LIST OF PROJECTS (3)

MD PHD SCHOLARSHIPS

MARCH 2021

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PROJECT MD1

Title : Early biomarkers of neurodegeneration in Parkinsonian syndromes: an ultra high field (7T) brain MRI study

Supervisor : GUYE Maxime

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Co-supervisor : EUSEBIO Alexandre

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State of the art
At an early stage, the differential diagnosis between Parkinson's disease (PD) and each of the Atypical Parkinson's Syndromes (such as progressive supranuclear palsy, PSP) is a challenge for clinicians. Although clinically similar, these different diseases are underpinned by partly different pathophysiological mechanisms and have a very variable evolution and prognosis. As trials with targeted therapies begin, there is a growing urgency to develop early biomarkers to better differentiate diseases for early and more accurate diagnosis. Classically, cerebral MRI at 1.5 T or 3T does not help in the positive or differential diagnosis of Parkinsonian syndromes. Recent studies (few in number) suggest that the contribution of ultra high field imaging (7T) could bring new positive arguments for these diseases
Objectives
1/ To compare the accumulation of intracellular sodium at brain level measured by ultra high field (7T) brain MRI between subjects with PD and subjects with suggestive signs or possible PSP. 2/ To compare subjects with PD, PSP and control subjects in terms of: cerebral atrophy (Global and by regions of interest) (brainstem, deep grey matter, frontal, prefrontal and bilateral lower parietal regions) in VBM; Intracellular accumulation of iron with QSM; structural and functional connectivity in diffusion and tractography
Methods
A clinical evaluation of patients will be performed in addition to cerebral MRI. The evaluation of each patient will be performed by the neuroschool student in the laboratory of CRMBM-CEMEREM. 15 patients per group are expected: PD, PSP, controls. The images acquired in sodium MRI will have to be reconstructed, corrected, normalized and smoothed to obtain quantitative maps of total sodium concentration of the whole brain. The images acquired in proton MRI (MP2RAGE) will be segmented and normalized in the MNI model, and the resulting transformation will be applied to quantitative sodium maps. The quantitative maps of total sodium concentration of the three groups will then be compared to each other. Similar processing for QSM and DTI. Intergroup comparisons and correlations between imaging and clinical data will be performed.
Expected results
To date, there are no published data on sodium metabolism in PD, a marker that has already shown interest in understanding the pathophysiological mechanisms of other neurological diseases such as Multiple Sclerosis and Amyotrophic Lateral Sclerosis. These results could help in the diagnosis of the various parkinsonian syndromes in order to better adjust patient management. They would also help to better target patients to be included in the various therapeutic trials based on their diagnosis.
Feasibility
CEMEREM hosts new 3T and 7T MRI machines with a CE label allowing routine clinical exploration in addition to conventional research protocols. The lab has extensively published in the field of neurological disorders over the past 20 years. The Movement disorders unit is expert center for PSP and the active list of patients will allow the collection of the necessary number of subjects to meet the stated objectives. The CEMEREM has the necessary expertise in imaging tools and techniques. BaGaMoRe and the Department of Movement Disorders has the necessary expertise in terms of clinical aspects of parkinsonism and access to patients
Expected candidate profil
MD specializing/zed in Neurology, Interest and expertise in parkinsonism, Interest in MRI techniques and image analysis

SUPERVISED PHDS & PUBLICATIONS : GUYE Maxime

- **Currently supervised PhD students**

- Mikhael AZILINON
- Stephan GRIMALDI

- **Previously supervised PhD students**

- Ben RIDLEY
- Jonathan WIRSICH

- **Publications of previously supervised PHD students**

Modular slowing of resting-state dynamic functional connectivity as a marker of cognitive dysfunction induced by sleep deprivation.

- Lombardo D, Cassé-Perrot C, Ranjeva JP, Le Troter A, Guye M, Wirsich J, Payoux P, Bartrés-Faz D, Bordet R, Richardson JC, Felician O, Jirsa V, Blin O, Didic M, Battaglia D.Neuroimage. 2020 Nov 15;222:117155. doi: 10.1016/j.neuroimage.2020.117155. Epub 2020 Jul 29.

