GENETICS, ENVIRONMENT, SIGNALLING & SYNAPTIC PLASTICITY IN DEVELOPMENTAL BRAIN DISORDERS: FROM BENCH TO BEDSIDE

GENETIQUE, ENVIRONNEMENT, SIGNALISATION ET PLASTICITE SYNAPTIQUE DANS LES MALADIES DU DEVELOPPEMENT DU CERVEAU : DU LABORATOIRE A LA CLINIQUE

President: **Barbara Bardoni**
IPMC - CNRS UMR7275, 660, Route des Lucioles SOPHIA-ANTIPOLIS
06560 Valbonne, France

Vice-President: **Mara Dierssen**
Centre for Genomic Regulation (CRG), C/ Dr. Aiguader, 88, PRBB Building, 08003 Barcelona, Spain

***Roscoff** (Brittany), France*
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Rapport sur la Conférence

Conference Report

General description of the conference

The Jacques Monod Conference *« Genetics, environment, signalling, and synaptic plasticity in developmental brain disorders: from bench to bedside »* took place in Roscoff from April 11th to April 15th, 2022. The President was Dr. **Barbara BARDONI** (Valbonne, France) and Vice-President Prof. **Mara DIERSSEN** (Barcelona, Spain). Participants were 89 in total, among them:

- 26 invited speakers (scientists with a tenure position) were selected on the basis of their scientific excellence in neurobiology and neurogenetics. The female representation among the invited speakers was 58%.

- 63 applicants selected upon abstract submission (32 tenure positions, 7 post-docs and 24 students). Females represented 65% of participants.

Country	Invited Speakers	Scientists (application)	Students (application)
France	11	24	10
Italy	2	11	7
USA	3	0	1
Germany	0	1	0
Netherlands	1	0	2
Spain	2	1	0
Portugal	1	0	0
UK	0	1	0
Canada	1	0	0
Poland	0	0	4
Ireland	1	1	
Australia	1		
Hungary	1		
Israel	1		
Sweden	1		
Total	**26**	**39**	**24**

The meeting was organized in 10 sessions of oral presentations including the opening of the meeting on April 11th, with two speakers (Prof. Fiona Miller and Prof. Victor Faundez) giving a virtual talk. Each session was a mix of talks given by an invited speaker (25 minutes + 5-10 minutes of discussion) and short talks (10 minutes + 5 minutes of discussion) given by participants whose presentation was selected on the basis of their submitted abstract. A total of 18 short oral presentations were selected based on the scientific interest of the subject and the consistence with the specific session of the meeting. The female representation among the selected speakers was 67%. At least one chairperson of each session was selected among young scientists.

Two poster sessions with a total of 45 posters were presented and half of the number of posters were presented in each session. Two Blitz Poster sessions allowed 14 participants to introduce their posters during three minutes with only one slide. The female representation among the selected speakers in the blitz poster session was 57%. Two awards for the two best posters (500 €/each – sponsored by the Fondation Jerôme Lejeune) were assigned to **Gabriele CHELINI** (post-doc at the Center for Mind/Brain Sciences-University of Rovereto,Italy; Supervisor: Prof. Yuri BOZZI) Title of the poster: "*Proteoglycan Clusters as a Site of Coordinated, Multi-Dendritic Plasticity*" and to **Federica QUICI** (PhD Student at the Institut Interdisciplinaire des Neurosciences, IINS, Université de Bordeaux, CNRS UMR 5297; supervisor: Prof. Valentin Nägerl). Title of the poster: "*Dual-scanner STED microscope for simultaneous photo-stimulation and fast fluorometric imaging".*

Mrs Nathalie BABIC took perfectly care of the practical organization of the meeting and her support to the organizers was absolutely essential for the success of the meeting. The technical support and the logistic offered by the Biological Station in Roscoff were strongly appreciated, as well as the accommodations in several hotels in Roscoff and the quality and variety of food served at the Gulf Stream Hotel. CNRS provided the main funding to support the conference. Furthermore, the organizers received a substantial financial support by the **Jérôme Lejeune Foundation, Frontiers and T21 Research Society**. The support of Frontiers is associated with the topic *"Innovative approaches and therapeutic perspectives for early-onset neurodevelopmental disorders: from bench to bedside"* on Frontiers in Neuroscience - Neurodevelopment.

