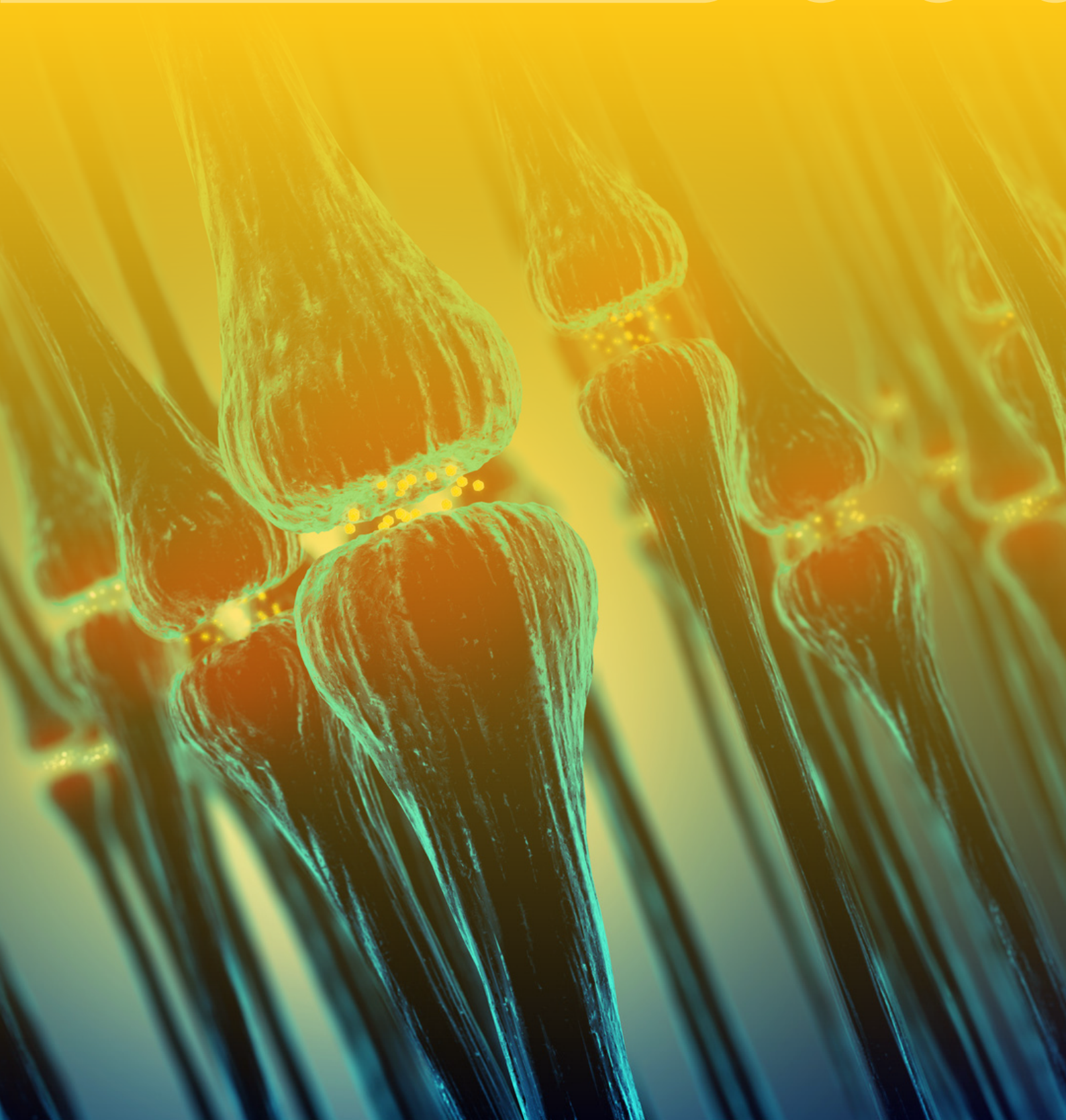
*cibersam*

Centro de Investigación Biomédica en Red  
*Salud Mental*

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# 1. ORGANIZATION





## Letter from the Scientific Director

**Dr. Celso Arango.**

Scientific Director, CIBERSAM

In the olden days, baskets were primarily made of canes, which were taken from river willows. In order to not end production, harvesters had to make sure that they took good care of those willows, such that the quality of the baskets improved over the years. Finally, and as years went by, the willows were no longer cared for, were not pruned every year and were damaged by droughts. At first, this resulted in baskets having worse quality, and ultimately they disappeared. The wise Spanish proverb, which is virtually now obsolete, states that “Con estos mimbres no se puede hacer más que este cesto”, which literally means that with these canes, all that can be made is this basket. In the same way, this CIBER has excellent canes which, as a result of the structure of the CIBER, allows being integrated in a common project common with a result that none of them would have achieved on their own. Despite the lack of water and lack of interest of those who should have cared for it, alternatives are sought year after year which allows maintaining productivity and end product quality. However, like everything in life, there is a limit and the preparation, motivation, international impact and excellence of its groups end up needing a nutritive medium so as not to perish while making the effort.

Unquestionably, our centre is turning into a structure that is increasingly more competitive at the international level, drawing the interest of private industry to enable safely and efficiently carrying out some of its projects with the quality assurance offered by a centre with annual evaluations and which is under national and international scrutiny. However, imposed management difficulties (hiring of researchers, for example) only contribute to increasing the burden given the funding cuts over the years.

The last four years of work of all the CIBER subject areas, and therefore the Mental Health subject area, has been evaluated this year. While awaiting the results, all the researchers in this CIBER should be proud of the work they have done under this innovative research structure. It is easy to make out a before an after in the collaborative and translational research culture in neurosciences and mental health in our country. In 2014, like every year since its creation, this CIBER conducted an annual evaluation of each of the groups. This comprehensive evaluation, which I believe should be extended to other public research structures in order to break away from the highly bureaucratic research that is so typical of us and causes so much harm to this country, results in a more efficient distribution of the resources available for research of excellence. Our research proves that synaptic pruning results in better-prepared functional circuits. An example of translation consists of applying that knowledge to the management team of our CIBER and discontinuing those groups that have lost their working capacity, so that other new, up and coming groups can grow and provide added value to the CIBER. Research groups inside and outside this CIBER are dynamic groups with varying research quality over the years. We believe that a Centre receiving public funding cannot have groups outside the institution which are better than groups inside it. One of the greatest strengths of this Centre is that it is a dynamic structure which can and must adapt to internal and external changes by means of transparent and objective evaluation mechanisms. There is no system more inefficient than one that allows those joining an institution to remain in said institution regardless of their effort, ability and results. This ancient, outdated and inefficient system that has been with us for so long must finally be put to rest. In 2015 we will be incorporating two new groups in the CIBER that will most definitely contribute to reinforcing and enriching it. We can thereby meet one of the objectives laid out in our 2014-2016 strategic plan. In following with this line of action, we decided to change a third of the head positions within the CIBER every year, making it more dynamic. In brain research this is referred to as plasticity. Also, Dr. Eduard Vieta, who

is an example of a professional who has a proven international impact and scientific research excellence in mental health in our country, was appointed Assistant Scientific Director of this CIBER in 2014.

The main objective of favouring translational research of excellence in mental health is sought through programmes and platforms. All the programmes (depression, schizophrenia, bipolar disorder, therapeutic innovation, child and adolescent psychiatry and psychosomatic, anxiety and impulse control disorders) consist of preclinical research groups which are one of the greatest assets of this CIBER. The working of transversal structures, such as research platforms, has been reinforced in 2014. The number of genetic samples in our DNA platform, which already totals 12,000, is increasingly more appealing for international consortiums, and it also allows being able to conduct national studies that would otherwise be impossible. The CIBER is part of or is in the process of becoming part of the most important international consortiums dealing with genetics in mental disorders, and these consortiums are the only way to get enough samples for the genetic study of complex pathologies like ours. We have continued to work hard on the application joining the DNA platform with the common database. At present, any researcher of this CIBER can know about the availability of samples with specific characteristics (diagnosis, age of onset of the disorder, sex, race, existence family members in the platform, etc.) and the groups to contact to be able to use this platform in the most efficient manner. The instrument bank platform continues to provide excellent service to clinical researchers inside and outside this CIBER. Improvement to the GRIDSAM tool, which allows entering data in multicentre projects, continues and it currently includes data from thousands of patients.

We continue to be committed to Europe, especially considering the delicate economic situation of our country. We are sure that a return can be further improved through participation and coordination by our groups in projects funded by the European Union. The participation of more than half the CIBERSAM groups in European projects and our Centre's coordination in strategic projects within the European Union attest to this. The final recommendations of the Roadmap for Mental Health Research in Europe (ROAMER), coordinated by the CIBERSAM and presented in the European Parliament by Josep Maria Haro, will mark the future priority lines for mental health funding within Horizon 2020.

In 2014, we continued to foster and enhance our relations with family and patient associations by holding meetings and joint acts with many of them, and by participating, in collaboration with the industry and other agents, in campaigns against the stigma of people with disabilities or mental health myths. We participated in the "Semana de la Ciencia" and have supported a growing number of scientific activities. We continued to work on having a more dynamic, intuitive web page, providing access to the priority content of the page. Our Twitter account, @CIBER\_SAM, which communicates our activities and most important discoveries, already has over 700 followers, and our Facebook page is increasingly more active.

One of the key objectives of this CIBER since its incorporation was to train young researchers in the pleasing and stimulating task of mental health research. In 2014, we held the second year of our Master's course in Introduction to Mental Health Research with the participation of five of the best universities in the country. There was such a large number of applicants that we had to select those which would have the greatest future impact and had to discard most applicants. It was a success which proves that an existing need in our country has been covered.

Now more than ever, it is time to conduct efficient research aimed at improving the health and quality of life of individuals at the lowest possible cost, without jeopardizing all that has been achieved over recent years. Only through the common effort of those best prepared for doing this task together with the support of the new generations of talented researchers integrated in groups of excellence will get us out of this situation and make us strong enough to face current and future challenges.

## LIST OF GROUPS AND INSTITUTIONS

The consortium consists of 24 research groups from 8 different Spanish Regions: Principality of Asturias, Cantabria, Basque Country, Aragón, Catalonia, Madrid, Region of Valencia and Andalusia.

Group	Center	City	Principal Investigator
Group 1	Hospital Gregorio Marañón	Madrid	Celso Arango
Group 2	Instituto de investigaciones Biomédicas	Barcelona	Francesc Artigas
Group 3	Hospital Universitario La Princesa	Madrid	José Luis Ayuso
Group 4	Hospital Clínico de Barcelona	Barcelona	Miguel Bernardo
Group 5	Univ. de Oviedo. Facultad de Medicina	Oviedo	Julio Bobes
Group 6	Univ. de Granada. Facultad de Medicina	Granada	Jorge A. Cervilla
Group 7	Hospital Gregorio Marañón	Madrid	Manuel Desco
Group 8	Univ. de Barcelona. Facultad de Biología	Barcelona	Lourdes Fañanas
Group 10	Hospital Santiago Apóstol	Vitoria- Gasteiz	Ana González-Pinto
Group 11	Fundación Sant Joan de Deu	Barcelona	Josep María Haro
Group 12	UCM. Facultad de Medicina	Madrid	Juan Carlos Leza
Group 13	Hospital Clínico Universitario	Zaragoza	Antonio Lobo
Group 15	FIDMAG Hermanas Hospitalarias. Unidad de investigación Benito Menni CASM	Barcelona	Peter J. McKenna
Group 16	Universidad del País Vasco	Leioa, Bizkaia	José Javier Meana
Group 17	Hospital Universitario de Bellvitge	Barcelona	José Manuel Menchón
Group 18	Univ. de Cádiz. Facultad de Medicina	Cádiz	Juan Antonio Micó
Group 19	Hospital Universitario 12 de Octubre	Madrid	Tomás Palomo
Group 20	Univ. de Cantabria. Facultad de Medicina	Santander	Ángel Armando Pazos
Group 21	Hospital de Santa Creu i Santa Pau	Barcelona	Víctor Pérez
Group 22	Hospital Universitario Ramón y Cajal	Madrid	Jerónimo Saiz
Group 23	Univ. de Valencia. Facultad de Medicina	Valencia	Julio Sanjuán
Group 24	Univ. de Valencia. Facultad de Medicina	Valencia	Rafael Tabarés
Group 25	Hospital Clínico de Barcelona	Barcelona	Eduard Vieta
Group 26	Hospital Univ. Marqués de Valdecilla	Santander	Benedicto Crespo

## ORGANISATIONAL STRUCTURE OF CIBERSAM

The CIBERSAM is a cooperative networking structure formed by 24 groups located in some of the most important main research in Spain. These groups are structured in 6 Research Programmes where they conduct projects which allow us, through multidisciplinary work, to pool efforts, optimise resources and take maximum advantage of the knowledge that is generated in order to transfer it to clinical practice and, ultimately, offer it to patients and to society as a whole.

The governance and administration of the CIBERSAM is the responsibility of the following bodies: the Board of Trustees and its Permanent Commission (which are common for all CIBER Research Areas), and the management bodies represented by the Steering Committee, the Scientific Director and General Management.

### External Scientific Advisory Committee

The External Scientific Advisory Committee provides general scientific support and advice to the Board of Trustees. It consists of internationally renowned scientists in the health sciences field who stand out in their professional and scientific careers aligned with CIBERSAM objectives. The members of this committee include:

**Mr. Jim Van Os.** Maastricht University. Netherlands

**Mr. Guy Goodwin.** Department of Psychiatry, University of Oxford, Warnerford Hospital. United Kingdom

**Mr. Michael Hamon.** Institut National de la Santé et de la Recherche, Université Pierre et Marie Curie, Paris. France

**Ms. Maria Ron.** Institute of Neurology, University College London, Queen Square, London. United Kingdom

**Ms. Marion Leboyer.** Groupe Henri Mondor- Albert Chenevier, Pôle de Psychiatrie, Créteil, Paris. France

### Steering Committee

The Steering Committee consists of a collegial body which assures the development of the Consortium by looking after the needs of the groups and its strategic objectives. This committee is made up of:

Dr. Celso Arango	Scientific Director
Dr. Francesc Artigas	Therapeutic Innovation Programme Manager
Dr. Víctor Pérez	Depression Programme Manager
Dr. Eduard Vieta	Bipolar Disorder Programme Manager
Dr. Julio Sanjuán	Schizophrenia Programme Manager and Common Databases Platform Manager
Dr. Antonio Lobo	Psychosomatic, Anxiety and Impulse Control Disorders Programme Manager
Dr. Ángel Pazos	Training and Mobility Manager
Dr. Josep María Haro	Platforms Manager
Dra. Josefina Castro	Child and Adolescent Psychiatry Programme Manager
Dra. Ana M <sup>a</sup> González-Pinto	Quality Manager
D. Manuel Sánchez	General Manager

### Technical Unit

As of 1 January 2014, the CIBERSAM Technical Unit has been centralized in the CIBER Technical Unit, and it now has the following address and contacts: <http://www.ciberisciii.es/quienes-somos/oficina-tecnica>

Contact: CIBERSAM Scientific Secretary: Pura Moran, secretaria. [cientifica@cibersam.es](mailto:cientifica@cibersam.es), 91 586 75 15.

## 2014 CIBERSAM BUDGET

EXPENSES		INCOME	
<b>I.- ACTIVITY</b>		<b>I. FUNDING</b>	
Group Funding	1.898.328,43	ISCIII	2.199.190,00
Training	60.000	Bank	10000
Coordination	37.000		
Technical Unit	340.000		
Institutional Relations	60.000	<b>II.- REMAINDER PREVIOUS YEARS</b>	<b>286.138,43</b>
Platforms	100.000		
<b>II.- INTERNAL CALLS FOR PROPOSALS</b>	<b>0</b>		
C. Intramural Proposals	0		
<b>TOTAL</b>	<b>2.495.328,43</b>		<b>2.495.328,43</b>
<b>III PROJECTS</b>	<b>2,336.311, 94</b>	<b>IV.-PROJECTS</b>	<b>2.336.311,94</b>
Intramural Projects	912.918, 03	Intramural Projects	912.998,03
Calls for Proposals	559.676,57	Calls for Proposals	559.677,57
Industry	863.637,34	Industry	863.637,34
<b>TOTAL</b>	<b>4.831.640,37</b>		<b>4.831.640,37</b>



## CIBERSAM STAFF

Number of employees during the year to December 31 distinguishing by category and gender.

	WOMEN			Total WOMEN
	Indefinite	Works and Services	Postdoctoral	
CIBERSAM	14	39	2	55
PhD	5	9	2	16
Degree Holder	5	16		21
Diploma Holder	1	5		6
Technician	3	9		12
Grand total	14	39	2	55

	MEN			Total MEN
	Indefinite	Works and Services	Postdoctoral	
CIBERSAM	3	11	1	15
PhD		2	1	3
Degree Holder	3	9		12
Diploma Holder				
Technician				
Grand total	3	11	1	15

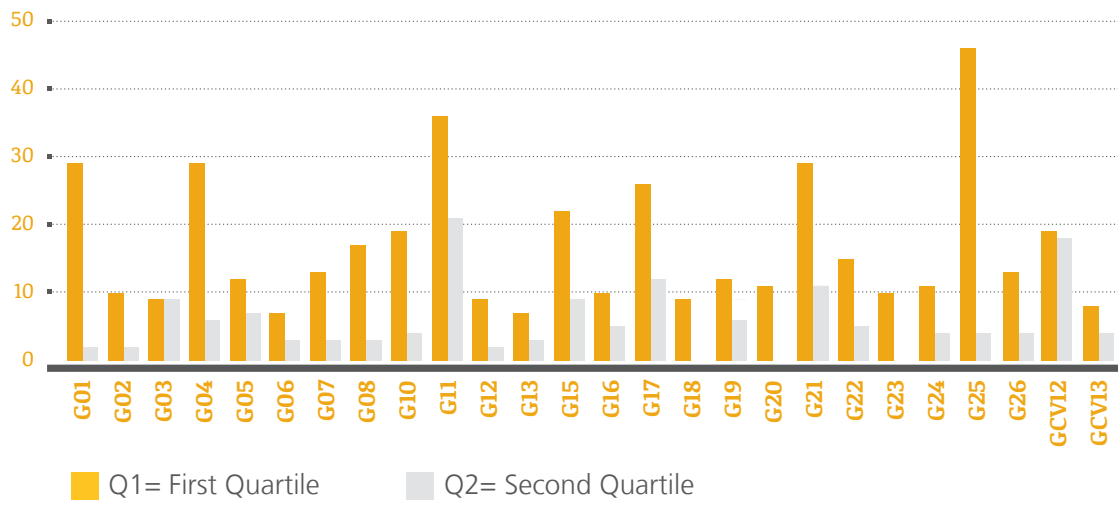
  

	Indefinite	Works and Services	Postdoctoral	Grand total
CIBERSAM	17	50	3	70
PhD	5	11	3	19
Degree Holder	8	25		33
Diploma Holder	1	5		6
Technician	3	9		12
<b>Grand total</b>	<b>17</b>	<b>50</b>	<b>3</b>	<b>70</b>

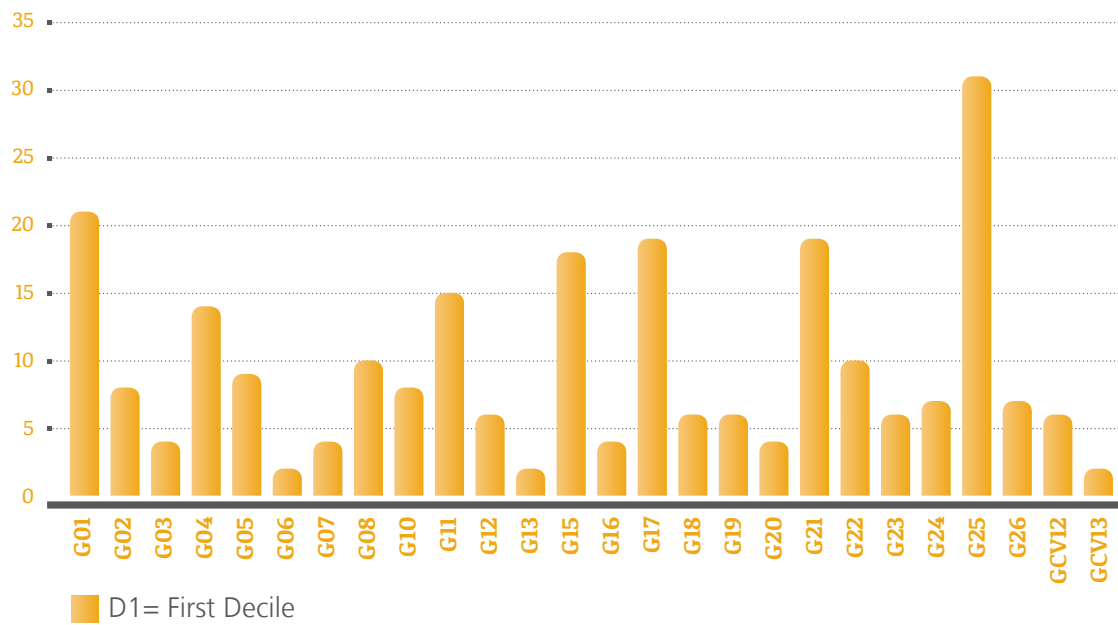
## PUBLICATIONS (studies published in international magazines)

Ips	Groups	Total	D1	Q1	Q2
ARANGO LÓPEZ, CELSO	G01	36	21	29	2
ARTIGAS PÉREZ, FRANCESC	G02	13	8	10	2
AYUSO MATEOS, JOSÉ LUIS	G03	23	4	9	9
BERNARDO ARROYO, MIGUEL	G04	47	14	29	6
BOBES GARCÍA, JULIO	G05	28	9	12	7
CERVILLA BALLESTEROS, JORGE A	G06	20	2	7	3
DESCO MENÉNDEZ, MANUEL	G07	30	4	13	3
FAÑANAS SAURA, LOURDES	G08	25	10	17	3
GONZÁLEZ PINTO ARRILLAGA, ANA	G10	28	8	19	4
HARO ABAD, JOSEP MARIA	G11	68	15	36	21
LEZA CERRO, JUAN CARLOS	G12	12	6	9	2
LOBO SATUÉ, ANTONIO	G13	13	2	7	3
MCKENNA, PETER J	G15	38	18	22	9
MEANA MARTÍNEZ, JOSÉ JAVIER	G16	19	4	10	5
MENCHON MAGRIÑA, JOSÉ MANUEL	G17	43	19	26	12
MICO SEGURA, JUAN ANTONIO	G18	11	6	9	0
PALOMO ÁLVAREZ, TOMAS	G19	26	6	12	6
PAZOS CARRO, ANGEL ARMANDO	G20	12	4	11	0
PÉREZ SOLA, VÍCTOR	G21	52	19	29	11
SAIZ RUIZ, JERÓNIMO	G22	28	10	15	5
SANJUÁN ARIAS, JULIO	G23	20	6	10	0
TABARÉS SEISDEDOS, RAFAEL	G24	16	7	11	4
VIETA PASCUAL, EDUARD	G25	56	31	46	4
CRESPO FACORRO, BENEDICTO	G26	21	7	13	4
CASAS BRUGUÉ, MIGUEL	GCV12	52	6	19	18
VILELLA CUADRADA, ELISABET	GCV13	15	2	8	4