Connectivity strength, time lag structure and the epilepsy network in resting-state fMRI

- Bandt SK, Besson P, Ridley B, Pizzo F, Carron R, Regis J, Bartolomei F, Ranjeva JP, Guye M. Neuroimage Clin. 2019;24:102035. doi: 10.1016/j.nicl.2019.102035. Epub 2019 Oct 23.

Structural Connectivity Alterations in Amyotrophic Lateral Sclerosis: A Graph Theory Based Imaging Study.

- Fortanier E, Grapperon AM, Le Troter A, Verschueren A, Ridley B, Guye M, Attarian S, Ranjeva JP, Zaaraoui W. Front Neurosci. 2019 Oct 2;13:1044. doi: 10.3389/fnins.2019.01044. eCollection 2019.

Quantitative Brain Sodium MRI Depicts Corticospinal Impairment in Amyotrophic Lateral Sclerosis

- Grapperon AM, Ridley B, Verschueren A, Maarouf A, Confort-Gouny S, Fortanier E, Schad L, Guye M, Ranjeva JP, Attarian S, Zaaraoui W.Radiology. 2019 Aug;292(2):422-428. doi: 10.1148/radiol.2019182276. Epub 2019 Jun 11.

Dynamic 23Na MRI - A non-invasive window on neuroglial-vascular mechanisms underlying brain function

- Bydder M, Zaaraoui W, Ridley B, Soubrier M, Bertinetti M, Confort-Gouny S, Schad L, Guye M, Ranjeva JP. Neuroimage. 2019 Jan 1;184:771-780. doi: 10.1016/j.neuroimage.2018.09.071. Epub 2018 Oct 4.

Distribution of brain sodium long and short relaxation times and concentrations: a multi-echo ultra-high field 23Na MRI study.

- Ridley B, Nagel AM, Bydder M, Maarouf A, Stellmann JP, Gherib S, Verneuil J, Viout P, Guye M, Ranjeva JP, Zaaraoui W. Sci Rep. 2018 Mar 12;8(1):4357. doi: 10.1038/s41598-018-22711-0.

Brain Networks are Independently Modulated by Donepezil, Sleep, and Sleep Deprivation

- Wirsich J, Rey M, Guye M, Bénar C, Lanteaume L, Ridley B, Confort-Gouny S, Cassé-Perrot C, Soulier E, Viout P, Rouby F, Lefebvre MN, Audebert C, Truillet R, Jouve E, Payoux P, Bartrés-Faz D, Bordet R, Richardson JC, Babiloni C, Rossini PM, Micallef J, Blin O, Ranjeva JP; Pharmacog Consortium. Brain Topogr. 2018 May;31(3):380-391. doi: 10.1007/s10548-017-0608-5. Epub 2017 Nov 23.

Metabolic counterparts of sodium accumulation in multiple sclerosis: A whole brain 23Na-MRI and fast 1H-MRSI study.

- Donadieu M, Le Fur Y, Maarouf A, Gherib S, Ridley B, Pini L, Rapacchi S, Confort-Gouny S, Guye M, Schad LR, Maudsley AA, Pelletier J, Audoin B, Zaaraoui W, Ranjeva JP. Mult Scler. 2019 Jan;25(1):39-47. doi: 10.1177/1352458517736146. Epub 2017 Oct 24.

Complementary contributions of concurrent EEG and fMRI connectivity for predicting structural connectivity

- Wirsich J, Ridley B, Besson P, Jirsa V, Bénar C, Ranjeva JP, Guye M.Neuroimage. 2017 Nov 1;161:251-260. doi: 10.1016/j.neuroimage.2017.08.055. Epub 2017 Aug 24.

Brain sodium MRI in human epilepsy: Disturbances of ionic homeostasis reflect the organization of pathological regions

- Ridley B, Marchi A, Wirsich J, Soulier E, Confort-Gouny S, Schad L, Bartolomei F, Ranjeva JP, Guye M, Zaaraoui W. Neuroimage. 2017 Aug 15;157:173-183. doi: 10.1016/j.neuroimage.2017.06.011. Epub 2017 Jul 3.

Simultaneous Intracranial EEG-fMRI Shows Inter-Modality Correlation in Time-Resolved Connectivity Within Normal Areas but Not Within Epileptic Regions

- Ridley B, Wirsich J, Bettus G, Rodionov R, Murta T, Chaudhary U, Carmichael D, Thornton R, Vulliemoz S, McEvoy A, Wendling F, Bartolomei F, Ranjeva JP, Lemieux L, Guye M. Brain Topogr. 2017 Sep;30(5):639-655. doi: 10.1007/s10548-017-0551-5. Epub 2017 Feb 13.

