Cortical Connections Conference

June 13-14, 2019
Imagine Institute, Paris, France

Imagine Institute's auditorium, 6th floor
24 boulevard Montparnasse
75015, Paris

Coordinated and organized by:

IRC5
International Research Consortium for the Corpus Callosum and Cerebral Connectivity

UNIVERSITÉ PARIS DESCARTES

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Welcome to the Cortical Connections Conference 2019 !

The IRC5 is thrilled to welcome you at the Imagine Institute, a research and innovative healthcare institute created in 2007, where research and clinical care come together to help to better understand genetic diseases to better treat them.

The IRC is a consortium composed of scientists and clinicians from around the world striving to make major discoveries that will make a significant difference to the lives of affected individuals affected with a corpus callosum anomaly.

This 2 days of conference will give everyone the opportunity to share their research results and their experiences, to move forward, and make progress on the characterization of these cortical connections disorders.

This conference will also be marked by an afternoon dedicated to the families and patients affected with corpus callosum anomaly. We are happy to host this first French family meeting !

We'd like to thank the Imagine Institute, Paris Descartes University, the Simons Foundation, the Rare-disease networks AnDDI-Rares and DefiSciences for their help and support.

We wish you an exciting and enjoyable meeting !

IRC5 Board

CONFERENCE SCHEDULE : 13th June 2019

8:45– 9:00 *Welcome to Imagine (**Stanislas Lyonnet**) & Introduction to IRC5 **(Lynn Paul)**, IRC5 President*

Session 1: Brain Development (chair: Elliott Sherr)

9:00-9:20 ***Linda Richards**: Mutations in human DCC affect cell morphology which may underlie altered interhemispheric remodeling of the septum and agenesis of the corpus callosum.*

9:20-9:40 ***Alessandra Pierani**: Life and death of transient neurons in the maturation of functional and dysfunctional cortical circuits.*

9:40-10:00 ***Alain Chedotal**: Role of netrin 1 and DCC in axonal wiring: from spinal cord to cortex.*

10:00-10:20 ***Anaïs Bellon**: Epigenetic control of cortical wiring: role of axonal miRNAs in fetal alcohol spectrum disorders.*

10:20 - 10:40 Morning Break

Session 2: Models (chair: Linda Richards)

10:40-11:00 ***Binnaz Yalcin**: Large-scale neuroanatomical study uncovers 198 gene associations in mouse brain morphogenesis.*

11:00-11:20 ***Marta Nieto Lopez**: Developmental plasticity underlies the diversity of cortical maps.*

11:20-11:40 ***Christine Laclef**: Role of primary cilia in corpus callosum development.*

11:40-12:00 ***Sonia Garel**: Microglia at the crossroads of cortical wiring and environmental signals.*

12:00-12:20 ***Diego Szczupak**: Assessing interhemispheric connectivity in animal models of dysgenesis of the corpus callosum.*

12:20-14:00 - Lunch Break

Session 3: Connectivity and plasticity (chair: Fernanda Tovar-Moll)

14:00-14:20 ***Roberto Lent****: Cortical connectivity changes after severe peripheral traumas.*

14:20-14:40 ***Jorge Moll****: Mapping and modulating social emotions.*

14:40-15:00 ***Ghislaine Dehaene****: Corpus callosum and functional hemispheric asymmetries in human infants.*

15:00-15:20 ***Gregor Kasprian****: Clinical Fetal Magnetic Resonance Imaging of Brain Connectivity.*

15:20-16:00 **Posters flash session (chair : Lynn Paul).**

16:00 - 16:20 Afternoon Break

Session 4: Long-term outcomes (chair: Paul Lockhart)

16:20-16:40 ***Stéphanie Valence****: Prenatal diagnosis of ACC: what have they become? Prospective follow-up of a cohort of children born between 2005 and 2015.*

16:40-17:00 ***Romina Romaniello****: Long-term follow-up of a cohort of subjects affected by corpus callosum agenesis detected during fetal life: Neuropsychological, neuroimaging and genetic correlations.*

17:00-17:20 ***Vincent Des Portes****: Outcome of isolated agenesis of the corpus callosum: a population-based prospective study.*

17:20-17:25 Sponsor presentation: Agilent Technologies

17h30-19h30: Posters session and Welcome Cocktail

CONFERENCE SCHEDULE : 14th June 2019

Session 5: Prenatal diagnosis (chair: Christel Depienne)

9:00-9:20 ***Laurent Guibaud****: Prenatal imaging diagnosis of corpus callosum anomalies.*

9:20-9:40 ***Zvi Leibowitz****: The many faces of the fetal corpus callosum, on our experience and difficulties in diagnosing and counselling parents of fetuses with suspected callosal anomalies.*

9:40-10:00 ***Tally Lerman-Sagie****: Autopsy findings in fetuses with agenesis of the corpus callosum diagnosed in utero.*

10:00-10:20 ***Laurent Salomon*** *: Lumière prenatal research platform.*

10:20-10:40 Morning Break

Session 6: Behavior (chair: Warren Brown)

10:40-11:00 ***Jessica Dubois****: Imaging the structural and functional development of brain connectivity.*

11:00-11:20 ***Vanessa Siffredi****: Agenesis of the corpus callosum: Exploring neuroplastic responses in the anterior and posterior commissures.*

11:20-11:40 ***Laurence Vaivre-Douret****: Patients with ARID1B mutations (Coffin-Siris syndrome): specific neuropsychological and neuropsychomotor deficits correlated with corpus callosum metrics.*

11:40-12:00 ***Alice Wright****: Social cognition: A comparison of Agenesis of the Corpus Callosum and Autism Spectrum Disorder*

12:00-12:20 ***Lynn Paul****: Behavioural Consequences of Callosal Malformations.*

12:20 - 14:00 Lunch Break

13:30 Welcome of families

Session Applications Cliniques / Clinical Applications (with Families)

14:00-14:20 ***Catherine Garel****: Imagerie prénatale de l'agénésie du corps calleux: intérêt et limites. / Prenatal imaging of corpus callosum agenesis : interest and limits.*

14:20-14:50 ***Tania Attié-Bitach & Solveig Heide****: Génétique des anomalies du corps calleux / Genetics of corpus callosum anomalies.*

14:50-15:10 ***Delphine Héron****: Séquençage d'exome en prénatal dans les agénésies du corps calleux : résultat d'une étude pilote. / Prenatal whole exome sequencing in agenesis of the corpus callosum: a French experience.*

15:10-15:30 ***Emmanuelle Lacaze & Kim Giraudat****: Aspects cognitifs et comportementaux des anomalies du corps calleux / Cognitive and behavioral aspects of corpus callosum anomalies.*

15:30-15:50 ***Jean-Marie Jouannic****: Les grandes étapes du diagnostic prénatal des anomalies calleuses. / The main steps of prenatal diagnosis of callosum abnormalities.*

16:00 - 16:20 Afternoon Break

16:20-16:40 ***Béatrice Langellier-Bellevue****: Prise en charge médico-sociale des agénésies du corps calleux. / Medico-social care of corpus callosum agenesis.*

16:40-17:00 ***Laëtitia Domenighetti****: Maladies rares en France et en Europe, intérêt d'une association de patients. / Rare diseases in France and Europe, interest of a patient organisation.*

17:00- 17:30 ***Round table with families.***

*Concluding Remarks****: Linda Richards****, PhD, IRC5 Secretary*

ABSTRACTS

Session 1: Brain Development

Mutations in human DCC affect cell morphology which may underlie altered interhemispheric remodeling of the septum and agenesis of the corpus callosum.

Linda Richards, Australia

Members of the IRC5 recently published an international study of individuals with corpus callosum dysgenesis associated with mutations in the gene called DCC-netrin1 receptor (DCC, Marsh et al., 2017). Our laboratory has been investigating the function of DCC in corpus callosum formation using both mouse models and in vitro cell culture. Several of the mutations identified in the publication were generated in plasmids and transfected into neuroblast cell cultures. Overexpression of wildtype DCC causes the cells to form extra filopodial processes but over-expression of mutated forms failed to elicit this change in cellular morphology. We previously showed that DCC mouse mutants displayed complete agenesis of the corpus callosum and axonal guidance defects (Fothergill et al., 2014). More recent work demonstrates that an additional phenotype that these mice display is a failure of interhemispheric remodeling of the septum causing retention of the interhemispheric fissure and open septal leaves. This phenotype may arise due to defects in glial morphology at the midline that are required for the remodeling to occur. The work suggests that DCC functions in both axonal guidance and glial development in the formation of the corpus callosum.

Acknowledgements: Australian National Health and Medical Research Council projects GNT1126153 and GNT1059666. LJR is supported by an NHMRC Principal Research Fellowship. LM, APLM and TJE were each supported by an Australian Postgraduate Research Award.

Life and death of transient neurons in the maturation of functional and dysfunctional cortical circuits.

Alessandra Pierani, France

Abnormal brain development participates to the pathophysiology of multiple neurodevelopmental disorders. Programmed cell death is emerging as a key player in the wiring of cortical circuits. Cajal-Retzius cells (CRs) are among the first born cortical neurons and reside in the most superficial layer of the developing cerebral cortex from where they coordinate multiple crucial steps in the construction of functional circuits. CRs completely undergo programmed cell death at the end of brain maturation in mice as well as in primates and their abnormal persistence is associated with pathological conditions in humans. We have shown that although all CR subtypes undergo cell death they do so at least through two molecularly distinct pathways. We produced the first mouse model in which one CR subtype survives to adulthood. These animals display neuronal hypertrophy and imbalanced excitatory/inhibitory (E/I) ratio. We will discuss the effects of maintaining immature neurons in the mature cortex and the role of a subtype-specific control of CR programmed cell death in the construction of functional and dysfunctional cortical circuits.

Acknowledgements: Agence Nationale de la Recherche Imagine Fondation pour la Recherche Médicale Fondation de France Bio SPc CNRS INSERM Université Paris Diderot et Descartes

Role of netrin1 and DCC in axonal wiring: from spinal cord to cortex.

Alain Chedotal, France.

Netrin is a secreted molecule which is best known for its role in the guidance of axons across the midline of the CNS. Its main receptor is DCC (deleted in colorectal cancer). Both netrin-1 and DCC knockout mice exhibit midline crossing defects in the brain (including the corpus callosum) and the spinal cord. Moreover, in humans, mutations of DCC and NTN1 are associated with congenital mirror movements. Although netrin-1 was thought to act as a chemo-attractive molecule, I will discuss our recent studies revisiting netrin-1 mechanism of action in the mammalian CNS. I will also present new functions for netrin-1 and DCC in the development of the visual system.

Epigenetic control of cortical wiring: role of axonal miRNAs in fetal alcohol spectrum disorders.

Anaïs Bellon, France.

Prenatal exposure to environmental factors, such as maternal nutrition, drug use or air pollutants, influences fetal brain development resulting in neurological diseases. Converging data suggest that environmental factors act through epigenetic mechanisms, including the deregulation of microRNAs. Recently, subsets of microRNAs specifically located in the axon have been identified and are thought to regulate brain wiring. Our research aims to determine whether axonal microRNAs are involved in the pathological rewiring of brain circuits induced by in utero exposure to environmental agents. To answer this question, we have developed a new mouse model of Fetal Alcohol Spectrum Disorders (FASD), in which embryos are exposed to moderate doses of alcohol during the stage when the major axon tracts develop. Mapping the connectivity of the entire brain using 3D imaging of cleared brains has revealed that prenatal exposure to alcohol causes axonal guidance anomalies that affect different tracts such as the corpus callosum and striatonigral projections. A screening of microRNAs deregulated by prenatal alcohol exposure allowed us to identify candidate microRNAs present in vivo in growing callosal axons. We are currently testing how the deregulation of these candidates could be responsible for alcohol-induced abnormalities of the interhemispheric connectivity, via functional knockdown approaches by in utero electroporation of microRNA-sponges. The results of this study will provide new insights into the mechanisms by which epigenetic changes may be responsible for the cognitive and behavioral abnormalities associated with FASD.

Acknowledgements: ANR-WIRING-FASDBRAIN.

Session 2: Models

Large-scale neuroanatomical study uncovers 198 gene associations in mouse brain morphogenesis.

Binnaz Yalcin, France.

Brain morphogenesis is an important process contributing to higher-order cognition, however our knowledge about its biological basis is largely incomplete. Here we analyzed 118 neuroanatomical parameters in 1,566 mutant mouse lines and identified 198 genes whose disruptions yield Neuro-Anatomical Phenotypes (NAP), mostly affecting structures implicated in brain connectivity. Groups of functionally similar NAP genes participate in pathways involving the cytoskeleton, the cell cycle and the synapse, display distinct fetal and postnatal brain expression dynamics and importantly, their disruption can yield convergent phenotypic patterns. 17% of human unique orthologues of mouse NAP genes are known loci for cognitive dysfunction. The remaining 83% constitute a vast pool of genes newly implicated in brain architecture, providing the largest study of mouse NAP genes and pathways. This offers a complementary resource to human genetic studies and predict that many more genes could be involved in mammalian brain morphogenesis.

Acknowledgements: This study was funded by the Swiss National Science Foundation (Ambizione PZ00P3_142603), the Jerôme Lejeune Foundation, the French National Research Agency (ANR-11-PDOC-0029), the Gutenberg Circle, and the grant ANR-10-LABX-0030-INRT, a French State fund managed by the Agence Nationale de la Recherche under the frame program Investissements d'Avenir ANR-10-IDEX-0002-02.