At the conclusion of the meeting on April 15th afternoon, Mara Dierssen (Barcelona, Spain) was confirmed chairman for the next conference and Marie-Claude Potier (Paris, France) was nominated vice-chairman.

Report on scientific aspects

The opening session was chaired by **Christine METIN** (Paris, France). The first speaker was **Freda MILLER** (Vancouver, Canada) presenting a large overview on the cortical stem cells during normal and abnormal development. The second speaker, **Victor FAUNDEZ** (Atlanta, USA), presented his approach to identify biomarkers for RETT syndrome by performing proteomics in cerebrospinal fluid obtained from animal models and patients of this disorder.

The session "From circuits to systems (Part I)" had as Chairpersons **Valery MATARAZZO** (Marseille, France) and **Sophie SAKKAKI** (Montpellier, France). The first speakers, **Gabor TAMAS** (Szeged, Hungary), focused his talk speaking on similarities and differences among human and rodent neocortical synapses, neurons and networks during development. The second speaker, **Michela**

FAGIOLINI (Boston, USA), discussed about circuit dissection in neurodevelopmental disorders and the characterization of biomarkers in the Rett syndrome. Daniela TROPEA (Dublin, Ireland) gave a short talk describing the molecular and genomic signatures predictive of response to mecasermin in children with Rett syndrome. Nicoletta LANDSBERGER (Milan, Italy) presented a new treatment for RETT syndrome based on the modulation of the neuronal activity.

The second part of the session I "From circuits to systems" was chaired by **Charlotte KILSTRUP-NIELSEN** (Busto-Arsizio, Italy) and **Luca PANGRAZZI** (Rovereto, Italy). This session was open ed by **Orly REINER** (Rehovot, Israel) describing the generation of brain organoids as a bottom-up approach for studying human neurodevelopment. The second speaker **Alessandra PIERANI** (Paris, France) focused her talk on Cajal-Retzius neurons (CRs) and their role in normal and pathological neurodevelopment. Indeed, CRs are initially embedded into the immature neuronal network before being almost completely eliminated by cell death at the end of cortical development. **Michèle STUDER** (Nice, France) talked about the work of her team on the BBSOA syndrome, a form of neurodevelopmental disorder characterized by intellectual disability and caused by mutations in the *Nr2f1* gene encoding an orphan nuclear hormone receptor and transcriptional regulator. In particular she described their ability to model the disease both in mouse and brain organoids. **Sara BONZANO** (Torino, Italy) gave a short talk on BBSOA syndrome too. She presented evidence about the role of *Nr2f1* on mitochondrial architecture in adult-born mouse hippocampal neurons. **Àlex BAYÉS PUIG** (Barcelona, Spain) gave a short talk focused on his approach to system biology to decipher the synaptic molecular alterations underpinning intellectual disability caused by synGAP1. This gene encodes the synaptic Ras/Rap GTPase-activating protein (synGAP) which is one of the most abundant proteins in the postsynaptic density of excitatory synapses. His studies on *Syngap1*$^{+/-}$ mice revealed that proteins related to small GTPases, translation and energy production were significantly altered in these animals.