Improvement of spasticity following intermittent theta burst stimulation in multiple sclerosis is associated with modulation of resting-state functional connectivity of the primary motor cortices

- Boutière C, Rey C, Zaaraoui W, Le Troter A, Rico A, Crespy L, Achard S, Reuter F, Pariollaud F, Wirsich J, Asquinazi P, Confort-Gouny S, Soulier E, Guye M, Pelletier J, Ranjeva JP, Audoin B. Mult Scler. 2017 May;23(6):855-863. doi: 10.1177/1352458516661640. Epub 2016 Aug 1.

Alien Hand, Restless Brain: Salience Network and Interhemispheric Connectivity Disruption Parallel Emergence and Extinction of Diagonistic Dyspraxia.

- Ridley B, Beltramone M, Wirsich J, Le Troter A, Tramoni E, Aubert S, Achard S, Ranjeva JP, Guye M, Felician O. Front Hum Neurosci. 2016 Jun 20;10:307. doi: 10.3389/fnhum.2016.00307. eCollection 2016

Whole-brain analytic measures of network communication reveal increased structure-function correlation in right temporal lobe epilepsy

- Wirsich J, Perry A, Ridley B, Proix T, Golos M, Bénar C, Ranjeva JP, Bartolomei F, Breakspear M, Jirsa V, Guye M. Neuroimage Clin. 2016 May 19;11:707-718. doi: 10.1016/j.nicl.2016.05.010. eCollection 2016.

Corrigendum: Neural substrate of quality of life in patients with schizophrenia: a magnetisation transfer imaging study.

- Faget-Agius C, Boyer L, Wirsich J, Ranjeva JP, Richieri R, Soulier E, Confort-Gouny S, Auquier P, Guye M, Lançon C. Sci Rep. 2016 Feb 15;6:21055. doi: 10.1038/srep21055.

Neural substrate of quality of life in patients with schizophrenia: a magnetisation transfer imaging study

- Faget-Agius C, Boyer L, Wirsich J, Ranjeva JP, Richieri R, Soulier E, Confort-Gouny S, Auquier P, Guye M, Lançon C. Sci Rep. 2015 Dec 3;5:17650. doi: 10.1038/srep17650.

Nodal approach reveals differential impact of lateralized focal epilepsies on hub reorganization

- Ridley BG, Rousseau C, Wirsich J, Le Troter A, Soulier E, Confort-Gouny S, Bartolomei F, Ranjeva JP, Achard S, Guye M. Neuroimage. 2015 Sep;118:39-48. doi: 10.1016/j.neuroimage.2015.05.096. Epub 2015 Jun 10.

Single-trial EEG-informed fMRI reveals spatial dependency of BOLD signal on early and late IC-ERP amplitudes during face recognition

- Wirsich J, Bénar C, Ranjeva JP, Descoins M, Soulier E, Le Troter A, Confort-Gouny S, Liégeois-Chauvel C, Guye M. Neuroimage. 2014 Oct 15;100:325-36. doi: 10.1016/j.neuroimage.2014.05.075. Epub 2014 Jun 5. PMID: 24910070

SUPERVISED PHDS & PUBLICATIONS : EUSEBIO Alexandre

- **Currently supervised PhD students**

- Stephan GRIMALDI

- **Previously supervised PhD students**

- Cyril ATKINSON-CLEMENT

- **Publications of previously supervised PHD students**

Psychosocial Impact of Dysarthria: The Patient-Reported Outcome as Part of the Clinical Management

- Atkinson-Clement C, Letanneux A, Baille G, Cuartero MC, Véron-Delor L, Robieux C, Berthelot M, Robert D, Azulay JP, Defebvre L, Ferreira J, Eusebio A, Moreau C, Pinto S. Neurodegener Dis. 2019;19(1):12-21. doi: 10.1159/000499627. Epub 2019 May 21. PMID: 31112944 Free article.

Effects of subthalamic nucleus stimulation and levodopa on decision-making in Parkinson's disease.