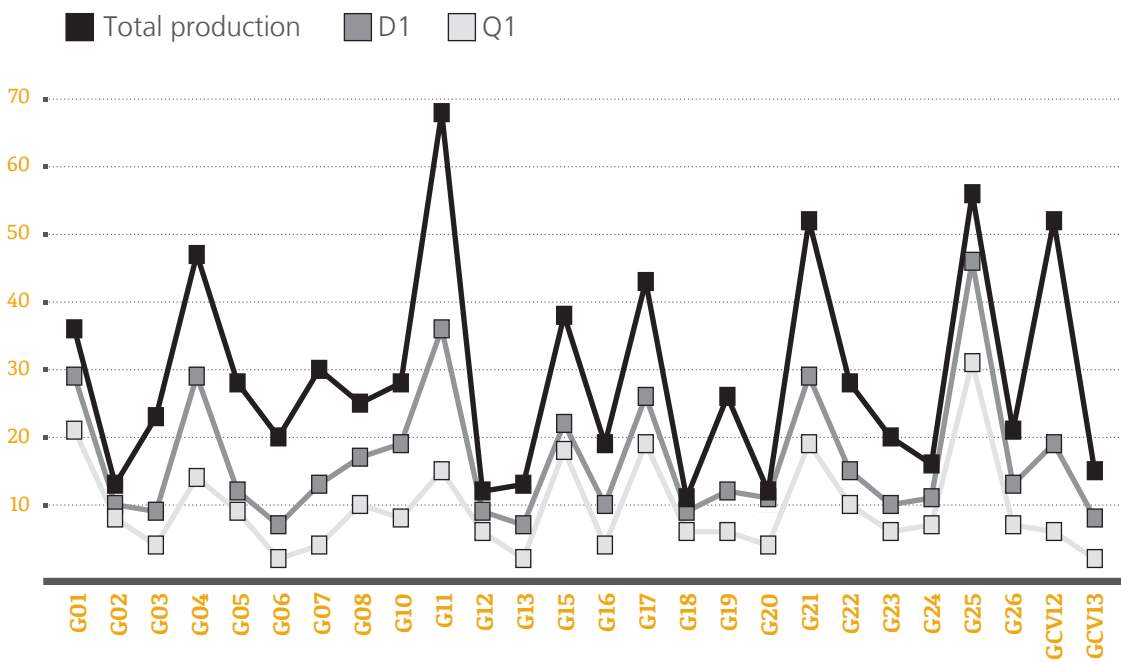
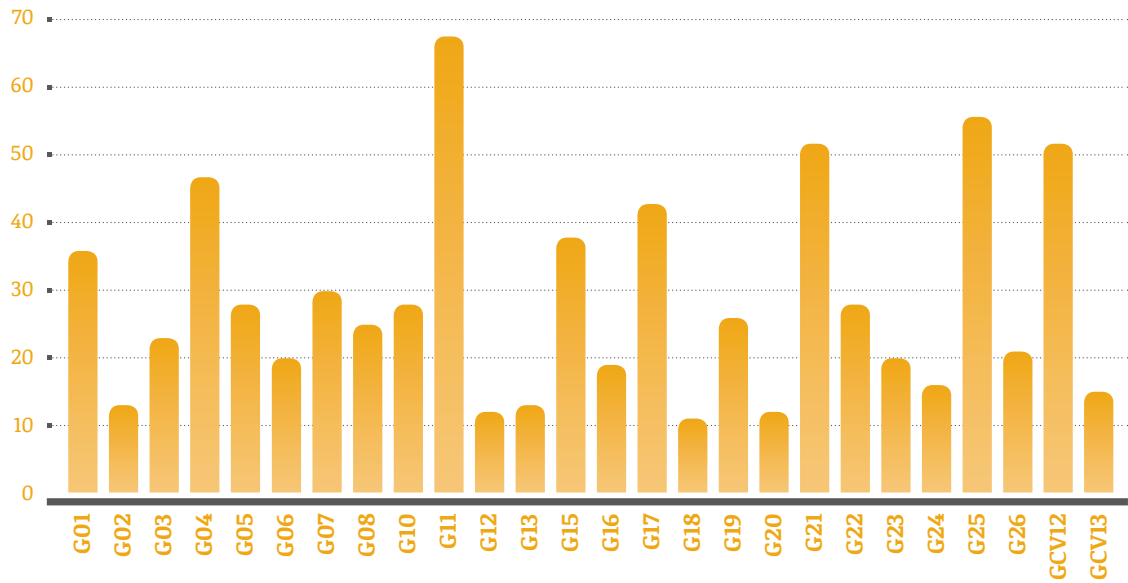
PUBLICATIONS FOR GROUP (Q1-Q2)



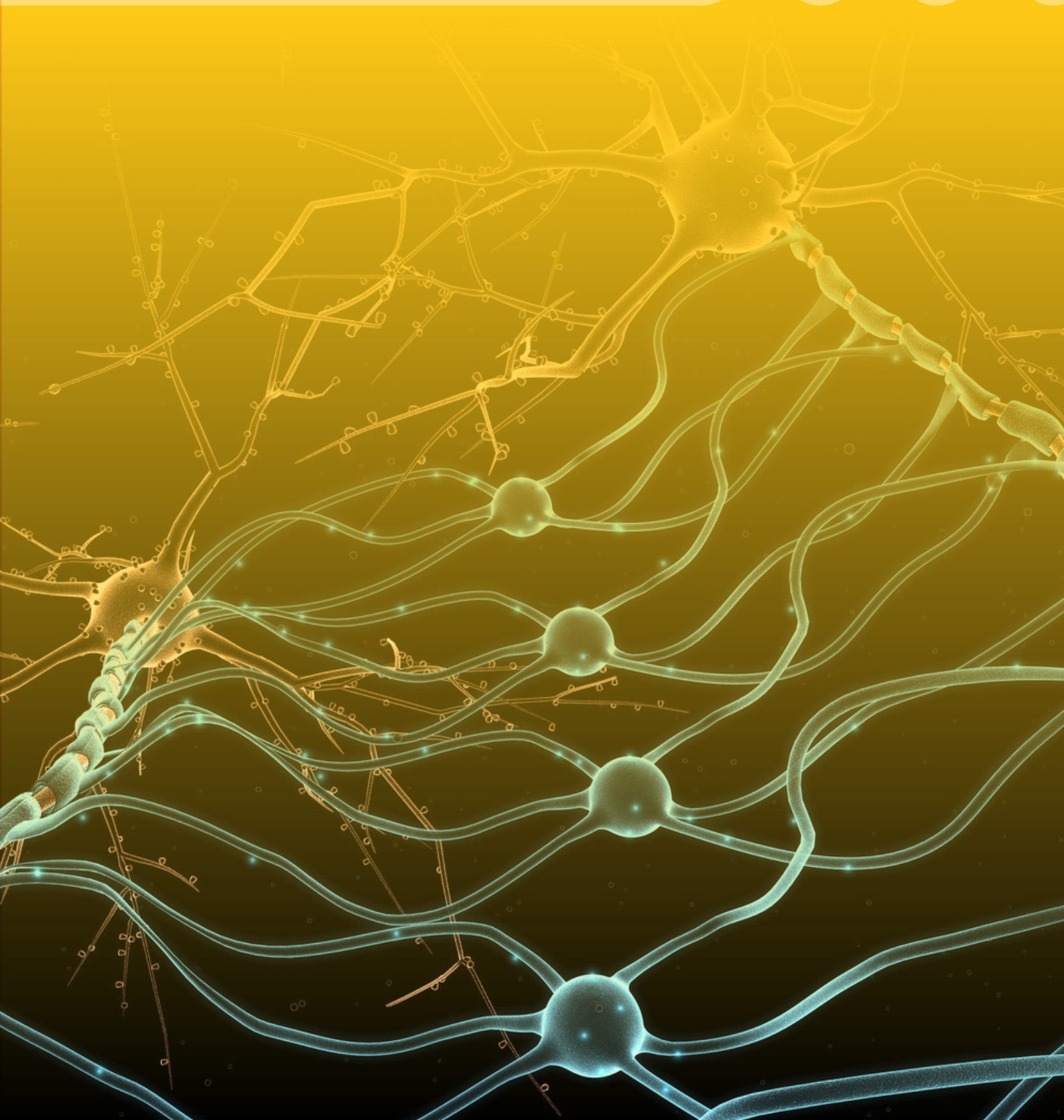
PUBLICATIONS FOR GROUP (D1)



## TOTAL PUBLICATIONS FOR GROUP



## 2. SCIENTIFIC PROGRAMMES





**Eduard Vieta Pascual (G25)**  
Coordinator

### Programme Description

Created in 2008, the CIBERSAM Bipolar Disorder Programme is essentially formed by national groups having expertise in translational research with a very high tendency of applying the results to clinical practice. The main objective of this programme is to enhance knowledge about bipolar disorder causes and treatment.

### Identification of the Coordinator and Affiliated Groups:

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

- Hospital Universitario La Princesa (José Luis Ayuso Mateos)
- Universidad de Oviedo. Facultad de Medicina (Julio Bobes García)
- Hospital Universitario de Álava (Ana González - Pinto Arrillaga)
- FIDMAG Hermanas Hospitalarias (Peter J. Mckenna)
- Universidad de Valencia. Facultad de Medicina (Rafael Tabares Seisdedos)

The Bipolar Disorder Programme has a high rate of internationalization and scientific productivity. Some of the most important work conducted in 2014 includes the epidemiological collaborative works between CIBERSAM groups and international groups, genetic studies, structural and functional neuroimaging work, the development and validation of specific psychometric instruments, staging models, participation in the development of guidelines for clinical practice to be applied in the health system, and innovative clinical trials. Examples of said works are the study of the genetic association of lithium response predictors, international consensus on bipolar disorder staging, the guideline for the evaluation of the effectiveness of the psychological intervention in the first psychotic episodes, studies in that same population who have neurocognitive deficiencies and the associated disability, the characterisation of functional cerebral changes in different stages of bipolar disorder, the clinical trial on the effectiveness of a psychoeducational programme for family group intervention in reducing hospitalizations, and the neurocognitive and functional rehabilitation trial. Work continued in the collaborative study with NASA which has allowed advancing in the knowledge about the mechanisms involved in the age of onset of bipolar disorder and in the description of neural networks involved in the manic and depressive stages of the disease. The findings of all these studies have been published in prestigious journals, such as The New England Journal of Medicine, JAMA Psychiatry, Schizophrenia Bulletin, Neuropsychopharmacology, Psychotherapy and Psychosomatics, Journal of Clinical Psychiatry, Acta Psychiatrica Scandinavica and European Neuropsychopharmacology.

### THE MAIN LINES OF RESEARCH DEVELOPED BY THE BIPOLAR DISORDER PROGRAMME TO DATE INCLUDE:

- Databases: Creating a broad collaborative database with epidemiological, clinical and biological information about bipolar disorder.
- Clinical trials: Conducting clinical trials to determine the efficacy and tolerability of new treatments for bipolar disorder.

- Epidemiology: studies aimed at determining the prevalence, comorbidity and disability associated with bipolar disorder.
- Identifying new biomarkers, therapeutic targets and novel mechanisms of action for the treatment of bipolar disorder.
- Early intervention: Studying a broad representative sample of bipolar patients in early stages of the disease (first episode) and genetic and environmental factors.
- Neuropsychology: Analysing the role of neurocognition as an endophenotype and as a potentially treatable prognostic factor.
- Neuroimaging: Analysing changes in structural and functional neuroimaging associated with the disease, its pathophysiology, symptoms, and neuropsychological manifestations
- Psychometry: Validating psychometric instruments for use in bipolar disorder.
- Psychotherapies: Studying the efficacy of innovative psychosocial interventions for improving disease prognosis.

## Objectives

- Make efficient use of resources and funding.
- Disseminate the findings.
- Conduct research with the maximum ethical and quality standards.
- Stimulate translational research and innovation.
- Initiate epidemiological studies and clinical trials.
- Improve knowledge and mental health in this area.
- Promote collaborative research relating to bipolar disorder.
- Train researchers to be experts in this disease.



**Josefina Castro Fornieles (G04)**  
Coordinator

The Mental Disorders in Children and Adolescents Programme was created in 2010 and consists of five CIBERSAM groups. The main objective of the programme is to study mental disorders that start during childhood and adolescence.

In 2014 our programme conducted the following work in each of its vertical lines:

**LINE 1: STUDY OF RISK FACTORS, GENETICS, CLINICAL CHARACTERISTICS, NEUROIMAGING, TREATMENT, PROGRESSION AND PHYSICAL AND PHYSICAL INVOLVEMENT OF PSYCHOTIC AND EMOTIONAL DISORDERS IN CHILDREN AND ADOLESCENTS.**

- Work has been continued in the already initiated studies on risk factors, genetics, clinical characteristics, neuroimaging, treatment and progression of psychotic and emotional disorders in children and adolescents.
- Work has been continued in collaborative studies in samples of children and adolescents at a high risk for psychosis (clinical and genetic), increasing follow-up time.
- Work has been initiated in study of the physical health consequences of psychotic disorders.
- Work has been initiated in the study of factors and markers for prognosis of disease progression.

**LINE 2: STUDY OF RISK FACTORS, GENETICS, CHARACTERISTICS CLINICAL, NEUROIMAGING, TREATMENT AND PROGRESSION OF THE EATING DISORDERS.**

- Work has been continued in earlier studies on the progression of eating disorders, conducting longitudinal studies.
- Work has been continued in the study of the efficacy of various pharmacological and psychological treatments in the treatment of eating disorders.

**LINE 3: STUDY OF GENETIC CHARACTERISTICS AND NEUROIMAGING IN CHILDREN AND ADOLESCENTS WITH OBSESSIVE-COMPULSIVE DISORDERS AND OTHER ANXIETY DISORDERS IN CHILDREN AND ADOLESCENTS.**

- Work has been continued in studies on common and differential characteristics between eating disorders and obsessive-compulsive disorder.
- Several studies were additionally initiated in 2014 on the genetic characteristics of children and adolescents who have developed these disorders, relating them to the response to some treatments pharmacological.

**LINE 4: STUDY OF THE GENETIC CHARACTERISTICS, NEUROIMAGING, TREATMENT AND PROGRESSION OF AUTISTIC SPECTRUM DISORDERS.**

- Throughout this year work has been continued in studies that began in previous years on the clinical, cognitive and of neuroimaging characteristics of children diagnosed with an autistic space disorder.



- Work has also been continued with research on the efficacy of various pharmacological and psychological treatments.
- Research has been conducted on the relationship of autistic spectrum disorders with other types of disorders, such as schizophrenia spectrum disorders or Rett Syndrome.

#### LINE 5: STUDY IN THE SAFETY AND EFFICACY OF THE PSYCHOTROPIC DRUGS AND OTHER TREATMENTS IN CHILDREN AND ADOLESCENTS.

- Work has been continued in the study of the efficacy and safety of antipsychotic treatments as a result of the participation of several groups in our programme in European projects.
- The study of new non-antipsychotic drugs such as fluoxetine was incorporated into this line this year.
- Work has been initiated in the study of the efficacy of other non-pharmacological treatments in several psychiatric disorders that begin during childhood.

#### LINE 6: DEVELOPMENT AND VALIDATION OF SPECIFIC EVALUATION INSTRUMENTS IN CHILDREN AND ADOLESCENTS AND OF THE NEUROIMAGING TECHNIQUE.

- Validation of some measurement instruments were concluded in 2014.
- Work has been initiated in the validation into Spanish of a scale assessing the impact of obsessive-compulsive disorder symptoms in children and adolescents.

#### LINE 7: STUDY OF IMMUNOLOGICAL IMPAIRMENTS IN VARIOUS PSYCHIATRIC DISORDERS CHILD AND ADOLESCENT.

- Work has been continued with the studies that were started in previous years assessing the relationship between autoimmune impairments and psychopathology in children and adolescents
- New international collaboration projects have been initiated, all of which are linked to Tourette's Syndrome and Tics.

#### LINE 8: STUDY OF THE BEHAVIOURAL DISORDERS IN CHILDREN AND ADOLESCENTS.

- Two European studies have been initiated in which research is done on different subtypes of behavioural disorders according to the presence of impulsivity or psychopathic features.

### Identification of the Coordinator and Affiliated Groups:

**Coordinator:** Dra. Josefina Castro Fornieles (Hospital Clínic de Barcelona, G04)

#### Affiliated Groups:

- Universidad de Valencia. Facultad de Medicina, G24 (Rafael Tabares Seisdedos)
- Hospital General Universitario Gregorio Marañón, G07 (Manuel Desco Menéndez)
- Universidad de Barcelona. Facultad de Biología, G08 (Lourdes Fañanás Saura)
- Hospital General Universitario Gregorio Marañón, G01 (Celso Arango López)
- Hospital Clínico y Provincial de Barcelona, G04 (Dra. Josefina Castro Fornieles).



**Víctor Pérez Sola** (G21)  
Coordinator

The mission of the CIBERSAM Depression Programme is to carry out collaborative projects between basic and clinical researchers: ranging from animal models to patients, genetics to clinical, including neurochemistry and molecular biology. For that purpose, the programme includes clinical and basic groups with extensive experience in translational research. In 2014 and as a result of the work conducted in previous years, several collaborative intramural and extramural projects focusing on basic research, new therapeutic targets and genes-environment interaction, neuroimaging studies and clinical trials that have allowed evaluating pharmacological and physical therapies in refractory depression were concluded in the programme. A line of research focusing on the risk factors of suicide, and on the consolidation and evaluation of specific programmes for the prevention of suicidal behaviour was also consolidated.

The research projects in the programme focus on 3 main focal points: Epidemiology and prevention of depression and suicide; neurobiological basis of mood disorders; efficacy, resistance and new therapeutic targets in depression.

### Structure of the Programme

**Coordinator:** Víctor Pérez Sola – G21

**Groups involved in the programme:**

- G02 Instituto de Investigaciones Biomédicas (Francesc Artigas Pérez)
- G03 Hospital Universitario La Princesa (José Luis Ayuso Mateos)
- G06 Universidad de Granada. Facultad de Medicina (Jorge A. Cervilla Ballesteros)
- G17 Hospital Universitario de Bellvitge (José Manuel Menchón Magriña)
- G20 Universidad de Santander. Facultad de Medicina (Ángel Armando Pazos Carro)
- G21 Hospital Santa Creu i Sant Pau / Hospital Mar (Víctor Pérez y María J. Portella)

### Specific objectives of the Depression Programme

Description of the main lines of research of the programme:

- Analysis of suicidal behaviour; development and evaluation of prevention programmes. Incidence of the suicide, related factors and use of antidepressants in the child and youth population.
- Genes-environment interaction in depression. Genetic predisposition and drug response factors.
- Psychosocial difficulties and occupational disability in patients with depression.
- Sociodemographic, clinical and/or pharmacological factors involved in the response to different therapeutic strategies.

- Cellular and molecular basis of depression and of the mechanism of action of the antidepressants. Intracellular signalling targets. Phenotypic and molecular characterisation.
- New therapeutic targets. Neuroplasticity and serotonergic neurotransmission. Endocannabinoid system and antidepressant responses.
- New therapeutic tools in depression: small interfering RNA (siRNA), ketamine, new psychotherapeutic strategies.
- Deep brain stimulation. Clinical trials in patients and animal models.
- Validation of various instruments of evaluation and change in patients with depression.
- MRI study in different stages of major depression.
- Origin and consequences of the neuroinflammation in depression.
- Treatment with ECT: relationship with neuropsychological impairments and quality of life.



**Francesc Artigas Pérez (G2)**  
Coordinator

### Description

The Therapeutic Innovation Programme is a top-quality transversal programme that has an international exposure and channels the efforts of CIBERSAM in the identification of new therapeutic targets and strategies for the purpose of improving treatments existing. The programme is made up of basic and clinical groups and conducts translational and back-translational research, also working on the improvement of experimental models of mental disease. The programme has a long-standing tradition of identifying and developing new pharmacological and non-pharmacological therapeutic strategies.

### Identification of the Coordinator and Affiliated Groups

The Therapeutic Innovation Programme is currently made up of 9 research groups, and its **coordinator** is **Dr. Francesc Artigas Pérez**:

- Hospital Clínico y Provincial de Barcelona (Dr. Eduard Vieta Pascual)
- Hospital Gregorio Marañón (Dr. Manuel Desco Menéndez)
- Hospital Universitario Marqués de Valdecilla (Dr. Benedicto Crespo Facorro)
- Instituto de Investigaciones Biomédicas de Barcelona. CSIC (Dr. Francesc Artigas Pérez)
- Universidad Complutense de Madrid. Facultad de Medicina (Dr. Juan Carlos Leza Cerro)
- Universidad de Cádiz. Facultad de Medicina (Dr. Juan Antonio Micó Segura)
- Universidad de Cantabria. Instituto de Biomedicina y Biotecnología de Cantabria. (Dr. Ángel Armando Pazos Carro)
- Universidad de Valencia. Facultad de Medicina (Dr. Julio Sanjuán Arias)
- Universidad del País Vasco (Dr. José Javier Meana Martínez)

The Programme includes the groups of the coordinators of the Bipolar Disorder Programme (Dr. E. Vieta) and Schizophrenia Programme (Dr. J. Sanjuán), and there is excellent collaboration between several groups with the group of the Depression Programme coordinator (Dr. V. Pérez). This favours the integration of various programmes. In addition, there are a number of collaborations with various CIBERSAM groups and other CIBERS.

The mission of the Therapeutic Innovation Programme (TIP) consists of conducting multidisciplinary and translational research in the fields of depression, schizophrenia and bipolar disorder for the purpose of improving already existing treatments for these diseases.

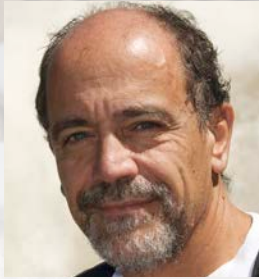
The programme includes highly trained staff, developing a wide range of lines of work, as well as a range of basic and clinical methodologies.

## THE MAIN LINES OF RESEARCH DEVELOPED BY THE THERAPEUTIC INNOVATION PROGRAMME TO DATE INCLUDE:

- Neurochemistry/Neurobiology: Studies on neurotransmitters, receptors (mGluR2, 5-HT1A, 5-HT2A, 5-HT3, CB1, DA, NA-Alpha-2, opioids, etc.) and intracellular signalling mechanisms (AMPC, CREB, ERK-1/2, etc.).
- The role of neuroplasticity/neuroproliferation pathways in psychiatric disorders.  $\beta$ -catenin, mTOR and BDNF as new targets for psychotropic drugs.
- Brain circuits in schizophrenia (GABA interneurons, NMDA-R, thalamocortical circuits, etc.). Mechanism of action of antipsychotic drugs.
- Mechanism of action of new antidepressant strategies: deep brain stimulation, (preclinical and clinical studies), ketamine, 5HT4 receptor, siRNA.
- The role of stress and its regulating mechanisms in psychiatric disorders.
- Regulation of inflammatory mechanisms, of their origin and consequences in neuropsychiatric disorders.
- Neurobiological mechanisms of hallucinations and sensitivity to psychotropic drugs.
- Genes and neuroimaging (clinical and preclinical studies).
- Study of the early stages of Schizophrenia: molecular models for the early identification of psychosis.
- Neurobiological relations between depression-chronic pain.
- New classifications (for example polarity index) and treatments for bipolar disorder.
- Methodology for evaluating the efficacy and tolerability of drugs and non-pharmacological interventions for mental disorders.
- Brain neuroimaging. Diagnostic and prognostic variables. Neural circuits and networks as therapeutic targets.

## Objectives:

- To integrate basic and clinical research in a more efficient and multidisciplinary manner by means of collaborative projects in genetics, neuroimaging, identification of therapeutic targets, animal models of mental disorders and mechanism of action of psychotropic drugs.
- To study the neurobiological basis of resistance to treatments and the mechanism of action of new therapeutic strategies.
- To identify new therapeutic targets and biomarkers in mental disorders, particularly depression, schizophrenia and bipolar disorder.
- To study of the mechanism of action and to design antidepressant, antipsychotic and mood stabilizing drugs.
- To examine and incorporate new non-pharmacological treatment strategies.
- To develop, improve and evaluate new basic and clinical research methodologies for evaluating the effect of drugs and other therapeutic interventions.
- To transfer basic knowledge to clinical practice and vice versa.
- To reposition drugs.
- To provide early identification of psychosis by means of biological markers.