Part I of Session II entitled "The complex multilayer scenario in neurodevelopmental disorders" was chaired by **Véronique BRAULT** (Illkirch, France) and **Marianne BÉNARD** (Paris, France). The first speaker **Peter TODD** (Ann Arbor, USA) focused on the role of expansion of nucleotide repeats in human neurological diseases such as Autism Spectrum Disorder (ASD) and Fronto Temporal Dementia (FTD). The studies of the group of Dr. Todd revealed that the mechanisms by which repeat expansions cause disease is a combination of toxic RNA gain-of-function mechanisms and the unconventional translation of repeats in the absence of an AUG start codon ("RAN translation"). He discussed recent data of his team concerning the mechanisms by which RAN translation occurs and its role in disease pathogenesis in Fragile X-associated disorders. The second speaker of the session, **Mara DIERSSEN** (Barcelona, Spain), presented recent data of her laboratory showing the epigenic impact on Down Syndrome (DS). Indeed, she focused on lncRNAs that are involved in learning and memory. The critical role of lncRNAs for the adult hippocampal GABAergic circuit and their association of with adult neurogenesis has been established thus covering several of the DS pathogenicity mechanisms. She discussed new findings showing deregulated expression of lncRNAs in the hippocampus of a DS mouse model, the Ts65Dn, and their involvement in DS specific neuropathology. **Clement CARRÉ** (Paris, France) gave a short talk about the role of the ribose methylation enzyme FTSJ1 in neuron morphology and learning performance in a *Drosophila* model. Another study concerning the role of epigenetics in brain development was presented by **Valérie MEZGER** (Paris, France) showing her data about the contribution of stress-responsive pathways in normal neurodevelopment and pathological forms such as Fetal alcohol Syndrome and Rubinstein-Taybi Syndrome.

The second part of Session II entitled "The complex multilayer scenario in neurodevelopmental disorders" was chaired by **Gabriele CHELINI** (Rovereto, Italy). The first speaker, **Brigitte KIEFFER**

(Strasbourg, France), talked about the role of opioid receptors in brain function and during brain development. In particular, she presented recent data linking mu opioid receptor gene and drug activities to whole-brain functional networks, using by fMRI in mice. The second speaker, **Kenneth O'RIORDAN** (Cork, Ireland), made an overview about the role of the intestinal microbiome as a regulator of gut-brain axis signaling. He discussed his data providing strong evidence that modulation of the gut microbiome is intrinsically linked with cellular plasticity in the brain, and likely to be important in the behavioral phenotype of these animals, further implicating the gut microbiome in brain and behavior processes.

The Session III "Blitz posters" was chaired by **Mara DIERSSEN** (Barcelona, France). In this session seven participants selected on the basis of their abstract had three minutes to introduce their posters in front to all the participants:

Francesco BEDOGNI (Cardiff, UK) *"Interactions between Neurod1 and ERK signaling in mechanisms of cerebral cortex development and their role in the genesis of neurodevelopmental disorders"*

Gabriele CHELINI (Rovereto, Italy) "*Proteoglycan Clusters as a Site of Coordinated, Multi-Dendritic Plasticity*"

Sébastien DELHAYE (Valbonne, France) *"A new model of neurodevelopmental disorder"*

Florelle DOMART (Göttingen, Germany) *"Mover/TPRG1L: a novel presynaptic protein upregulated in Schizophrenia"*

Alessandra FOLCI (Milan, Italy) *"Oligophrenin-1: a novel sumo target in synaptic function and dysfunction"*

Matteo FOSSATI (Milan, Italy) "*UBE3A-dependent regulation of synaptic development: implications for the pathogenesis of neurodevelopmental disorders"*

Angelisa FRASCA (Milan, Italy) "*Neural precursor/stem cell-based therapy for Rett syndrome"*

Session IV entitled "Inhibitory neurons: Keeping the Brain's Traffic in Check" was chaired by **Francesco BEDOGNI** (Cardiff, UK) and **Florelle DOMART** (Göttingen, Germany). The first speaker **Alberto BACCI** (Paris, France) presented his data concerning the dendritic over-inhibition of cortical circuits in DS. On the same subject, the second speaker **Marie-Claude POTIER** (Paris, France) discussed the role of GABA-ergic interneurons inhibition in DS and the consequent possible therapeutic approaches. Melody ATKINS (Paris, France) gave a short talk and she presented her results focused on the role of primary cilium-elicited signalling pathways and cortical interneuron migration in DS. The second short talk by **Evelyne BLOCH-GALLEGO** (Paris, France) described her analysis of the migration of GABAergic interneurons in the absence of TRIO whose mutations are associated with neurodevelopmental disorders. This gene encodes a large protein that functions as a GDP to GTP exchange factor. She observed delayed migration, and misplacement of INs in different cortical layers.