Developmental plasticity underlies the diversity of cortical maps.

Marta Nieto-Lopez, Spain.

Axons of the corpus callosum (CC) establish selective interhemispheric connections that facilitate the high functions of the cerebral cortex. How developing cortical neurons wire such stereotyped networks following ostensibly strict rules of target selection, yet are capable of remarkable early plasticity enabling optimal functional circuits and alternative rewiring in non-canonical scenarios, has not been reconciled. Current models establish that early fate-restrictions on axonal development preemptively sort callosal or non-callosal identities at a neuron's birth and impose fundamental limitations to the possible interhemispheric maps. Using a novel axonal-retrotracing strategy we instead demonstrate that virtually all cortical pyramidal neurons project callosally initially. Precise adult connectivity emerges when developmental contralateral axons are extensively refined in area- and layer-specific manners under the influence of circuit activity. Surgical and genetic interventions demonstrate that refinement is plastic and depends on specific sensory input. Loss of thalamic innervation results in structural and functional interhemispheric hyperconnectivity, demonstrating the bonafide early callosal potential of most cortical neurons. Thus, we show that during their selective wiring, most young cortical neurons overshoot and subsequently discard primed alternative circuits as instructed by circuit input. This uncommitted wiring mode may ensure the optimal formation of complex functional circuits and explains the higher plasticity observed in young brains. It helps to understand how diverse non-canonical alternative circuits can emerge in the context of neurodevelopmental diseases, and suggest that impaired sensory integration, early damage of sensory organs, failures of plasticity, or defects in neuro-modulatory signals during development, lead to aberrant interhemispheric maps yet to comprehend.

Acknowledgements: This work was funded by grants from MINECO BFU2016-81887-REDT, PCIN-2015-176-C02-02/ERA-Net Neuron (Era-Net, MINECO), MICINN SAF2017-83117-R, BES-2015-071690 and a grant from Ramón Areces Foundation.

Primary cilia in corpus callosum development.

Christine Laclef, France.

Agenesis of the Corpus callosum (ACC) is characterized by partial or complete absence of the callosal structures. This frequent brain malformation is found in over 80 human congenital syndromes, including ciliopathies. ACC, combined with severe neurodevelopmental defects, has been identified in mouse mutants, deficient for ciliary genes, which provide valuable models of ciliopathies. We thus aim to investigate the role of primary cilia in brain development and corpus callosum (CC) formation. We first analyzed the developmental origin of ACC in *Rpgrip1l* knock-out mouse, a model for Meckel-Grüber syndrome, in which ciliogenesis is altered due to the lack of RPGRIP1L, a protein of the ciliary transition zone. We showed that ACC is associated with the disrupted location of guidepost cells in the dorsomedial telencephalon, which results from early patterning defects and abnormal cortico-septal boundary establishment. We then demonstrated by rescue experiments that ACC primarily originates from an abnormal processing of GLI3, the main SHH transcriptional effector in the dorsal telencephalon. Overexpressing the short repressor form of GLI3 (GLI3R), in Rpgrip1l-/- embryos is sufficient to rescue both the positioning of callosal guidepost cells and the CC formation. We next confirmed that GLI3R can compensate for cilia deficiency caused by a mutation in another ciliary gene, Rfx3, which encodes a transcription factor regulating several target genes involved in ciliogenesis. Finally, by rescuing CC formation in two independent ciliary mutant mice, we have demonstrated that processing of the GLI3 protein is a major outcome of primary cilia, at least in the developing dorsal telencephalon.

Microglia at the crossroads of cortical wiring and environmental signals.

Sonia Garel, France.

Prenatal inflammation and dysfunction of microglia, the brain resident macrophages, have both been associated with the etiology of several neuropsychiatric disorders, including schizophrenia and autism spectrum disorders. Consistently, microglia were shown to regulate neurogenesis, synaptic remodeling and maturation at postnatal stages. However, microglia invade the brain during mid-embryogenesis and could thus exert earlier prenatal and perinatal roles during normal and pathological brain wiring. Here we show that embryonic microglia, which display a transient uneven distribution, regulate the wiring of forebrain circuits. By taking advantage of multiple mouse models, including cell-depletion approaches, we found that perturbing microglia activity affects the development of neocortical inhibitory interneurons, which constitute main actors in neuropsychiatric diseases. In particular, absence, prenatal inflammation or functional perturbation of microglia affects the timely positioning of specific subsets of interneurons as well as their subsequent functional integration in the neocortex. We furthermore found that responses of microglia to environmental signals, including the ones from the microbiome, are sexually dimorphic in males and females. This remarkable finding has major implications for our comprehension of sexual biases in the occurrence of microglia-related diseases, such as the prevalence in males of neurodevelopmental disorders. Our work reveals key roles for immune cells during the normal assembly of cortical circuits and provides novel insights onto how microglia dysfunction or immune risks lead to pathological brain wiring.

Acknowledgements: ERC, ENP, INSERM, CNRS, PSL, Labex Memolife.

Assessing interhemispheric connectivity in animal models of dysgenesis of the corpus callosum.

Diego Szczupak, USA.

A characterization of the normal and abnormal interhemispheric connections with diffusion weighted MRI and histology in mice, monkeys and humans with normal and abnormal corpus callosum morphology. To characterize the Balb/c strain long distance plasticity and compare to the human dysgenesis of the Corpus Callosum (dCC), we employed MRI to evaluate the white matter plasticity. We found that Balb/c strain presents abnormal bundles similar to the human dCC patients. More than that, we found that the brain anatomy of Balb/c strain is different from C57bl6 even in animals with apparently normal CC. Using a histological tracer technique, aav9, we were able to confirm these bundles and we found that the strain C57bl6 also has these supposed abnormal fibers. We also used a connectomic approach and discovered that the Balb/c strain variability is not only related to the size of the CC, but also to the global connectivity with the frontal pole as the most affected cortical region. Then we focused on the human patients, and with the same connectomic approach, we evaluated the whole brain connectivity and found that, in a similar way to the mice, the humans with dCC present many intra-hemispheric alterations and a shift from the interhemispheric connectivity to intra-hemispheric. We also have found that there are marmoset monkeys with a hypoplasic corpus callosum and using diffusion weighted MRI and fMRI, we are characterizing how the brain networks are altered in face of the altered white matter structure.

Acknowledgements: NIH intra mural funding, Cappes and CNPq.

Session 3: Connectivity and plasticity

Cortical connectivity changes after severe peripheral traumas.

Roberto Lent, USA.

Limb amputation is an example of severe peripheral trauma that causes short- and long-distance plasticity of callosal and other cortical connections. To reveal the plastic changes in connectivity we performed different MRI studies in human lower limb amputees, and reverse-translated them to animal models using electron microscopy and axonal tracing. Results revealed that somatotopic maps in the cortex of humans were expanded in both hemispheres. In addition, structural connectivity was reduced between the hemispheres, but expanded within each of them. The corpus callosum showed lowered fractional anisotropy, suggesting microstructural changes demanding a reductionist explanation. To model this condition in animals, early (neonatal) and late (adult) single limb amputations were performed in anesthetized rats, and after long-term survival their brains were either injected with axonal tracers into the limb representation of somatosensory cortex or submitted to imaging and ultrastructural studies of the corpus callosum and other tracts. Results showed a reduction of fractional anisotropy in the corticospinal tract contralateral to the amputated side, and a similar trend in the corpus callosum. Electron microscopy analyses showed a reduction of myelination in both tracts. Anterograde tracers revealed an expansion of callosal axon arbors in the hemisphere ipsilateral to the amputation, with significant increases in the number of synaptic boutons. In sum, we concluded that the somatotopic map reorganization in the cerebral cortex of amputees is possibly explained by an extensive plastic reorganization of connectivity, including a decrease of callosal and corticospinal myelination, with alterations in axonal arborization and synaptic coverage in the cortex.

Acknowledgements: CNPq, FAPERJ, CAPES.

Functional imaging of social reward and moral motivation.

Jorge Moll, Brazil.

Morality enables humans to act according to socio-cultural norms and the needs of others. Over the past decade, functional imaging studies have provided fundamental evidence on the brain network supporting moral cognition and behaviour (Moll et al., J Neurosci 2002). These systems include sectors of the frontal and temporal lobes involved in sequential action knowledge, social concept representations and basic emotional states (Moll et al, Nature Rev Neurosci, 2005). More recently, significant advances have been made in identifying the key neural systems enabling moral motivation. Interestingly, these networks overlap with evolutionarily older systems of kinship bonding and include subgenual frontal and septo-hypothalamic areas (Insel and Young, Nature Rev Neurosci, 2001; Moll et al., PNAS, 2006). My aim will be to review the rapid progress made in this area, provide a novel perspective on how understanding the neural architecture of moral motivation can illuminate certain aspects of neuropsychiatric disorders such as frontotemporal dementia, major depression and psychopathy (Green et al, JAMA Psychiatry, 2012; Moll et al., Neuroimage 2011), thereby guiding future research aiming at understanding and promoting prosocial behaviour and developing new technology such as brain-machine interfaces and emotional neurofeedback (Moll et al., 2014).

Corpus callosum and functional hemispheric asymmetries in human infants.

Ghislaine Dehaene, France.

In humans, structural and functional hemispheric asymmetries are observed as early as the prenatal period suggesting genetically determined differences between both hemispheres. What is the role of the corpus callosum in this asymmetric brain? During the talk, I will present studies in infants during the first semester of life investigating callosal maturation and its functional role during the first semester of life. In collaboration with J. Dubois and P. Adibpour.

Acknowledgements: Fondation NrJ-Institut de France.

Clinical fetal Magnetic Resonance Imaging of brain connectivity.

Gregor Kasprian, Austria.

Developmental neurobiology has developed various complex pathophysiological concepts, which help to understand the origin and consequences of developmental disorders of the human brain. These concepts are mainly derived from rodent or primate animal models, which cannot fully be translated to the human fetus. Thus, human fetal in vivo imaging data constitutes an important source to promote our understanding of normal and pathological brain development. From early second trimester (18 gestational weeks) onwards, fetal MRI provides structural and recently even functional imaging data of the developing human brain. Partly overcoming the problem of fetal motion, modern MR neuroimaging techniques (Diffusion tensor imaging, functional BOLD imaging, spectroscopy) have been successfully adapted to fetal MR imaging. Using fetal brain atlases, even subtle anatomical deviations of the fetal brain can be identified. Comparing in vivo fetal MR data to post mortem MRI and histology in cases after termination of pregnancy allows to validate fetal brain imaging data. Following fetuses with prenatally detected brain pathologies, provides important insights into structure-function relationships. These ongoing efforts ultimately aim to optimize the ability to prognosticate the consequences of structurally abnormal and/or atypical findings detected by prenatal screening ultrasound.

Acknowledgements: The research has been supported by the Austrian science fund (FWF).

Session 4: Long-term outcomes

Long-term neurodevelopment of 126 children born after agenesis of the corpus callosum diagnosed prenatally.

Stéphanie Valence, France.

Agenesis of the corpus callosum (ACC) is usually diagnosed by prenatal ultrasound examination (US) during the 2nd trimester of pregnancy. In the absence of an etiological diagnosis, the neurodevelopment prognosis is uncertain : if ACC is isolated, 20-30 % of patients will present with mild to severe intellectual disability whereas 70-80 % of patients will have development in the normal range. If ACC is associated with other malformations (cerebral or extra-cerebral), poor prognosis is usually considered, despite the lack of accurate data. Thus, neurodevelopmental outcome of prenatal agenesis of the corpus callosum (ACC) remains a major concern with uncertain prognosis.
From 2005 to 2014, 437 women were referred to our unit for fetal ACC, diagnosed by prenatal ultrasound examination (US) and confirmed by brain MRI. 162 (37%) pregnancies were terminated, 84 (20%) pregnancy outcomes were unknown and 192 (42%) babies were born. In this cohort of patients with ACC, 62 (32%) were lost to follow-up, and 4 died. We present here the neuro-developmental outcome for the 126 children (90 males/ 36 females) aged 3 to 15 years. 95 (75%) had isolated ACC (defined by the absence of other malformation) and 31 (25%) had associated ACC. All the enrolled patients underwent post-natal brain MRI, and genetic analysis including at least karyotype, and array-CGH. Psychomotor development data were reported for patients aged 3 to 5 years (n=38), while neuropsychological data (in accordance with the age) and/or school level were reported for patients aged >5 years (n=88), of which 45 had neuropsychological tests. The results show that 75/95 patients (78%) with ACCi and 17/31 patients (55%) with ACCa had a good clinical outcome (normal psychomotor data, neuropsychological data or school level). The data will be detailed and perspectives considered.

Long-term follow-up of a cohort of subjects affected by corpus callosum agenesis detected during fetal life. Neuropsychological, neuroimaging and genetic correlations.

Romina Romaniello, Italy.