**Julio Sanjuán Arias (G23)**  
Coordinator

### Description

The main objective of the Schizophrenia Programme is the multidisciplinary study of this serious mental disorder by trying to integrate research on animal models, research on new molecules, the neurobiological basis and psychosocial needs. All this is geared towards reducing the distance, which is still quite large today, between research and clinical practice.

The Schizophrenia Programme involves the largest number of groups (12). As a result of this broad participation combined with the Common Database and various collaborative studies, this programme has the largest clinical and genetic database. Important collaborative projects on the progression of the first psychotic episodes have been developed through this programme.

2014 has been particularly important for this programme because it is the year in which results and publications relating to important collaborative projects have started to appear.

### Coordination and Participating Groups:

**Coordination:** Dr. Julio Sanjuán Arias - Universidad de Valencia. Facultad de Medicina. G23

#### Participating Groups:

- G01. Hospital Gregorio Marañón (Dr. Celso Arango López)
- G04. Hospital Clínico y Provincial de Barcelona (Dr. Miquel Bernardo Arroyo)
- G05. Universidad de Oviedo. Facultad de Medicina (Dr. Julio Bobes García)
- G08. Univ. de Barcelona. Facultad de Biología (Dra. Lourdes Fañanás Saura)
- G10. Hospital Universitario de Álava (Dra. Ana González-Pinto Arrillaga)
- G11. Fundación Sant Joan de Deu (Dr. Josep Maria Haro Abad)
- G15. Benito Menni Complex Assistencial (Dr. Peter J. Mckenna)
- G16. Universidad del País Vasco (Dr. José Javier Meana Martínez)
- G19. Hospital Universitario 12 de Octubre (Dr. Tomás Palomo Álvarez)
- G22. Hospital Ramón y Cajal (Dr. Jerónimo Saiz Ruiz)
- G23. Universidad de Valencia. Facultad de Medicina (Dr. Julio Sanjuán)
- G26. Hospital Univ. Marques de Valdecilla (Dr. Benedicto Crespo-Facorro)

## Lines of Research.

- To continue the study of the follow-up and predictive variables in first psychotic episodes.

The results of the FPE study on first psychotic episodes have begun to be published in 2014. Work has been continued on the second project on FPEs, both of which are coordinated by Dr. M. Bernardo. The first results of the European project EU-GEI, coordinated in Spain by Dr. C. Arango, have also been published.

- To study the possible neurobiological (genetic, immunological and neuroimaging) markers of different symptomatological phenotypes of schizophrenia.

The main results of the GWAS study, which replicate the findings of broad genome studies in a sample of over 3000 patients diagnosed with schizophrenia, have been published in 2014.

- Study the predictive response variables (neuroimaging, neuroimmunology, neurophysiology) in relation to different pharmacological treatments.

Various basic CIBERSAM groups have published and proposed new antipsychotic response prediction models. There have also been important contributions concerning the role of immunological response as a prognosis variable in these patients.

- To conduct research on the efficacy and effectiveness of psychotherapeutic treatments in combination with standard pharmacological treatments in schizophrenia.

Several European projects have been initiated which include the participation of CIBERSAM groups (Dr. Arango, Dr. Crespo-Facorro, Dr. Bernardo). The main objectives of these projects, among others, are optimisation of pharmacological and psychosocial treatment.

- To study the repercussions of schizophrenia on the state of health, psychosocial adjustment, quality of life, the individual's levels of disability and on patient service use patterns and the effect on comorbidity.

The research meeting on Psychosis, including the participation of family members of these patients, was held again. Various multicentre projects concerning the importance of physical health in schizophrenic patients, with a particular emphasis on metabolic disorder, were started up.



**Antonio Lobo Satué** (G13)  
Coordinator

## Programme Description

The Psychosomatic Disorders, Anxiety and Impulse Control Programme is geared towards epidemiological, clinical and basic research of a broad group of mental disorders and conditions related to somatic factors, anxiety and behavioural disorders. The programme includes specific mental disorders, such as personality disorders, anxiety and obsessive-compulsive disorder, the relationship between mental disorders and somatic aspects, such as pain, inflammation, and psychosomatics, from both the clinical perspective and the basic perspective, genetic studies, ageing, epidemiological studies encompassing primary care, and research on services in primary care and general hospitals. The programme is of great interest given the high prevalence of mental disorders and conditions of this type and because of the high social costs and the impact they have on the quality of life of people who suffer from them.

## Identification of the Coordinator and Affiliated Groups:

**Programme Coordinator:** **Antonio Lobo Satué** (Hospital Clínico Universitario de Zaragoza)  
 Universidad de Granada. Facultad de Medicina (Dr. Jorge A. Cervilla Ballesteros)  
 Fundación Sant Joan de Déu (Dr. Josep Maria Haro Abad)  
 Universidad Complutense de Madrid. Facultad de Medicina (Dr. Juan Carlos Leza Cerro)  
 Hospital Clínico Universitario de Zaragoza (Dr. Antonio Lobo Satué)  
 Hospital Universitario de Bellvitge (Dr. José Manuel Menchón Magriña)  
 Universidad de Cádiz. Facultad de Medicina (Dr. Juan Antonio Micó Segura)  
 Hospital Universitario 12 de Octubre (Dr. Tomás Palomo Álvarez)  
 Hospital de la Santa Creu i Sant Pau (Dr. Víctor Pérez)  
 Hospital Ramón y Cajal (Dr. Jerónimo Saiz Ruiz)

## Main Lines of Research:

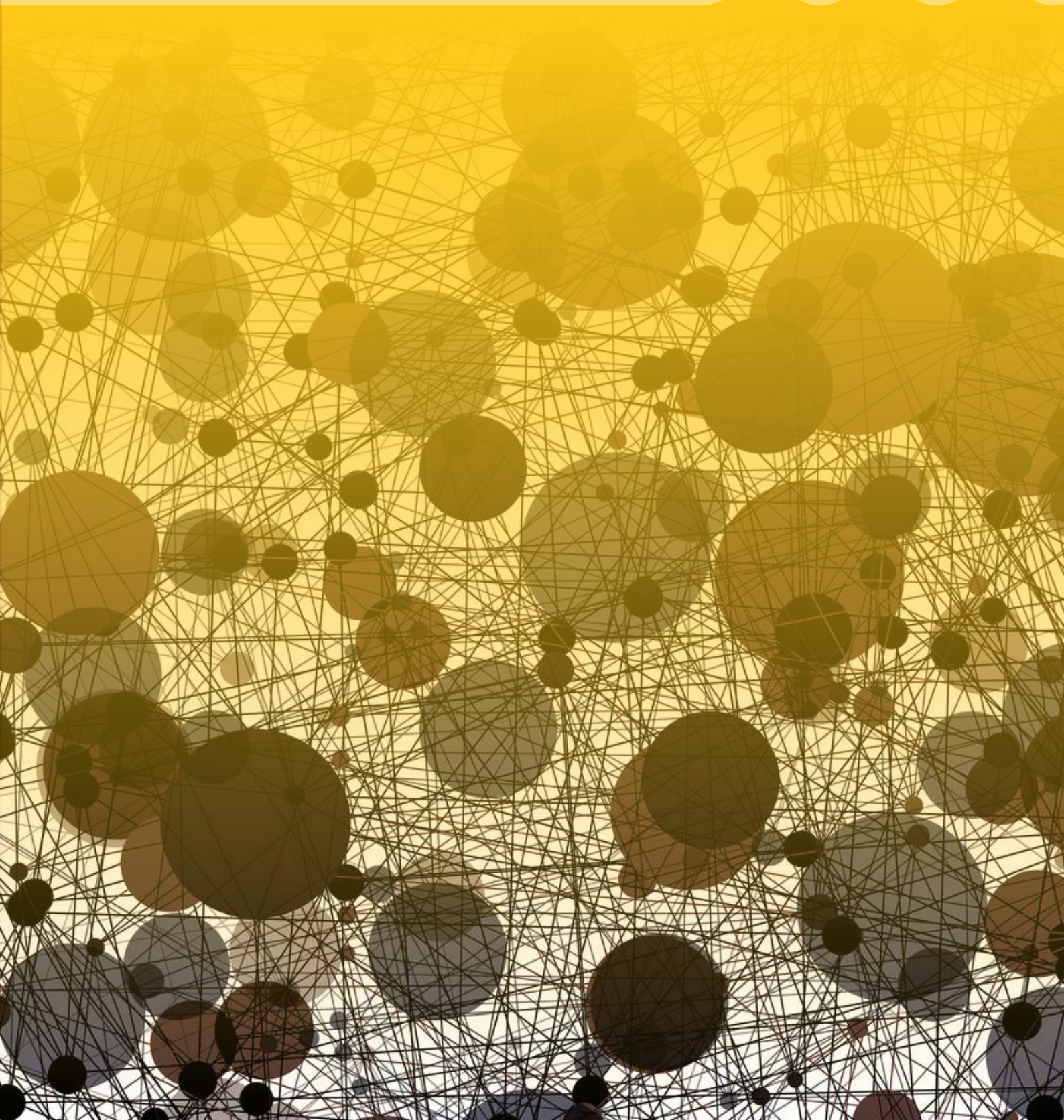
- Ageing, specifically healthy ageing, and its relationship with the disorders of this programme.
- Biological markers and physiopathological mechanisms of neuroinflammation, in relation to stress disorders, anxiety and other mental disorders.
- Neurobiological and psychosocial factors of the pain.
- Personality: features, genetic factors and therapeutic strategies in borderline personality disorder.
- Impulse control disorders and suicidal behaviours.



- Obsessive-compulsive disorder: clinical aspects, neurobiological aspects, genetic aspects and therapeutic strategies.
- Use of health care resources and mental health services in general hospitals and Primary Care Centres.
- Longitudinal epidemiological and risk factor studies in medical populations, including the Primary Care population.
- Population-based study of psychiatric morbidity. Development of epidemiological databases.
- Disorders with psychological and somatic comorbidity.



### 3. TRANSVERSAL PROGRAMMES





**José Luis Ayuso Mateos (G03)**

European Programmes and International Relations Area Coordinator

### Description

The European Programmes and International Relations Area of CIBER works closely with other areas and programmes to promote the participation of its researchers in international projects and initiatives and in the development of specific actions for exposing and promoting the international presence of CIBERSAM.

In recent years, the CIBER has already reached a leadership position in the field of psychiatry both in Spain and abroad. In 2014, the main objective has been to establish and maintain contacts with institutions of the European Commission, not only by submitting proposals and collaborating in international consortiums, but also by advocating for international calls for proposals in the CIBERSAM priority research areas. Furthermore, and as a result of the international recognition achieved by CIBERSAM, the attempt has been made to increase participation of the CIBER in outside of Europe programmes.

### Objectives

- To enhance CIBERSAM group participation in calls for proposals for European and international projects, offering support to groups that want to embark on such initiatives.
- To encourage CIBERSAM researchers to coordinate European projects.
- To establish contacts with the authorities involved in funding mental health research in Europe and abroad to stimulate the creation of calls for proposals in the CIBERSAM priority research areas.

### Summary of 2014 Activities

In 2014, the Mental Health CIBER has reinforced its participation in the international research community of excellence. In 2014 the first proposals were submitted for the new European programme, Horizon 2020. Furthermore, the participation in calls for proposals outside of Europe, particularly in the USA has been increased, and by means of its calls for proposals in intramural projects, the CIBER has funded in 2014 the participation of 4 groups in a non-commercial European clinical trial on new intervention strategies in bipolar disorder - MEMAP - aimed at proving the efficacy of methylphenidate (stimulant) in the control of the acute mania symptoms in patients with bipolar disorder. Four CIBERSAM groups participated in collaboration with groups from Germany and Belgium.

Even more worth highlighting is the increase in synergies with international reference institutions in the field of health, such as the World Health Organization (WHO) and the National Institute of Mental Health (NIMH) of the United States, which is an indication of the international positioning that has been achieved.

The main results of these actions obtained in 2014 were:

- Participation of 8 of the 24 (33%) CIBERSAM groups in active European projects in 2014.
- 256 papers published in collaboration with international researchers and teams (corresponding to 44% of the total of 581 papers published in 2014 by groups affiliated with CIBERSAM).
- Coordination of the “Roadmap for Mental Health Research in Europe” - ROAMER project.
- Collaboration with the NIMH, the WHO and the ROAMER Project in the organization of the meeting entitled “Future Directions in Research Diagnostic Criteria for Mental Disorders”, which was held at the School of Medicine at the Universidad Autónoma de Madrid on 17-19 February 2014.
- Participation in the research and management of 4 FP7 projects and one NIH project.
- Approval of a European project for the H2020 programme which will begin in 2015.
- Recruitment of international researchers for internships and PhDs with European mention through the Marie Curie MARATONE network, which is part of CIBERSAM.
- NARSAD grant (Independent Investigator Grant) awarded to a researcher in group G25.
- Translation into Spanish of DSM-5 (Diagnostic and Statistical Manual of Mental Disorders).

#### ACTIVE EUROPEAN/INTERNATIONAL PROJECTS MANAGED THROUGH CIBERSAM IN 2014:

(The groups managing the project directly through CIBERSAM are in bold)

- **ROAMER** | Roadmap for Mental Health Research in Europe. G01, G03, G06, G10, G11, G25, G26 (Coordinador Haro)(IP Ayuso).
- **STOP** | Suicidality: Treatment Occurring in Paediatrics. G01, G04 (IPs Arango y Castro).
- **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 Arango).

#### EUROPEAN/INTERNATIONAL PROJECTS GRANTED IN 2014 WHICH WILL BE MANAGED THROUGH CIBERSAM IN 2015:

- **RE**factoring Parallel Heterogeneous Resource-Aware Applications - a Software Engineering Approach (Rephrase) – IP DESCO.



**Ana González-Pinto** (G10)

Quality and Internal Evaluation Area Manager

Actions such as administrative procedure standardisation were carried out in 2014, and by means of an audit, it was verified that the Mental Health CIBER complies with ISO 9001:2008 standard requirements.

### 2014 INDICATORS

	2013 Situation Indicator	2014 Objective	2014 Situation	Observations
Number of meetings, quality group	5	5	5	Five meetings were held in 2014.
Number of meetings, quality group with other areas	3	3	3	Three meetings were held in 2014.
Number of areas of improvement detected	4	3	3	Renewal of management positions, coordination positions, committees and responsibilities in internal CIBERSAM management (every 4 years). Creation of CIBERSAM pre-doctoral grants for young researchers Change in intranet management provider Annual meeting compulsory for Principal Investigators in which the working of projects in each Area and/or Programme is discussed.
Number of preventive actions implemented	3	2	2	Introduction of additional indicators in the 2014-2016 Strategic Plan in the Quality Area: ("Percentage of surveys issued to internal and external users that were answered with respect to the total number of surveys performed"; "No. of non-conformities").
Number of internal satisfaction surveys performed.	1	1	1	CIBERSAM Principal Investigator satisfaction survey.
Number of external opinion surveys performed.	1	1	1	Pharmaceutical laboratory satisfaction survey.
Number of survey analyses.	1	2	2	Principal Investigator satisfaction survey and pharmaceutical laboratory satisfaction survey.
Percentage of surveys given to internal and external users that were answered with respect to the total number of surveys performed	sd	>65%	19/24 79%	
No. of non-conformities	sd	-1		

In this context of improvement, evaluation is necessary and CIBERSAM stresses the evaluation of its structure, processes, and scientific production:

- Structure: the qualification, technological capacity, infrastructure, economic-administrative organization, management of human and material resources are taken into account.
- Processes: the accomplishment of CIBER's mission, the relevance of its activity on a national and international level and the coherence in planning, disclosing and disseminating its results stand out.
- Scientific production: production is assessed with respect to the available funds, the number of publications, the projects, the patents and the development over time.

CIBERSAM has a code of Good Research Practices adopted by all its researchers. Complying with a code of Good Scientific Practice means maintaining ethical principles and legal requirements in accordance with international ethical standards in research stated in the Declaration of Helsinki (obtaining informed consent, comprehensive assessment of the risk/benefit ratio of the study and impartiality in selecting study participants and performing follow-up), as well as the CIBERSAM Good Scientific Conduct Committee (GSCC). These are the essential elements in any research work that seeks to expand scientific knowledge within a framework of credibility and respect from society.

Furthermore, CIBERSAM has added to its Quality Management System an operating protocol based on national and international ethical standards for handling and transferring biological samples between CIBERSAM laboratories (from test animals or experiments with cells and from patients or controls). This protocol assures the quality and stability of the samples under its control and of the data relating to said samples at all times.

The Mental Health CIBER has a quality control system for research and management activities. The Steering Committee, the Scientific Committee as well as the area, line and/or project coordinators and managers make sure that the objectives are complied with and that the scientific methods have the appropriate quality attributes.

In 2014, actions for evaluating and monitoring objectives, indicators and processes defined in the Strategic Plan based on the ISO standard were conducted:

- Defining and monitoring areas of improvement and prevention detected in areas of management and research activity.
- Detecting and monitoring areas of improvement resulting from analyzing satisfaction surveys.
- Analysing results of the external pharmaceutical laboratory satisfaction survey.

## TRAINING PROGRAMME

A Training Programme which seeks to become the point of reference in mental health training in this country and to facilitate the access of young researchers to new scientific knowledge has been operating since CIBERSAM was created. The core element of said Programme is the development of a Master's course in Introduction to Mental Health Research that began in 2013-2014. Along with said Master's course, this Programme also contemplates the possibility of funding CIBERSAM member participation in other courses related to the various areas of work, preferably those courses offered by CIBERSAM itself. Furthermore, the Programme also provides funding for research internships in other CIBERSAM Units, in other CIBERs, or abroad.

The Master's course for the Introduction to Mental Health Research is an interuniversity Master's course which includes the participation of the Universidad Complutense, Universidad de Barcelona, Universidad Autónoma de Barcelona, Universidad de Cádiz and Universidad de Cantabria which coordinated the study. Eleven CIBERSAM groups officially take part in teaching, and all the other groups participate in a more indirect manner. The Master's Programme (worth 60 credits) is characterised by having a strong virtual component as well as mandatory basic and clinical internships. It addresses aspects relating to research foundations, the neurobiological basis and diagnostic, clinical and therapeutic approaches. In 2014 all the courses corresponding to the second four-month period of the first year (2013-2014), including the bulk of the part corresponding to work internships; furthermore, in the final trimester of the year the first courses of the second year were taught, one of them being a classroom course and 5 being online. The number of students registered to this first ever Master's course offered by CIBERSAM amounted to 33. They were from all over Spain and have different research backgrounds (medicine, psychology, biology, etc).

As regards funding provided by the Programme, CIBERSAM has assigned two thirds of its training budget for partial funding of researcher participation in the Master's course, either directly for CIBERSAM staff or in the form of grants for people who are not yet part of the CIBERSAM but who are closely related to it. In the first year, a total of 11 consortium groups benefited from partial registration subsidy. Five people were given the grant in the second year.

Obviously, attendance to courses linked with the Master's course is fundamental. However, apart from the Master's course, the Training Programme has funded 17 attendances to other courses for CIBERSAM members: 13 of them were in Spain (5 in courses organized or directed by their groups) and 4 abroad (Netherlands, Germany). The significant attendance to the Intensive Courses for an Introduction to Neurosciences should be pointed out.

In addition, 3 internships have been funded for CIBERSAM members, 2 in Spain and the rest in Great Britain. It should be pointed out that this number of internships does not include all of those which are done in the various CIBERSAM groups within the aforementioned Master's course. In reference to only CIBERSAM members or students who have been given a grant by CIBERSAM, and exclusively considering those internships which entailed going to another city, there were a total of 8 internships. Taking into account the part of the budget that was set aside as mentioned above, it is important to indicate that the funding objectives set forth in the Programme have for the most part been met in 2014.

The Master's course for the Introduction to Mental Health Research is an official interuniversity programme with partial classroom attendance. It is organized by research groups belonging to five Spanish universities (Universidad de Cantabria; Universidad Complutense de Madrid; Universidad Autónoma de Barcelona; Universidad de Barcelona and Universidad de Cádiz) and which are part of a national networking research structure, known as CIBERSAM. The Master's course is coordinated by the Universidad de Cantabria (Dr. Elsa Valdizán, G20). Its mission is to improve clinical care relating to mental health of our society through the knowledge generated by innovation and translational research in psychiatry and neurosciences. The Master's course targets national and international students who are interested in research in psychiatry and mental health, and it particularly targets young researchers in CIBERSAM.



The purpose of the Master's course is to train mental health researchers in both basic and clinical aspects, and to encourage the exchange between mental health work groups, which helps carry out joint projects.

The classes within the curriculum studies are taught by research groups that are leaders in their area, in order to provide students with in-depth knowledge about the neurobiological, psychological, genetic and environmental bases of normal psychological activity and mental disorders, the bases of treatment, as well as in the methods of research in mental health. Eleven CIBERSAM groups officially take part in teaching, and all the other groups participate in a more indirect manner.

The Master's course offers a total of 133 credits, 60 of which are required to complete the course. These credits are distributed into theoretical class modules and two supervised internship cycles in mental health research units. The theoretical module is done for the most part online.

The second year of this Master's course, which is a pioneer in the Mental Health field in Spain, started in the final trimester of 2014, and the maximum number of registered students, i.e., 50, has been covered.

## COMMUNICATION PROGRAMME

The Communication initiatives in the CIBERSAM during this period were:

### PRESS RELEASES:

“Demuestran que SAME empeora la neurogénesis y contribuye al deterioro cognitivo” (Investigación CIBERSAM y CIBEREHD) 2 de mayo de 2014.

“Presentado el Máster de Investigación en Salud Mental”. (La Universidad de Cantabria coordina este programa de posgrado, impulsado por el CIBERSAM e impartido por cinco universidades. Santander) 14 de marzo de 2014.

“El CIBER cocina sus proyectos para la Semana de la Ciencia” (Investigación representativas de las 8 áreas temáticas del CIBER. CIBERSAM: ROAMER) 6 de noviembre de 2014.

“El consumo de cocaína cuadruplica el riesgo de muerte súbita en personas de 19 a 49 años” (Investigación de la UPV/EHU, Instituto Vasco de Medicina Legal y el CIBERSAM) 28 de noviembre de 2014.

### HITS IN THE MEDIA

Total number of hits: 751 (85% internet and 15% print media)

Audience: 86% internet/ 14% print media

Hits in the most important media outlets:

Date	Headline/ subject addressed	Mentioned member	No. of hits
05/11/2014	La cocaína provoca anomalías en el corazón	Department of Psychiatry, Hospital General de Valencia	82
10/12/2014	La cocaína cuadruplica el riesgo de muerte súbita	Research conducted by UPV/EHU, Instituto Vasco de Medicina Legal and CIBERSAM	71
20/05/2014	Identifican un desequilibrio inflamatorio celular al inicio de la esquizofrenia	Miquel Bernardo, Ana González-Pinto, Mónica Martínez-Cengotitabengoa and Juan Carlos Leza	40
21/02/2014	Relación inversa entre Alzheimer y cáncer	Rafael Tabarés-Seisdedos	37
04/12/2014	Los pacientes con esquizofrenia que abandonan el tratamiento tienen más posibilidades de recaer	Paz García-Portilla, CIBERSAM	20

### TWITTER STATISTICS [https://twitter.com/ciber\\_sam](https://twitter.com/ciber_sam)

Updates					Followers					Following					Klout*				
ENR	MRZ	JL	MRZ	DIC	ENR	MRZ	JL	SEP	DIC	ENR	MRZ	JL	SEP	DIC	ENR	MRZ	JL	MRZ	DIC
70	141	264	317	<b>414</b>	249	332	438	492	<b>587</b>	323	343	350	350	<b>352</b>	43	43	43	44	<b>44</b>

\*Klout (influence level values between 1 and 100).