The first part of Session V "From gene to mechanism and pathophysiology" was chaired by **Gaëlle FRIOCOURT** (Brest, France) and **Aurélie DE THONEL** (Paris, France). The first speaker, **Barbara BARDONI**, described the approach of her laboratory to define an effective treatment for the Fragile X Syndrome (FXS), a very frequent form of intellectual disability and ASD. Starting from RNA targets of FMRP, the protein causing FXS, they identified the cAMP and cGMP signaling as main altered pathways in the FXS neurons. The normalization of this altered signaling allowed the rescue of socio-cognitive deficits in the FXS mouse and rat models. The second speaker **Julie PERROY** (Montpellier, France) described her recent study focused on the signaling NMDA receptors-metabotropic mGlu5 receptors-

PSD95-GKAP-Shank3-Homer. Combining BRET imaging and electrophysiology, they showed that a transient neuronal depolarization inducing NMDA-dependent plasticity disrupts glutamate receptosome in a long-lasting manner at synapses and activates signaling pathways required for the expression of the initiated neuronal plasticity, such as ERK and mTOR pathways in the Shank3-ΔC mice, a model of ASD. The group of **Flavia ANTONUCCI** (Milan, Italy) identified Ataxia Telangiectasia Mutated (ATM) as a novel kinase that orchestrates GABA development by controlling *KCC2* expression. By using the ATM kinase inhibitor KU55933, they were able to normalize molecular, functional and behavioral defects in two mouse models of ASD (Mecp2y/- mouse model of Rett syndrome and mice prenatally-exposed to valproic acid) both having increased ATM levels. **Frédéric LAUMONNIER** (Tours, France) gave a short talk focused on *de novo* missense mutations identified in his laboratory in the *DPYSL5*. This gene causes intellectual disability with brain malformations that lead to dendritic outgrowth dysregulation through interaction defects with cytoskeleton-associated proteins. The second selected short talk of the session was presented by **Anne DEBANT** (Montpellier, France). She collected and studied the largest international cohort of 24 individuals with confirmed pathogenic missense or non-sense variants in TRIO. In particular, she showed that spectrin and GEFD1 TRIO variants cause opposite modulation of RAC1 activity and observed a striking correlation between RAC1 activation levels and the head size of the individuals with intellectual disability.

Session VI "Dissecting Synaptopathies" was chaired by **Alessandra FOLCI** (Milan, Italy) and **Ludovic TRICOIRE** (Paris, France). The first speaker of this session, **Christophe MULLE** (Bordeaux, France), discussed physiological and pathological functions of the amyloid precursor protein APP in CA3 hippocampal region in the normal and pathological brain, considering neurodegenerative and neurodevelopmental disorders. The second speaker, **Ana Luisa CARVALHO** (Coimbra, Portugal), investigated a mutant form – variant V143L - of the TARP family member stargazin (AMPA receptor auxiliary proteins), associated to intellectual disability in a patient. Knock-in mice carrying this variant manifest cognitive and social deficits resembling phenotypes displayed by intellectual disability patients. In their hippocampus, CA1 neurons show impaired synaptic transmission and plasticity, and alterations in spine maturation in basal dendrites and in the synaptic ultrastructure. Laurent GROC (Bordeaux, France/ Goteborg, Sweden) presented evidence that alteration of the NMDA receptor dynamics and synaptic anchoring play an instrumental role in different developmental and acute rodent models of psychosis, *i.e.* immune challenge and autoimmunity as well as in patients. For personal/health reasons, two talks were canceled in this section. Maria Vincenza CATANIA (Catania, Italy) was initially scheduled to present an overview about the synaptic dysfunction of metabotropic glutamate receptors in synaptic plasticity with a focus on the Fragile X Syndrome. A short talk of Hanna ZIEGER (Bordeaux, France) entitled "The disease-associated synaptic protein synGAP is involved in AMPA receptor organization" was also initially scheduled in this session.