Since 2003, about 100 fetal MRI were performed in corpus callosum agenesis detected by a second-level ultrasound at the Department of Neuroradiology, Children's Hospital Buzzi, Milan. Only isolated corpus callosum agenesis oldest two years of age (from 2 to 16 years old) were selected for a detailed neuropsychological evaluation at the Neuropsychiatry and Neurorehabilitation Unit, Scientific Institute E. Medea, Bosisio Parini. Fetal MRI have been classified based on the presence or absence of commissural structures (anterior commissure, hippocampal commissural, heterotopic vestigial commissures) into 4 subgroups of anatomical variants of corpus callosum agenesis. A postnatal MRI (1.5 or 3 Tesla) was performed in order to confirm the isolated corpus callosum agenesis. All the enrolled patients underwent genetic analysis including Karyotype, ArrayCGH and a NGS-based panel sequencing of all known genes causative of defects of the corpus callosum development. A neuropsychological assessment has been performed in accordance with the age and the skills of the subjects to obtain data on cognition, motor abilities, memory, attention, executive functions, language,

behavior. Outcome data of the first two years of life have been obtained in all the 49 enrolled cases; outcome data of the preschool age (3-6 years) have been obtained in 45 patients, data on scholar age (7-16 years) on 40 subjects (7-11 years n= 29; 12-16 years n= 11). Fetal MRI findings have been compared with postnatal MRI data, neuropsychological data and genetic results in search of prognostic indicators to predict neurodevelopmental outcome, to develop early rehabilitation strategies and to address the prenatal counselling.
Acknowledgements: RC 2018- 2019 to RR; 5x1000 funds for biomedical research 2018 to RR.

Outcome of isolated agenesis of the corpus callosum: a population-based prospective study.

Vincent Des Portes, France.

Objectives: Neurodevelopmental outcome of apparently isolated agenesis of the corpus callosum (ACC) remains a major concern with uncertain prognosis. Despite normal IQ reported in a majority of patients, the rates of learning disabilities and severe outcome (ranging from 0% to 20%) are not clearly established. Methods: A large population-based series was investigated based on a longitudinal follow-up until school age, using Wechsler Intelligence scales at 3, 5, and 7 years. Results: Fifty women were referred to a tertiary referral unit for an apparently isolated ACC confirmed by ultrasound, foetal MRI, and karyotyping or array CGH. Twelve pregnancies were terminated, one foetus died in utero, one pregnancy outcome was unknown, and 36 babies were born. Two were lost to follow-up. Thirty-four children could be classified into three groups. Group 1 comprised two children (6%) with severe intellectual disability (one Mowat-Wilson syndrome and one ASD). Group 2 comprised 10 children (29%) who had learning disabilities and borderline intellectual functioning (VIQ and/or PIQ scores >70 and < 85); three patients had hypopituitarism with additional MRI anomalies revealed after birth. Group 3 comprised 22 children (65%) who had both VIQ and PIQ > 85 (-1 SD) with a normal school level. Longitudinal follow-up revealed weaker PIQ in younger children which improved with age. Conclusion: Our data indicate that intellectual ability is normal (IQ > 85) in approximately two thirds and borderline in just over a quarter of patients. However, a low risk of severe cognitive impairment exists, and this information should be shared with couples during prenatal counselling.

Session 5: Prenatal diagnosis

Prenatal imaging diagnosis of corpus callosum anomalies.

Laurent Guibaud, France.

Corpus callosum anomalies have an incidence of about 1:4000 live births. Prenatal diagnosis is based on ultrasound and magnetic resonance imaging (MRI). Callosal dysgenesis included complete or partial agenesis, short corpus callosum and callosal hypoplasia. These callosal anomalies can be isolated or associated with other central nervous system (CNS) anomalies (e. g., cortical developmental disorders, callosal lipoma, intracranial cysts...) or extra-CNS anomalies. Imaging findings of callosal anomalies will be presented from routine examination to dedicated prenatal cerebral imaging.

The many faces of the fetal corpus callosum, on our experience and difficulties in diagnosing and counselling parents of fetuses with suspected callosal anomalies.

Zvi Leibowitz, Israel.

The fetal corpus callosum (CC) is detectable on the sagittal sonographic plane by 18-20 gestational weeks. The CC steadily elongates during the second half of gestation, whereas the average CC body thickness remains stable (2-2.5 mm). This growth pattern results in a relatively "thin" CC appearance in late gestation. Although all CC parts are well formed by 20-22 weeks, its final modelling is achieved by 3 years of age. While the diagnosis and prognostication in fetuses with complete CC agenesis is straightforward, the assessment and counselling in other forms of CC dysgenesis are more challenging and there is insufficient information in the literature. The evaluation of the fetal CC is complicated and requires accurate demonstration of the rostrum, genu, body, and splenium; the use of reference charts for CC length and thickness of its components; follow-up of CC development during gestation; dedicated neurosonography/MRI for assessment of extracallosal malformations; and a thorough anatomical scan for extracranial anomalies. Even after this meticulous approach, precise counselling is difficult for the following reasons: 1) there is prominent postnatal remodelling and growth of the CC; 2) the uncertain correlation between the prenatal and postnatal findings; 3) there are no optimal cut-offs of the fetal callosal biometry for prediction of CC dysgenesis; 4) the differentiation between hypoplasia and partial agenesis is not clear; 5) the sonographic definition of fetal hypoplasia is usually a short CC, while the postnatal definition refers to a thin one; 6) the significance of an abnormally shaped fetal CC is unknown.

Autopsy findings in fetuses with agenesis of the corpus callosum diagnosed in utero.

Tally Lerman-Sagie, Israel.

Objective: To describe the callosal defects and additional autopsy findings in a series of fetuses whose pregnancies were terminated. To assess the frequency of syndromic compared to isolated callosal defects. To evaluate the difference between fetuses with different types of callosal defects. To examine the added value of fetal autopsy in cases of A-CC. Methods: Among 1,290 fetal autopsies which were carried out at Meir Medical Center between 1997 and 2013, there were 50 cases with a callosal defect. Based on

the callosal defect, the cases were divided into 4 groups: complete agenesis, partial agenesis, hypoplasia and dysgenetic. Specific diagnoses were made based on additional autopsy findings, including abnormalities in the brain and internal organs, as well as external dysmorphic features. Results: Among the 50 cases, 68% were syndromic, 10% isolated, 8% encephaloclastic and 14% undetermined. Abnormalities of the cerebral hemispheres as well as of internal organs were more common in cases of hypoplastic and dysgenetic callosal defects, compared to complete and partial. The groups did not differ in gender, external dysmorphism and abnormalities in the cerebellum and brain stem. Conclusions: Autopsy, through its detailed careful evaluation of external and internal gross histological features can suggest specific diagnoses and elucidate the pathomechanism of agenesis of the corpus callosum, that are currently impossible by other modalities. The autopsy findings enable more accurate genetic evaluations and counseling.

The Lumiere research platform.

Laurent Salomon, France.

The first 1,000 days of life - the time spanning roughly between conception and one's second birthday - is a unique period of opportunity when the foundations of optimum health, growth, and neurodevelopment across the lifespan are established. However, amongst these first 1000 days, perhaps the most critical, and also those with the greatest potential, are the period of pregnancy during which the placenta is responsible for nutrition of the fetus. Magnetic Resonance Imaging (MRI) is a technique that has developed significantly in recent years. It is safe, and provides information on pregnancy that would otherwise be totally inaccessible by using other imaging modalities. It is now possible to understand and study the function of the placenta, the engine of fetal development, and to better decipher the mechanisms of onset of fetal growth disorders that may result, decades later, in adverse health outcomes, such as diabetes or cardiovascular disease and stroke. The Necker-Enfants Malades academic hospital of the Assistance Publique-Hôpitaux de Paris has over two centuries of history fighting for and advancing children's health. It is now developing, in partnership with the University and the Faculty of Medicine Paris Descartes, a unique, internationally one of a kind, imaging platform, dedicated to the exploration of pregnancy, the placenta and the fetus. This integrated platform of clinical research in medical imaging of the fetus and placenta called "LUMIERE" will revolutionize fetal medicine and improve the health of generations to come. This platform will be available to all clinical and related partner research teams, either publicly funded academic teams or privately funded industry research groups. It will quickly acquire data and unique knowledge by taking advantage of new imaging techniques, as well as artificial intelligence and big data technologies, in order to facilitate research for the entire scientific community. This work has as its overarching goal the optimization of early development through improved nutrition, management of diseases starting before birth, and improving the care and health of children and their families. LUMIERE will allow us to understand the importance and function of the placenta in these 1000 days with a depth and breadth previously not achievable. This understanding will no doubt allow us to customize and optimize the nutrition of newborns based on observations made during the pregnancy. For example, expectant mothers and

eventually their newborns may benefit from specific and different nutritional supplements based on the specific types of placental function supporting in utero development prior to birth. This level of nutritional customization opens a new horizon and perspective into the emerging field of personalized medicine. We need you to accompany and support this medical revolution!

Acknowledgements: AP-HP, Université et Faculté de Médecine Paris Descartes, Fondation EDF, Eiffage Energie Systèmes, Forbo, La Pelucherie, General Electric, Fondation LUMIERE

Session 6: Behavior

Imaging the structural and functional development of brain connectivity.

Jessica Dubois, France.

Studying how the infant's brain develops and becomes functional is essential to understand the complexity of neurodevelopmental disorders and the cognitive specificities of the human species. To do so, we need non-invasive neuroimaging approaches that can relate the structural and functional development of the brain in vivo. In the recent years, major advances have been made in magnetic resonance imaging (MRI) techniques that can be combined with complementary electrophysiological approaches or behavioral follow-up to evaluate the children's acquisitions. In particular, the development of brain connectivity has been studied in infants using diffusion MRI and resting-state functional MRI. These studies suggest an early architecture of cerebral networks, with efficient inter-hemispheric connections, as well as asynchronous periods of maturation between functions.

Acknowledgements: Fondation de France, Fondation Fyssen, Human Brain Project.

Agenesis of the corpus callosum : exploring neuroplastic responses in the anterior and posterior commissures.

Vanessa Siffredi, Switzerland.

Developmental absence (agenesis) of the corpus callosum (AgCC) is a congenital brain malformation resulting from the disruption of corpus callosum formation, a structure that is crucial for the transfer and integration of information across the brain. The anterior and posterior commissures have been suggested as potential candidates for alternative inter-hemispheric pathways in individuals with AgCC. I will discuss work from the "Paediatric Agenesis of the Corpus Callosum Project" examining structural and functional properties of the anterior and posterior commissures, including potential neuroplastic responses in the anterior and posterior commissures for cognitive functioning. The project recruited a cohort of 28 children with AgCC from The Royal Children's Hospital in Melbourne, Australia as well as 30 typically developing children aged 8 to 17 years. Children underwent comprehensive neuropsychological and brain MRI. In this work we have used T1-weighted, diffusion-weighted and functional MR sequences to calculate volume, microstructural parameters, tractography and functional connectivity of the anterior and posterior commissures. Changes in the properties of the anterior and posterior commissures will be described, as well as their potential role in understanding the heterogeneity in cognitive functioning.

Acknowledgements: This study was supported by Victorian Government's Operational Infrastructure Support Program, and the Murdoch Children's Research Institute and the Alain Patry Grant from the Geneva Academic Society. Dr Vanessa Siffredi was supported by the Swiss National Science Foundation Doc.CH scholarship. Professor Amanda Wood is supported by a European Research Council Consolidator Fellowship [682734]. Associate Professor Richard Leventer is supported by a Melbourne Children's Clinician Scientist Fellowship. Professor Vicki Anderson was supported by the Australian National Health and Medical Research Council Senior Practitioner Fellowship.

Patients with *ARID1B* mutations (Coffin-Siris syndrome): specific neuropsychological and neuropsychomotor deficits correlated with corpus callosum metrics.

Laurence Vaivre-Douret, France.

ARID1B mutations in Coffin–Siris syndrome are a cause of intellectual disability (0.5–1%), with various degrees of autism spectrum disorder (ASD) and agenesis of the corpus callosum (10%). We aimed to select a paramedian sagittal section of the brain MRI, and corpus callosum was measured in anteroposterior length, genu and trunk width to investigate with standardized assessment tools the neuropsychomotor, neuropsychological and neurovisual phenotypage. Eight patients (mean age: 11 years ± 6 months, range: 3–23 years) with *ARID1B* mutations were included and were recruited from Necker- Hospital and Hospices Civils de Lyon clinical genetics units. Global cognitive testing indicated mild-severe intellectual deficiency in all patients. Three patients met some criteria for ASD and one patient full criteria, but all exhibited inappropriate gaze direction. Spearman analyses show a tendency for negative correlation between a wider genu and with specific variables including neuromotor, motricity, oculomotor and visual fixation, bimanual and digital praxis, rhythm, digital tactile and visual gnosis, perceptivomotor and visual/spatial perception, visuo-spatial attention, visual memory and mental planification functions. Positive correlation was found between the anteroposterior length of the corpus callosum and those neuromotor and cognitive functions. Positive correlation between genu width and visuo-perceptive skills (e.g. visual perception of position) and immediate visual memory. Retro-cerebellar cysts were associated with corpus callosum anomalies. Severity of sensory-motricity and neurovision dysfunctions are linked to the corpus callosum volumetric contributing to identify a deficit of social cognitive skills, language impairment and behavior disturbances that are likely to be associated with some criteria of ASD in *ARID1B* mutations patients.

Social cognition: a comparison of agenesis of the corpus callosum and autism spectrum disorder.