**2013 ANNUAL REPORTS** (Spanish/English version) (pdf and flip/flop)

<http://www.ciberisciii.es/comunicacion/memorias-anuales>

**CIBER NEWSLETTERS EVERY TWO MONTHS.** It includes the top 4 news items of the CIBERSAM during that period <http://www.ciberisciii.es/comunicacion/boletines>

**PARTICIPATION IN THE SEMANA DE LA CIENCIA. ACTIVITY: TAPACONCIENCIA.**

Carla Obradors (Mental Health CIBER and Parc Sanitari Sant Joan de Déu) presented at “TapaConCiencia”, an interCIBER activity at the Semana de la Ciencia of Madrid, the ROAMER project to 250 attendees.

The act was covered by over 20 general and specialized media sources.

<http://www.ciberisciii.es/ficheros/CIBER/DossierTapaConCienciaFlip.html#p=16>


**NEWS UPDATES ON THE CIBERSAM WEB PAGE**

<http://cibersam.es/>

**III FORO INTERNACIONAL NUEVOS ABORDAJES EN EL TRATAMIENTO DE LA ESQUIZOFRENIA**

The III Foro Internacional Nuevos abordajes en el tratamiento de la esquizofrenia, organised by CIBERSAM, was held at the Ateneo in Madrid on 20-21 November 2014. This time there was a larger presence of researchers from the network who could listen to the contributions made by basic, translational and clinical research to the field of schizophrenias. Twenty-three of the top experts in neuroscience from both Spain and abroad participated in this event.





Some of the foreign guests held a debate on the attenuated psychosis syndrome (William Carpenter and Robin Murray) and on the effectiveness of cognitive treatments in psychosis (Til Wykes).

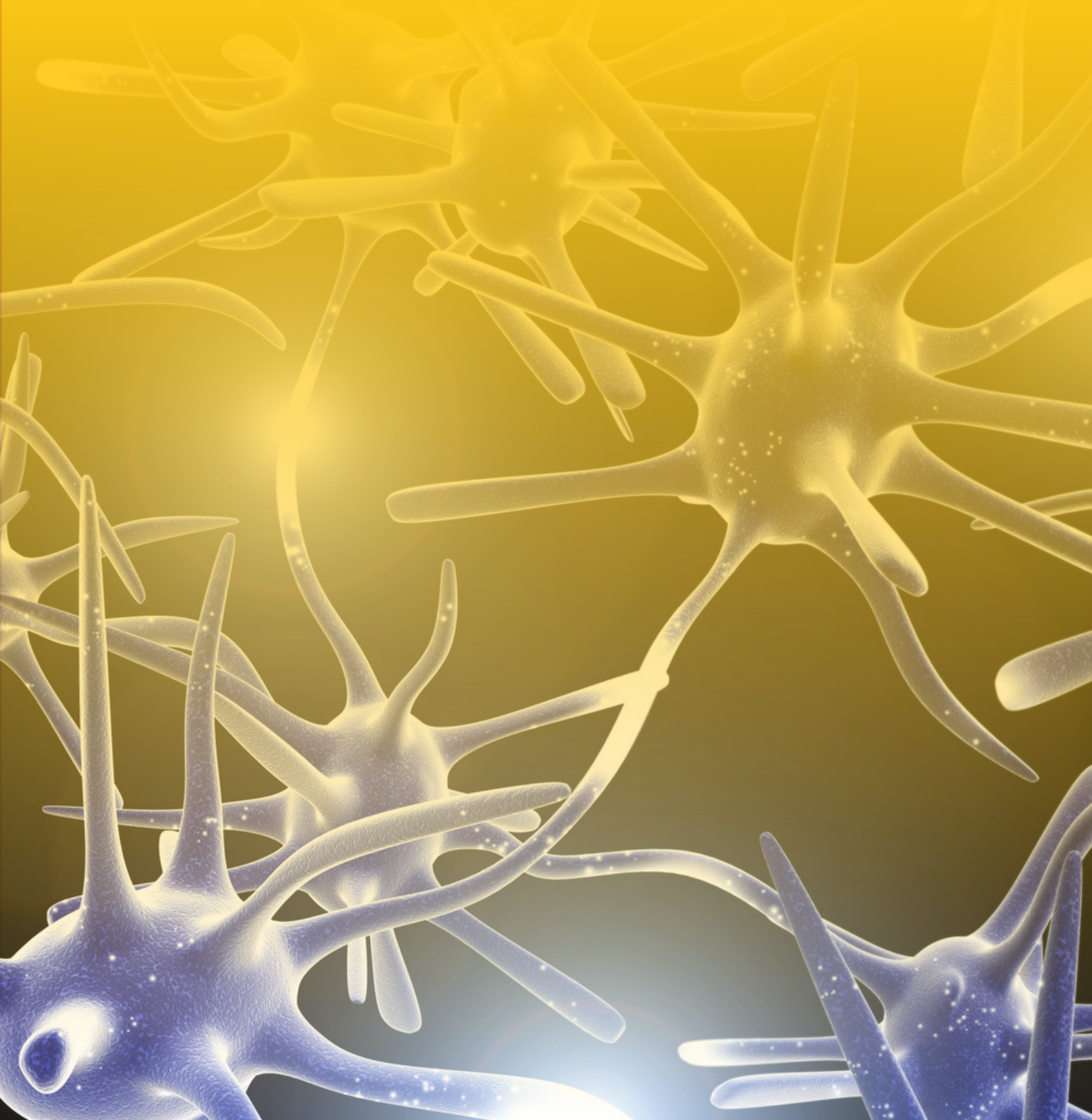
In addition, there were three round tables dedicated to research in schizophrenia in the Mental Health CIBER (CIBERSAM), to the physical health of the people with schizophrenia and to the role of GABAergic interneurons in schizophrenia.

Finally, there was a conference focusing on Health Economics in the field of schizophrenia given by Professor A-La Park of the London School of Economics and Political Sciences.

The assessment obtained through the evaluation questionnaire was also very positive this year, so the Forum has become one of the most highly recommended events for Spanish neuroscientists.

The CIBERSAM PIs met on 21 and 22 November (Friday afternoon, 21 November) and held specific meetings of the different CIBERSAM research programmes (schizophrenia, bipolar, etc.). This time each of the groups gave in-depth analysis of the current state and the development of each of the programmes and discussed and approved new trends and aspects to be enhanced.

## 4. PLATFORMS



## PLATFORMS



**Josep M. Haro Abad (G11)**  
Area responsable Platforms

CIBERSAM includes 5 research support platforms:

- **DNA Bank Platform**
- **Library of Mental Health and Disability Instruments Platform**
- **Brain Bank Platform**
- **Neuroimaging Platform**
- **Common Databases Platform**

These infrastructures are equipped with highly qualified staff providing significant research support. These platforms provide support both to CIBERSAM research groups and to external groups that conduct mental health research activities or in other areas of knowledge.

The DNA Bank Platform includes 11,696 samples obtained from individuals with mental disorders and controls.

The Library of Instruments Platform provides researchers with information and services with respect to mental health measuring instruments and surveys.

The Brain Bank Platform provides brain tissue samples obtained from individuals with mental disorders and controls.

The Neuroimaging Platform is a technical group the main objective of which is to enhance the use of quantitative analysis techniques in Neuroimaging. It has a collection of thousands of images.

The Clinical Data Platform provides an online tool to record sociodemographic, clinical, and research information. It has more than 24,176 patients with a total of 88,272 evaluations. The DNA and Neuroimaging Platforms are integrated with the clinical data platform.

## 2014 INDICATORS

Indicator	2013 Starting Situation	2014 Objective	2014 Situation	Objective Achieved
<b>INSTRUMENT BANK PLATFORM</b>				
No. of new instruments added to the database.	53	40	41	Yes
% increase in no. of queries made in the bank	7	10% incr.	8	Yes
<b>BRAIN BANK PLATFORM</b>				
No. of new samples	48	5% incr.	0	No
No. of intra-CIBERSAM donations.	82	10% incr.	60	No
No. of total donations.	112	10% incr.	144	Yes
No. of toxicology service collaborations	78	80	0	No
No. of CIBERSAM papers prepared with samples of the bank.	8	>=10	10	Yes
		* Inability to collect new samples due to internal biobank restructuring		
<b>NEUROIMAGING PLATFORM</b>				
No. of patients added in the platform.	619	10% incr.	1226	Yes
No. of processed images at the platform.	3059	10% incr.	700	Yes
Total no. of patients in the platform.	1460	10% incr.	2686	Yes
No. of images in the platform.	8785	10% incr.	11248	Yes
<b>DNA PLATFORM</b>				
No. of coordination group meetings.	6	2	6	Yes
No. of studies conducted using the platform.	8	8	8	Yes
No. of samples collected.	9721	10% incr.	11248	Yes
<b>CLINICAL DATA PLATFORM</b>				
No. of patients in the platform.	22493	5% incr.	24176	Yes
No. of papers prepared using the platform.	6	4	6	Yes
<b>OTHERS</b>				
No. of queries made in platforms by researchers outside CIBER.	6	4	4	Yes
No. of training activities organized by the platforms.	2	2	2	Yes
No. of networks with participation of the platforms	1	1		
% platforms cost covered by external income (CIBERSAM extra).	70000	10% incr.	35000	Yes
Organization of scientific conference for all platforms	0	2	2	Yes

\* Percent increase in all cases relative to baseline

## DNA BANK PLATFORM



**Dr. Celso Arango López (G11)**  
DNA Bank Platform Manager

### Scientific Committee formed by:

- Dr. Julio Sanjuán Arias (G23)
- Dra. Lourdes Fañanás Saura (G08)
- Dr. Jorge Cervilla Ballesteros (G06)
- Dr. Josep Maria Haro Abad (G11)

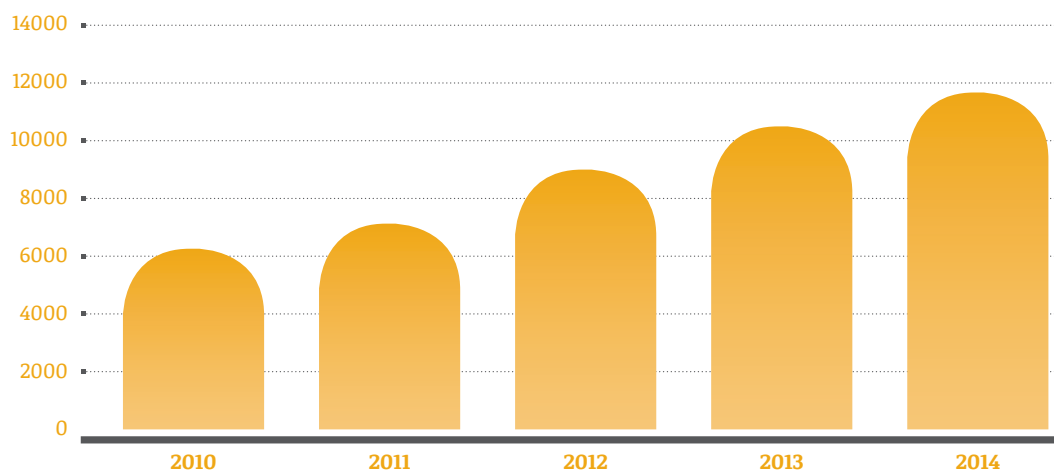
Throughout 2014, a total of 493 samples of patients with schizophrenia, emotional disorders and autism spectrum disorder have been included in the collection of CIBERSAM DNA samples. Furthermore, the number of healthy controls increased by 672. Last year's collection activities are summarized in the following table:

Center	City	Samples
Hospital Gregorio Marañón	Madrid	444
Universidad de Oviedo	Oviedo	48
Hospital Clínico Barcelona	Barcelona	60
Universidad de Valencia	Valencia	48
Hospital Clínico Santiago Compostela	Santiago Compostela	499
Otros		66
	Total	1165



Like in previous years, new projects were incorporated in the platform in 2014, with the inclusion of almost 1100 new samples. This brings the total number of samples to 11696. Progression in the number of samples since the creation of the platform can be verified in the following graph:

### ACCUMULATION OF SAMPLES



Several teleconferences between the committee members of this platform has led to an agreement to update and improve the protocol for sending samples to the bank, such that any CIBERSAM group can send samples to the platform in a clear and unequivocal manner (<http://www.cibersam.es/cibersam/Plataformas/Plataformas%20de%20Investigaci%C3%B3n/Banco%20de%20ADN/Plataforma%20de%20Banco%20de%20ADN>). This protocol and documents were approved by all CIBERSAM Pls. The collection has also been officially managed and registered and is now registered in the National Biobank Registry (Instituto de Salud Carlos III).

The platform is also linked to the CIBERSAM common data bank for better sample characterization and selection (GRIDSAM). The platform committee updated the procedures for assuring correct identification of samples and the existence of a minimum set of data assuring data use and facilitating data search. Any CIBERSAM group can therefore know the number of patients or controls that comply with a series of characteristics, the CIBERSAM group to which the data belong, the project to which each sample belongs, or if a specific sample is included in several projects.



**Josep M. Haro Abad (G11)**  
Library of Instruments Platforms Manager

**Scientific Committee formed by:**

- Dr. Josep M. Haro (G11)
- Dra. Ana González-Pinto (G10)
- Dr. Eduard Vieta Pascual (G25)
- Dr. José Luis Ayuso (G03)
- Dr. Julio Bobes (G05)
- Dr. Antonio Lobo (G13)
- Dr. Celso Arango (G01)

The Library of Mental Health and Disability Instruments has over 250 instruments distributed according to the different areas of interest.

The Bank includes 298 instruments: 24 correspond to the diagnosis area, 80 to the symptomatology area, 34 to childhood/adolescence, 15 to special populations, 35 to neuropsychology, 16 to disability and the rest to others (family burden, social skills, service satisfaction, adverse events, dual pathology and quality of life).

The objectives and proposals for 2015 are:

- Expand dissemination of bank instruments.
- Continue online consulting service.
- Expand the number of instruments and update the web page (design and operability).
- Improve the qualitative evaluation of the instruments.
- Bank of instruments call for proposals.
- Bank of instruments workshop.

Number of instruments added to the database in 2014	41
Number of queries made to the Bank in 2014	8

## BRAIN BANK PLATFORM



**Dr. José Javier Meana (G16)**  
Brain Bank Platform Manager

**Scientific Committee formed by:**

Dr. Josep M. Haro (G11)

Dr. Ángel Pazos (G20)

Dr. J. Javier Meana (G16)

The Brain Bank Platform and brain sample collections are the basic structure in translational psychiatric research. There are currently three nodes linked to the Fundación Sant Joan de Déu, Universidad del País Vasco and Universidad de Cantabria groups.

The platform amasses samples with quality criteria, donor's clinical data and toxicological data. A total of 144 samples have been given to multiple national and international intra-CIBERSAM groups. Fundación Sant Joan de Déu has successfully earned biobank accreditation and is now not part of the Biobanks Network supported by the Instituto de Salud Carlos III.

In 2014, the process of incorporating donors and for obtaining samples to be transferred out for national and international scientific projects has continued.

Number of intra-CIBERSAM donations.	60
Number of total donations.	144
Number of toxicology service collaborations	0
Number of CIBERSAM papers prepared with samples from the Bank	10



**Dr. Manuel Desco (G07)**  
Neuroimaging Platform Manager

### Scientific Committee formed by:

- Dr. Joost Hansen (G01)
- Dra. Núria Bargalló (G04)
- Dr. Manuel Desco (G07)
- Dr. Josep Maria Haro (G11)
- Dr. Raymond Salvador (G15)
- Dr. Julio Sanjuán (G23)
- Dr. Benedicto Crespo (G26)

The Neuroimaging Platform is a technical group within CIBERSAM having the main objective of enhancing the use of quantitative analysis techniques in neuroimaging. This Platform is the link between groups specializing in processing and analysis in the Mental Health CIBER. It also acts as a bridge between clinical users and external groups having a technical profile and proven experience in image processing.

The permanent resources of the Neuroimaging Platform are located in the Medical Imaging Laboratory of the Experimental Surgery and Medicine Unit of Hospital General Universitario Gregorio Marañón, Madrid. The services of this Platform are available for all researchers of the Mental Health CIBER.

Among the activities developed in the Neuroimaging Platform in 2014 the highlights are:

- Maintenance and Optimisation of the DICOM server (<http://dicomserver.hggm.es>).
- Improvements in Parallel Processing Cloud Servers.
- 70 virtual machines (very useful in multicentre studies).
- Update and Improvement in the Magnetic Resonance Acquisition sequences: DTI (HARDI) and Resting-State fMRI.
- Advanced Processing Pipeline configuration for Structural studies, DTI and Rs-fMRI.

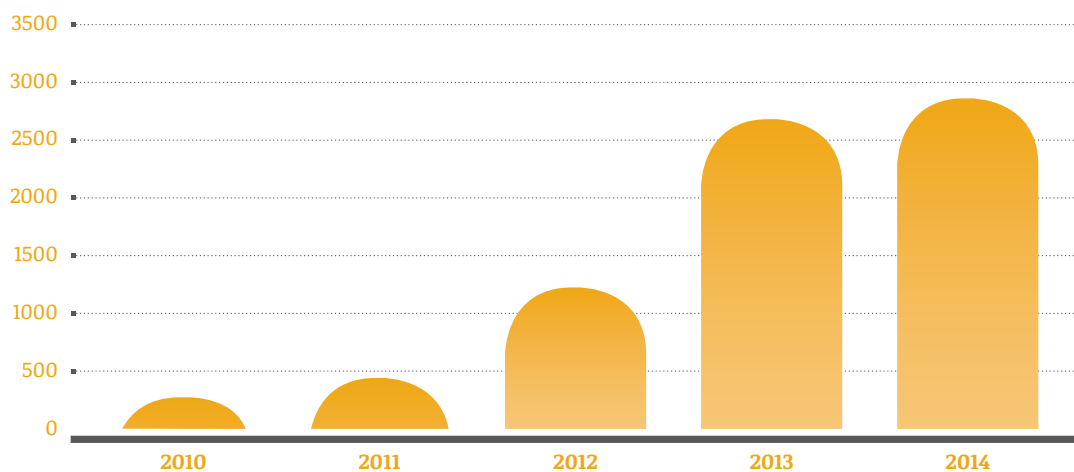
In relation to the available resources within the Platform, maintenance of the DICOM images server via web has been of very useful for the storage of a large volume of anonymised images, including different types of Magnetic Resonance Imaging. Highly efficient neuroimaging processing is maintained as a result of the management of the parallel processing server using virtualization, being very useful in multicentre studies. The development of tools for the processing and statistical analyse of fMRI images in small animals is also maintained.

## Activity in 2014:

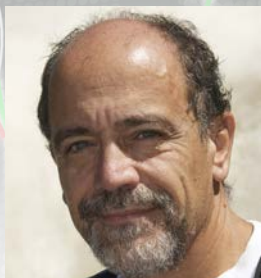
Collaborations with external groups: Universidad Carlos III de Madrid (UC3M), Philips, Instituto de Investigación en Ingeniería de Aragón (I3A), Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Unitat de Recerca en Neurociència Cognitiva (URNC), Centro Nacional de Investigaciones Oncológicas (CNIO), Centre d'Imatge Molecular (CRC CIM), Sociedad Española de Electromedicina y Calidad (SEDECAL).

Number of projects using the Platform.	23
Number of processed studies.	700

## NUMBER OF PATIENTS



## COMMON DATABASE PLATFORM



**Dr. Julio Sanjúan Arias** (G23)

Responsible for the Base Platform Common Data

The Platform for data collection (<http://gridsam.grycap.upv.es>) was developed by the Grid and High Performance Computing Group (GRyCAP) of the Universidad Politécnica de Valencia with the clinical coordination of Group G23 (Universidad de Valencia). The Platform's objective is to allow systematic data collection that is distributed in CIBERSAM projects. Each project included in the platform can have customised data and questionnaires to be collected. It is also possible to obtain data from several projects simultaneously, so the platform becomes a strategic element for collaborative projects. This platform is linked to the DNA and Imaging Platforms so it can provide extensive clinical and sociodemographic data about the collected samples.

The number of projects included in the common database increases constantly. Some of said projects currently include:

- Analysis of risk polymorphisms in whole-genome association studies (WGAS) in psychosis.
- A case-control study on the interaction between polymorphic variation at genes implicated in neurogenesis and environmental risk factors in major depression: "DEPREGENE" Study.
- First psychotic episodes (FPEs). Led by Miguel Bernardo.
- EU-GEI. Led by Celso Arango.
- The DNA Bank project brings together all subjects (patients and controls) providing DNA samples.
- Autism Biobank Project, led by Mara Parellada.
- FlamDepre Project, led by Juan Carlos Leza.
- Psychoeducational project, led by Ana González Pinto.
- 2EPS project (ongoing), led by Miquel Bernardo.
- AGES-CM, Environment and Genes in Schizophrenia project – Research Groups from the Spanish Region of Madrid, led by Celso Arango.
- Inverse co-morbidity project.

This Platform provides centralised storage through a web application housed in a server located at the Universidad Politécnica de Valencia for all structured and duly coded data corresponding to the CIBERSAM projects mentioned above.

- Total no. of cases: 24,176
- Total no. of forms: 88,272
- No. of cases added in 2014: 1,653
- No. of forms added in 2014: 6,422

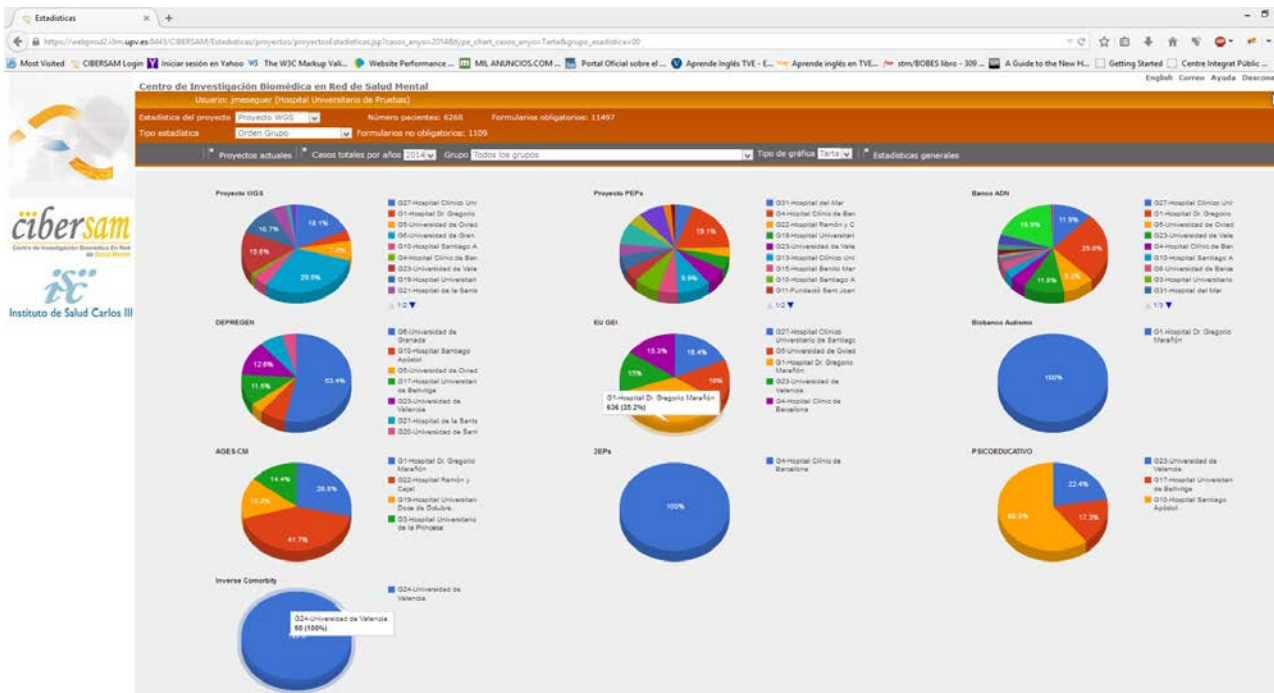


Fig. New statistical structure of cases entered

## Supported Tasks

Consolidating the platform requires a number of telephone calls and emails, therefore the researchers are provided with a customised helpline. The system is available 24/7 and provides services to staff during working hours (from 8 am to 7 pm) which allows reacting to problems suitably. To prevent data loss in the event of a technical problem, total and partial database backups are scheduled on a daily and weekly basis. The system has a built-in helpdesk option as well as help documents explaining the content of all the system's variables.