- Atkinson-Clement C, Cavazzini É, Zénon A, Witjas T, Fluchère F, Azulay JP, Baunez C, Eusebio A. Mov Disord. 2019 Mar;34(3):377-385. doi: 10.1002/mds.27625. Epub 2019 Jan 25. PMID: 30681186

Diffusion tensor imaging in Parkinson's disease: Review and meta-analysis.

- Atkinson-Clement C, Pinto S, Eusebio A, Coulon O. Neuroimage Clin. 2017 Jul 15;16:98-110. doi: 10.1016/j.nicl.2017.07.011. eCollection 2017

PROJECT MD2

Title : Regulation mechanisms of visual thalamic neuron excitability, a route to treatment of amblyopia?

Supervisor : DEBANNE Dominique

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Co-supervisor : MARQUEZE POUEY Béatrice

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State of the art

Neuronal circuits in the brain are shaped by activity-dependent plasticity in early postnatal life. Thus, abnormal visual experience during childhood results in amblyopia, a visual deficit that affects 2-5% of the population (Holmes JM and Clarke MP, 2006). When a child develops an eye turn (strabismus) or a substantial difference in refractive error between the eyes (anisometropia), the unequal input causes the brain to ignore information from the weaker eye during brain development. The treatment is possible only during the first 6-7 years of life by handling the cause of abnormal vision and reversed occlusion. When this sensitive period is exceeded, the visual deficit is irreversible

Objectives

The project aims to identify the mechanisms at the origin of the loss of visual responsiveness in a rodent model of amblyopia induced by blocking vision in one eye (monocular deprivation). We have already some preliminary results suggesting that intrinsic excitability plasticity is involved in that process, in the dorsal lateral geniculate thalamic (LGN) neurons, primary recipients of retinal inputs. Our goal is to understand ion channel regulations inducing such intrinsic excitability plasticity. We are currently comparing ion channel interacting protein networks in thalamic area of the deprived eye versus the open eye. The PhD project concerns in situ characterization of these potential interactions. This will be done by imaging protein interactions on individual monocular and binocular thalamic neurons using the Proximity Ligation Assay, method allowing characterization of two antigens proximity (30 nm)

Methods

Eyelid will be sutured during the developmental sensitive period in young rats before eye opening (P12; Nataraj K et al., 2010). LGN slices connected to the deprived and open eyes from the same animal will be incubated with a couple of primary antibodies obtained from two different species directed against the two putative interacting proteins. Secondary antibodies conjugated with complementary oligonucleotides directed against each of the primary antibodies will be added (Duolink, Sigma). In case of close proximity, a fluorescent PCR amplified signal will occur and be observed on a confocal microscope.

Expected results

We are expecting to establish signaling complexes specifically driven by activity, by comparing the results of thalamic neurons connected to the open or deprived eye. We will be able to test the function of these interactions in long-term change of intrinsic excitability using electrophysiology techniques.

Feasibility

The project is fully feasible as the scientific expertise and methodological skills needed for that aim are already mastered. The D. Debanne group has long and solid expertise in the neurophysiological study of visual cortical plasticity and intrinsic plasticity. B. Marquèze-Pouey has wide competence in membrane receptor biochemistry and immunohistology. Clinicians from the Department of Ophtalmology of Prof D. Denis will bring their skill and knowledge in the physiopathology of the developing visual system. Facilities for biochemistry and cellular immunohistology are available at the U1072 laboratory. The north medical school campus provides animal housing and surgery rooms for lid sutures. We have already obtained a “Technical Boost” grant in Neurosciences in 2021 from Institut NeuroMarseille with The PINT proteomic platform to perform mass spectrometry, initial stage of the project, which will lead to the more physiological in situ characterization of ion channel regulations.

Expected candidate profil

Candidates should have a curious mind-set with a strong interest in understanding neurosciences at a molecular level. They should be able to integrate in a multidisciplinary research team. The PhD student will have to perform experiments on rats and mice, critically examine its data and present them in regular meeting and discussions.