Alice Wright, Rhonda Booth, UK

Agenesis of the Corpus Callosum (AgCC) is associated with a range of neuropsychological outcomes. Difficulties with social communication are common in AgCC and similarities to Autism Spectrum Disorder (ASD) have been highlighted. It has been proposed that the range of outcomes found in AgCC result from a core neuropsychological syndrome, characterized by limited inter-hemispheric transfer of complex information, slowed cognitive processing and difficulties processing tasks which are novel and complex. This suggests that social communication difficulties in people with AgCC are qualitatively different to those found in ASD and should be more pronounced in tasks which require greater interhemispheric transfer and integration of complex information. This study analyses quantitative and qualitative data from a range of social cognition measures including both first and second order Theory of Mind (ToM) tasks (e.g. unexpected transfer task, appreciating humour, faux pas and social attribution). It is hypothesized that the nature of the social cognition impairments in AgCC will be different to those in ASD. Specifically, children with AgCC will only show impairments on complex ToM tasks, which require verbal reasoning compared to more

simple ToM tasks (i.e. those tasks requiring greater interhemispheric transfer and processing of complex, novel tasks) and there will be qualitative differences in responses given. Data comparing three groups, AgCC (n=23), ASD (n=22) and typically developing controls (n=23) will be presented.
Acknowledgements : Alice Wright is funded to complete the MSc in Clinical Paediatric Neuropsychology at UCL Great Ormond Street Institute of Child Health by NHS Firth Valley. This research was kindly supported by a private donor through the Anglo-American Charity Ltd.

Behavioral consequences of callosal malformations.

Lynn Paul, USA.

The corpus callosum, whose roughly 200 million axons constitute the largest white matter tract in the human brain, remains enigmatic in its contribution to cognition and behavior. For two decades, we have been characterizing the cognitive and behavioral features shared among individuals with agenesis of the corpus callosum (ACC), a congenital brain malformation defined by the complete or partial absence of callosal structures. ACC can be an isolated finding but can also co-occur with additional brain malformations and systemic conditions. Adolescents and adults with isolated ACC and normal-range intellectual scores exhibit a shared pattern of limitations in fundamental aspects of cognition including interhemispheric transfer of complex information and processing speed, as well as higher order cognitive skills such as complex novel problem solving, comprehension of second-order meanings in language, and complex theory of mind and social interpretation. Preliminary results are also available from longitudinal studies of cognitive development in infants with ACC. Our research aims to provide a foundation for more accurate cognitive and psychosocial profiling and intervention for people with corpus callosum disorders, while also informing wider central issues in neuroscience, such as functional development of the cortex and neuroplasticity.
Acknowledgements: L. Paul's research on ACC has been supported by the Simons Foundation, a NARSAD Young Investigator Grant, and NIH.

Session Applications Clinique

Imagerie prénatale de l'agénésie du corps calleux : intérêt et limites.

Catherine Garel, France.

Le diagnostic prénatal des anomalies du corps calleux repose sur l'échographie à partir de 22 semaines d'aménorrhée (5 mois). Ce diagnostic est fondé sur la présence de signes directs et indirects observés dans les différents plans de coupe. Les conditions d'examen dépendant du morphotype maternel et de la position fœtale expliquent que certains diagnostics soient faits plus tardivement. Par ailleurs, il existe différents types d'anomalies du corps calleux comprenant son absence totale ou partielle ou des anomalies de sa forme, de sa longueur ou de son épaisseur. Certaines anomalies sont subtiles et peuvent être difficiles à identifier. Par exemple, les lipomes péri-calleux qui sont associés à des anomalies calleuses, peuvent être de très petite taille et identifiés seulement après la naissance. La découverte d'une anomalie du corps calleux en prénatal implique sur le plan de l'imagerie la recherche en échographie d'anomalies associées soit intra, soit extra-cérébrales qui peuvent avoir un impact sur le pronostic. La recherche d'anomalies intracérébrales repose également sur l'IRM qui est réalisée idéalement vers 32 semaines d'aménorrhée (7 mois) car il faut prendre en compte la chronologie du développement cérébral. Toutefois, au terme de ce bilan d'imagerie, il est possible que des anomalies ne soient pas détectées pendant la période anténatale.

Génétique des anomalies du corps calleux.

Tania Attié-Bitach, Solveig Heide.

Le corps calleux (CC) est la principale commissure cérébrale connectant les aires corticales homologues des deux hémisphères. Les anomalies du corps calleux sont classiquement subdivisées en agénésie complète ou partielle, hypoplasies et dysplasies ou hypodysplasies. Leur prévalence est estimée à 1/4,000 naissances. Les causes sont variables, comprenant des anomalies chromosomiques, géniques, ou exogènes. Le pronostic neurodéveloppemental est variable, dépendant de la cause sous-jacente, et le plus souvent sans déficience intellectuelle dans les anomalies isolées. Les méthodes actuelles d'exploration du génome (caryotype, CGH, panel de gènes, exome) permettent d'identifier une cause génétique dans 30 à 40 % des cas. L'apport et les limites de ces méthodes, ainsi que les principales causes génétiques seront présentées.

Séquençage d'exome en prénatal dans les agénésies du corps calleux: résultat d'une étude pilote.

Delphine Héron, France.

Les agénésies du corps calleux (ACC) sont diagnostiquées en prénatal par échographie pendant le 2ème trimestre de la grossesse. Si l'ACC est isolée, le pronostic neuro-développemental est incertain : 70 à 80% des patients auront un développement normal, alors que 20 à 30% des patients auront des troubles intellectuels plus ou moins sévère. Le pronostic des ACC dépend de l'étiologie génétique. En France, seules les atteintes chromosomiques sont inspectées dans le cas d'un diagnostic prénatal d'ACC, et aucune étude moléculaire n'est proposée. Objectif : Notre étude a pour but d'évaluer la faisabilité d'une étude prénatale des gènes responsables des ACC par whole exome

sequencing (WES), dans le cas d'une ACC détecté par échographie. Matériel et méthodes : Nous avons effectué des séquençages haut débit du whole exome (WES) en trio, avec de l'ADN fœtal extrait du liquide amniotique. Nous avons seulement regardé les variants pathogènes connus dans les cas d'ACC. Les variants de significations inconnus (VUS) et les autres observations n'ont pas été prise en compte. Résultats : Nous avons inclus 18 couples. Les résultats du séquençage haut débit du whole exome sont généralement disponible en 21 jours. 13 WES étaient normaux (pas de variant pathogènes connu dans les ACC). Dans deux cas, un variant pathogène dans un gène responsable d'ACC avec déficience intellectuelle a été identifié (BRAT1, PPP2R1A) et une variation du nombre de copie (VNC) pathogène a également était identifié dans un cas (6q27del). Nous avons retrouvé un VUS dans 2 cas. Conclusion : Les études préliminaires confirment la faisabilité d'un whole exome sequencing quand une ACC est diagnostiquée pendant la grossesse. Cette méthode est nécessaire pour affiner le pronostic et aider les couples à prendre une décision sur le futur de la grossesse. Cependant, cette approche durant la période anténatale pose un nombre de question éthique.
Acknowledgements: APHP

Aspects cognitifs et psychoaffectifs des enfants suivis pour une agénésie du corps calleux

Emmanuelle Lacaze & Kim Giraudat, France.

Un certain nombre de travaux de recherche portant sur les enfants qui naissent avec une agénésie du corps calleux ont été menés afin de répondre aux questionnements suscités par cette malformation cérébrale : Comment se développent-ils ? Quel est leur fonctionnement cognitif ?
Ces études ont montré l'existence de capacités intellectuelles préservées dans 70 à 80% des cas, mais aussi d'un certain nombre de troubles des apprentissages, le profil neuropsychologique et la sévérité des troubles cognitifs de ces enfants variant selon l'étiologie génétique (ACC associée ou isolée).
Cette présentation aura pour objectif de présenter l'évolution du discours médical et du suivi de ces enfants au regard des connaissances médicales et neuropsychologiques ainsi que les données issues des évaluations neuropsychologiques réalisées depuis 2004 au sein du service de neuro-pédiatrie de l'Hôpital Trousseau.

Les grandes étapes du diagnostic prénatal des anomalies calleuses.

Jean-Marie Jouannic, France.

Le diagnostic prénatal d'agénésie calleuse impose la réalisation d'une neuro-imagerie de référence reposant sur l'échographie et l'IRM idéalement réalisée vers 7 mois de grossesse afin de vérifier le caractère isolé ou associé de l'anomalie. Dans le cadre du bilan prénatal une étude du caryotype et par ACPA est proposée aux patientes. De nouvelles techniques de génétique devraient permettre de mieux affiner le pronostic de ces anomalies. L'ensemble de ces examens a pour but d'estimer le risque de survenue d'un retard du neuro-développement, notamment observé dans les formes d'anomalies calleuses associées. L'attente des rendez-vous et des résultats d'examens en cours de grossesse est une grande source d'anxiété pour les couples.

Accompagnement médico-social.

Béatrice Langellier-Bellevue, France

Les conséquences d'une agénésie du corps calleux sont très variables d'une personne à l'autre et nous ne pouvons pas préconiser une prise en charge médico-sociale type. Cependant, il nous parait important, d'informer les familles des droits auxquels ils peuvent prétendre afin d'améliorer leur vie quotidienne, des personnes ressources existantes qui pourront les guider dans leur prise en charge.

Maladies rares en France et en Europe, intérêt d'une association de patients.

Laëtitia Domenighetti, France.

Chaque jour les associations apportent un soutien moral aux familles touchées par les maladies rares, information et réconfort pour sortir de l'isolement dans lequel le diagnostic ou la maladie nous plongent. Il est fondamental de pouvoir s'entourer et trouver une aide dans ces situations, auprès d'une association de patients. Les Associations en France ont joué un rôle majeur pour les maladies rares: par la force du Collectif, elles portent la voix des millions de malades. Cette mobilisation a permis que soient mis en place trois plans nationaux maladies rares

Clinical Applications session (with Families).

Abstracts in English.

Prenatal imaging of corpus callosum agenesis : interest and limits.

Catherine Garel, France

Prenatal diagnostic of corpus callosum abnormalities is based on ultrasound from the 22nd week of amenorrhea (5 months). This diagnosis is based on the presence of direct and indirect signs observed on different sectional plans. The ultrasound examination depends on the maternal morphotype and the fetal position, explaining why some diagnosis are made later in pregnancy. There are different types of corpus callosum abnormalities, including a total or partial absence, an abnormal shape, length or thickness. Some anomalies can be subtle and difficult to identify. For example, pericallosal lipomas, which are associated to callosal abnormalities, can be very mall and identified only after birth. The prenatal discovery of an abnormality of the corpus callosum leads to the search, by echography, for intra or extra cerebral associated anomalies, which may have an impact on the prognosis. The intra-cerebral search of abnormality is also done by a MRI, ideally performed around 32 weeks of gestation (7months), because we have to take into account the chronology of the cerebral development. However, some abnormalities might be not detected prenatally.

Genetics of corpus callosum agenesis.

Tania Attié-Bitach & Solveig Heide, France

The corpus callosum (CC) is the main cerebral commissure connecting the homologous cortical areas of both hemispheres. Abnormalities of the corpus callosum are classically classified as complete or partial agenesis, hypoplasias (HCC) and dysplasias or hypodysplasias. Their prevalence is estimated at 1/4 000 births. Their causes are highly variable including chromosomal and monogenic disorders, or exogenous etiologies. The neurodevelopmental outcome is variable, depending on the underlying cause, and most often without intellectual disability in isolated agenesis of the corpus callosum. Current technologies used for genetic analysis (karyotyping, arrayCGH, gene panel, whole exome sequencing) make it possible to identify a genetic cause in 30 to 40% of cases. Impact and limits of these methods as well as the main genetic causes will be presented.

Prenatal whole exome sequencing in agenesis of the corpus callosum: a French experience.

Delphine Héron, France

Introduction: Agenesis of the corpus callosum (ACC) is diagnosed by prenatal ultrasound examination (US) during the 2nd trimester of pregnancy. If ACC is isolated, the neurodevelopment prognosis is uncertain: 70 - 80 % of patients will have normal development whereas 20 - 30 % of patients will present with mild to severe intellectual disability. The prognosis of ACC depends on its genetic etiology. In France, only chromosomal causes are investigated in case of prenatal diagnosis of ACC and no

molecular study is proposed. Objective: Our study aims to evaluate the feasibility of prenatal study of genes responsible for ACC by whole exome sequencing (WES), in case of ultrasound diagnosis of ACC. Material and methods: We performed trio WES with fetal DNA extracted from amniotic fluid. We reported only pathogenic variants in known genes for ACC. Variants of unknown significance (VUS) and secondary findings were not reported/sought. Results: We included 18 couples. The WES results were available within 21 days in average. Thirteen WES were normal (no pathogenic variant in known genes of ACC). In two cases, a pathogenic variant in a gene responsible for ACC with ID were identified (BRAT1, PPP2R1A) and a pathogenic copy number variant was identified (6q27 deletion) in one case. We identified a VUS in 2 cases. Conclusion: Preliminary results confirm the feasibility of prenatal WES when ACC is diagnosed during the pregnancy. WES is necessary to refine the prognosis and helps the couples to take a decision about the outcome of the pregnancy. However, this approach during the prenatal period arises questions about its ethical implications.