This application was developed taking the following options into account:

- Recruitment of patients and controls for transversal and longitudinal projects.
- Mandatory and optional forms.
- Sharing of patients between different projects (particularly important for controls).
- Collection of clinical, demographic, genetic and imaging data.
- Support for different user profiles (project leader, data collection, centre manager, etc.).
- Report management.
- Data collection and activity statistics in the last period.
- Consolidated data export for statistical analyses through standard applications.
- Multiuser, multicentre, ubiquitous access.
- Support for standardised questionnaires.
- Support for several languages.
- Internal quality control on data and data collection quality indicators.

## Specific Activity conducted in 2014

- Update and improvement of statistics tools.
- Update of global search tools.
- Improvements in the search response time generating time tables updated overnight.
- 3 new projects implemented in 2014.
- 2EPS, Psychoeducational and Inverse Co-morbidity.
- Intensive use: 1653 new cases and 6422 new forms in 2014, Total number of forms 88272.
- Introduction of new Web tools in new projects.
- HTML5, JSON (JavaScript Object Notation), Ajax, etc.
- Continued update of computing equipment where it is hosted.
- 20% improvement in performance.



## 5. RESEARCH GROUPS



## RESEARCH GROUPS

### Group 1

Programme: Trastornos Mentales del Niño y el Adolescente; Esquizofrenia



**Lead Researcher:** Arango López, Celso

### Group members

**STAFF MEMBERS:** Kehrmann Irisarri, Lara | Merchan Naranjo, Jessica | Morán Moya, Purificación | Recio Lamparero, Sandra | Rodríguez Latorre, Pamela | Rodríguez Quiroga, Alberto | Tapia Casellas, Cecilia

**ASSOCIATED MEMBERS:** Boada Muñoz, Leticia | De Portugal Fernández, Enrique | Fraguas Herráez, David | García Amador, Margarita | 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 | Rapado Castro, Marta | Romo Villa, José | Corral Zarapuz, Azucena.

### Main lines of research

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

## Most relevant scientific articles

- ARANGO C., FRAGUAS D., PARELLADA M. Differential neurodevelopmental trajectories in patients with early-onset bipolar and schizophrenia disorders. *Schizophrenia Bulletin* 2014 Mar;40 Suppl 2:S138-46.
- DE RUBEIS S., HE X., GOLDBERG A.P., POULTNEY C.S., SAMOCHA K., CICEK A.E. et al. Synaptic, transcriptional and chromatin genes disrupted in autism. *Nature*. 2014;515(7526):209-215.
- ARANGO C., GIRALDEZ M., MERCHAN-NARANJO J., BAEZA I., CASTRO-FORNIELES J., ALDA J.-A. et al. Second-Generation. Antipsychotics in Children and Adolescents: A Six-Month Prospective Cohort Study in Drug-Naïve. Patients. *Journal of the American Academy of Child and Adolescent Psychiatry* 2014 Nov;53(11):1179-90
- CALVO A., MORENO M., RUIZ-SANCHO A., RAPADO-CASTRO M., MORENO C., SANCHEZ-GUTIERREZ T. et al. Intervention for adolescents with early-onset psychosis and their families: A randomized controlled trial. *Journal of the American Academy of Child and Adolescent Psychiatry*. 2014;53(6):688-696.
- DIAZ-CANEJA C.M., MORENO C., LLORENTE C., ESPLIEGO A., ARANGO C., MORENO D.. Practitioner Review: Long-term pharmacological treatment of pediatric bipolar disorder. *Journal of Child Psychology and Psychiatry and Allied Disciplines*. 2014;55(9):959-980.

## Highlights

The research team at the Department of Psychiatry of Hospital General Universitario Gregorio Marañón (CIBERSAM group 1, G01) is internationally recognised due to its expertise in the field of Child and Adolescent Psychiatry and its accredited human and technical resources. In 2014, the group has obtained competitive funding for four national projects in the “ Strategic Action for Health Research” (Acción Estrategia en Salud) call from Instituto de Salud Carlos III, focused on the study of endophenotypes in autism (PI: Mara Parellada), ethiopathogenic mechanisms involved in the development of early-onset affective disorders (PI: Carmen Moreno), cellular aging in early-onset psychosis (PI: David Fraguas) and the development of new tools for image analysis to assess brain connectivity in patients with schizophrenia and autism spectrum disorders (PI: Joost Janssen). The group also participates in one InterCIBER Excellence Project, together with CIBERSAM groups G24 (PI: Rafael Tabarés Seisdedos) and G26 (PI: Benedicto Crespo Facorro), funded by the same call.

The group participates in nine European projects funded by the EU under the Seventh Framework Programme and one international project funded by the US National Institute of Mental Health (NIMH). In 2014, members of the group have published thirty-seven articles in national and international peer-reviewed journals and have collaborated in the development of the White Book of Child and Adolescent Psychiatry and two clinical practice guidelines. Furthermore, three doctoral theses supervised by members of the group have been successfully completed during this period.

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**Institution:** Servicio Madrileño de Salud

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Website: www.ua.hggm.es

## Group 2

Programme: Therapeutic Innovation; Depression



**Lead Researcher:** Artigas Pérez, Francesc

### Group members

**STAFF MEMBERS:** Jaramillo Muñumer, María | Paz Silva, Verónica | Santana Ramos, Noemí

**ASSOCIATED MEMBERS:** Bortolozzi Biasoni, Analia | Campa Montobbio, Leticia | Castañe Forn, Anna | Celdada Pedrosa, María Paz | Ferres Coy, Albert | Galofre Centelles, Mireia | Gasull Camós, Júlia | Llado Pelfort, Laia | Masana Nadal, Merce | 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: brain circuits involved.
- Study on the brain circuits involved in the psychotomimetic action of non-competitive NMDA receptor antagonists.
- Neurobiological basis of new novel antidepressant strategies (deep brain stimulation, interference RNA, ketamine).
- Transgenic mouse models of schizophrenia.
- Neurochemistry and neuropharmacology of brain neurotransmitters.

## Most relevant scientific articles

- Troyano-Rodríguez E., Llado-Pelfort L., Santana N., Teruel-Martí V., Celada P., Artigas F.. Phencyclidine inhibits the activity of thalamic reticular gamma-aminobutyric acidergic neurons in rat brain. *Biological Psychiatry*. 2014;76(12):937-945.
- Sanchez C., Asin K.E., Artigas F.. Vortioxetine, a novel antidepressant with multimodal activity: Review of preclinical and clinical data. *Pharmacology and Therapeutics*. 2014;:-.
- Jimenez-Sanchez L., Campa L., Auberson Y.P., Adell A.. The Role of GluN2A and GluN2B Subunits on the Effects of NMDA Receptor Antagonists in Modeling Schizophrenia and Treating Refractory Depression. *Neuropsychopharmacology*. 2014;:-.
- Riga M.S., Soria G., Tudela R., Artigas F., Celada P.. The natural hallucinogen 5-MeO-DMT, component of Ayahuasca, disrupts cortical function in rats: reversal by antipsychotic drugs. *International Journal of Neuropsychopharmacology*. 2014;:-.
- Mocci G., Jimenez-Sanchez L., Adell A., Cortes R., Artigas F.. Expression of 5-HT<sub>2A</sub> receptors in prefrontal cortex pyramidal neurons projecting to nucleus accumbens. Potential relevance for atypical antipsychotic action. *Neuropharmacology*. 2014;79:49-58.

## Highlights

The group has led a total of 10 grants during 2014, including 1 EU grant (IMI-NEWMEDS, Grant 115008), 6 Spanish competitive grants (SAF2012-35183, IPT-2012-1208-300000, PI10/01103, PI10/00290, PI12/00156 and RTC-2014-2812-1), 1 international grant (The Brain & Behavior Research Foundation Grant 20003), 1 autonomous community grant (20145GR798) and 1 contract with a pharmaceutical company. Additionally, two patents have been published on May 1, 2014 (US 2014/0120158 and WO 2014/064258).

From the studies carried out during 2014, we highlight a) development of novel antidepressant strategies using RNAi and deep brain stimulation, b) study of the mechanism of action of novel antidepressant drugs, c) development of preclinical models of schizophrenia, and d) identification of thalamocortical circuits as therapeutic targets in schizophrenia. In particular, we highlight the identification of NMDA receptors in the reticular nucleus of the thalamus as a target for the psychotomimetic actions of phencyclidine.

The group activity has resulted in a total of 13 papers (9 original articles, 3 reviews and 1 editorial commentary requested by the editor of *Biol Psychiatry*). From these, 10 papers are from 1st quartile journals and 8 from 1st decile journals, with 9 national and 4 international collaborations.

Overall, these results keep a solid reputation of the group in the field of Neuropsychopharmacology, as shown by its high level of citations (h-index of PI = 55, with more than 10.000 citations). Among the awards and distinctions received during 2014, the PI gave the presidential plenary lecture at the annual congress of the Canadian College of Neuropsychopharmacology (CCNP) in June 2014 (Banff, Canada).

**Institution:** Agencia Estatal Consejo Superior De Investigaciones Científicas

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## Group 3

Programme: Depression; Bipolar disorder



**Lead Researcher:** Ayuso Mateos, José Luis

### Group members

**STAFF MEMBERS:** Caballero Díaz, Francisco Felix | Cabello Salmerón, Maria | Kamenov, Kaloyan | Miret Garcia, Marta.

**ASSOCIATED MEMBERS:** Leal Leturia, Itziar | López Garcia, Pilar | Martorell Cafranga, Almudena | Mellor Marsa, Blanca | Nuevo Benítez, Roberto | Provencio Ortega, María | Rico Uribe, Laura Alejandra | Rivas Rodríguez, María del Mar.

### Main lines of research

- Epidemiology and nosology of mental disorders.
- Assessment of the efficacy of different therapeutical interventions in patients with major depression and bipolar disorders.
- Road map for mental health and well-being research in Europe.
- Evaluation of health status, quality of life and well-being in the general population.
- Analysis and prevention of suicide behaviour.
- Use of the ICF model as theoretical framework for the assessment of functioning and disability in mental disorders.
- Strategies for improvement mental health service coverage in low and middle income countries.
- Analyses of factors associated with the onset of first psychotic episodes.

## Most relevant scientific articles

- MIRET M., CABALLERO F.F., CHATTERJI S., OLAYA B., TOBIASZ-ADAMCZYK B., KOSKINEN S. et al. Health and happiness: Cross-sectional household surveys in Finland, Poland and Spain. *Bulletin of the World Health Organization*. 2014;92(10):716-725.
- NUEVO R., CHATTERJI S., VERDES E., NAIDOO N., AYUSO-MATEOS J.L., MIRET M.. Prevalence of Alcohol Consumption and Pattern of Use among the Elderly in the WHO European Region. *European Addiction Research*. 2014;:88-96.
- KOYANAGI A., GARIN N., OLAYA B., AYUSO-MATEOS J.L., CHATTERJI S., LEONARDI M. et al. Chronic conditions and sleep problems among adults aged 50 years or over in nine countries: A multi-country study. *PLoS ONE*. 2014;9(12):-.
- LARA E., OLAYA B., GARIN N., AYUSO-MATEOS J.L., MIRET M., MONETA V. et al. Is cognitive impairment associated with suicidality? A population-based study. *European Neuropsychopharmacology*. 2014;:-.
- MIRET M., CABALLERO F.F., HUERTA-RAMIREZ R., MONETA M.V., OLAYA B., CHATTERJI S. et al. Factors associated with suicidal ideation and attempts in Spain for different age groups. Prevalence before and after the onset of the economic crisis. *Journal of Affective Disorders*. 2014;163:1-9.

## Highlights

Following H2020 strategic plan, we are consolidating our research line on active aging and wellbeing. In 2014 we presented two European proposals that received funding for the upcoming years: ATHLOS - Ageing Trajectories of Health: Longitudinal Opportunities and Synergies and PATHWAYS - Participation To Healthy Workplaces And inclusive Strategies in the Work Sector. In addition, two other H2020 projects are currently being prepared and have already been selected by the European Commission for the second stage of the evaluation. Both projects (IMPACD and EU-PATIO) aim to improve mental health in older population by means of a comprehensive and integrated approach to health and well-being and are intended to be managed by CIBER.

In 2014 we continued working in the development of an European roadmap in mental health (ROAMER project) and we pursued our work within MARATONE project: the e-learning platform for MARATONE Marie Curie fellows has been created and we maintained important networking contacts with our European partners. Our researchers participated as trainers and as students within MARATONE's training programme.

We also continued to contribute to the promotion of mental health not only at a European level but also in Low and middle income countries (LAMICs) and focus in improvement of health systems. One example is our participation in the international project EMERALD.

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## Group 4

Programme: Schizophrenia; Child and Adolescent Psychiatry



**Lead Researcher:** Bernardo Arroyo, Miguel

### Group members

**STAFF MEMBERS:** Bioque Alcazar, Miguel | De la Serna Gomez, Elena | Folch Espada, Anna.

**ASSOCIATED MEMBERS:** Andrés Perpiña, Susana | Baeza Pertegaz, María Inmaculada | Cabrera Llorca, Bibiana | Calvo Escalona, Rosa | Castro Fornieles, Josefina | Catalán Campos, Rosa | Fernández Egea, Emilio | Flamarique Valencia, Itziar | García Rizo, Clemente | Lafuente Flo, Amalia | Lazaro García, Luisa | Lomeña Caballero, Francisco | Mane Santacana, Anna | Mas Herrero, Sergio | Massana Montejo, Guillem | Morer Liñán, Astrid | Parellada Rodón, Eduardo | Penades Rubio, Rafael | Pons Villanueva, Alexandre | Puig Navarro, Olga | Romero Cela, Soledad | Sánchez Gistau, Vanesa.

### Main lines of research

- Physical health.
- 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

- GARCIA-RIZO C., KIRKPATRICK B., FERNANDEZ-EGEA E., OLIVEIRA C., MESEGUER A., GRANDE I. et al. "Is bipolar disorder an endocrine condition?" Glucose abnormalities in bipolar disorder. *Acta Psychiatrica Scandinavica*. 2014;129(1):73-74.
- GASSO P., MAS S., MOLINA O., LAFUENTE A., BERNARDO M., PARELLADA E.. Increased susceptibility to apoptosis in cultured fibroblasts from antipsychotic-naïve first-episode schizophrenia patients. *Journal of Psychiatric Research*. 2014;48(1):94-101.



- GARCIA-BUENO B., BIOQUE M., MAC-DOWELL K.S., BARCONES M.F., MARTINEZ-CENGOTITABENGOA M., PINA-CAMACHO L. et al. Pro-/anti-inflammatory dysregulation in patients with first episode of psychosis: Toward an integrative inflammatory hypothesis of schizophrenia. *Schizophrenia Bulletin*. 2014;40(2):376-387.
- BERNARDO M., BIOQUE M.. What have we learned from research into first-episode psychosis?. *Revista de Psiquiatria y Salud Mental*. 2014;7(2):61-63.
- PUJOL N., PENADES R., JUNQUE C., DINOVI I., FU C.H.Y., CATALAN R. et al. Hippocampal abnormalities and age in chronic schizophrenia: Morphometric study across the adult lifespan. *British Journal of Psychiatry*. 2014;205(5):369-375.

## Highlights

Schizophrenia Clinic Unit responds to a medical clinical approach, research and teaching, including care protocols, aimed at responding to problems of schizophrenia and integrates the various devices of Hospital Clínic of Barcelona with activity against this disease. Our goals are the expansion of theoretical and practical knowledge related to schizophrenia, longitudinal follow-up of patients with chronic schizophrenia and patients with first psychotic episodes. They are further objectives of the Unit the development and validation of psychopathological scales and integration into routine care, teaching and research.

### PROJECTS

#### INTERNATIONAL PROJECTS:

- Diabetes in neuropsychiatric disorders (USA)
- European Network of National schizophrenia Networks studying Gene-environment Interactions (EU-GEI)
- Optimization of Treatment and Management of Schizophrenia in Europe- OPTiMiSE
- PSYSCAN – Translating neuroimaging findings from research into clinical practice
- European Long-acting Antipsychotics in Schizophrenia Trial

#### NATIONAL PROJECTS (ISCIII):

- Evaluació coste/efectivitat de la intervenció farmacogenètica en la optimització del tractament amb antipsicòtics en pacients amb esquizofrènia.
- Determinants clínics i neurobiològics de segons episodis de esquizofrènia. Estudi longitudinal de primers episodis psicòtics.
- Apoptosis i canvis estructurals progressius en pacients amb un primer episodi de esquizofrènia: estudi longitudinal i multimodal de neuroimatge i biologia molecular.
- El BDNF (Brain-derived neurotrophic factor) com a possible biomarcador del tractament de rehabilitació neurocognitiva en la esquizofrènia de predomini negatiu.

### PATENTS

- Method for predicting the onset of extrapyramidal symptoms (EPS) induced by an antipsychotic-based treatment. Mas, S, Gassó P, Malagelada C, Bernardo M, Lafuente A

### CLINICAL GUIDES 2014

- Pla director de salut mental i addiccions. Guia de bona pràctica clínica sobre la teràpia electroconvulsiva a Catalunya. Barcelona: Direcció General de Planificació i Recerca en Salut, Generalitat de Catalunya; 2014
- Bernardo M., Safont G., Oliveira C., Valiente A. Recomanacions per al monitoratge i la promoció de la salut física dels pacients amb esquizofrènia i altres trastorns greus. Pla director de salut mental i addiccions. Departament de Salut. 2014

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## Group 5

Programme: Schizophrenia; Bipolar disorder



**Lead Researcher:** Bobes García, Julio

### Group members

**STAFF MEMBERS:** Al-Halabi Díaz, Susana | Bascarán Fernández, María Teresa | García Álvarez, Leticia

**ASSOCIATED MEMBERS:** Bombín González, Igor | Bousoño García, Manuel | Buron Fernández, Patricia | Díaz Mesa, Eva María | Flórez Menéndez, Gerardo | García Portilla González, Mari Paz | Iglesias García, Celso Angel | Jiménez Treviño, Luis | Muñiz Fernández, José | Sáiz Martínez, Pilar Alejandra.

### 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

- Carli V., Hoven C.W., Wasserman C., Chiesa F., Guffanti G., Sarchiapone M. et al. A newly identified group of adolescents at “invisible” risk for psychopathology and suicidal behavior: Findings from the SEYLE study. *World Psychiatry*. 2014;13(1):78-86.
- Kasper S., Iglesias-Garcia C., Schweizer E., Wilson J., Dubrava S., Prieto R. et al. Pregabalin long-term treatment and assessment of discontinuation in patients with generalized anxiety disorder. *International Journal of Neuropsychopharmacology*. 2014;17(5):685-695.
- Garcia-Bueno B., Bioque M., Mac-Dowell K.S., Barcones M.F., Martinez-Cengotitabengoa M., Pina-Camacho L. et al. Pro-/anti-inflammatory dysregulation in patients with first episode of psychosis: Toward an integrative inflammatory hypothesis of schizophrenia. *Schizophrenia Bulletin*. 2014;40(2):376-387.
- Brunner R., Kaess M., Parzer P., Fischer G., Carli V., Hoven C.W. et al. Life-time prevalence and psychosocial correlates of adolescent direct self-injurious behavior: A comparative study of findings in 11 European countries. *Journal of Child Psychology and Psychiatry and Allied Disciplines*. 2014;55(4):337-348.
- Grande I., Bernardo M., Bobes J., Saiz-Ruiz J., Alamo C., Vieta E.. Antipsychotic switching in bipolar disorders: A systematic review. *International Journal of Neuropsychopharmacology*. 2014;17(3):497-507.

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## Group 6

Programme: Schizophrenia; Depression



**Lead Researcher:** Cervilla Ballesteros, Jorge A.

### Group members

**STAFF MEMBERS:** Ibáñez Casas, Inmaculada | Muñoz Negro, José Eduardo

**ASSOCIATED MEMBERS:** Gutiérrez Martínez, Blanca | Lorente Acosta, José Antonio | Perez 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).
- Psycogeriatrics (J. Cervilla).
- Medical Issues in Mental Disorder (M. Rivera).

## Most relevant scientific articles

- GUTIÉRREZ B, BELLÓN JA, RIVERA M, MOLINA E, KING M, MARSTON L et al. The risk for major depression conferred by childhood maltreatment is multiplied by BDNF and SERT genetic vulnerability: a replication study. *Journal of psychiatry & neuroscience : JPN*. 2014;39(6):140097.
- HUNG C.-F., RIVERA M., CRADDOCK N., OWEN M.J., GILL M., KORSZUN A. et al. Relationship between obesity and the risk of clinically significant depression: Mendelian randomisation study. *British Journal of Psychiatry*. 2014;205(1):24-28.
- IVORRA J.L., RIVERO O., COSTAS J., INIESTA R., ARROJO M., RAMOS-RIOS R. et al. Replication of previous genome-wide association studies of psychiatric diseases in a large schizophrenia case-control sample from Spain. *Schizophrenia Research*. 2014;159(1):107-113.
- KALISOVA L., RABOCH J., NAWKA A., SAMPOGNA G., CIHAL L., KALLERT T.W. et al. Do patient and ward-related characteristics influence the use of coercive measures? Results from the EUNOMIA international study. *Social Psychiatry and Psychiatric Epidemiology*. 2014;49(10):1619-1629.
- MORENO-PERAL P., DE DIOS LUNA J., MARSTON L., KING M., NAZARETH I., MOTRICO E. et al. Predicting the onset of anxiety syndromes at 12 months in primary care attendees. The predictA-Spain study. *PLoS ONE*. 2014;9(9):-.

## Highlights

CIBERSAM 06 Group has obtained two Marie Curie Grants to focus on: 1) Physical-Psychiatris comorbidity among community dwellers in a sample of 5309 individuals and, 2: to test a neuropsychological intervention on psychotic patients in collaboration with Duke University, USA. We have also participated on the Spanish Consensus Clinical Guide on Management of Physical disorders in Depressive Patients. In addition, we finished our large epidemiological study on prevalence and risk factors for common mental disorders in Andalusia (Southern Spain) and got financing for a follow-up of such cohort focused on psychosis. We have also developed a network and tools to develop naturalistic studies on the treatment of delusional psychosis. Finally, we have continued adding evidence to our research field on genetic and environmental interactions as determinants of depression.

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## Group 7

Programme: Therapeutic Innovation;  
Child and Adolescent Psychiatry



**Lead Researcher:** Desco Menéndez, Manuel

### Group members

**STAFF MEMBERS:** Garrido Huerta, Rosa Trajana.

**ASSOCIATED MEMBERS:** Alemán Gómez, Yasser | Calvo Manuel, Felipe | Cusso Mula, Lorena | Domínguez Montero, Pedro Luis | García Barreno, Pedro | Guzmán de Villoria Lebieziejewski, Juan | Lafuente Martínez, Javier | Navas Sánchez, Francisco Javier | Pascau González Garzón, Javier | Soto Montenegro, María Luisa.

**CONTRIBUTORS:** De Francisco López, Alejandra

### 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

- HERNANDEZ-PORRAS I., FABBIANO S., SCHUHMACHER A.J., AICHER A., CANAMERO M., CAMARA J.A. et al. K-RasV14I recapitulates noonan syndrome in mice. *Proceedings of the National Academy of Sciences of the United States of America*. 2014;111(46):16395-16400.
- NAVAS-SANCHEZ F.J., ALEMAN-GOMEZ Y., SANCHEZ-GONZALEZ J., GUZMAN-DE-VILLORIA J.A., FRANCO C., ROBLES O. et al. White matter microstructure correlates of mathematical giftedness and intelligence quotient. *Human Brain Mapping*. 2014;35(6):2619-2631.
- LACALLE-AURIOLES M., MATEOS-PEREZ J.M., GUZMAN-DE-VILLORIA J.A., OLAZARAN J., CRUZ-ORDUNA I., ALEMAN-GOMEZ Y. et al. Cerebral blood flow is an earlier indicator of perfusion abnormalities than cerebral blood volume in Alzheimer's disease. *Journal of Cerebral Blood Flow and Metabolism*. 2014;34(4):654-659.
- JANSSEN J., ALEMAN-GOMEZ Y., SCHNACK H., BALABAN E., PINA-CAMACHO L., ALFARO-ALMAGRO F. et al. Cortical morphology of adolescents with bipolar disorder and with schizophrenia. *Schizophrenia Research*. 2014;158(1-3):91-99.
- MONTESINOS P., ABASCAL J.F.P.J., CUSSO L., VAQUERO J.J., DESCO M.. Application of the compressed sensing technique to self-gated cardiac cine sequences in small animals. *Magnetic Resonance in Medicine*. 2014;72(2):369-380.