SUPERVISED PHDS & PUBLICATIONS : DEBANNE Dominique

- **Currently supervised PhD students**

- Johanna Extrémet (2018-2022) 50% (other supervisor: Michael Russier, 50%)
- Malika Sammari (2019-2022) 100%

- **Previously supervised PhD students**

- Yanis Inglebert (2014-2018)
- Aurélié Fékété (2014-2018)
- Mickaël Zbili (2012-2016)
- Célia Gasselin (2009-2013)
- Andrzej Bialowas (2008-2012)
- Emilie Campanac (2004-2008)
- Philippe Gastrein (2003-2007)
- Sami Boudkkazi (2003-2006)
- Gaël Daoudal (1999-2003)
- Valérie Sourdet (1998-2002)

- **Publications of previously supervised PHD students**

- Fékété et al., ***PNAS*** in review
- Inglebert et al. ***PNAS*** 2020
- Zbili, Rama, Yger, Inglebert et al., ***Sci Adv*** 2020
- Debanne, Inglebert & Russier. ***Curr Opin Neurobiol*** 2019
- Fékété & Debanne ***J Physiol*** 2018
- Rama, Zbili, Fékété et al. ***Sci Rep*** 2017
- Gasselin*, Inglebert* et al. ***Sci Rep*** 2017
- Rama*, Zbili*, et al. ***Nat Commun*** 2015
- Gasselin et al. ***J Physiol*** 2015
- Bialowas et al., ***EJN*** 2015
- Debanne, Bialowas & Rama ***Nat Rev Neurosci*** 2013
- Campanac*, Gasselin* et al., ***Neuron*** 2013
- Gastrein*, Campanac*, Gasselin et al. ***J Physiol*** 2011
- Boudkkazi et al., ***J Physiol*** 2011
- DiGiovanni*, Boudkkazi* et al., ***Neuron*** 2010
- Campanac, Daoudal et al., ***J Neurosci*** 2008
- Campanac & Debanne ***J Physiol*** 2008
- Boudkkazi et al. ***Neuron*** 2007
- Carlier, Sourdet, Boudkkazi et al. ***J Physiol*** 2006
- Sourdet et al. ***J Neurosci*** 2003
- Daoudal et al. ***PNAS*** 2002

SUPERVISED PHDS & PUBLICATIONS : MARQUEZE POUEY Béatrice

- **Currently supervised PhD students**

- none

- **Previously supervised PhD students**

- Frédérique Berton (1995-1998)
- Vincent Rouger (20%, 2012-2013)

- **Publications of previously supervised PHD students**

- Marquèze, Berton et al., ***Biochimie*** 2000
- Berton et al., ***EJN*** 2000
- Berton et al., ***J Neurosci*** 1997
- Marquèze-Pouey, Rouger et al., **Plos One**, 2014

PROJECT MD3

Title : Therapeutic development in KCNQ2-related Developmental and Epileptic Encephalopathies (DEE)

Supervisor : VILLARD Laurent

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LABORATORY WEBSITE : https://www.marseille-medical-genetics.org/l-villard/

State of the art
Developmental and Epileptic Encephalopathies (DEE) are rare disorders in babies. They are characterized by early-on set intractable seizures. The prognosis is severe with a high mortality rate in the first years of life or severe encephalopathy. To date, there are neither prenatal signs norcurative treatment for these patients. At the molecular level, the KCNQ2 gene is the most frequently involved. Loss-of-function (LoF) and gain-of-function (GoF) variants in the KCNQ2 gene cause DEE whereas KCNQ2 haploinsufficiency leads to Benign Familial Neonatal Epilepsy (BFNE).
Objectives
The project will be to design therapeutic approaches. We will develop an RNA interference (RNAi) therapy following our hypothesis that the inactivation of the KCNQ2 mutated allele could transform the patient prognosis from severe (DEE) to benign (BFNE). In parallel, we will test pharmacological molecules as retigabine analogues, repurposed drugs, and newly developed compounds, pre-selected from our collaborative network (EJP RD 2020 and ANR 2019)
Methods
Over the years, the neurogenetics team has built a cohort of 73 patients affected by KCNQ2-DEE. Patients iPSC-derived-neurons will be used to demonstrate the feasibility of Kcnq2 allele-specific knock down and to test other molecules. The phenotype of these cells will be characterized, before and after each potential therapeutic strategy, using electrophysiological analysis (microelectrode arrays).A knock-in mouse model produced by our team is also available to perform in vivo treatments
Expected results
We expect to obtain a specific electrophysiologic alread-out that could discriminate in vitro therapeutic effect. In particular, we intend to demonstrate RNAi feasibility and efficiency in KCNQ2-DEE patients' cells. Positive results will be used to treat our KCNQ2knock-in mouse model
Feasibility
The KCNQ2-DEE study is a long-term team project. Three KCNQ2-DEE patient iPSC lines are already available and are differentiated into cortical neurons by the team. Regarding the RNAi project, we have strong support from our MMG collaborators to carry out experiments. This project is supported by grants from ANR2019 and EJP-RD2020" preclinical research to develop effective therapies for rare diseases"
Expected candidate profil
Young M.D. doing a Ph.D. with a specific interest in developmental and epileptic encephalopathies. The candidate should have a clinical and molecular genetic background and a strong research interest