Cognitive and psycho-affective aspects of children followed for agenesis of the corpus callosum.

Emmanuelle Lacaze & Kim Giraudat, France

Several research studies on children born with agenesis of the corpus callosum were conducted to answer the questions raised by this cerebral malformation: How do they develop? How is their cognitive functioning?

These studies have shown that intellectual abilities are preserved in 70 to 80% of cases, but also the existence of learning disorders, the neuropsychological profile and the severity of the cognitive disorders of these children are variable, according to the genetic etiology (associated or isolated ACC).

This presentation will present the evolution of the medical discourse and the follow-up of these children with regard to the medical and neuropsychological knowledge as well as the data resulting from the neuropsychological evaluations carried out since 2004 within the neuropediatric department of Trousseau hospital.

The main steps of prenatal diagnosis of callosum abnormalities.

Jean-Marie Jouannic, France

Prenatal diagnosis of corpus callosum agenesis implies a neuro-imaging including an echography and a MRI ideally performed around the 7th month of pregnancy, to check weather this anomaly is isolated or associated. As part of the prenatal statement, a chromosomal analysis is also proposed to the patients. New genetic techniques should help make a better prognostic of these abnormalities. These investigations aim to estimate the neurodevelopmental outcome, as delay are mainly observed in associated form of corpus callosum abnormalities. Parents should be accompanied during the whole prenatal diagnosis process as uncertainty on the prognosis is a source of major anxiety.

Overview of medico-social support.

Beatrice Langellier-Bellevue, France

The consequences of a corpus callosum agenesis are very different from a person to another, and we can not suggest a "standard" medico social care. However, it is important to inform families of their rights, existing resources and persons that might improve their lives, and support their care.

Rare diseases in France and Europe, interest of a patient organization.

Laetitia Domeghetti, France

Every day, organizations provide psychological support to families affected by rare diseases, information and comfort to get out of the isolation in which the diagnosis or disease leaves us. It is very important in these situations to be surrounded and find help with a patient organization. Patient organizations in France played a major role for rare diseases: by the strength of alliance, they carry the voice of millions of patients. This mobilization allowed the establishment of three national rare disease plans.

Abstracts / Posters

Mutations in the *KIF21B* kinesin gene are associated with intellectual disability and cause microcephaly and corpus callosum agenesis.

Laure Asselin*, Solveig Heide, José Riveira Alvarez, Camille Bonnet, Peggy Tilly, Hélène Vitet, Chantal Weber, Carlos Bacino, Anna Chassevent, Sonal Desai, Laurence Faivre, Cyril Mignot, Caroline Nava, Agnès Rastetter, Janneke M Weiss, Petra Zwijnerburg, Frédéric Saudou, Christel Depienne, Christelle Golzio, Delphine Héron, Juliette D Godin*, **Institut de Génétique et de Biologie Moléculaire et Cellulaire, Illkirch, **France**.*

Cortical development is a highly regulated process that progresses through concurrent steps, including progenitor proliferation, neuronal migration, differentiation and formation of axonal connections within and between right and left hemisphere. Proper cortical development relies on dynamic cell shape remodeling which largely depends on the tight regulation of the microtubules (MT) cytoskeleton. KIF21B is a plus-end directed kinesin motor protein highly enriched in neurons that promotes intracellular transport and controls microtubule dynamics. Here we identified four variants in KIF21B in individuals with intellectual disability associated with cortical malformations including corpus callosum agenesis (ACC) and microcephaly. In support of the pathogenic potential of the discovered alleles, expression of missense KIF21B variants in mice using in utero electroporation or in zebrafish embryos recapitulated key neurodevelopmental phenotypes, including impaired neuronal positioning, microcephaly and decreased intra- and inter-hemispheric connectivity. We establish that *KIF21B* variants act both as gain-of-function and dominant negative mutations, likely through dysregulation of canonical kinesin motor activity. We further show that the ACC-related KIF21B variant independently perturbs axonal growth and ipsilateral axon branching through gain-of-function and dominant negative mechanisms respectively, deregulating KIF21B motor activity. Altogether, our data indicate that disturbance in KIF21B autoregulation and function plays a critical role in the pathogenicity of human cortical malformations including corpus callosum agenesis.

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Laure is a PhD student under the supervision of Dr. Juliette Godin at the IGBMC. Her work focuses on the functions of the kinesin KIF21B during cortical development.

An absence of axonal rerouting through alternative commissural pathways in corpus callosum dysgenesis.

Ryan J. Dean*, Timothy J. Edwards,Yunan Ye, Jacquelyn Knight, Laura R. Fenlon, Simon A. Mandelstam, Gail A. Robinson, Linda J. Richards*

Queensland Brain Institute, The University of Queensland, St. Lucia, Queensland **Australia.*

Individuals with corpus callosum dysgenesis (CCD) lack the clear disconnection syndrome characteristic of individuals in whom the corpus callosum has been surgically severed. One possible explanation for this paradox is the rerouting of axons via alternative commissural routes to connect the contralateral hemisphere. To investigate this possibility, a cohort of eleven individuals with complete and partial CCD and eleven age- and sex-matched controls were scanned at 3T and 7T using a multi-shell diffusion magnetic resonance imaging (MRI) sequence. We found no significant difference in midsagittal anterior commissure area between CCD and controls, nor in measures of commissural axon diameter, density, compartmental volume fraction, fractional anisotropy or mean diffusivity. To test for brain rewiring through the anterior and posterior commissures, we also performed diffusion tractography on all participant data sets. While we were able to replicate a previous finding of homotopic connections in CCD between parietal cortices from the anterior commissure and posterior commissure, these connections were also generated in controls with an intact corpus callosum. These findings were reproducible using different probabilistic and deterministic tractography algorithms, seeding strategies, and streamline parameters. To examine this further we performed tractography and histological tract tracing in BTBR/C57Bl6 mice with CCD and identified the formation of ectopic Probst bundles but no evidence of significant re-routing of axons via the anterior or posterior commissures. Together, this data suggests that in both mice and humans in our cohort with CCD, homotopic neocortical projections are not re-routed via the anterior and posterior commissures.

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Ryan graduated with his PhD from Western Sydney University in 2016 where he studied the physics of magnetic resonance imaging under Prof. William S. Price. Since graduating, Dr Dean has been employed at the Queensland Brain Institute (QBI), first as research assistant and later as a postdoctoral researcher, under the supervision of Prof. Linda Richards. Dr Dean currently leads several human imaging projects under Prof. Richards leadership, including investigations into the structural and functional reorganisations in disorders of the corpus callosum and autism spectrum disorders, and also currently holds the position of secretary for the IRC5 Imaging Working Group.

A novel MR based scoring system for prenatal neurodevelopmental outcome prediction in isolated callosal agenesis.

Sarah Glatter*, Mariana C. Diogo, Rainer Seidl, Dieter Bettelheim, Gregor J. Kasprian*. **Department of Pediatrics and Adolescent Medicine, Medical University of Vienna, **Austria.***

Objectives: Predicting neurodevelopmental outcome in children with agenesis of the corpus callosum (ACC) remains a challenge. Until now, prenatal imaging was unable to reliably identify those 20% of "isolated" ACC cases, who reportedly suffer from significant cognitive impairments postnatally. In this prospective study, a novel fetal MRI based scoring system was applied to predict neurodevelopmental outcomes in complete and/or partial ACC cases, which were classified as "isolated" by state-of-the-art prenatal neuroimaging. Methods: The MR based scoring system included a variety of morphological features such as brain opercularization, (a-)symmetry, sulcation/gyration, lamination, colpocephaly, parenchymal loss as well as hippocampal positioning and size. MRI features were scored independently by two neuroradiologists, blinded to the cognitive outcome, using a standard fetal MRI protocol (T2, T1, DWI, EPI). Neurodevelopmental outcomes were tested by a neuropediatrician and/or psychologist using Bayley Scales - Third Edition (BSID-III) and the Kaufman Assessment Battery for Children – Second Edition (KABC-II), depending on the age of the children. Results Average gestational age at MRI was 28 weeks. Average age at postnatal evaluation was 24.5 months (range 7-69 months). Neurodevelopmental cognitive outcome was normal in 71% (10/14) and motor outcome was in the average range in 64% (9/14) of the children. There was significant negative correlation between ACC MRI-Score and neurodevelopmental outcomes for cognition ($r = -.66$, $p = .01$) and motor skills ($r = -.55$, $p = .04$). All patients could be classified by MR Score in three predicting outcome groups: good, moderate and severe. Conclusions: The MR based score improves prognostication of fetuses with partial and/or complete isolated callosal agenesis. Specific fetal MR features seem to correlate to deficits in certain neurocognitive domains.

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Sarah has been studying human medicine (MD, N202) for 5 years at the Medical University of Vienna. From 2016, she has completed a BSc at the University of Vienna, and is in a MSc-Program Psychology (diploma thesis: developmental psychology). From 2018, she has entered a excellence-PhD Program (094). Sarah has in neuroscience lab experience: immunohistochemistry and cell culture.

Functional and structural plasticity in one hour: a neurofeedback by fMRI study.

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Introduction The corpus callosum (CC) is the greatest commissure of the human brain, and understanding its plastic proprieties and investigating effective ways of induce changes in its structure and function are important steps toward rehabilitation and development of new therapeutic tools. In this randomized, double-blind and placebo-controlled study, we used brain training with neurofeedback (NFB) by fMRI (1,2) to induce brain plasticity at record speed. Methods Thirty-six healthy volunteers (NFB group, n= 19; sham (control) group, n=17) underwent the study that consisted in 3 runs (6 minutes each) of NFB training with motor imagery. With the aid of the real-time NFB, participants were instructed to mimic motor execution brain patterns while performing motor imagery. Diffusion-weighted and resting state imaging were acquired before and after the training. Sham group participants were unwittingly trained with false feedback. Total scan time was approximately 1 hour, performed in a single visit. Results/Conclusion The present study was recently published (3) and showed that less than one hour of NFB training can induce increased connectivity strength of both default mode (DMN) and sensorimotor networks, and in the FA of the sensorimotor segment of corpus callosum. These results were not observed in the Sham group. Development of optimized therapeutic approaches relies on our understanding of the depth of how we can promote brain plasticity in the normal and diseased brain, thus the present study paves the way for improvement of future strategies. *References (1) Sitaram, R., Ros, T., Stoeckel, L., Haller, S., Scharnowski, F., Lewis-Peacock, J., Weiskopf, N., Blefari, M.L., Rana, M., Oblak, E., Birbaumer, N., Sulzer, J., 2017. Closed-loop brain training: The science of neurofeedback. Nat. Rev. Neurosci. 18, 86–100. (2) Marins, T.F., Rodrigues, E.C., Engel, A., Hoefle, S., Basílio, R., Lent, R., Moll, J., Tovar-Moll, F., 2015. Enhancing Motor Network Activity Using Real-Time Functional MRI Neurofeedback of Left Premotor Cortex. Front. Behav. Neurosci. 9, 1–12. (3) Marins, T; Rodrigues, E; Bortolini, T; Melo, B; Moll, J; Tovar-Moll, F, Structural and functional connectivity changes in response to short-term neurofeedback training with motor imagery. Neuroimage, in press.*

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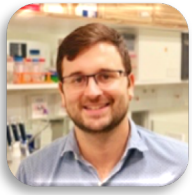

Theo holds an MSc and a Ph.D. degree in Morphological Sciences obtained at Federal University of Rio de Janeiro, Brazil, in 2014 and 2018, respectively. As a postdoctoral at the D'Or Institute for Research and Education (IDOR), Marins has been using advanced protocols of brain imaging to investigate the impact of brain malformations, congenital blindness, amputation and training on brain structural and function. Alongside his activities as a young neuroscientist, his interests are to develop science communication and public engagement on neuroscience and to train and develop new students on brain imaging methods.

Early callosal fate of most cortical neurons.

Noelia Sofia De León Reyes*, Sara Mederos, Inés Varela, Linnea Weiss, Gertrudis Perea, María Galazo, Marta Nieto López*. **Centro Nacional de Biotecnología (CNB-CSIC), **Spain**.*

Axons of the corpus callosum (CC) establish selective interhemispheric connections that facilitate the higher order functions of the cerebral cortex. According to current views, neurons wire following strict rules that are set intrinsically, and early decisions on axonal development determine callosal or non-callosal fate at a neuron's birth. Using a novel axonal-retrotracing strategy we instead demonstrate that most cortical pyramidal neurons project calosally initially. Precise adult connectivity emerges when developmental contralateral axons are extensively refined in area- and layer-specific manners. Surgical and genetic interventions demonstrate that refinement is plastic and depends on specific sensory input from distinct thalamic-nuclei. Loss of thalamic innervation results in structural and functional interhemispheric hyperconnectivity, demonstrating the bonafide early callosal fate of cortical neurons. Thus, during their selective wiring, cortical neurons overshoot and subsequently discard primed alternative circuits according to the circuit input. This wiring mode may ensure the optimal formation of complex functional circuits and explains the remarkable early plasticity of neurons.

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Noelia is on her 4th year of thesis. Her thesis project has been focused on understanding the mechanisms that governs the formation of the Corpus Callosum during development. They have demonstrated that contrary to current knowledge most cortical neurons have early callosal projections that are lately refined in a sensory-specific manner during postnatal life. She really is motivated to continue her formation and research in order to help the understanding of cortical networks and how different developmental alterations can lead to alternative circuits or neuronal pathologies.