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## Group 8

Programme: Schizophrenia;  
Child and Adolescent Psychiatry



**Lead Researcher:** Fañanas Saura, Lourdes

### Group members

**STAFF MEMBERS:** Fatjo Vilas Mestre, Mar | Martin Garcia, M José | Valldeperas Llaberia, Anna

**ASSOCIATED MEMBERS:** Alemany Sierra, Silvia | Arias Sanperiz, Barbara | Barrantes Vidal, Neus | Cordova Palomera, Aldo | Ibáñez Ribes, Manuel Ignacio | Miret Fallada, Salvador | Mitjans Niubo, Marina | Moya Higuera, Jorge | Ortet Fabregat, Generos | Papiol Miro, Sergi | Prats Balado, Claudia | Rosa de la Cruz, Araceli.

### Main lines of research

- Genetic studies based on clinical and brain phenotypes (fMRI\_MRI) in schizophrenia, autism spectrum and affective disorders.
- Study of genetic and early environmental factors (GxE mechanisms), psychopathological status in adulthood and associated brain correlates (MRI): studies based on twins, families and individuals from the general population.
- Pharmacogenetics of antidepressants, antipsychotics and mood stabilizers.
- Population analysis of schizotypy and attenuated psychotic symptoms from the etiopathogenic psychosis continuum model.
- Personality, addiction and identification of risk markers.



## Most relevant scientific articles

- RIPKE S., NEALE B.M., CORVIN A., WALTERS J.T.R., FARH K.-H., HOLMANS P.A. et al. Biological insights from 108 schizophrenia-associated genetic loci. *Nature*. 2014;511(7510):421-427.
- STEINBERG S., DE JONG S., MATTHEISEN M., COSTAS J., DEMONTIS D., JAMAIN S. et al. Common variant at 16p11.2 conferring risk of psychosis. *Molecular Psychiatry*. 2014;19(1):108-114.
- TOULOPOULOU T., VAN HAREN N., ZHANG X., SHAM P.C., CHERNY S.S., CAMPBELL D.D. et al. Reciprocal causation models of cognitive vs volumetric cerebral intermediate phenotypes for schizophrenia in a pan-European twin cohort. *Molecular Psychiatry*. 2014.
- DEBBANÉ M, BARRANTES-VIDAL N. Schizotypy From a Developmental Perspective. *Schizophrenia bulletin*. 2014.
- KWAPIL TR, BARRANTES-VIDAL N. Schizotypy: Looking Back and Moving Forward. *Schizophrenia bulletin*. 2014.

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## RESEARCH GROUPS

### Group 10

Programme: Bipolar disorder; Schizophrenia



**Lead Researcher:** González Pinto Arrillaga, Ana

### Group members

**STAFF MEMBERS:** Alberich Mesa, Susana | Barbeito Resa, Sara | Martínez Cengotitabeitia, Mónica.

**ASSOCIATED MEMBERS:** De Leon Molina, José Alfonso | Echeburua Odriozola, Enrique | Echevarria Orella, Enrique | Fernández Hernández, Miryam | Gil Goikouria, Javier | González Ortega, Itxaso | Irazusta Astiazaran, Jon | López Peña, Maria Purificacion | Martin Carrasco, Manuel | Mosquera Ulloa, Fernando | Vega Pérez, Patricia | Zorrilla Martínez, Iñaki.

**CONTRIBUTORS:** Alonso Pinedo, Marta | Besga Basterra, Adriana | Fernandez de Corres Aguiriano, Blanca | González-Pinto Arrillaga, Asunción | Hernánz Manrique, Margarita M | Karim Haidar, Mahmoud | Ruiz de Azua García, Sonia | Sáenz Herrero, Margarita | Ugarte Ugarte, Amaia.

### Main lines of research

- Epidemiology. Bipolar Disorder.
- Epidemiology. First Episodes of Psychosis.
- Aetiopathogenesis. Genes and Environment.
- Psychopathology.
- Treatment.

## Most relevant scientific articles

- FERNANDES B.S., STEINER J., BERK M., MOLENDIJK M.L., GONZALEZ-PINTO A., TURCK C.W. et al. Peripheral brain-derived neurotrophic factor in schizophrenia and the role of antipsychotics: meta-analysis and implications. *Molecular Psychiatry*. 2014.
- GARCIA-BUENO B., BIOQUE M., MAC-DOWELL K.S., BARCONES M.F., MARTINEZ-CENGOTITABENGOA M., PINA-CAMACHO L. et al. Pro-/anti-inflammatory dysregulation in patients with first episode of psychosis: Toward an integrative inflammatory hypothesis of schizophrenia. *Schizophrenia Bulletin*. 2014;40(2):376-387.
- POPOVIC D., TORRENT C., GOIKOLEA J.M., CRUZ N., SANCHEZ-MORENO J., GONZALEZ-PINTO A. et al. Clinical implications of predominant polarity and the polarity index in bipolar disorder: A naturalistic study. *Acta Psychiatrica Scandinavica*. 2014;129(5):366-374.
- KAPCZINSKI F., MAGALHAES P.V.S., BALANZA-MARTINEZ V., DIAS V.V., FRANGOU S., GAMA C.S. et al. Staging systems in bipolar disorder: An International Society for Bipolar Disorders Task Force Report. *Acta Psychiatrica Scandinavica*. 2014;130(5):354-363.
- POPOVIC D., BENABARRE A., CRESPO J.M., GOIKOLEA J.M., GONZALEZ-PINTO A., GUTIERREZ-ROJAS L. et al. Risk factors for suicide in schizophrenia: Systematic review and clinical recommendations. *Acta Psychiatrica Scandinavica*. 2014;130(6):418-426.

## Highlights

The G10 group, led by Ana González- Pinto, is known for its research in the study of Bipolar Disorder, First Psychotic Episodes, Alzheimer, Schizophrenia and Depression, participating both in basic research (neurotrophins, inflammation, oxidative stress), and clinical and psychopharmacological: development of new treatments, new methods of treatment application (online, e- learning), intervention strategies for prevention (postpartum depression, in patients at high risk of developing psychosis). One of the areas of greatest impact of the group focuses on the detection and treatment of psychiatric patients with cannabis and other substances consumption. The G -10 has developed a specific treatment for psychotic patients with cannabis use, to achieve its abandonment.

Besides, is has been published the clinical guide: *Evaluation of the effectiveness of psychological intervention in the first psychotic episodes by multidisciplinary treatment*. (Ministry of Health. Service Health Technology Assessment of the basque Country; 2014. OSTEBA. Intellectual property record: 00/2012/1686).

The G10 research group has numerous projects awarded continuously, both at national level (FIS, MINECO, MSPSI), and at regional level (Basque Government, Kronikgune), as at European level (FISTAR and MASTERMIND).

Finally, several doctoral theses have been presented (Sara Barbeito and Sonia Ruiz de Azúa) and the incorporation of new talent for research is been promoted (Carlos III Institute Predoctoral Grant).

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## RESEARCH GROUPS

### Group 11

Programme: Schizophrenia; Psychosomatic, Anxiety and Impulse Control Disorders



**Lead Researcher:** Haro Abad, Josep Maria

### Group members

**STAFF MEMBERS:** Aguado Carne, Jaume | Farreny Sero, Aida | Maliandi, María Victoria | Moneta, Victoria | Obradors Tarrago, Carla | Ramos José María, Belén | Tyrovolas, Stefanos

**ASSOCIATED MEMBERS:** Araya la Rivera, Susana | Arránz Martí, Belén | Brebion, Gildas | Dolz Abadia, Montserrat | Foix Sanjuan, Alexandrina | Fuste Boadella, Montserrat | Garín Escriva, Noe | Koyanagi, Ai | Moreno Bote, Ruben | Navarra Ordoño, Jordi | Ochoa Guerre, Susana | Olaya Guzmán, Beatriz | San Molina, Luis | Usall Rodie, Judith.

**CONTRIBUTORS:** Iniesta Benedicto, Raquel | López Carrilero, Raquel | Roca Casaus, Mercedes | Stephan Otto Attolini, Christian.

## Most relevant scientific articles

- MURRAY C.J.L., ORTLAD K.F., GUINOVART C., LIM S.S., WOLOCK T.M., ROBERTS D.A. et al. Global, regional, and national incidence and mortality for HIV, tuberculosis, and malaria during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *The Lancet*. 2014.
- DE JONGE P., ALONSO J., STEIN D.J., KIEJNA A., AGUILAR-GAXIOLA S., VIANA M.C. et al. Associations between DSM-IV mental disorders and diabetes mellitus: A role for impulse control disorders and depression. *Diabetologia*. 2014;57(4):699-709.
- DE JONGE P., ALONSO J., STEIN D.J., KIEJNA A., AGUILAR-GAXIOLA S., VIANA M.C. et al. Erratum: Associations between DSM-IV mental disorders and diabetes mellitus: A role for impulse control disorders and depression (*Diabetologia* DOI 10.1007/s00125-013-3157-9). *Diabetologia*. 2014;57(6):1269-1270.
- IBANEZ A., AGUADO J., BAEZ S., HUEPE D., LOPEZ V., ORTEGA R. et al. From neural signatures of emotional modulation to social cognition: Individual differences in healthy volunteers and psychiatric participants. *Social Cognitive and Affective Neuroscience*. 2014;9(7):939-950.
- MCDOWELL R.D., RYAN A., BUNTING B.P., O'NEILL S.M., ALONSO J., BRUFFAERTS R. et al. Mood and anxiety disorders across the adult lifespan: A European perspective. *Psychological Medicine*. 2014;44(4):707-722.

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## Group 12

Programme: Psychosomatic, Anxiety and Impulse Control Disorders; Therapeutic Innovation



**Lead Researcher:** Leza Cerro, Juan Carlos

### Group members

**STAFF MEMBERS:** Martín Hernández, David

**ASSOCIATED MEMBERS:** Carrasco Perera, José Luis | Díaz Marsa, Marina | García Bueno, Borja | Macdowell Mata, Karinas | Muñoz Madrigal, José Luis | Rodríguez Maus, Sandra | Sayd, Aline.

### Main lines of research

- Search for inflammation biomarkers in plasma and blood cells from neuropsychiatric disease patients in order to identify and develop new therapeutic strategies.
- Study of protection mechanisms against oxidative and inflammatory cell damage after stress exposure. Identification of potential therapeutic targets and evaluation of neuroprotection strategies.
- Study of individual mechanisms of susceptibility to stress-induced cell damage.
- Study of mechanisms through which noradrenaline acts as an anti-inflammatory mediator in stress. Among them, the key role of the chemokine MCP-1.
- Study of stress-induced colonic bacteria translocation during brain response to stress.
- Elucidation of the mechanisms through which stress exposure increases susceptibility and cell damage in Alzheimer's disease, Parkinson's disease, brain hypoxia and demyelinating diseases models. Identification of potential therapeutic targets and evaluation of neuroprotective strategies.
- Elucidation of the mechanisms through which stress exposure increases susceptibility and cell damage in the intestine. Identification of potential therapeutic targets and evaluation of cytoprotective strategies.
- Evaluation of the therapeutic potential of the endocannabinoid system in neuropsychiatric and gastrointestinal pathologies caused by stress.

- Potential new mechanisms: role of innate immunity receptors (TLRs) in stress-related processes in neuro-psychiatric pathologies models.
- Study of the neuroprotective effects resultant from the administration of different types of antidepressant and antipsychotic drugs in animal models (in vivo and in vitro) of psychiatric diseases.

## Most relevant scientific articles

- GARATE I., GARCIA-BUENO B., MADRIGAL J.L.M., CASO J.R., ALOU L., GOMEZ-LUS M.L. et al. Toll-like 4 receptor inhibitor TAK-242 decreases neuroinflammation in rat brain frontal cortex after stress. *Journal of Neuroinflammation*. 2014;11:8.
- GARCIA-BUENO B., BIOQUE M., MAC-DOWELL K.S., BARCONES M.F., MARTINEZ-CENGOTITABENGOA M., PINA-CAMACHO L. et al. Pro-/anti-inflammatory dysregulation in patients with first episode of psychosis: Toward an integrative inflammatory hypothesis of schizophrenia. *Schizophrenia Bulletin*. 2014;40(2):376-387.
- ZOPPI S., MADRIGAL J.L., CASO J.R., GARCIA-GUTIERREZ M.S., MANZANARES J., LEZA J.C. et al. Regulatory role of the cannabinoid CB2 receptor in stress-induced neuroinflammation in mice. *British Journal of Pharmacology*. 2014;171(11):2814-2826.
- MACDOWELL K, CASO J, MARTÍN-HERNÁNDEZ D, MADRIGAL J, LEZA J, GARCÍA-BUENO B. Paliperidone Prevents Brain Toll-Like Receptor 4 Pathway Activation and Neuroinflammation in Rat Models of Acute and Chronic Restraint Stress. *The international journal of neuropsychopharmacology*. 2014;18(3).
- GARCÍA-BUENO B, BIOQUE M, MACDOWELL KS, SANTABÁRBARA J, MARTÍNEZ-CENGOTITABENGOA M, MORENO C et al. Pro-/antiinflammatory dysregulation in early psychosis: results from a 1-year follow-up study. *The international journal of neuropsychopharmacology*. 2014;18(2).

## Highlights

During 2014 our group published several articles in scientific journals. Our main goal has been the search for inflammatory biomarkers in various psychiatric pathologies. Most of these articles were performed in collaboration with several clinical groups, and are focused on the origin and consequences of immune response and inflammation in various diseases. Also, in our preclinical studies (in vivo, ex vivo and in vitro) we shed some light on the way inflammatory signals enter brain structures and their main intracellular pathways. Some of the papers published in 2013 achieved the "highly cited" category during 2014. Moreover, the group obtained funds in competitive calls from public and private institutions and foundations. In particular, this group during the year 2014 has had received funding for three projects from public institutions (FIS and MINECO). From a private standpoint, the group has been involved in 4 different projects funded by private institutions (Mutua Madrileña Foundation and Alicia Koplowitz Foundation), collaborating with clinical groups in CIBERSAM. As an essential part of our goals, the academic/scientific training of pre- and postgraduate students has a special chapter. During 2014 one PhD Thesis has been completed (obtaining the highest score), based on a collaborative study (FlammPEPs), codirected by our PI. Our group has a very important participation in the development of the first course of the Interuniversity Master on Initiation of research in mental health. Finally, it is important to mention that our group is part of different Research Consortia, such as the Instituto de Investigación Hospital 12 de Octubre and the Instituto Universitario de Investigación en Neuroquímica (UCM).

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## Group 13

Programme: Depression



**Lead Researcher:** Lobo Satué, Antonio

### Group members

**ASSOCIATED MEMBERS:** Barcones Molero, María Fe | Campayo Martínez, Antonio Jesús | De la Cámara Izquierdo, Concepción | Día Sahún, José Luis | Gutiérrez Galve, Leticia Beatriz | Lobo Escolar, Elena | Marcos Aragues, Guillermo | Roy Delgado, Juan Francisco | Saz Muñoz, Pedro | Ventura Faci, Tirso.

**CONTRIBUTORS:** Posadas de Miguel, Mar.

### Main lines of research

- PSYCHOSOMATIC AND LIAISON PSYCHIATRY

Our group has a long tradition in the study of psychiatric and somatic comorbidity, in the study of “complex patients” (because of this co-morbidity), and in particular of depression in medical illness, including the biological and psycho-social complications. It has designed and implemented a number of network studies, including the coordination in Spain of EU, cross-national projects such as the ECLW studies; it also coordinated the Spanish Network for Research in Psychosomatics and Liaison Psychiatry (REPEP, FIS-ISCIII). Recently (2014) has been granted with the first “*Frits Huyse Award*”, given by the European Association of Psychosomatic Medicine, EAPM, for a relevant trajectory in the discipline.

- GERIATRIC PSYCHIATRY

A different research line with a long tradition in this group is related to the psychiatric study in the elderly of major neuro-degenerative disorders, mainly dementias (and Alzheimer’s disease); of depression; and of somatic-psychiatric comorbidity, in general and in specific diseases such as the car-



diovascular diseases, and the relation with mortality. The main project here is the ZARADEMP Study, a longitudinal research in a large cohort of the general population (n= 5,000), now in the “wave”, more than 12 follow-up years. Papers in this study, including the participation in the EURODEM and EURODEP Projects of the EU are referenced as classical in the discipline.

- NEW TRENDS OF RESEARCH IN PSYCHIATRY

As a result of the collaboration in the CIBERSAM network, our group has started new research lines to join the ones of other CIBERSAM groups, contributing with our previous experience. Primarily, we have initiated lines on the study of genotype -phenotype interactions in first psychotic episodes and pragmatic clinical trials using new therapeutic strategies in major depressive disorder resistant to treatment with SSRIs.

## Most relevant scientific articles

- BRAAM A.W., COPELAND J.R.M., DELESPAUL P.A.E.G., BEEKMAN A.T.F., COMO A., DEWEY M. et al. Depression, subthreshold depression and comorbid anxiety symptoms in older Europeans: Results from the EURODEP concerted action. *Journal of Affective Disorders*. 2014;155(1):266-272.
- GARCIA-BUENO B., BIOQUE M., MAC-DOWELL K.S., BARCONES M.F., MARTINEZ-CENGOTITABENGOA M., PINA-CAMACHO L. et al. Pro-/anti-inflammatory dysregulation in patients with first episode of psychosis: Toward an integrative inflammatory hypothesis of schizophrenia. *Schizophrenia Bulletin*. 2014;40(2):376-387.
- DE MIGUEL-ETAYO P., MORENO L.A., SANTABARBARA J., MARTIN-MATILLAS M., PIQUERAS M.J., ROCHA-SILVA D. et al. Anthropometric indices to assess body-fat changes during a multidisciplinary obesity treatment in adolescents: EVASYON Study. *Clinical Nutrition*. 2014.
- GUTIERREZ-GALVE L., CHU E.M., LEESON V.C., PRICE G., BARNES T.R.E., JOYCE E.M. et al. A longitudinal study of cortical changes and their cognitive correlates in patients followed up after first-episode psychosis. *Psychological Medicine*. 2014.
- ASCASO F.J., CRUZ N., MODREGO P.J., LOPEZ-ANTON R., SANTABARBARA J., PASCUAL L.F. et al. Retinal alterations in mild cognitive impairment and Alzheimer’s disease: An optical coherence tomography study. *Journal of Neurology*. 2014;261(8):1522-1530.

## Highlights

The contributions in this period of time include “first quartil” articles such as the new EURODEP paper about European differences in depression-anxiety in the elderly community; the anti-inflammatory profile in first episode psychosis and, in a different article with British authors coordinated from our Group, the study of cortical changes in neuroimage, also in first episode psychosis; the longest follow-up (17 years) in the elderly community showing the increased mortality risk in individuals with cognitive impairment; and the first study in the international literature documenting by means of optical coherence tomography (OCT) the reduced volume of retinal nerve fibers in Alzheimer’s disease, but also changes suggesting inflammatory processes in mild cognitive impairment (MCI). We continue the field work in the ZARADEMP Project, with the 5th wave in the 20-year follow-up of the 5,000 individuals aged 55 or more years and living in the community. Papers are published systematically, and this has been the base for the new application for a European project related to dementia and AD, in the *Joint Programme in Neurodegenerative Diseases*.

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## Group 15

Programme: Schizophrenia; Bipolar disorder



**Lead Researcher:** Mckenna, Peter J.

### Group members

**STAFF MEMBERS:** Canales Rodríguez, Erick Jorge | García Arribas, Alicia | Moreno Alcazar, Ana | Salgado Pineda, Pilar.

**ASSOCIATED MEMBERS:** Alonso Lana, Silvia | Amann, Benedikt | Gomar Soñes, Jesús Joaquin | Monte Rubio, Gemma Cristina | Pomarol Clotet, Edith | Radua Castaño, Joaquin | 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 (these neuroimaging techniques are combined with clinical and neuropsychological data in order to study their neuro-anatomical correlates) and b) the execution of clinical trials on new drugs and other treatment strategies.

- Neuroimaging of severe mental illnesses:
  - Multimodal imaging: Usage of new methods of image analysis on different pathologies. Design of new studies involving the development and implementation, in MRI, of new cognitive paradigms in patients and healthy subjects. This has led to several significant findings including the abnormality in the Default Mode Network observed in several mental disorders.
  - Clinical applicability: New methods are applied and results checked in different clinical populations. The research team mainly works with populations of schizophrenic patients, bipolar patients, schizoaffective patients and first episodes. We currently have several ongoing projects on learning machine algorithms for diagnostic prediction in psychosis (mainly schizophrenia and bipolar disorder) which we hope to eventually lead to more personalized treatments.
- Development of new clinical methods and MRI methods from different modalities (brain connectivity, diffusion MRI (DTI and tractography) and structural MRI), including new meta-analytical tools for these type of images. New statistical models for diffusion and functional connectivity are being developed. This also includes the generation of a tractographic atlas (atlas of white matter fiber tracts) based on healthy brains, but intended for future clinical applications.
- Development of new therapeutic approaches.
- Development and validation of scales and tests aimed at symptom evaluation.
- Studies on language, cognition and symptoms in psychiatric and neuropsychiatric pathologies (severe mental disorders, Huntington's disease, autism).

## Most relevant scientific articles

- LAWS K., MCKENNA P.. Cognitive therapy for patients with schizophrenia. *The Lancet*. 2014;384(9941):399.
- SALVADOR R., VEGA D., PASCUAL J.C., MARCO J., CANALES-RODRIGUEZ E.J., AGUILAR S. et al. Converging Medial Frontal Resting State and Diffusion-Based Abnormalities in Borderline Personality Disorder. *Biological Psychiatry*. 2014.
- LANDIN-ROMERO R., MCKENNA P.J., SALGADO-PINEDA P., SARRO S., AGUIRRE C., SARRI C. et al. Failure of deactivation in the default mode network: a trait marker for schizophrenia?. *Psychological Medicine*. 2014.
- CANALES-RODRIGUEZ E.J., POMAROL-CLOTET E., RADUA J., SARRO S., ALONSO-LANA S., DEL MAR BONNIN C. et al. Structural abnormalities in bipolar euthymia: A multicontrast molecular diffusion imaging study. *Biological Psychiatry*. 2014;76(3):239-248.
- RODRIGUEZ-CANO E., SARRO S., MONTE G.C., MARISTANY T., SALVADOR R., MCKENNA P.J. et al. Evidence for structural and functional abnormality in the subgenual anterior cingulate cortex in major depressive disorder. *Psychological Medicine*. 2014.

## Highlights

Our research team has a long experience in the field of neuroimaging, specially applied to psychiatric disorders, including schizophrenia and bipolar disorder but in 2014 also other disorders such as schizoaffective, delusional, major depressive, attention deficit hyperactivity or borderline personality.

In 2014 the team has been granted several economical helps to conduct research projects and has kept a good scientific production. Three of the new projects will together help predict the risk of poor outcome after a maniac episode or a first episode of psychosis, as well as help an early diagnosis and prognosis of these episodes, from the combination of both clinical and different types of neuroimaging data, using new learning machines and survival analyses. Another novel project will characterize the schizophrenia negative symptoms using functional magnetic resonance virtual-reality paradigms. We also have several ongoing projects investigating new therapeutic approaches, such as the use of deep brain stimulation in schizophrenia (in collaboration with Hospital de Sant Pau team) and the use of eye movement desensitization and reprocessing therapy in bipolar disorder.