SUPERVISED PHDS & PUBLICATIONS : VILLARD Laurent

- **Currently supervised PhD students**

- Lucile BRUN
- Florence RICCARDI, M.D

- **Previously supervised PhD students**

- Affef ABIDI 2013-2016
- Nancy CHOUCAIR 2010-2013
- Bilal EL WALY 2009-2012
- Marie-Reine HADDAD 2006-2009
- Vincent CANTAGREL 2004-2007
- VéroniqueSAYWELL 2002-2006

- **Publications of previously supervised PHD students**

Affef ABIDI (2013-2016)

Early-onset epileptic encephalopathy as the initial clinical presentation of WDR45 deletion in a male patient.

- Abidi A, Mignon-Ravix C, Cacciagli P, Girard N, Milh M, Villard L. Eur J Hum Genet. 2016 Apr;24(4):615-8. doi: 10.1038/ejhg.2015.159. Epub 2015 Jul 15.PMID: 26173968.

A recurrent KCNQ2 pore mutation causing early onset epileptic encephalopathy has a moderate effect on M current but alters subcellular localization of Kv7 channels.

- Abidi A, Devaux JJ, Molinari F, Alcaraz G, Michon FX, Sutera-Sardo J, Becq H, Lacoste C, Altuzarra C, Afenjar A, Mignot C, Doummar D, Isidor B, Guyen SN, Colin E, De La Vaissière S, Haye D, Trauffler A, Badens C, Prieur F, Lesca G, Villard L, Milh M, Aniksztejn L.Neurobiol Dis. 2015 Aug;80:80-92. doi: 10.1016/j.nbd.2015.04.017. Epub 2015 May 22.PMID: 26007637.2Supervisors who obtained a fellowship in 2020(Ecole Doctoralor NeuroSchool PhD program) cannot apply. Reminder:a maximum of 3 full-time PhD studentsper HDR is accepted.

A Kv7.2 mutation associated to early onset epileptic encephalopathy with suppression-burst enhances Kv7/M channel activity.

- Devaux JJ, Abidi A, Roubertie A, Molinari F, Becq H, Lacoste C, Villard L, Milh M, Aniksztejn L.Epilepsia. 2016 May;57(5):e87-93. doi: 10.1111/epi.13366. Epub 2016 Mar 31.PMID: 27030113.4/Variable Clinical Expression in Patients with Mosaicism for KCNQ2 Mutations.

- MilhM, LacosteC,CacciagliP,Abidi A, Sutera-SardoJ, TzelepisI, ColinE, BadensC,AfenjarA, Dieux CoeslierA, DaillandT, LescaG, PhilipN,and VillardL.Am J Med Genet A. 2015 Oct;167A(10):2314-8. doi: 10.1002/ajmg.a.37152. Epub 2015 May 10.PMID: 25959266.

  Epileptic patients with de novo STXBP1 mutations: Key clinical features based on 24 cases.
- Di Meglio C, Lesca G, Villeneuve N, Lacoste C, Abidi A, Cacciagli P, Altuzarra C, Roubertie A, Afenjar A, Renaldo-Robin F, Isidor B, Gautier A, Husson M, Cances C, Metreau J, Laroche C, Chouchane M, Ville D, Marignier S, Rougeot C, Lebrun M, De Saint Martin A, Perez A, Riquet A, Badens C, Missirian C, Philip N, Chabrol B, Villard L, and Milh M.Epilepsia. 2015 Dec;56(12):1931-40. doi: 10.1111/epi.13214. Epub 2015 Oct 29.PMID: 26514728.