A reduced version of corpus callosum? The pattern of transcallosal connections in the partial dysgenesis of corpus callosum.

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The dysgenesis of the corpus callosum (DCC) is a congenital malformation that affects the correct formation of the corpus callosum (CC). In cases of partial DCC, it is common to observe a hypoplasic CC or the anterior remnant of the CC (genu). Despite advances on the plastic changes in DCC, including the observation of the Sigmoid Bundle (1,2), it is not clear whether the interhemispheric cortical connectivity via CC in partial DCC follows the connectivity pattern observed in neurotypical individuals. Here, we hypothesized that in both cases of partial DCC (hypoplasia and when only the genu is present) the cortical projections of CC might not resemble those observed in controls. Five subjects with DCC (four with hypoplasia and one with partial agenesis) and four controls underwent the anatomical and diffusion-weighted magnetic resonance brain imaging protocol (Siemens 3T Prisma), according to the Human Connectome Project Pipelines. We used probabilistic tractography to perform the hard segmentation of the CC based on its pattern connectivity (3,4) to the prefrontal, temporal, motor, somatosensory, posterior parietal and occipital cortices. Contrary to what is observed in typical individuals, preliminary results point that in cases of partial DCC the CC shows abnormal projections to the cortex. Despite radiological/anatomical midline similarities to the typical portions of the normal CC, the remnant genu or the hypoplasic CC assume an abnormal pattern of connectivity. However, more studies are necessary to confirm our findings and to investigate their impact on behavioral aspects of DCC.

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Lucas holds a degree in psychology. In parallel, he develops research on neuroplasticity in patients with dysgenesis of the corpus callosum, at the interface with magnetic resonance imaging and cerebral connectivity.

Mutations in tubulin genes are associated with abnormal decussation of the corticospinal tract and mirror movements.

Ashley PL Marsh*, Timothy J. Edwards, Charles Galea, Ryan Dean, Jennifer Dempsey, Vesna Lukic, Wei Shern Lee, Greta Gillies, Kate Pope, Zornitza Stark, George Mcgillivray, Simone Mandelstam, Mai Raabus, Peter Farlie, Dong Zhang, Don Newgreen, Bryn Webb, Ethylin Jabs, Guy Rouleau, Sarah Stephenson, Delphine Heron, Mathilde Nizon, Tally Lerman-Sagie, Melanie Bahlo, Linda Richards, Richard Leventer, Dan Doherty and **Paul Lockhart*** ** Bruce Lefroy Centre for Genetic Health Research, Murdoch Children's Research Institute, Royal Children's Hospital, Parkville, Victoria,* ***Australia.***

Background: Tubulinopathies are a spectrum of disorders characterized by disturbances to neuronal development and axon guidance. These disorders are caused by mutations in tubulin genes, whose translated products form the building blocks of microtubules, proteins indispensable for nervous system development. While the spectrum of brain abnormalities stemming from neuronal defects are well-characterized, those potentially arising from abnormal axon guidance remain poorly defined. Methods: Clinical information was obtained by review of medical records and examination of affected individuals. Genetic sequencing studies were used to investigate the molecular basis of disease. MRI and probabilistic constrained spherical deconvolution MRI tractography were utilized to assess brain structure and corticospinal (CS) tract wiring. Findings: We identified a novel *TUBB3* mutation in a family with three affected individuals presenting with a complex array of developmental brain malformations, including callosal dysgenesis, and mirror movements (MMs). Tractography identified decreased crossing of descending CS tract projections at the pyramidal decussation in the affected individual available for scanning. Subsequent clinical examination of a tubulinopathy cohort detected MMs in at least one affected individual from all 11 additional families screened (TUBB3, n=7; TUBB, n=2; TUBA1A, n=1 or TUBB2B, n=1). Interpretation: We describe 12 families with classical tubulinopathy features, in addition to MMs, a phenotype not previously associated with this spectrum of disorders. Tractography revealed a failure of CS axonal decussation at the midline, consistent with previous MMs studies. Overall, this study provides insight into a potential novel function of tubulins in the guidance of the CS tract at the midline.

Acknowledgements : NHMRC Project Grant (APP1059666) and NHMRC Early Career Fellowship (APP1156820).

Ashley : Postdoctoral Scholar and NHMRC CJ Martin Early Career Fellow working in the Gleeson Laboratory for Pediatric Brain Disease at the University of California, San Diego. Ashley received her PhD in Neurogenetics (Dissertation: Determining the Genetic Control of Corpus Callosum Development) from the University of Melbourne in 2018, under the supervision of Assoc. Pr. Paul Lockhart and Assoc. Pr. Richard Leventer, at the Murdoch Children's Research Institute. She utilized modern genomic technologies to identity and characterize novel disease genes, including the first genetic cause of isolated ACC, published in Nature Genetics (Marsh et al., 2017). Ashley has a strong interest in brain wiring and brain rewiring in the context of neurodevelopmental disorders such as ACC and mirror movements.

Conference Speakers, IRC5 Members & Affiliates Biography

Tania Attie-Bitach, is Professor at Paris Descartes University and a human geneticist specialized in molecular genetics and fetal pathology. She developed a clinical and genetic research on human fetal disorders at Imagine institute, in Necker Medical School. She has driven several projects leading to the identification of genes responsible for ciliopathies and other lethal disorders such as Matthew-Wood and Fowler syndromes. She recently lead a national project (ABM, ANR Cilaxcal) aiming to characterize the genetic causes of isolated and syndromic causes of corpus callosum anomalies in human. **IRC5 Board Member & Conference Speaker.**

Nadia Bahi-Buisson, is Child Neurologist, conducting the rare disease program on Rett syndrome and brain malformation at Necker Enfants Malades University Hospital in Paris. Paris. She is part of the group "Genetics and Cerebral cortex development" (A. Pierani) at Imagine Institute (INSERMU1163). She's interested in understanding the cellular and molecular mechanisms of brain development, especially neurogenesis, and neuronal migration. Her main goal is to understand the molecular basis of Malformations of Cortical Development that are important causes of intellectual disability and account for 20-40% of drug-resistant childhood epilepsy. She conducts integrated multidisciplinary studies involving cellular and molecular biologists, foetal pathologists and radiologists with a wide range of approaches including genetics, biochemistry and cellular biology to better understand the signaling pathways involved in these processes and how their dysregulations can lead to pathologies. **IRC5 Affiliate.**

Anais Bellon is a research scientist at the Mediterranean Institute of Neurosciences of the University of Aix-Marseille, France. Her research focuses on the molecular mechanisms, including epigenetic regulations that control brain wiring. She has recently developed a new mouse model of fetal alcohol spectrum disorders and is investigating whether the deregulation of axonal microRNAs induced by prenatal alcohol exposure contributes to the pathological rewiring of brain circuits, including the callosum corpus. **Conference Speaker.**

Nathalie Boddaert is head of pediatric radiology department in Necker's Hospital. **IRC5 Affiliate.**

Ronda Booth is a Senior Teaching Fellow at UCL Great Ormond Street Institute of Child Health for the MSc in Clinical and Applied Paediatric Neuropsychology. Her primary research interests are in the neurological underpinnings of cognitive and social development. Dr Booth worked as an Applied Psychologist specializing in the assessment and remediation of specific learning disabilities in Auckland, New Zealand, prior to completing her PhD at the Institute of Psychiatry, King's College London. Postdoctoral work included studying the social and cognitive profile of individuals with disorders of the corpus callosum. **IRC5 Member.**

Lucile Boutaud is a medical biologist, and worked for 4 years in Necker Hospital in the molecular embryology Team directed by Pr. Tania Attie Bitach. She was especially on charge of molecular diagnosis in patients and fetus with corpus callosum malformations by a next generation sequencing panel at the lab. She's now doing her PhD with Pr Attie Bitach, on functional analysis of a candidate gene in human cerebral development. **IRC5 Affiliate.**

Warren S. Brown is Professor of Psychology and Director of the Lee Travis Research Institute at the Graduate School of Psychology, Fuller Theological Seminary. He is a research neuropsychologist /neuroscientist interested in the cognitive and psychosocial impact of a congenital brain malformation (agenesis of the corpus callosum and hemispherectomy) and has coauthored over 80 peer reviewed scientific articles. He is also author or editor of 4 books on neuroscience and philosophy/religion (Whatever Happened to the Soul, edited with Nancey Murphy and H. Newton Malony; Did My Neurons Make Me Do It?, with Nancey Murphy; Neuroscience, Psychology and Religion, with Malcolm Jeeves; and Physical Nature of Christian Life with Brad Strawn). **IRC5 Board Member.**

Alain Chedotal is currently Research director (DRCE) at INSERM, and group leader at the Vision institute in Paris. He was an undergraduate at the ENS and Lyon University and received his PhD degree from Pierre & Marie Curie University in Paris for graduate work with Constantino Sotelo on cerebellum development. He moved to UC Berkeley and completed his postdoctoral research with Corey Goodman where he worked on axon guidance and semaphorins. He was recruited at INSERM in 1997 and started his own laboratory at the Salpetriere Hospital in Paris. He moved to the Institut de la Vision in 2008. Dr Chedotal was elected at the Academia Europaea, the French Academy of Sciences and is a member of the European Dana alliance for Brain Initiatives (EDAB). His lab studies axon guidance, neuronal migration and angiogenesis and has pioneered the use of tissue-clearing methods and light sheet microscopy to study embryogenesis. **IRC5 Affiliate & Conference Speaker**

Ryan Dean is graduated with his PhD from Western Sydney University in 2016 where he studied the physics of magnetic resonance imaging under Prof. William S. Price. Since graduating, Dr Dean has been employed at the Queensland Brain Institute (QBI), first as research assistant and later as a postdoctoral researcher, under the supervision of Prof. Linda Richards. Dr Dean currently leads several human imaging projects under Prof. Richards leadership, including investigations into the structural and functional reorganizations in disorders of the corpus callosum and autism spectrum disorders, and also currently holds the position of secretary for the IRC5 Imaging Working Group. **IRC5 Affiliate.**

Ghislaine Dehaene-Lambertz is a pediatrician and director of the developmental brain imaging lab (INSERM U992, Neurospin/CEA, Paris-Saclay, France), she and her team investigate the development of cognitive functions in infants and children using brain imaging techniques. Their goal is to understand how complex cognitive functions, such as language, music, mathematics, etc., emerge in the human brain, thanks to a thorough description of the brain initial structural and functional organization. **Conference Speaker.**

Christel Depienne is Associate Professor at the University Hospital of Essen, Germany. She received a PhD in molecular and cellular biology in 2000 and has been working on genetics of human brain disorders since 2002. She has been responsible for genetic testing of neurological disorders (hereditary spastic paraplegia, epilepsy, intellectual disability) and in parallel, has developed research projects as principal investigator focusing on the identification of genes involved in several neurodevelopmental disorders (epilepsies, intellectual disability, autism spectrum disorders, mirror movements and more recently agenesis of the corpus callosum) and establishment of genotype-phenotype correlations. **IRC5 Board Member.**

Vincent Des Portes is Professor of Pediatrics at Medical School Lyon Sud, University Lyon 1 in France. He is the head of the department of child neurology at University Hospital HFME in Lyon and leads the French Rare disease Network "DefiSciences". He coordinates three Inter University Diploma in the field of neurodevelopmental disorders. He is a scientific expert for START Project: translational Teaching in NDD (funded by CNSA, ARS IDF/ARA). His research activity at Institute for Cognitive Science (ISC) in Lyon is oriented towards Neuronal Networks and cognitive processes in X-Linked Intellectual Disabilities. He is investigator (PI for France) in 5 Multisite pharmacological trials in Fragile X Syndrome. Publications: 148 citations in PubMed. **Conference Speaker.**

Laëtitia Domenighetti is a project manager within AnDDI-Rares (Rare Disease Health Network). She is also the mother of a child with a rare disease, she was president of a national patient organization for 3 years and still in charge of Communication for this organization. **Conference Speaker.**

Jessica Dubois is a neuroscience researcher at INSERM (Paris, France), in the NeuroSpin center (CEA) and the Robert Debré Children's Hospital (Neuro-Diderot Unit). She obtained an engineering degree in 2001 and a PhD in Physics in 2006. Her researches are focused on the early development of the human brain, which she studies in premature newborns and infants with non-invasive neuroimaging techniques such as MRI combined with dedicated post-processing tools. She has detailed how the infant brain is organized at the structural level, showing the early architecture and the progressive myelination of white matter bundles. She also described how the brain cortex develops by measuring the intense folding process and microstructural changes from the pre-term to early post-term period. For the visual and auditory modalities, she has linked the speed of functional responses and the maturation of underlying pathways by studies combining MRI and EEG. **Conference Speaker.**

Timothy J. Edwards is a medical doctor and PhD student from the Queensland Brain Institute in Brisbane, Australia. The focus of his research is how structural connectivity is reorganized in brain malformations such as agenesis of the corpus callosum. To achieve this, he uses high field diffusion MRI in humans and animal models to investigate in vivo models of structural plasticity. **IRC5 Affiliate.**