Our most relevant contributions have been in the field of multimodal neuroimaging studies and meta-analyses. In 2014 we applied the former to major depression, finding converging evidence of functional and structural abnormalities in subgenual anterior cingulate cortex, and to borderline personality disorder, where functional and structural abnormalities were found in the fronto-limbic system. We also characterized the functional brain changes in the different phases of bipolar disorder including euthymia.

Regarding meta-analyses, these have addressed both clinical and neuroimaging unsolved issues. In a meta-analysis published in the *British Journal of Psychiatry*, for example, we questioned the efficacy of cognitive behavioral therapy in schizophrenia. In the field of neuroimaging, several meta-analyses were conducted to help elucidate specific brain abnormalities in depression, Alzheimer, childhood maltreatment, obsessive-compulsive disorder, attention deficit hyperactivity disorder, individuals at elevated genetic risk of developing schizophrenia, and a rather long etcetera.

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## Group 16

Programas: Schizophrenia; Therapeutic Innovation



**Lead Researcher:** Meana Martínez, José Javier

### Group members

**STAFF MEMBERS:** Corada Galarreta, Leire | Gil de la Pisa, Itziar | Munarriz Cuezva, Eva.

**ASSOCIATED MEMBERS:** Ballesteros Rodríguez, Francisco Javier | Barrondo Lakarra, Sergio | Callado Hernando, Luis Felipe | Díez Alarcía, Rebeca | Gabilondo Urquijo, Ane Miren | Gutiérrez Fraile, Miguel | Horrillo Furundarena, Igor | López de Jesús, Maider | Miranda Azpiaz, María Patricia | Ortega Calvo, Jorge Emilio | Rivero Calera, Guadalupe | Salles Alvira, Joan | Urigüen Echeverria, Leyre.

**CONTRIBUTORS:** Eguiluz Uruchurtu, Iñaki | Elizagarate Zabala, Edorta | Montaña Muro, Mario | Muguruza, Carolina | Palomo Lerchundi, Javier | Querejeta Ayerdi, Imanol | Segarra Echebarria, 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

- RIVERO G., GABILONDO A.M., GARCIA-SEVILLA J.A., LA HARPE R., CALLADO L.F., MEANA J.J.. Increased  $\alpha 2$ - and  $\beta 1$ -adrenoceptor densities in postmortem brain of subjects with depression: Differential effect of antidepressant treatment. *Journal of Affective Disorders*. 2014;167:343-350.
- ERDOZAIN A.M., RUBIO M., VALDIZAN E.M., PAZOS A., MEANA J.J., FERNANDEZ-RUIZ J. et al. The endocannabinoid system is altered in the post-mortem prefrontal cortex of alcoholic subjects. *Addiction Biology* 2014; en prensa. Doi: 10.1111/adb.12160.
- MORENTIN B., BALLESTEROS J., CALLADO L.F., MEANA J.J.. Recent cocaine use is a significant risk factor for sudden cardiovascular death in 15-49-year-old subjects: A forensic case-control study. *Addiction* 2014; 109: 2071-2078.
- MUGURUZA C., MIRANDA-AZPIAZU P., DIEZ-ALARCIA R., MORENTIN B., GONZALEZ-MAESO J., CALLADO L.F. et al. Evaluation of 5-HT<sub>2A</sub> and mGlu<sub>2/3</sub> receptors in postmortem prefrontal cortex of subjects with major depressive disorder: Effect of antidepressant treatment. *Neuropharmacology*. 2014;86:311-318.
- ERDOZAIN A.M., MORENTIN B., BEDFORD L., KING E., TOOTH D., BREWER C. et al. Alcohol-related brain damage in humans. *PLoS ONE*. 2014;9(4).

## Highlights

### NEW PROJECTS:

- Alterations of noradrenergic system in cognitive deficits of schizophrenia: localization, mechanisms and pharmacological reversion. SAF2013-48586R. PI: Luis Felipe Callado
- Evaluation of the role of 5-HT<sub>2A</sub> receptors and Akt/GSK3 pathway as molecular mechanisms of cannabis induced psychosis. PI13/01529. PI: Leyre Urigüen
- Development of cognitive therapies for schizophrenia and Parkinson's disease. RTC-2014-1645-1 PI: J. Javier Meana

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## RESEARCH GROUPS

### Group 17

Programme: Depression; Psychosomatic, Anxiety and Impulse Control Disorders



**Lead Researcher:** Menchón Magriña, José Manuel

### Group members

**STAFF MEMBERS:** Giménez Navarro, Mónica

**ASSOCIATED MEMBERS:** Alonso Ortega, María del Pino | Cardoner Álvarez, Narcis | Contreras Fernández, Fernando | Crespo Blanco, José Manuel | Hernández Ribas, Rosa | López Sola, Clara | Real Barrero, Eva | Segalas Cosi, Jacinto | Soria Tomas, Virginia | Soriano Mas, 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

- DE WIT S.J., ALONSO P., SCHWEREN L., MATAIX-COLS D., LOCHNER C., MENCHON J.M. et al. Multicenter voxel-based morphometry mega-analysis of structural brain scans in obsessive-compulsive disorder. *American Journal of Psychiatry*. 2014;171(3):340-349.
- VAN AMERINGEN M., SIMPSON W., PATTERSON B., DELL'OSSO B., FINEBERG N., HOLLANDER E. et al. Pharmacological treatment strategies in obsessive compulsive disorder: A cross-sectional view in nine international OCD centers. *Journal of Psychopharmacology*. 2014;28(6):596-602.
- LOPEZ-SOLA C., FONTENELLE L.F., ALONSO P., CUADRAS D., FOLEY D.L., PANTELIS C. et al. Prevalence and heritability of obsessive-compulsive spectrum and anxiety disorder symptoms: A survey of the Australian twin registry. *American Journal of Medical Genetics, Part B: Neuropsychiatric Genetics*. 2014;165(4):314-325.
- VIA E., CARDONER N., PUJOL J., ALONSO P., LOPEZ-SOLA M., REAL E. et al. Amygdala activation and symptom dimensions in obsessive-compulsive disorder. *British Journal of Psychiatry*. 2014;204(1):61-68.
- JIMENEZ-MURCIA S., FERNANDEZ-ARANDA F., GRANERO R., MENCHON J.M.. Gambling in Spain: Update on experience, research and policy. *Addiction*. 2014;109(10):1595-1601.

## Highlights

Our group has developed research lines which are interrelated. At present, our group participates in the international consortium OCD Brain Imaging Consortium in which different international OCD groups have joined their imaging data to carry out a mega-analysis, which their first data have been published this year (de Wit et al, 2014). Further, the group is involved in an international multicenter clinical trial on deep brain stimulation, which has finished the clinical recruitment phase. This technique is carried out only in some OCD specialized centers and the participation in this study has placed our group as a reference center in this technique applied in OCD.

Regarding the OCD spectrum, we have participated in the researches promoted by ICOCS (International College of Obsessive-Compulsive Spectrum Disorders) and by Obsessive-Compulsive Research Network (OCCRN, which belongs to European College of Neuropsychopharmacology, ECNP). Further, in the context of studying compulsivity as a behavioral construct, we have been collaborating with other CIBER groups in studies on gambling disorder and behavioural addiction.

In the field of mood disorders, the group has collaborated in multicenter studies on bipolar disorder. On the other hand, in the field of unipolar depression, the group is in charge of the development of two work packages within project ('Epigenetic and environmental factors bracing cognitive impairment and late-onset depression in elderly and early stages of Alzheimer disease') which has been awarded this year in a specific call for research institutions ('Excellence Integrated Projects'). Further, regarding depression and physical therapies, the group has kept the development of a clinical trial on electroconvulsive maintenance in unipolar depression as well as a training course on convulsive therapy and other physical therapies that is organized by our group biannually.

The neuroimaging team in our group has actively participated within the different clinical research lines and has led neuroimaging studies that have been conducted in different mental disorders.

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## RESEARCH GROUPS

### Group 18

Programme: Psychosomatic, Anxiety and Impulse Control Disorders; Therapeutic Innovation.



**Lead Researcher:** Micó Segura, Juan Antonio

### Group members

**STAFF MEMBERS:** Rey Brea, Raquel

**ASSOCIATED MEMBERS:** Alba Delgado, Cristina | Berrocoso Domínguez, Esther | Bravo Garcia, Lidia | Gilbert Rahola, Juan | Romero Grimaldi, Carmen | Torres Sánchez, Sonia.

**STAFF MEMBERS:** Gallego Gamo, Jesús

### Main lines of research

- Pain & Depression.
- Mechanisms of action of Deep Brain Stimulation in CNS Disorders.
- Neurobiology and Treatment of Schizophrenia and related mental disorders.



## Most relevant scientific articles

- PEREZ-CABALLERO L., PEREZ-EGEA R., ROMERO-GRIMALDI C., PUIGDEMONT D., MOLET J., CASO J.-R. et al. Early responses to deep brain stimulation in depression are modulated by anti-inflammatory drugs. *Molecular Psychiatry*. 2014;19(5):607-614.
- GARCIA-BUENO B., BIOQUE M., MAC-DOWELL K.S., BARCONES M.F., MARTINEZ-CENGOTITABENGOA M., PINA-CAMACHO L. et al. Pro-/anti-inflammatory dysregulation in patients with first episode of psychosis: Toward an integrative inflammatory hypothesis of schizophrenia. *Schizophrenia Bulletin*. 2014;40(2):376-387.
- BRAVO L., TORRES-SANCHEZ S., ALBA-DELGADO C., MICO J.A., BERROCOSO E.. Pain exacerbates chronic mild stress-induced changes in noradrenergic transmission in rats. *European Neuropsychopharmacology*. 2014;24(6):996-1003.
- BERROCOSO E.. Gabapentin, a double-agent acting on cognition in pain?. *Pain*. 2014;155(10):1909-1910.
- BORGES G., NETO F., MICO J.A., BERROCOSO E.. Reversal of monoarthritis-induced affective disorders by diclofenac in rats. *Anesthesiology*. 2014;120(6):1476-1490.

## Highlights

Our group in 2014 continued to enhance its strategic lines in 2013 focused on research in both the Therapeutic Innovation Program and the Psychosomatic Disorders Program. As most relevant results, we would emphasize the participation in different studies in the field of schizophrenia, depression and psychiatric diseases associated with pain.

In depression, we have demonstrated the involvement of a neuro-inflammatory mechanism associated with the known early therapeutic response of Deep Brain Stimulation in resistant depression. Also, we have demonstrated the interrelationship of the nucleus Locus coeruleus and the noradrenergic system in the affective-emotional symptoms in situation of chronic pain. We have also evidenced as a peripheral nociceptive stimulus affects the affective-emotional response.

In schizophrenic patients, we have been able to establish, in conjunction with other CIBERSAM groups, a possible plasma biomarker for the first psychotic episodes, specifically the anti-inflammatory mediator 15d-PGJ2. Regarding the cognitive symptoms in schizophrenia, our group in collaboration with other CIBERS and other international institutions has shown that an alteration in the concentration of SAME (S-adenosylmethionine) impairs neurogenesis and that this would result in a cognitive decline.

In 2014 we have obtained a research project funded by the Instituto de Salud Carlos III, to study the neurobiological mechanisms underlying the comorbidity depression, anxiety and cognitive deficits associated with chronic pain. In addition, we have obtained a Research Transfer Project for the study of some antagonist's drugs of histamine receptor type 3 (R-H3) as possible target for the depression-pain comorbidity. Moreover, in the area of Therapeutic Innovation and Technology Transfer we have applied for a new patent of encapsulated nanoparticles of a cannabinoid (CB13), with possible therapeutic indication in neurology and psychiatry.

Finally, in epidemiology, we have conducted the first national survey on the emotional impact of chronic pain in the Spanish population.

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## Group 19

Programme: Schizophrenia; Psychosomatic, Anxiety and Impulse Control Disorders



**Lead Researcher:** Palomo Alvarez, Tomás

### Group members

**STAFF MEMBERS:** Dompablo Tobar, Monica | Gómez Núñez, M del Carmen

**ASSOCIATED MEMBERS:** Aguera Ortíz, Luis Fernando | Aragues Figuero, Maria | Caso Fernández, Javier Rubén | Hoenicka Blanco, Janet | Jiménez Arriero, Miguel Angel | Jurado Barba, Rosa | Molina Rodríguez, Vicente | Moreno Ortega, Marta | Rodríguez Jiménez, Roberto | Sanz Fuentenebro, Francisco Javier.

**CONTRIBUTORS:** Bagnay Lifante, Alexandra | Guerra Martín Polanco, Noelia | Navio Acosta, M. Mercedes

### Main lines of research

- Psychotic disorders. Vulnerability to schizophrenia. Neurocognition. Social cognition. Disorder's evolution.
- Psychotic disorders. Treatment for schizophrenia. First episodes. Treatment for resistant symptoms.
- Psychotic disorders. Psychosis and dual pathology. Addictive disorders.
- Psychosomatics. Psychiatric morbidity in medical-surgical patients. Population psychiatric morbidity and use of care services.
- Personality. Traits and disorders. Attention deficit hyperactivity disorder (ADHD). Antisocial disorder.
- Affective disorders. Suicide.
- Aging. Dementia.
- Neuroinflammation. Psychiatric disorders. Stress.
- Molecular and genetic basis of neuropsychiatric disorders.

## Most relevant scientific articles

- PEREZ-CABALLERO L., PEREZ-EGEA R., ROMERO-GRIMALDI C., PUIGDEMONT D., MOLET J., CASO J.-R. et al. Early responses to deep brain stimulation in depression are modulated by anti-inflammatory drugs. *Molecular Psychiatry*. 2014;19(5):607-614.
- GARCIA-BUENO B., BIOQUE M., MAC-DOWELL K.S., BARCONES M.F., MARTINEZ-CENGOTITABENGOA M., PINA-CAMACHO L. et al. Pro-/anti-inflammatory dysregulation in patients with first episode of psychosis: Toward an integrative inflammatory hypothesis of schizophrenia. *Schizophrenia Bulletin*. 2014;40(2):376-387.
- SANTOS J.L., APARICIO A., BAGNEY A., SANCHEZ-MORLA E.M., RODRIGUEZ-JIMENEZ R., MATEO J. et al. A five-year follow-up study of neurocognitive functioning in bipolar disorder. *Bipolar Disorders*. 2014.
- MOLINA V., TABOADA D., ARAGUES M., HERNANDEZ J.A., SANZ-FUENTENEbro J.. Greater clinical and cognitive improvement with clozapine and risperidone associated with a thinner cortex at baseline in first-episode schizophrenia. *Schizophrenia Research*. 2014;158(1-3):223-229.
- IVORRA J.L., RIVERO O., COSTAS J., INIESTA R., ARROJO M., RAMOS-RIOS R. et al. Replication of previous genome-wide association studies of psychiatric diseases in a large schizophrenia case-control sample from Spain. *Schizophrenia Research*. 2014;159(1):107-113.

## Highlights

In Research the main novelty have being the study of neuroinflammation markers in relation to vulnerability to psychiatric disorders, both in animal models and in patients, in collaboration with group G12 (IP Juan Carlos Leza).

We have continued the study of genetic factors and neuroimaging in Schizophrenia in relation to clinical and cognitive symptoms progression. Among our results, we found clinical and cognitive improvement, associated with brain cortex thickness, in patients treated with both Clozapine and Risperidone.

Molecular genetic studies have continued characterizing ANKK1 gen in relation to dopaminergic function.

The important cognition and schizophrenia research line has continued in several research projects comparing bipolar, schizophrenia and dual pathology patients.

We have started also a collaboration with Columbia University in New York for the study of brain connectivity and TMS treatments.

In Education and Teaching, the main activity in CIBERSAM has been the creation of a new Master Degree course for Research in Mental Health, organized and coordinated by group G20 (Angel Pazos), involving several universities and CIBERSAM groups. Our group G19 coordinates UCM groups G1, G12 and G19 and the three UCM University Hospitals Gregorio Marañón, Clínico de San Carlos and 12 de Octubre.

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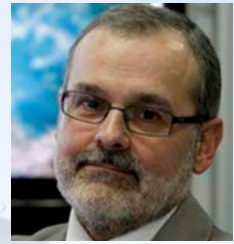
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## Group 20

Programme: Depression; Therapeutic Innovation



**Lead Researcher:** Pazos Carro, Ángel Armando

### Group members

**STAFF MEMBERS:** Amigo Riu, Josep | Berrueco Sáiz, Rubén | Pilar Cuellar, María Fuencisla.

**ASSOCIATED MEMBERS:** Castro Fernández, Elena | Díaz Martínez, Alvaro Marcelino | Garro Martínez, Emilio | Linge Mendez, Raquel | Marrón Souto, Eva | Valdizan Ruiz, Elsa Maria | 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

- PILAR-CUÉLLAR F, VIDAL R, DÍAZ A, CASTRO E, DOS ANJOS S, VARGAS V et al. Signaling pathways involved in antidepressant-induced cell proliferation and synaptic plasticity. *Current pharmaceutical design*. 2014;20(23):3776-94.
- VIDAL R, CASTRO E, PILAR-CUÉLLAR F, PASCUAL-BRAZO J, DÍAZ A, ROJO ML et al. Serotonin 5-HT4 receptors: A new strategy for developing fast acting antidepressants?. *Current pharmaceutical design*. 2014;20(23):3751-62.
- ROIZ-SANTIANEZ R., AYESA-ARRIOLA R., TORDESILLAS-GUTIERREZ D., ORTIZ-GARCIA DE LA FOZ V., PEREZ-IGLESIAS R., PAZOS A. et al. Three-year longitudinal population-based volumetric MRI study in first-episode schizophrenia spectrum patients. *Psychological Medicine*. 2014;44(8):1591-1604.
- ERDOZAIN A.M., RUBIO M., VALDIZAN E.M., PAZOS A., MEANA J.J., FERNANDEZ-RUIZ J. et al. The endocannabinoid system is altered in the post-mortem prefrontal cortex of alcoholic subjects. *Addiction Biology*. 2014.
- CORRALES A., VIDAL R., GARCIA S., VIDAL V., MARTINEZ P., GARCIA E. et al. Chronic melatonin treatment rescues electrophysiological and neuromorphological deficits in a mouse model of Down syndrome. *Journal of Pineal Research*. 2014;56(1):51-61.

## Highlights

Our group is focused in three major lines of research. Our main activity is dedicated to meet the aims proposed in our SAF2011-25020 project ("Mecanismos de neuroplasticidad involucrados en la respuesta antidepressiva rápida de los agonistas del receptor 5-HT4: papel de las vías Wnt/ $\beta$ -catenina y mTOR"). Animal models of depression/anxiety and **genetically** manipulated are used. Our results demonstrate a depression/anxiety-like phenotype in  $\beta$ -catenin conditional knockout mice in hippocampal progenitor neurons, which correlates with impaired proliferation and maturation of hippocampal neurons. In addition, 5-HT4 ko mice do not exhibit apparent behavioral changes in paradigms of depression/anxiety, although some neuroplasticity biomarkers appear to be altered. In this sense, preliminary results suggest that the presence of the 5-HT4 is not crucial for certain antidepressant responses. However, this receptor may be a relevant therapeutic target under certain pathophysiological conditions associated with impaired neuroplasticity, since the subchronic treatment (7 days) with the partial agonist 5-HT4 RS67333 in the  $\beta$ -catenin conditional ko mouse shows antidepressant efficacy. Furthermore, this outcome is associated to adaptive changes in elements of the serotonergic pathway (5-HT1A and 5-HT4 receptors), as described for conventional antidepressants.

A second line of research is aimed at evaluating the antidepressant potential of cannabidiol (CBD). This compound exhibits short-term antidepressant efficacy, increasing serotonin and glutamate levels in frontal cortex, and modulating neuroplasticity markers as BDNF and mTOR.

Finally, under a collaborative framework with SERVIER S.L. pharmaceutical, we are evaluating the biological activity of AMPA receptor modulators in order to develop new compounds with antidepressant potential.

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## RESEARCH GROUPS

### Group 21

Programme: Depression; Psychosomatic, Anxiety and Impulse Control Disorders



**Lead Researcher:** Pérez Sola, Víctor

### Group members

**STAFF MEMBERS:** Allende Leal, Saiko | Grasa Bello, Eva M | Justicia Diaz, Azucena | Pujol Nuez, Jesús

**ASSOCIATED MEMBERS:** Alonso Solis, Ana | Álvarez Martínez, Enrique | Antoni Joan Arbos, Rosa María | Arranz Calderon, María Jesús | Clos Batet, Susana | Corripio Collado, Iluminada | De Diego Adeliño, Francisco Javier | Durán-Sindreu Terol, Santiago | Feliu Soler, Albert | Giménez Badia, Sandra | Martín Blanco, Ana | Pascual Mateos, Juan Carlos | Pérez Blanco, Josefina | Pérez Egea, Rosario | Portella Moll, María Jesús | Puigdemont Campos, Dolors | Ramos Ferraz, Liliana | Riba Serrano, Jordi | Sauras Quetcuti, Rosa Blanca | Serra Blasco, Maria | Soler Ribaudi, Joaquin | Tiana Sastre, Thais | Trujols Albet, Joan | Valle Cano, Marta.

**CONTRIBUTORS:** Ballester Verneda, M Rosa | Gich Saladich, Ignacio Jose | 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 and functional neuroimaging; biological and genetic biomarkers; identification and evaluation of new therapeutic targets and programs; pharmacogenetics.
- Psychotic disorders: environmental, biological and genetic factors; efficacy and effectiveness of anti-psychotic drugs; first episodes of psychosis; genotype-phenotype and environment interaction; neuroimaging; pharmacogenetics.

- Personality disorders: mixed treatment in patients with Borderline Personality Disorder (BPD), validation of diagnostic instruments; genetic-neuroimaging studies.
- Mental health therapeutics: efficacy and resistance to treatment; validation of diagnostic and assessment scales; systematic reviews; neuropsychology; neurophysiology; neuroimaging.

#### NEW RESEARCH LINES:

- New therapeutic strategies: DBS in treatment-resistant schizophrenia; methylphenidate in mania; determination of cortisol in hair; brain effects of mindfulness in BPD; Apps and ICT application in the prevention and treatment of depression and schizophrenia.

## Most relevant scientific articles

- PEREZ-CABALLERO L., PEREZ-EGEA R., ROMERO-GRIMALDI C., PUIGDEMONT D., MOLET J., CASO J.-R. et al. Early responses to deep brain stimulation in depression are modulated by anti-inflammatory drugs. *Molecular Psychiatry*. 2014;19(5):607-614.
- SALVADOR R., VEGA D., PASCUAL J.C., MARCO J., CANALES-RODRIGUEZ E.J., AGUILAR S. et al. Converging Medial Frontal Resting State and Diffusion-Based Abnormalities in Borderline Personality Disorder. *Biological Psychiatry*. 2014.
- DE WIT S.J., ALONSO P., SCHWEREN L., MATAIX-COLS D., LOCHNER C., MENCHON J.M. et al. Multicenter voxel-based morphometry mega-analysis of structural brain scans in obsessive-compulsive disorder. *American Journal of Psychiatry*. 2014;171(3):340-349.
- USALL J., LOPEZ-CARRILERO R., INIESTA R., ROCA M., CABALLERO M., RODRIGUEZ-JIMENEZ R. et al. Double-blind, placebo-controlled study of the efficacy of reboxetine and citalopram as adjuncts to atypical antipsychotics for negative symptoms of schizophrenia. *Journal of Clinical Psychiatry*. 2014;75(6):608-615.
- TRUJOLS J., DE DIEGO-ADELINO J., FELIU-SOLER A., IRAURGI I., PUIGDEMONT D., ALVAREZ E. et al. The Spanish version of the Quick Inventory of Depressive Symptomatology-Self-Report (QIDS-SR16): A psychometric analysis in a clinical sample. *Journal of Affective Disorders*. 2014;169:189-196.