Session VII "From gene to mechanism and pathophysiology (Part II)" was chaired by **Delara SABERAN DJONEIDI** (Paris, France) and **Angelisa FRASCA** (Milan, Italy). The first speaker **Barbara FRANKE** (Nijmegen, The Netherlands) focused her talk on neurodevelopmental psychiatric disorders– attention-deficit/hyperactivity disorder (ADHD). ADHD is a common neurodevelopmental psychiatric disorder in both children and adults. Although the first description of ADHD dates back more than 200 years, the knowledge about its aetiology is still limited. This speaker described a set of complementary data science and experimental approaches to extract biological meaning from the findings of large-scale gene-finding studies, such as bioinformatic approaches, research in animal and human cellular model systems, as well as neuroimaging genetics analyses. The second speaker, **Yann HERAULT** (Illkirch,France), presented the molecular complexity underpinning the DS. They generated new mouse

models, refined an old one such as the Ts(1716)65Dn/J (Ts65Dn), and developed rat models for DS that they characterized by performing a standardized behavioral and brain pipeline with hippocampal gene expression profiling. While the important role of DYRK1A, a gene located on the critical DS region on chromosome 21 and encoding a kinase, as a main driver of cognitive dysfunction in DS was confirmed, they have also found new loci which are involved in cognition and behavior, highlighting the complexity of the altered neurological mechanisms in DS and contributing to altering brain cognition, function and structure. This study represents a novel vision of the disorder to start innovative therapeutic approaches. In her short talk, **Amélie PITON** (Illkirch, France) presented the collection of mutations responsible for the DYRK1A syndrome. To provide a better understanding of the clinical and molecular consequences of the loss-of-function variants responsible for this syndrome, they used a human neural precursor model to better understand the consequences of loss-of-function mutations. They established the DYRK1A interactome in these cells and identified novel protein partners, such as RNF114, an E3 ubiquitin ligase. Then, they demonstrated that inactivation of DYRK1A led to a decrease in the proliferation of neuronal precursors as well as a decrease in both the expression of the P21 protein, an important player in the cell cycle and the activation of the ERK pathway. The second short talk was presented by **Laurent MEIJER**, the director of 1Perha Pharmaceuticals Perharidy Research Center (Roscoff, France) the only non-academic researcher presenting his data at the meeting. He found that Leucettamine B, a natural product extracted from the marine sponge Leucetta microraphis, inhibits DYRK1A with relatively good selectivity. Inspired by this initial hit, they first synthesized, optimized and extensively characterized >500 analogues. Since genetic and pharmacological inhibition of DYRK1A correct cognitive deficits in various animal models of DS, they hope that these new molecules could be an innovative treatment for DS.

Session VII was part III of “From gene to mechanism and pathophysiology” and was chaired by **Sébastien DELHAYE** (Valbonne, France) and Annapia VERRI (Pavia, Italy). The first speaker, **Jozef GECZ** (Adelaide, Australia), described the Protocadherin 19 (PCDH19) Clustering Epilepsy pathology that is an X-chromosome disorder of cellular mosaics. Heterozygous females with one PCDH19 allele are affected by a loss of function mutation. In addition, males with a postzygotic somatic mutation are affected by loss of function of P CDH19 only in a proportion of their cells. At the molecular point of view, they showed that PCDH19 interacts with the Androgen Receptor. This result supports the hypothesis of the dual role of PCDH19 in cell adhesion and gene expression (co)regulation. **Maria PASSAFARO** (Milan, Italy) studied the *Pcdh19* c-KO mice and showed that the brain of these animals is characterized by the presence of PCDH19-negative hyperexcitable neurons, a global reduction of network activity with increased neuronal synchronization. Furthermore, PCDH19 mosaic expression compromised the excitatory/inhibitory balance and lead to aberrant functional connections within limbic system regions. **Jean-Vianney BARNIER** (Paris, France) in his short talk presented a genotype/molecular phenotype correlation of a large cohort of patients affected by intellectual disability and carrying mutations in the PAK (PAK1, Pak2 and PAK3) genes. **Françoise MUSCATELLI** (Marseille, France) in a short talk presented recent results on a Prader-Willi syndrome model, the *Magel2* deficient mice. Using electrophysiological recordings in acute brain slices of juvenile mice, they were able to reveal an increase of GABAergic activity in the CA2/CA3 hippocampal pyramidal neurons. An oxytocin-treatment in the first week of life has long-term effects as it restored social memory and normalized the GABAergic activity. **Hervé MOINE** (Illkirch, France) displayed the impact of a reduced expression level of Diacylglycerol kinase kappa in the pathophysiology of the FXS. In the last short talk of the session, **Valerie DUPÉ** (Rennes, France) presented her work on the cohort of a cerebral congenital malformation called Holoprosencephaly (HPE). HPE is defined by an incomplete separation