Sonia Garel heads the team Brain Development and Plasticity at the Institut de Biologie de l'Ecole Normale Superieure (IBENS) in Paris (France). Her research focuses on understanding the logic that controls the assembly of forebrain neural circuits during embryogenesis and postnatal development, with a particular emphasis on interactions with the immune system and the environment. After earning her PhD in Developmental Biology in Paris, she completed a post-doctoral stay in UCSF (San Francisco, USA). Since 2008, she is heading the team Brain Development and Plasticity and is a recipient of the HSFP Career Development Award, the European Young Investigator Award (EURYI), the ERC consolidator program and is an EMBO member. **Conference Speaker.**

Catherine Garel is a Consultant Pediatric Radiologist and an Associate Professor, she is also a visiting Senior Lecturer of the Sackler Faculty of Medicine in Tel Aviv. She works in Paris in a tertiary prenatal center, in a pediatric hospital, Hôpital d'Enfants Armand-Trousseau, which belongs to Sorbonne University. She is specialized in prenatal imaging and has written four books in this field and about 180 peer-reviewed articles in international journals. She started performing prenatal ultrasound in 1992 and is considered a referent specialist in this field in France and worldwide. She gives second (or very often third) opinions in many cases and women coming from France. Very few physicians worldwide perform prenatal US as well as MRI. She gives a lot of lectures and organizes or participates to numerous post-graduate educational programs in France and abroad. She is also a member of the editorial boards of Pediatric Radiology and Ultrasound Obstetrics and Gynaecology. **IRC5 Affiliate & Conference Speaker.**

Kim Giraudat works as a neuropsychologist in paediatric neurology and sees the patients who have agenesis of the corpus callosum to assess their neurocognitive functioning. **IRC5 Affiliate & Conference Speaker.**

Laurent Guibaud is Professor of radiology with a special expertise in prenatal imaging, especially in both ultrasound and MR analysis of fetal brain, which the main topic of his international publications. **Conference Speaker.**

Solveig Heide is a clinical geneticist in Pitié-Salpétrière Hospital, in Delphine Heron's team. During her master degree, she worked on genetic causes of ACC. **IRC5 Affiliate & Conference Speaker.**

Delphine Héron is a Pediatrician and geneticist at the Pitié-Salpétrière Hospital in Paris. **IRC5 Member & Conference Speaker.**

Ruiji Jiang is an MD/PhD candidate at the University of California San Francisco, currently completing his graduate work in Elliott Sherr's lab researching disorders of the corpus callosum, specifically how genes *C12ORF57* and *DDX3X* contribute to brain development and disease. He earned his BS at Duke University where he previously worked in the lab of Rasheed Gbadegesin. **IRC5 Affiliate.**

Jean-Marie Jouannic is professor in OB/GYN qualified in fetal medicine since 1998, head of department of fetal medicine in Trousseau Hospital in Paris. **Conference Speaker.**

Gregor Kasprian is Associate Professor at the Department of Biomedical Imaging and Image-guided Therapy of the Medical University of Vienna. He was trained in Radiology and Neurology and is recognized for his contribution to both research and clinical development of novel neuroimaging methods in the field of pediatric neuroradiology. His special interest lies in the field of fetal neuroimaging. He applies novel MR imaging techniques in cases with suspect fetal brain pathologies. With the departments of pediatrics and neuropediatrics (Rainer Seidl) and the clinical institute of neurology (Christine Haberler) he has set up a joint effort in the prenatal in vivo imaging characterization of fetal brain pathologies, their neuropathological confirmation and postnatal functional follow up. **Conference Speaker.**

Emmanuelle Lacaze has a cognitive psychology master research and thesis, two university diploma in Somatic Psychology at the Fondation Vallée and Support of patients affected with a genetic disorder at the Pitié-Salpétrière Hospital. She worked in adult neurology and reeducation (Rothshild ophthalmologic foundation, retirement residence in Bagnolet, CMP Jacques Arnaud), Children neurology (pediatric oncology at Gustave Roussy Institute, general pediatrics at Ivry Hospital, at the reference center of learning disabilities in Kremlin Bicêtre Hospital, and in neuropediatry and reference center of cerebellum disorders in Trousseau Hospital). **IRC5 Affiliate & Conference Speaker.**

Christine Laclef is Associate Professor at Sorbonne University, Paris, France. As developmental biologist she works on mouse models of ciliopathies. Her primary research interests are to address the functions of primary cilia in neural development and brain morphogenesis, and more particularly in telencephalon patterning, corpus callosum formation and interneuron migration during embryonic development. **Conference Speaker.**

Béatrice Langellier-Bellevue worked as a social worker at Necker Hospital for the last 13 years and she worked for 6 years in the medical genetic department of Pr. Arnold MUNNICH. In 2013, the Necker Hospital developed a rare / chronic disease space that she coordinated. From that space, dedicated to improving practices of rare disease centers, she had the opportunity to drive a project on teen-to adult transition, that gave birth in 2017 to a physical space of hospitality for young people, a website as well as a smartphone app. **Conference Speaker.**

Zvi Leibowitz is 62 years old, director of Ultrasound Unit, OB/GYN department, Bnai Zion Medical Center, Haifa, Israel and co-director of Fetal Neurology Clinic, Wolfson Medical Center, Holon, Israel. His main research interests are fetal neurosonography and prenatal sonographic diagnosis of CNS malformations. His teaching experience in the field of fetal neurosonography includes numerous local and international Fetal Neurosonography masterclass courses held under the auspices of International Society of Ultrasound in Obstetrics and Gynecology in USA, Israel, Romania, Russia, and Ukraine. **Conference Speaker.**

Roberto Lent received his MD at Federal University of Rio de Janeiro (1972), PhD at the Instituto de Biofisica Carlos Chagas Filho (1973 and 1978 respectively), Fogarty postdoctoral fellow at the Massachusetts Institute of Technology (1979-1982). Full professor of Neuroscience at the Federal University of Rio de Janeiro (1992), former director of the Instituto de Ciencias Biomedicas. Full member of the Brazilian Academy of Sciences, member of the Technical-Scientific Council for Basic Education (CAPES, Brazilian Ministry of Education), and president of the Council of Instituto Ciencia Hoje, a social organization created by the Brazilian Society for the Progress of Science, dedicated to science popularization. At the University, RL heads a Laboratory at Instituto de Ciencias Biomedicas, working in Neuroembriology, Neuroplasticity and Evolution of the Nervous System. In this area, he has published 10 books and 100 papers with an average IF of 3 and an h factor of 21. He is active in science popularization for adults and children, with books published for both. He has recently been elected to direct the Brazilian Network of Science for Education, a non-profit association of scientists devoted to translational research in education. **IRC5 Member & Speaker.**

Tally Lerman-Sagie completed a residency in Pediatrics at Beilinson Medical Center in Israel in 1990. She did a fellowship in Pediatric Neurology at Mass. General Hospital, Boston, MA and a fellowship in Metabolic diseases at Children's Hospital, Boston, MA. She

is a Professor of Pediatrics and Pediatric Neurology at the Sackler School of Medicine, Tel-Aviv University and is chief of Pediatric Neurology at Wolfson Medical Center, Israel. She founded and is the head of the Metabolic-Neuro-Genetic service which diagnoses and treats rare metabolic and neurogenetic disorders. She is the neurologic co-director of the fetal neurology clinic, a multidisciplinary clinic that diagnoses and counsels pregnant women with fetal brain anomalies. Her main research is in the diagnosis of brain anomalies in utero, postnatal implications and the genetic basis of rare neurogenetic syndromes. She has written over 70 papers and chapters in textbooks on Fetal Neurology. **Conference Speaker.**

Paul Lockhart, A/Professor, received his PhD from the University of Melbourne in 2000. He was awarded a NHMRC CJ Martin Fellowship to study the genetics of neurodegenerative disorders, specifically Parkinson's disease, with Professor John Hardy and Professor Matthew Farrer at The Mayo Clinic, Florida. Paul returned to Australia in 2004 and joined the newly formed Bruce Lefroy Centre (BLC) at the Murdoch Children's Research Institute. In 2009 he became Co-Director of the Bruce Lefroy Centre and expanded his research activities to include gene identification utilizing modern genomic technologies. He works in close collaboration with the Victorian Clinical Genetics Service to identify and characterize the genetic basis of rare Mendelian genetic disorders in families presented to the clinic. Currently he leads a laboratory group that investigates the molecular basis of neurogenetic disorders. **IRC5 Board Member.**

Anne Elodie Millisher is Radiologist specialized in women and pediatric imaging. **IRC5 Affiliate.**

Theo Marins holds an MSc and a Ph.D. degree in Morphological Sciences obtained at Federal University of Rio de Janeiro, Brazil, in 2014 and 2018, respectively. As a postdoctoral at the D'Or Institute for Research and Education (IDOR), Marins has been using advanced protocols of brain imaging to investigate the impact of brain malformations, congenital blindness, amputation and training on brain structural and function. Alongside his activities as a young neuroscientist, his interests are to develop science communication and public engagement on neuroscience and to train and develop new students on brain imaging methods. **IRC5 Affiliate.**

Ashley Marsh is a Postdoctoral Scholar and NHMRC CJ Martin Early Career Fellow working in the Gleeson Laboratory for Pediatric Brain Disease at the University of California, San Diego. Ashley received her PhD in Neurogenetics (Dissertation: Determining the Genetic Control of Corpus Callosum Development) from the University of Melbourne in 2018, under the supervision of Assoc. Prof. Paul Lockhart and Assoc. Prof. Richard Leventer, at the Murdoch Children's Research Institute. During her candidature, she utilized modern genomic technologies to identity and characterize novel disease genes, including the first genetic cause of isolated agenesis of the corpus callosum, published in Nature Genetics (Marsh et al., 2017). Ashley has a strong interest in brain wiring and brain rewiring in the context of neurodevelopmental disorders such as agenesis of the corpus callosum and mirror movements. She is currently investigating the role of somatic mosaicism in malformations of cortical development, including focal cortical dysplasia. **IRC5 Affiliate.**

Jorge Moll Neto is the co-founder and Chairman of the board at the D'Or Institute for Research and Education. In research, his areas of interest include cognitive and social neuroscience, functional MRI, emotional neurofeedback, moral emotions, altruistic decision-making, psychological and neural bases of prosocial and antisocial behavior. Dr. Moll has contributed with key research, some of which is published in high visibility journals such as PNAS, Nature Reviews Neuroscience, Journal of Neuroscience, and Archives of General Psychiatry. During the last 10 years, Dr. Moll has had an active and continuous role in contributing to the cognitive and social neuroscience field nationally and internationally through invited talks and symposia. He is a board member for the biannual International Symposium Frontiers in Neuroscience and the annual World Congress on Brain, Behavior and Emotions. Furthermore, Dr. Moll has been successful in quickly establishing an initial "hub" for the cognitive neuroscience field in South America, which has been increasingly attractive to international visiting researchers and students. **Conference Speaker.**

Marie-Laure Moutard: PhD in 1981 (PARIS) / Specialization in child neurology since 1981 / Master in Neurourology and Urodynamics in 1988 / Master in Medical Ethics in 2001 / I have been working in a Children Hospital since 1976 (Hôpital Saint Vincent de Paul, Paris then Hôpital Trousseau, Paris, France). I am particularly involved in fetal neurology and in fetal brain malformations (corpus callosum).
IRC5 Affiliate.

Remya Nair is a Staff Scientist at the Emotion and Social Cognition Lab at Caltech. Her interests include fMRI analysis, studying functional organization in AgCC brains and neuroimaging data processing pipeline development and big data management. **IRC5 Affiliate.**

Marta Nieto-Lopez is a Principal Investigator of the Scientific Research Council of Spain. Her group is located at the National Center for Biotechnology, CNB-CSIC. Her group investigates activity dependent mechanisms of corpus callosum formation using the mouse as a model. They use retro-tracing experiments, confocal imaging and electrophysiology. **Conference Speaker.**

Lynn K. Paul, PhD, is a Senior Research Scientist at California Institute of Technology and an Associate Research Professor at Fuller Graduate School of Psychology. Dr Paul's research is broadly focused on understanding the role that cortical connectivity plays in development of higher-order social cognition and the brain's capacity for reorganization during development. At Caltech, she directs research programs studying brain structure, cognition and social processing in dysgenesis of the corpus callosum and hemispherectomy. She also collaborates with Dr. Ralph Adolphs on studies of social processing and brain structure in adults with psychiatric diagnoses such as autism and anxiety disorders, as well as studies of individuals with congenital bilateral amygdala lesions. Dr. Paul is director of the Psychological Assessment for Research Laboratory at Caltech and principal investigator for the Psychological Assessment Core of the NIH-funded Conte Center for Social Decision Making. / Dr Paul was the founding president of the National Organization for Disorders of the Corpus Callosum (NODCC), a not-for-profit that brings families, clinicians, and scientists together in the effort to improve quality of life for people with callosal disorders. She has co-authored two children's books about callosal agenesis: "ACC and Me" and "Emme and Me." / Finally, Dr Paul maintains a clinical psychology practice in Pasadena (L.K.Paul and Associates), where she sees adult outpatient psychotherapy clients and conducts neuropsychological assessments on individuals with callosal dysgenesis. Dr Paul received her PhD in Clinical Psychology from Fuller Graduate School of Psychology and completed a post-doctoral fellowship in clinical neuropsychology from the Department of Neurology, UCLA. **IRC5 Board Member & Conference Speaker.**