## Highlights

- First case of Deep Brain Stimulation in treatment-resistant schizophrenia. Clinical trial funded by a FIS project, coordinated with G15 of CIBERSAM.
- First double-blind, crossover, clinical trial of Deep Brain Stimulation in treatment-resistant depression, with positive results in relapse prevention (to be published in 2015).
- Grant of European project m-Resist for monitoring and follow-up using ICTs for patients with schizophrenia, with the participation of 8 European partners (2 CIBERSAM groups).
- Cortisol determination in hair by ELISA technique.
- Clinical trial funded by a FIS project to assess the efficacy of mindfulness in Borderline Personality Disorder and study of changes in the Default Mode Network, in collaboration with G15 of CIBERSAM.

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## Group 22

Programme: Schizophrenia; Psychosomatic, Anxiety and Impulse Control Disorders



**Lead Researcher:** Saiz Ruiz, Jerónimo

### Group members

**STAFF MEMBERS:** Almeida Nunes , Rosa M | Anaya Suárez., Celia | Grillo Durán, Beatriz.

**ASSOCIATED MEMBERS:** Artes Rodríguez, Antonio | Baca García, Enrique | Blasco Fontecilla, Hilario | Ibáñez Cuadrado, Angela | Lahera Forteza, Guillermo | Llerena Ruiz, Adrian | López Castroman, Jorge | Montes Rodríguez, José Manuel | Pérez Rodríguez, Mercedes.

### Main lines of research

- Suicidal behaviour.
- Application of data mining to mental health research.
- Genetic of mental disorders.
- Lipid metabolism in mental disorders.
- Phamacogenetics.



## Most relevant scientific articles

- OQUENDO M.A., SULLIVAN G.M., SUDOL K., BACA-GARCIA E., STANLEY B.H., SUBLETTE M.E. et al. Toward a bio-signature for suicide. *American Journal of Psychiatry*. 2014;171(12):1259-1277.
- OQUENDO M.A., BACA-GARCIA E.. Suicidal behavior disorder as a diagnostic entity in the DSM-5 classification system: Advantages outweigh limitations. *World Psychiatry*. 2014;13(2):128-130.
- LLERENA A., ALVAREZ M., DORADO P., GONZALEZ I., PENAS-LLEDO E., PEREZ B. et al. Interethnic differences in the relevance of CYP2C9 genotype and environmental factors for diclofenac metabolism in Hispanics from Cuba and Spain. *Pharmacogenomics Journal*. 2014;14(3):229-234.
- LOPEZ-CASTROMAN J., JAUSSENT I., BEZIAT S., GUILLAUME S., BACA-GARCIA E., GENTY C. et al. Increased severity of suicidal behavior in impulsive aggressive patients exposed to familial adversities. *Psychological Medicine*. 2014;:1-10.
- GRANDE I., BERNARDO M., BOBES J., SAIZ-RUIZ J., ALAMO C., VIETA E.. Antipsychotic switching in bipolar disorders: A systematic review. *International Journal of Neuropsychopharmacology*. 2014;17(3):497-507.

## Highlights

The activity of our group is reflected in the implementation of projects in progress:

- Environment and genes in schizophrenia, funded by the Community of Madrid, (S2010 / BMD- 2422 AGES), participating as two groups, Ramón y Cajal Hospital and Fundación Jiménez Díaz, with a successful achievement with regard to the objectives.
- Clinical and neurobiological determinants of second's episodes of schizophrenia. Longitudinal study of first psychotic episodes, funded by the FIS (PI11 / 00325 ). It is a continuation of the PEPs study in which we coordinated the Pharmacogenetics module, which is currently in a period of evaluation and diffusion of results.
- Identification of genetic determinants of suicidal behavior in depression (PI13 / 002200). International Latino Research Partnership (IRLP), funded by the National Institute on Drug Abuse (NIDA) of the United States, within a multinational multicentre initiative.
- Study of abnormalities in social cognition and its impact on the functionality.
- Pharmacogenetics in different ethnic populations, with special attention to the CYP enzyme system , and creation of common databases , including the creation of an Ibero-American network of pharmacogenetics and pharmacogenomics (RIBEF).
- Suicidal behaviour: its location in the diagnostic systems, risk and prevention factors, possibilities for intervention, genetics, clinical aspects, ...

In addition, we have actively participated in the development of recommendations and clinical practice guidelines such as:

- Clinical Practice Guideline on pharmacological and psychosocial therapy in Bipolar Disorder. Ministry of Health.
- Spanish Consensus on Physical Health in Depressive Patients. Spanish Society of Psychiatry.
- Clinical Practice Guideline on the management of OCD. Spanish Society of Psychiatry.

Monographic clinical programs remain focused on addictive behaviours (with special attention to gambling disorder) and in Bipolar Disorder and Obsessive–Compulsive disorder providing clinical information and possible cases for investigation. Likewise, the Functional Psychosurgery Program (CSUR) of which we are part.

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## Group 23

Programme: Therapeutic Innovation; Schizophrenia



**Lead Researcher:** Sanjuán Arias, Julio

### Group members

**STAFF MEMBERS:** Garcia Marti, Gracian | Gilabert Juan, Javier | Llacer Iborra, Blanca | Perez Roda, Inmaculada

**ASSOCIATED MEMBERS:** Aguilar Garcia Iturrospe, Eduardo Jesus | Carot Sierra, Jose Miguel | De La Iglesia Vaya, Maria | Gadea Domenech, Marien | Gonzalez Piqueras, Jose Carlos | Herrero Sebastian, Neus | Ivorra Martinez, Jose Luis | Leal Cercos, Carmen | Molto Ruiz, Maria Dolores | Nacher Rosello, Juan Salvador | Olucha Bordonau, Francisco | Rivero Martin, Olga | Tolosa Montero, Amparo.

**CONTRIBUTORS:** Brotons Girona, Olga | Escarti Fabra, M Jose | Jover Martinez, 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

- STEINBERG S., DE JONG S., MATTHEISEN M., COSTAS J., DEMONTIS D., JAMAIN S. et al. Common variant at 16p11.2 conferring risk of psychosis. *Molecular Psychiatry*. 2014;19(1):108-114.
- IVORRA J.L., RIVERO O., COSTAS J., INIESTA R., ARROJO M., RAMOS-RIOS R. et al. Replication of previous genome-wide association studies of psychiatric diseases in a large schizophrenia case-control sample from Spain. *Schizophrenia Research*. 2014;159(1):107-113.
- VAN OS J., RUTTEN B.P., MYIN-GERMEYS I., DELESPAUL P., VIECHTBAUER W., VAN ZELST C. et al. Identifying gene-environment interactions in schizophrenia: Contemporary challenges for integrated, large-scale investigations. *Schizophrenia Bulletin*. 2014;40(4):729-736.
- WEBER H., KLAMER D., FREUDENBERG F., KITTEL-SCHNEIDER S., RIVERO O., SCHOLZ C.-J. et al. The genetic contribution of the NO system at the glutamatergic post-synapse to schizophrenia: Further evidence and meta-analysis. *European Neuropsychopharmacology*. 2014;24(1):65-85.
- GUIRADO R., PEREZ-RANDO M., SANCHEZ-MATARREDONA D., CASTREN E., NACHER J.. Chronic fluoxetine treatment alters the structure, connectivity and plasticity of cortical interneurons. *International Journal of Neuropsychopharmacology*. 2014.

## Highlights

In the year 2014 our group has lead the publication of the first results of a large collaborative project coordinated from the G3 in Valencia. The GWAS project. In this estudy we have replicated the most relevant findings of previous GWAS studies psychosis, in a sample of 3000 patients. We have also collaborated with several international consortium in search of polymorphisms of risk for psychosis. We worked also in the European EU-GEI project in search of environmental & genetic factors in the first psychotic episodes.

In relation with the research line of animal models we have presented the first results on the of NO and glutamatergic systems in the synapse. We have also continued to define changes in synaptic connectivity after the chronic administration of fluoxetine.

In the field of neuroimaging, an important milestone for our group has been presenting a patent "Method for detecting anomalous areas in the brain from magnetic resonance imaging" No 000543.

Within this field of Neuroimaging we have completed the project (Marato TV3) in relation to changes in functional analysis before and after cognitive therapy in patients with persistent psychotic hallucinations.

Finally in this year 2014 we have participated in drafting the Mental Health Plan for the Valencian Community (Department of Health). In particular, our group has had active participation in the working grupo related with mental health research and in the consensus program for creating first psychotic episodes units.

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## RESEARCH GROUPS

### Group 24

Programme: Bipolar disorder; Child and Adolescent Psychiatry



**Lead Researcher:** Tabares Seisdedos, Rafael

### Group members

**STAFF MEMBERS:** Amezcua García, Cristina | Correa Ghisays, Patricia.

**ASSOCIATED MEMBERS:** Balanza Martínez, Vicent | Fuentes Dura, Inmaculada | Geijo Barrientos, Emilio | Giron I Giménez, Manuel | Gómez Beneyto, Manuel | Martínez Pérez, Salvador | Munárriz Ferrandis, Mikel | Salazar Fraile, José | Selva Vera, Gabriel.

### Main lines of research

- Longitudinal study of schizophrenia and bipolar disorder.
- Epidemiological study.
- Inverse comorbidity study.
- Cognitive endophenotypes (Endophenocognitypes) study.
- Neurogenetics.

## Most relevant scientific articles

- CATALA-LOPEZ F., SUAREZ-PINILLA M., SUAREZ-PINILLA P., VALDERAS J.M., GOMEZ-BENEYTO M., MARTINEZ S. et al. Inverse and direct cancer comorbidity in people with central nervous system disorders: A meta-analysis of cancer incidence in 577,013 participants of 50 observational studies. *Psychotherapy and Psychosomatics*. 2014;83(2):89-105.
- IBANEZ K., BOULLOSA C., TABARES-SEISDEDOS R., BAUDOT A., VALENCIA A.. Molecular Evidence for the Inverse Comorbidity between Central Nervous System Disorders and Cancers Detected by Transcriptomic Meta-analyses. *PLoS Genetics*. 2014;10(2).
- THOMPSON C.L., NG L., MENON V., MARTINEZ S., LEE C.-K., GLATTFELDER K. et al. A high-resolution spatiotemporal atlas of gene expression of the developing mouse brain. *Neuron*. 2014;83(2):309-323.
- KAPCZINSKI F., MAGALHAES P.V.S., BALANZA-MARTINEZ V., DIAS V.V., FRANGOU S., GAMA C.S. et al. Staging systems in bipolar disorder: An International Society for Bipolar Disorders Task Force Report. *Acta Psychiatrica Scandinavica*. 2014;130(5):354-363.
- MACEIRA A.M., RIPOLL C., COSIN-SALES J., IGUAL B., GAVILAN M., SALAZAR J. et al. Long term effects of cocaine on the heart assessed by cardiovascular magnetic resonance at 3T. *Journal of Cardiovascular Magnetic Resonance*. 2014;16(1).

## Highlights

First molecular evidence Inverse comorbidity. It has received more than 10,901 DISPLAYS in a year. "Molecular evidence for the inverse comorbidity Between Central nervous system disorders and Cancers detected by transcriptomic meta-analyzes" *PLoS Genet*. 2014.

Two of the five news pieces of greatest impact are regarding our group:

Long term effects of cocaine on the heart Assessed by cardiovascular magnetic resonance at 3T. *Journal of Cardiovascular Magnetic Resonance* 2014, 16:26.

Inverse and direct cancer comorbidity in people With Central nervous system disorders: a meta-analysis of cancer incidence in participants 577.013 of 50 observational studies. *Psychother Psychosom*. 2014; 83 (2): 89-105. Prize of the Royal Academy of Medicine of Valencia 2013-2014.

Atlas spatiotemporal gene expression. A high-resolution spatiotemporal atlas of gene expression of the Developing mouse brain. *Neuron*. 2014; 83 (2): 309-323.

INTERCIBER Project. Funded by the MINECO and Instituto de Salud Carlos III. "UNDERSTANDING OBESITY (OB), METABOLIC SYNDROME (METS), TYPE 2 DIABETES (T2DM) AND FATTY LIVER DISEASE (FL): A MULTIDISCIPLINARY APPROACH" (PIE14 / 00031).

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## Group 25

Programme: Bipolar disorder; Therapeutic Innovation



**Lead Researcher:** Vieta Pascual, Eduard

### Group members

**STAFF MEMBERS:** Bonin Roig, Caterina del Mar | Pacchiarotti, Isabella | Sanchez Moreno, José | Torrent Font, Carla.

**ASSOCIATED MEMBERS:** Benabarre Hernández, Antonio | Blanch Andreu, Jordi | Colom Victoriano, Francesc | De Dios Perrino, Consuelo | Gasto Ferrer, Cristobal | Goikolea Alberdi, José Manuel | Grande I Fullana, Iria | Martín Santos Laffont, Rocío | Martínez Aran, Anabel | Navarro Odriozola, Víctor | Navines de la Cruz, Ricard | Undurruga Fourcade, Juan Pablo.

**CONTRIBUTORS:** Comes Forastero, Merce

### 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

- COLOM F.. The evolution of psychoeducation for bipolar disorder: From lithium clinics to integrative psychoeducation. *World Psychiatry*. 2014;13(1):90-92.
- CANALES-RODRIGUEZ E.J., POMAROL-CLOTET E., RADUA J., SARRO S., ALONSO-LANA S., DEL MAR BONNIN C. et al. Structural abnormalities in bipolar euthymia: A multicontrast molecular diffusion imaging study. *Biological Psychiatry*. 2014;76(3):239-248.
- CATALA-LOPEZ F., SUAREZ-PINILLA M., SUAREZ-PINILLA P., VALDERAS J.M., GOMEZ-BENEYTO M., MARTINEZ S. et al. Inverse and direct cancer comorbidity in people with central nervous system disorders: A meta-analysis of cancer incidence in 577,013 participants of 50 observational studies. *Psychotherapy and Psychosomatics*. 2014;83(2):89-105.
- BHATTACHARYYA S, FALKENBERG I, MARTIN-SANTOS R, ATAKAN Z, CRIPPA JA, GIAMPIETRO V. et al. Cannabinoid Modulation of Functional Connectivity within Regions Processing Attentional Salience. *Neuropsychopharmacology* : official publication of the American College of Neuropsychopharmacology. 2014;.
- SCHUMANN G., BINDER E.B., HOLTE A., DE KLOET E.R., OEDEGAARD K.J., ROBBINS T.W. et al. Stratified medicine for mental disorders. *European Neuropsychopharmacology*. 2014;24(1):5-50.

## Highlights

- Functional characterization of brain changes in the different phases of bipolar disorder.
- Design a program that uses a behavioral neuro-cognitive approach to train patients in strategies to address the challenges and difficulties of daily life.
- Developing a staging model for bipolar disorder.
- Development of clinical recommendations on the recognition and management of risk factors in people with schizophrenia
- Development of a document proposing a common pathway among some pathologies in theory as diverse as neoplastic and neurodegenerative processes.
- Preparation of a document where the relationship between sunlight and age of onset of bipolar disorder is evident.

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## RESEARCH GROUPS

### Group 26

Programme: Schizophrenia, Therapeutic Innovation



**Lead Researcher:** Crespo Facorro, Benedicto

### Group members

**STAFF MEMBERS:** De la Fuente González, Noemi | Roiz Santiañez, Roberto M.

**ASSOCIATED MEMBERS:** Ayesa Arriola, Rosa | Gaité Pindado, Luis | Gómez del Barrio, José Andres | Herrán Gómez, José Andres | Herrera Castanedo, Sara | Mata Pastor, Ignacio | Ortiz 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.

**CONTRIBUTORS:** Tordesillas Gutierrez, Diana

### 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

- SCHIZOPHRENIA WORKING GROUP OF THE PSYCHIATRIC GENOMICS CONSORTIUM, CRESPO FACORRO B. Biological insights from 108 schizophrenia-associated genetic loci. *Nature*. 2014;511(7510):421-7.
- Psychosis Endophenotypes International Consortium, Wellcome Trust Case-Control Consortium 2, BRAMON E, PIRINEN M, STRANGE A, LIN K et al. A genome-wide association analysis of a broad psychosis phenotype identifies three loci for further investigation. *Biological psychiatry*. 2014;75(5):386-97.
- ROIZ-SANTIANEZ R., AYESA-ARRIOLA R., TORDESILLAS-GUTIERREZ D., ORTIZ-GARCIA DE LA FOZ V., PEREZ-IGLESIAS R., PAZOS A. et al. Three-year longitudinal population-based volumetric MRI study in first-episode schizophrenia spectrum patients. *Psychological Medicine*. 2014;44(8):1591-1604.
- PEREZ-IGLESIAS R., MARTINEZ-GARCIA O., PARDO-GARCIA G., AMADO J.A., GARCIA-UNZUETA M.T., TABARES-SEISDEDOS R. et al. Course of weight gain and metabolic abnormalities in first treated episode of psychosis: The first year is a critical period for development of cardiovascular risk factors. *International Journal of Neuropsychopharmacology*. 2014;17(1):41-51.
- PELAYO-TERAN J.M., DIAZ F.J., PEREZ-IGLESIAS R., SUAREZ-PINILLA P., TABARES-SEISDEDOS R., DE LEON J. et al. Trajectories of symptom dimensions in short-term response to antipsychotic treatment in patients with a first episode of non-affective psychosis. *Psychological Medicine*. 2014;44(1):37-50.

## Highlights

In 2014, our group has been involved in two EU projects: "PSYSCAN – Translating Neuroimaging Findings from Research into Clinical Practice" and "MENTHELDER – Preventing Mental Health-Related Problems In The Elderly". These projects provide an excellent opportunity to push forward our lines of research in neuroimaging and physical health.

In the National Plan calls we have achieved funding for the MINECO project "GEXANT - Novel candidate genes for treatment response to antipsychotics in schizophrenia: Evidence from pharmacogenetics in the light of personalized medicine" (SAF2013-46292-R) will explore genomic basis of treatment response and side effects in FES. Also for the AES health research projects numbers PI14/00639 and PI14/00918.

As the result of international consortiums ENIGMA, PEIC, and EnpactSz relevant data sets on schizophrenia (genetic and neuroimaging) have been created and will provide a unique opportunity to face new research issues.

Several clinical trials have been initiated during the 2014. Four in Spain: 10PAFIP, ADARFEP, GEXANT and ROAC2014. And EULAST, in Europe.

It is also of note the publication of "Guía de Hábitos de Vida Saludables para Personas con Enfermedad Mental Grave" (ISBN: 978-84-697-1243-6) and the clinical statements "Protocolo de Coordinación de Actividades Sanitarias y Educativas para la Detección y Seguimiento de personas con Trastorno por Déficit de Atención con/sin Hiperactividad durante la edad pediátrica" (ISBN: 978-84-95302-57-1).

Our group has applied for a patent to the OEPM on genomic variations and treatment response, named "Método de monitorización de tratamiento antipsicótico" (number P201431188).

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## Linked Group 1

Programme: Psychosomatic, Anxiety and Impulse Control Disorders



**Lead Researcher:** Casas Brugue, Miguel

### Group members

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### Main lines of research

The different research lines that are being developed include the study of:

- 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 diverse therapeutic approaches. We are also interested in the identification of how these different neurodevelopmental disorders and psychopathological factors influence school failure and, later on, in how the influence of adult everyday life.
- Impulsive and Disruptive behaviors. This research line concerns the study of diagnostic 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

- BOADA M., TARRAGA L., HERNANDEZ I., VALERO S., ALEGRET M., RUIZ A. et al. Design of a comprehensive Alzheimer's disease clinic and research center in Spain to meet critical patient and family needs. *Alzheimer's and Dementia*. 2014;10(3):409-415.
- HOEKZEMA E., CARMONA S., RAMOS-QUIROGA J.A., RICHARTE FERNANDEZ V., BOSCH R., SOLIVA J.C. et al. An independent components and functional connectivity analysis of resting state fMRI data points to neural network dysregulation in adult ADHD. *Human Brain Mapping*. 2014;35(4):1261-1272.
- VAN EMMERIK-VAN OORTMERSSEN K., VAN DE GLIND G., KOETER M.W.J., ALLSOP S., AURIACOMBE M., BARTA C. et al. Psychiatric comorbidity in treatment-seeking substance use disorder patients with and without attention deficit hyperactivity disorder: Results of the IASP study. *Addiction*. 2014;109(2):262-272.
- HOEKZEMA E., CARMONA S., RAMOS-QUIROGA J.A., CANALS C., MORENO A., FERNANDEZ V.R. et al. Stimulant drugs trigger transient volumetric changes in the human ventral striatum. *Brain Structure and Function*. 2014;219(1):23-34.
- MARTIN-BLANCO A., FERRER M., SOLER J., SALAZAR J., VEGA D., ANDION O. et al. Association between methylation of the glucocorticoid receptor gene, childhood maltreatment, and clinical severity in borderline personality disorder. *Journal of Psychiatric Research*. 2014;57(1):34-40.

## Linked Group 2

Programme: Schizophrenia



**Lead Researcher:** Vilella Cuadrada, Elisabet

### Group members

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### 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

- STOJANOVIC A., MARTORELL L., MONTALVO I., ORTEGA L., MONSENY R., VILELLA E. et al. Increased serum interleukin-6 levels in early stages of psychosis: Associations with at-risk mental states and the severity of psychotic symptoms. *Psychoneuroendocrinology*. 2014;41:23-32.
- MANZANARES N., MONSENY R., ORTEGA L., MONTALVO I., FRANCH J., GUTIERREZ-ZOTES A. et al. Unhealthy lifestyle in early psychoses: The role of life stress and the hypothalamic-pituitary-adrenal axis. *Psychoneuroendocrinology*. 2014;39(1):1-10.
- ABASOLO N, ROIG B, MARTORELL L, MARTÍNEZ-LEAL R, AGUILERA F, CAMACHO-GARCÍA RJ et al. Genetic study of NRXN1 $\beta$  variants in Spanish patients with schizophrenia. *Schizophrenia research*. 2014;159(2-3):554-5.
- MONTALVO I., GUTIERREZ-ZOTES A., CREUS M., MONSENY R., ORTEGA L., FRANCH J. et al. Increased prolactin levels are associated with impaired processing speed in subjects with early psychosis. *PLoS ONE*. 2014;9(2).
- TORRELL H., SALAS A., ABASOLO N., MOREN C., GARRABOU G., VALERO J. et al. Mitochondrial DNA (mtDNA) variants in the European haplogroups HV, JT, and U do not have a major role in schizophrenia. *American Journal of Medical Genetics, Part B: Neuropsychiatric Genetics*. 2014;165(7):607-617.

## Highlights

We highlight the development of three competitive projects:

- PI12/01885. Mutaciones en el ADN mitocondrial que contribuyen en el autismo y a las características propias de las enfermedades mitocondriales presentes en pacientes con trastorno del espectro autista. IP: Lourdes Martorell
- PI12/02111. Alteraciones de la melina en función del genotipo DDRI en pacientes esquizofrénicos: estudios clínico y molecular. IP: Elisabet Vilella
- PI10/01607. Mecanismos neurobiológicos del estrés en psicosis incipientes: relación del eje hipotálamo-pituitario-adrenal con el polimorfismo Val66Met del gen BDNF, volumen del hipocampo y rendimiento neuropsicológico. IP Javier Labad

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## 6. ANNEXE



## LIST OF PUBLICATION 1<sup>ST</sup> DECILE CIBERSAM 2014

Note: publications have listed only the first decile in their areas of expertise of downward by the impact factor of the journal in which they were published.

1. Consortium on Lithium Genetics, Hou L., Heilbronner U., Rietschel M., Kato T., Kuo P.-H., McMahon F.J., Schulze T.G. Variant GADL1 and response to lithium in bipolar I disorder. *New England Journal of Medicine*, 370(19): 1857-1859. 2014. F.I.: 54,4200.
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