  Heterogeneity of FHF1 related phenotype: Novel case with early onset severe attacks of apnea, partial mitochondrial respiratory chain complex II deficiency, neonatal onset seizures without neurodegeneration.
- Villeneuve N, Abidi A, Cacciagli P, Mignon-Ravix C, Chabrol B, Villard L, Milh M.Eur J Paediatr Neurol. 2017 Sep;21(5):783-786. doi: 10.1016/j.ejpn.2017.04.001. Epub 2017 Apr 29.PMID: 28506426

Nancy CHOUCAIR 2010-20131)

Intragenic rearrangements in X-linked intellectual deficiency: results of a-CGH in a series of 54 patients and identification of TRPC5 and KLHL15 as potential XLID genes.

- Mignon-Ravix C, Cacciagli P, Choucair N, Popovici C, Missirian C, Milh M, Mégarbané A, Busa T, Julia S, Girard N, Badens C, Sigaudy S, Philip N, Villard L.Am J Med Genet A. 2014 Aug;164A(8):1991-7. doi: 10.1002/ajmg.a.36602. Epub 2014 May 9.PMID: 24817631

Contribution of copy number variants (CNVs) to congenital, unexplained intellectual and developmental disabilities in Lebanese patients.

- Choucair N, Ghoch JA, Corbani S, Cacciagli P, Mignon-Ravix C, Salem N, Jalkh N, El Sabbagh S, Fawaz A, Ibrahim T, Villard L, Mégarbané A, Chouery E.Mol Cytogenet. 2015 Apr 9;8:26. doi: 10.1186/s13039-015-0130-y. eCollection 2015.PMID: 25922617

Evidence that homozygous PTPRD gene microdeletion causes trigonocephaly, hearing loss, and intellectual disability.

- Choucair N, Mignon-Ravix C, Cacciagli P, Abou Ghoch J, Fawaz A, Mégarbané A, Villard L, Chouery E.Mol Cytogenet. 2015 Jun 16;8:39. doi: 10.1186/s13039-015-0149-0. eCollection 2015. PMID: 26082802-

Bilal EL WALY 2009-2012

Deletion of YWHAE in a patient with periventricular heterotopias and pronounced corpus callosum hypoplasia.

- Mignon-Ravix C, Cacciagli P, El-Waly B, Moncla A, Milh M, Girard N, Chabrol B, Philip N, Villard L.J Med Genet. 2010 Feb;47(2):132-6. doi: 10.1136/jmg.2009.069112. Epub 2009 Jul 26.PMID: 196357262

Disruption of the ATP8A2 gene in a patient with a t(10;13) de novo balanced translocation and a severe neurological phenotype.

- Cacciagli P, Haddad MR, Mignon-Ravix C, El-Waly B, Moncla A, Missirian C, Chabrol B, Villard L.EurJ Hum Genet. 2010 Dec;18(12):1360-3. doi: 10.1038/ejhg.2010.126. Epub 2010 Aug 4.PMID: 206834873

Nhej1 Deficiency Causes Abnormal Development of the Cerebral Cortex.

- El Waly B, Buhler E, Haddad MR, Villard L.Mol Neurobiol. 2015 Aug;52(1):771-82. doi: 10.1007/s12035-014-8919-y. Epub 2014 Oct 7.PMID: 252881574/Molecular characterization of a 1p36 chromosomal duplication and in utero interference define ENO1 as a candidate gene for polymicrogyria.El Waly B, Mignon-Ravix C,Cacciagli P, Buhler E, Ben Zeev B, Villard L.Eur J Hum Genet. 2020 Dec;28(12):1703-1713. doi: 10.1038/s41431-020-0659-z. Epub 2020 Jun 2. PMID: 32488097

Marie-Reine HADDAD 2006-2009

Characterization of a de novo balanced translocation in a patient with moderate mental retardation and dysmorphic features.

- Haddad MR, Mignon-Ravix C, Cacciagli P, Mégarbané A, Villard L.Eur J Med Genet. 2009 Jul-Aug;52(4):211-7. doi: 10.1016/j.ejmg.2009.04.002. Epub 2009 Apr 18.PMID: 193798472

Spatiotemporal expression in mouse brain of Kiaa2022, a gene disrupted in two patients with severe mental retardation.

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