Alessandra Pierani is Director of Research at the National Center for Scientific Research (CNRS). She heads the team "Genetics and Development of the Cerebral Cortex" with a dual affiliation at the Imagine Institute (Institut des Maladies Génétiques, Hôpital Necker Enfants Malades, Paris) and the Institute of Psychiatry and Neurosciences of Paris (IPNP, Hôpital St Anne, Paris) (France). Her research focuses on the role of transient neuronal populations in cerebral cortex development, evolution and pathology. She obtained two PhDs in Biology at the University of Florence (1986) and University of Paris XI (1994) and trained first as a molecular biologist and biochemist at the Rockefeller University (New York). She then begun her work on neural development at the Institut Curie (Orsay) and pursued it at Columbia University (New York) and the Ecole Normale Supérieure (Paris). From 2006 until 2017, she was a group leader at the Institut Jacques Monod in Paris. She was awarded a CNRS-ATIPE grant (1999), a City of Paris prize (2006) and the Foulon Prize of the French Academy of Science (2012). **IRC5 Affiliate & Conference Speaker.**

Ferechté Razavi, As a paediatrician and neurodevelopmental pathologist with a backround of Embryology and Cytogenetics, Férechté Encha-Razavi, MD, Associate Professor at the University Paris-Descartes (France) is since 2009, a senior consultant in Necker's. She has conducted and participated in numerous research programs on developmental defects, with a special regard on normal and abnormal brain development. In 2012, her group received the Moore award, delivered by the American Association of Neuropathologists (AANP), where she is an active member since 90's. From 1989 to 2009, Dr Encha-Razavi has been head of the Unit of Fetal & Placental Pathology at Necker University Hospital, during which she developed an etiopathogenical approach of brain defects, initiated with her mentor Doctor Jeanne Claudie LARROCHE in 1983, impacting positively gene identification and the comprehension of morphological diversity and genetic heterogeneity of brain defects. During this time, she initiated and chaired a teaching program on human brain developmental disorders and promoted national and international collaborative researches in this field. She also participates in teaching programs on birth defects abroad (China, UK, Tunisia, Italy, Romania…) and served as tutor in IPPA teaching programs (International Paediatric Pathology Association).
She served as President (2005-2009) of the French Society of Fetal Pathology (SOFFOET), promoting teaching and research on fetal pathology and on its ethical and legal aspects. Prior to joining Paris, Dr Encha-Razavi worked for ten years at the Baharami University

Hospital (Teheran/Iran), involved in birth defects prevention and social paediatrics. She took part as author in international text books edited by Wigglesworth, Potter's reeditions, Escourolle & Poirier, Golden & Harding, Keeling, Scheimberg & Cohen….She co-edited in France textbooks on Human Embryology: From clinic to genes (Masson), and on fetal and placental pathology (Pathologie Foetale et placentaire pratique, Sauramps, 2009). Her numerous original scientific reports are signed ENCHA-RAZAVI Ferechte or RAZAVI Ferechte. **IRC5 Affiliate.**

Linda J. Richards, PhD, FAA, FAHMS is a Professor of Neuroscience and Deputy Director (Research) of the Queensland Brain Institute at The University of Queensland. She is an NHMRC Principal Research Fellow, past President of the Australasian Neuroscience Society and Co-Chair of the Australian Brain Alliance. She is patron and scientific advisor of AusDoCC, the Australian Disorders of the Corpus Callosum support group. **IRC5 Board Member & Conference Speaker.**

Romina Romaniello is specialized in Child Neurology and Psychiatry and works in the Department of Child Neurorehabilitation of the Medea Scientific Institute (Head Renato Borgatti) where she is engaged in clinical diagnostic evaluation and rehabilitative programs for patients affected by brain malformations, epilepsy and mental retardation. In the Institute she takes part to Neuro-radiological team to discuss neuroimaging of brain malformations and in Molecular Genetic Lab she is involved in research projects of the genetic of brain malformations. During the last four years she has been responsible of three research projects on brain malformations (corpus callosum agenesis; non progressive cerebellar ataxia and exome sequencing in brain malformations) and participate to several national and international projects. Recently she has published several studies, as first author, on clinical genetic and radiological aspects of bm. **IRC5 Member & Conference Speaker.**

Laurent J Salomon, MD, PhD is a senior consultant in the Department of Obstetrics and Fetal Medicine Necker-Enfants-Malades Hospital and full professor at Paris Descartes University since 2012. He has developed special interest and skills in fetal medicine and surgery, imaging technologies in pregnancy including fetal ultrasound and MRI, twin pregnancies, as well as teaching processes, quality control and statistics in healthcare. He is specialized in the management and follow up of high risk pregnancies and deliveries. He also offers maternity care to women with low risk pregnancies, with the expertise to provide care in cases when complications occasionally arise. He completed a PhD in Physics with distinction (Paris XI Sud, Science University –

Orsay), applied to Functional Imaging of the placenta. He also completed a MSc in Medical Statistics with distinction at the London School of Hygiene and Tropical Medicine (LSHTM). He is the associate director of the Master Degree in Prenatal Diagnosis and Fetal Medicine at Paris Descartes University. He is a previous Editor of Ultrasound in Obstetrics and Gynecology and involved in the board as well as many committees and task forces of the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG). He also serves on a regular basis as an expert for different Health Authorities, as well as for international research projects. He has co-authored more than 200 papers in the peer-reviewed English medical literature and several textbooks. He is also the co-founder and project co-leader of LUMIERE (www.fondation-lumiere.org). **IRC5 Affiliate & Conference Speaker.**

Elliott Sherr is a Professor in Neurology and Pediatrics at the Weill Institute of Neurosciences and the Institute of Human Genetics at UCSF. He directs the Brain Development Research Program, a group that studies the genetics and biology autism and epilepsy (brain.ucsf.edu). Specific areas of interest include understanding the link between advance brain imaging metrics, blood-based biochemical biomarkers and autism susceptibility. His lab also studies how brain function is altered in a "genetics first" model of ASD, as exemplified by deletion of duplication of a 600 kb interval in16p11.2, the most common genetic cause of autism. He studies the genetics of disorders of brain development, including agenesis of the corpus callosum. In this process, he has identified several genes that are mechanistically linking these to autism. He also is member of a large epilepsy genetics consortium (http://www.epgp.org/epi4k/) in which he lead a team trying to understand the genetic causes of severe childhood epilepsies, such as infantile spasms. For his research, he was the 2006 recipient of the Philip R. Dodge Young Investigator Award from the Child Neurology Society. He is a board-certified Child Neurologist and co-directs the Comprehensive Center for Brain Development at UCSF. In this capacity, he cares for children with neurodevelopmental disorders, including autism, intellectual disability and epilepsy. He is a native of California and completed his undergraduate degree in Philosophy and Biology at Stanford University. He obtained his M.D. and Ph.D. at Columbia University in New York and completed his clinical training in Pediatrics and Neurology at UCSF. **IRC5 Board Member.**

Vanessa Siffredi is a Postdoctoral Research Fellow at the Medical Image Processing Lab (MIP:lab) at the Ecole Polytechnique de Lausanne and at the Child Developmental Lab (ChilDlab) at the Faculty of Medicine, University of Geneva, Switzerland. Her postdoctoral

research examines brain plasticity and cognitive development in children (typically developing children, children with brain malformations, children born prematurely). Her research focuses on identifying early markers for the development of future cognitive impairment and examining interventions to support optimal development. **Conference Speaker.**

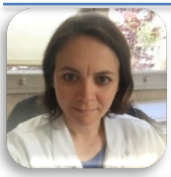
Diego Szczupak is an undergrad in the Biomedical Sciences course in the University of Rio de Janeiro in the lab of Dr. Roberto Lent where he started working with white matter of the brain. Later he was introduced to Fernanda Tovar Moll and did his Ph.D. thesis in the aberrant interhemispheric connections of the mouse brain and malformations of the corpus callosum, mentored by Dr. Moll, Dr. Lent and Dr. Afonso Silva. Now he is a postdoc in Dr. Silva's lab studying the callosal features of the marmoset monkey brain. **IRC5 Affiliate & Conference Speaker.**

Victor Tarabykin directs the Institute of Cell Biology and Neurobiology, Charite- Universitätsmedizin, Berlin. His research centers in the field of cerebral cortex development, specifically investigating molecular control of cell fate specification, cell type-specific axon navigation, neuronal migration and chromatin remodeling & epigenetic control of cell differentiation. **IRC5 Member.**

Sophie Thomas, PhD, is a INSERM Researcher at Imagine Institute (INSERM U1163). Her research focus on primary cilium and centrosome during neocortical development. **IRC5 Affiliate.**

Fernanda Tovar-Moll; MD degree (1999), Medical Residency in Radiology (2003) and PhD in Morphological Sciences (2007) at Federal University of Rio de Janeiro (UFRJ). Post-doctoral fellow at the National Institutes of Health (USA, 2004-2007). Adjunct professor of the National Center of Structural Biology and Bioimaging and of Institute of Biological Sciences at UFRJ and co-founder and director-president of the D'Or Institute for Research and Education. Affiliated member of the Brazilian Academy of Sciences. Research interest: clinical and translational research, employing in vivo imaging techniques in human and in other animal models to map brain circuits and its correlations with behavior, in order to improve the understanding of mechanisms related to brain connectivity and plasticity, in normal and pathological conditions. **IRC5 Board Member.**

Laurence Vaivre-Drouet, PhD, Full Professor of Developmental Neuropsychology at the University of Paris Descartes, Medicine Faculty. Clinical Neuropsychologist, and Physiotherapist, Psychotherapist in Children hospital AP-HP Necker in Paris. Member of Universitary Institute of France. Director of a research team entitled "Neuro-development and learning disabilities" in 1178-1018 Unit INSERM at Necker University Hospital. And associated researcher to the team of Endocrinological Pediatric department in the IMAGINE Institute of the genetic diseases. Area of expertise focus on the field of the neuro-developmental knowledges on children, from neonate to adolescent, from normal to pathology, with a transactional clinical assessment of phenotypage based on a fine semiology with the creation of new standardized assessment tools in neuro-sensory-motor and psychomotor functions. The aims being first to understand the underlying cerebral mechanism, the nature and the origin of an eventual disorder with the identification of homogeneous neurodevelopmental profiles and trajectories in order to enhance the knowledges from a physiological or pathological/genotyping-endophenotyping characterizations, on nosography, etiology, specific markers. Secondary, to contribute to remediation. **Conference Speaker.**



Stéphanie Valence is a Neuro-pediatric doctor at Hospital Trousseau, Paris. **IRC5 Affiliate & Conference Speaker.**

Alice Wright has previously trained as a Clinical Psychologist. This includes an undergraduate Psychology degree and a Masters in Research at the University of St Andrews and a Doctorate in Clinical Psychology at the University of Edinburgh. Throughout this training she has specialized in working with children with complex neurodevelopmental presentations. During this work she has developed an interest in neuropsychology and the link between underlying neurological impairment and the presenting difficulties in individuals. This has led her to undertake the MSc in Paediatric Clinical Neuropsychology with the long term aim of becoming a Clinical Neuropsychologist. Both her clinical work with young people with Agenesis of the Corpus Callosum (AgCC) and the taught elements of the MSc motivated her to seek out research opportunities in the field of AgCC. She's currently completing an MSc research project on the neural basis of social cognition difficulties in AgCC. **Conference Speaker.**

Binnaz Yalcin her research focuses on using mouse genetics to investigate genes involved in brain morphology and their role in human neurodevelopmental disease. The approach taken in the lab is to identify brain mutant phenotypes caused by gene inactivation on a large scale and then identify the underlying gene networks and biological mechanisms. This has provided the largest collection of gene knockouts that elicit the causal link between gene mutation and its associated neuroanatomical features to date. **IRC5 Affiliate & Conference Speaker.**

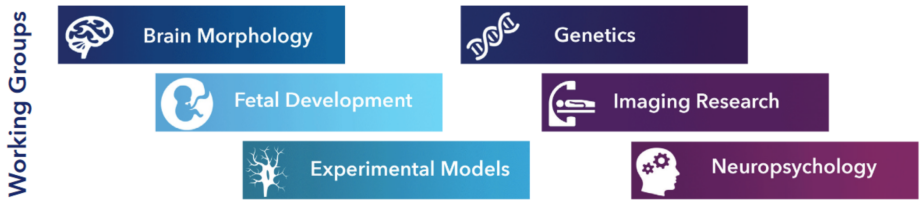
IRC5

International Research Consortium for the Corpus Callosum and Cerebral Connectivity

The International Research Consortium for the Corpus Callosum and Cerebral Connectivity (IRC5) is an international, multidisciplinary effort to discover the causes, consequences, and effective interventions for disorders of the corpus callosum and associated disorders of cerebral connectivity. It was established on March 20, 2015 by a group of investigators who are leading experts in corpus callosum developmental disorders and their neuropsychological and developmental outcomes and who have maintained long-standing involvement in patient support organizations.

IRC5 Mission

- Identify what causes malformation of brain connections before birth
- Discover ways to prevent or ameliorate these malformations
- Improve accuracy of predicting how child will be impacted by these malformation
- Develop effective interventions to prevent (or minimize) long-term disability from them, such as deficits in cognition and behavior, as well as neurologic conditions such as epilepsy, ataxia and spasticity



http://www.irc5.org