of the cerebral hemispheres during embryonic development. By highthrough put sequencing approach, 16 genes were implicated in HPE, associated with key pathways of forebrain development including sonic hedgehog.

Session VIII Blitz posters (Part II) was chaired by **Barbara BARDONI** (Valbonne, France). During this session 7 participants introduced their posters:

Véronique BRAULT (Illkirch, France) *"Investigating DYRK1A gene dosage effect in glutamatergic and GABAergic neurons in a mouse model of Down syndrome"*

Gaëlle FRIOCOURT (Brest,France) *"How much FOXP1 deregulation is responsible for the clinical features of ARX mutated patients?"*

Charlotte KILSTRUP-NIELSEN (Busto-Arsizio, Italy) "*Microtubules as a novel therapeutic target for CDKL5 deficiency disorder: targeting the microtubule +TIP CLIP170 with the neuroactive steroid pregnenolone-methyl-ether (PME) restores CDKL5-related defects in vitro and in vivo"*

Lisa PAVINATO (Turin, Italy) *"CAPRIN1 haploinsufficiency causes a novel neurodevelopmental disorder associated with morphological and functional impairment in hiPSCs-derived cortical neurons"*

Beatrice VIONE (Bologna,Italy) *"One-carbon pathway metabolites are altered in the plasma of subjects with Down syndrome: new insights for possible therapeutic approaches"*

Valery MATARAZZO (Marseille, France) *"Early life oxytocin treatment improves thermo-sensory reactivity and maternal behavior in neonates lacking the autism-associated gene Magel2"*

Luca PANGRAZZI (Rovereto, Italy) *"Cerebellar inflammation supports autism-related behaviors in the CNTNAP2 mouse model of autism spectrum disorders"*

Session IX was entitled "Looking to the future modelling of neurodevelopmental disorders" and was chaired by **Matteo FOSSATI** (Milan, Italy). The first speaker was **Paola BOVOLENTA** (Madrid, Spain) presenting her experience in studying neurodevelopmental visual disorders (NDVD). They generated a zebrafish Tg(E1-bhlhe40:GFP) line to track the retina pigment epithelium (RPE) morphogenesis and interrogated its participation in optic vesicle folding. Analysis of transcriptomic dynamics and chromatin accessibility in segregating neural retina and RPE populations highlighted an early recruitment of desmosomal genes in the flattening RPE, revealing Tead factors (TF) as upstream regulators. Investigation of GRNs dynamics uncovered an unexpected sequence of TF recruitment during RPE specification, which is conserved in human-derived organoids. The last presentation by **Pierre GRESSENS** (Paris, France) focused on the role the role of inflammation and the activation of immature microglia (pre-microglia) soon after birth in prematurity-associated neurodevelopmental disorders, and the specific features of pre-microglia during development. They also highlighted the relevance of immunomodulatory strategies for regulating activated microglia in a rodent model of perinatal brain injury. The scheduled presentation "New approaches and tools to investigate the extracellular space of the brain" by Valentin NÄGERL (Bordeaux, France) was canceled for the impossibility of the speaker to be present.

Conclusions and discussion

During oral and poster sessions, the discussion was intense and very interesting and stimulating. Several questions and concepts emerged during these discussions which need to be further addressed to improve the advance of the research in the field. The most noteworthy are here summarized:

- A large number of genes are involved in neurodevelopmental disorders (NDD). Even if each gene represents a niche of study for an entire scientific community, it seems important to define common altered signallings between NDD having different (genetic or environmental) causes that could result in common therapeutic approaches.
-The role of epigenetics and environment in the pathophysiology of NDD.
-The utilization of validated animal models to study NDD. This issue was particularly evident for NDD caused by complex genetic rearrangements, such us Down Syndrome.
-The role of interneurons in NDD.
-The importance of defining the temporal window for an early treatment in neurodevelopmental disorders, considering that neurons during development have a different behavior than mature neurons.
-The identification of biomarkers translatable between animal models and patients. In this context some talks correlating genotype of patients belonging to large cohorts of patients with molecular phenotypes were particularly appreciated.

We believe that we fulfilled our initial purpose of fostering interesting discussions and that for the success of the formula proposed and for the importance of the topics treated this type of meeting may get a high chance to have a great success in the future as well. In all discussion was clear as basic science is critical to advance research in this field, however, in future, it would be important to involve also clinicians to foster discussions about translation to patients of results concerning therapeutic approach obtained in various models and to increase the chance that treatments of NDD will be realized.

RÉSUMÉ

La Conférence Jacques Monod *« Génétique, environnement, signalisation et plasticité synaptique dans les troubles du développement cérébral : du banc au chevet »* s'est tenue à Roscoff du 11 au 15 avril 2022. La présidente était le Dr Barbara BARDONI (Valbonne, France) et Vice-Présidente Prof. Mara DIERSSEN (Barcelone, Espagne). Les participants étaient 89 au total. Parmi eux 26 conférenciers invités avec une représentation féminine parmi de 58 %. 63 participants ont été sélectionnés sur soumission de résumé (32 titulaires, 7 post-doctorats et 24 étudiants). Les femmes représentaient 65 % des participants.
La conférence a été organisée en 10 sessions de présentations orales. Chaque session était un mélange d'exposés donnés par un conférencier invité (25 minutes + 5-10 minutes de discussion) et de courts exposés (10 minutes + 5 minutes de discussion) donnés par des participants dont la présentation a été sélectionnée sur la base de leur résumé. Au total, 18 courtes présentations orales ont été sélectionnées La représentation féminine parmi les intervenants sélectionnés était de 67 %. Au moins un modèrateur/trice de chaque session a été choisi parmi les jeunes scientifiques. Deux sessions

d'affiches avec un total de 45 affiches ont été présentées. De plus, deux sessions de « Blitz Poster » ont permis à 14 participants de présenter leurs posters pendant trois minutes avec une seule diapositive. La représentation féminine parmi les conférenciers sélectionnés lors de la séance d'affiches éclair était de 57 %.

Plusieurs questions et concepts ont émergé lors des intenses discussions de chaque session, qui devraient être approfondis pour améliorer l'avancement de la recherche dans le domaine. Les plus remarquables sont ici résumées :

- Un grand nombre de gènes sont impliqués dans les troubles neurodéveloppementaux (TND). Même si chaque gène représente une niche d'étude pour toute une communauté scientifique, il semble important de définir des voies de signalisation altérées communes chez les TND ayant des causes (génétiques ou environnementales) différentes qui pourraient déboucher sur des approches thérapeutiques communes.
-Le rôle de l'épigénétique et de l'environnement dans la physiopathologie des TND.
-L'utilisation de modèles animaux validés pour étudier le TND. Ce problème était particulièrement évident pour les TDN causées par des réarrangements génétiques complexes, tels que le syndrome de Down.
-Le rôle des interneurones dans les TND.
-L'importance de définir la fenêtre temporelle pour un traitement précoce des TND, considérant que les neurones en cours de développement ont un comportement différent des neurones matures.
-L'identification de biomarqueurs traduisibles entre modèles animaux et patients. Dans ce contexte, certains exposés corrélant le génotype de patients appartenant à de larges cohortes avec des phénotypes moléculaires ont été particulièrement appréciés.