Activity Report 2019

Project-Team EMPENN

EMPENN

IN COLLABORATION WITH: Institut de recherche en informatique et systèmes aléatoires (IRISA)

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Creation of the Project-Team: 2019 January 01

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1. Team, Visitors, External Collaborators

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Aimery Louvet [Inria, until Jul 2019]
Natacha Perez [Inria, from Jun 2019 until Aug 2019]
Yris Brice Wandji Piugie [Inria, from Mar 2019 until Sep 2019]

Visiting Scientists

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Gregory Kiar [McGill University, from Apr 2019 until Jun 2019]

2. Overall Objectives

2.1. Overall Objectives

Empenn (means "Brain" in Breton language) ERL U1228 research team is jointly affiliated with Inria, Inserm (National Institute of Health and Scientific Research), CNRS (INS2I institute), and University of Rennes I. It is a team of IRISA/UMR CNRS 6074. Empenn is based in Rennes, at both the medical and science campuses. The team follows the "VisAGeS" one that was created for 12 years in 2006 by Inria, As for "VisAGeS", Empenn hosts the accreditation number U1228 renewed by Inserm in 2017, after a competitive evaluation conducted by both HCERES and Inserm.

Through this unique partnership, the ambition of Empenn is to establish a multidisciplinary team bringing together researchers in information sciences and medicine. Our medium- and long-term objective is to introduce our basic research to clinical practice, while maintaining the excellence of our methodological research.

Our goal is to foster research in medical imaging, neuroinformatics and population cohorts. In particular, the Empenn team targets the detection and development of imaging biomarkers for brain diseases and focus its efforts on translating this research to clinics and clinical neurosciences at large.

In particular, the objective of Empenn is to propose new statistical and computing methods, and to measure and model brain morphological, structural and functional states in order to better diagnose, monitor and deliver treatment for mental, neurological and substance use disorders. We propose combining advanced instrumental devices and new computational models to provide advanced diagnosis, therapeutic and neuro-rehabilitation solutions for some of the major disorders of the developing and aging brain.

Generic and challenging research topics in this broad domain include finding new ways to compare models and data, assist decisions and interpretation, and develop feedback from experiments. These activities are performed in close collaboration with the Neurinfo in vivo imaging platform, which is a critical environment for the experimental implementation of our research on challenging clinical research projects and the development of new clinical applications.

3. Research Program

3.1. Scientific Foundations

The scientific foundations of our team concern the design and development of new computational solutions for biological images, signals and measurements. Our objective is to develop a better understanding of the normal and pathological brain, at different scales.

This includes imaging brain pathologies in order to better understand pathological behavior from the organ level to the cellular level, and even to the molecular level (using molecule (e.g. through PET-MR imaging), as well as modeling with specific ligands/nanocarriers), and the modelling of normal and pathological large groups of individuals (cohorts) from image descriptors. It also includes the challenge of the discovery of episodic findings (i.e. rare events in large volumes of images and data), data mining and knowledge discovery from image descriptors, the validation and certification of new drugs from imaging features, and, more generally, the integration of neuroimaging into neuroinformatics through the promotion and support of virtual organizations of biomedical actors by means of e-health technologies.
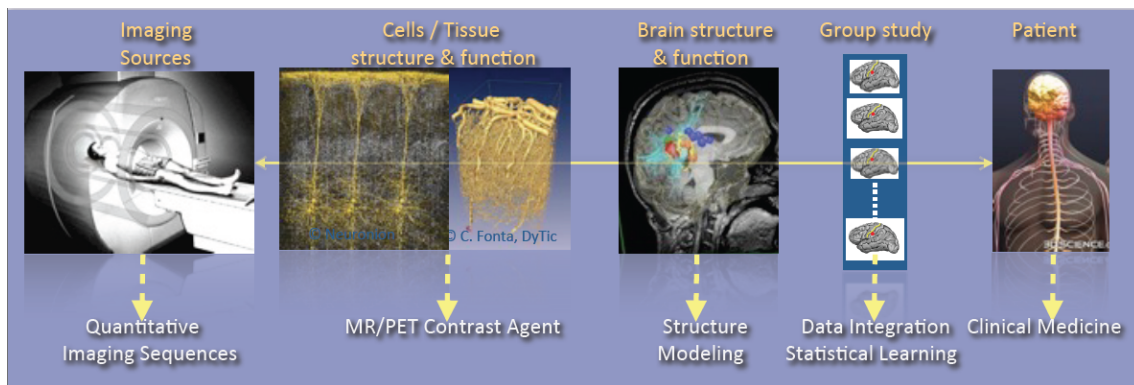
Figure 1. The major overall scientific foundation of the team concerns the integration of data from the Imaging source to the patient at different scales: from the cellular or molecular level describing the structure and function, to the functional and structural level of brain structures and regions, to the population level for the modelling of group patterns and the learning of group or individual imaging markers.

As shown in Fig. 1, the research activities of the Empenn team closely link observations and models through the integration of clinical and multiscale data, and phenotypes (cellular, and later molecular, with structural or connectivity patterns in the first stage). Our ambition is to build personalized models of central nervous system organs and pathologies, and to compare these models with clinical research studies in order to establish a quantitative diagnosis, prevent the progression of diseases and provide new digital recovery strategies, while combining all these research areas with clinical validation. This approach is developed within a translational framework, where the data integration process to build the models is informed by specific clinical studies, and where the models are assessed regarding prospective clinical trials for diagnosis and therapy planning. All of these research activities will be conducted in close collaboration with the Neurinfo platform, which benefited in 2018 from a new high-end 3T MRI system dedicated to research (3T Prisma™ system from Siemens), and through the development in the coming years of multimodal hybrid imaging (from the currently available EEG-MRI, to EEG-NIRS and PET-MRI in the future).

In this context, some of our major developments and newly arising issues and challenges will include:

- The generation of new descriptors to study brain structure and function (e.g. the combination of variations in brain perfusion with and without a contrast agent; changes in brain structure in relation to normal, pathological, functional or connectivity patterns; or the modeling of brain state during cognitive stimulation using neurofeedback).

- The integration of additional spatiotemporal and hybrid imaging sequences covering a larger range of observations, from the molecular level to the organ level, via the cellular level (arterial spin labeling, diffusion MRI, MR relaxometry, MR fingerprinting, MR cell labeling imaging, MR-PET molecular imaging, EEG-MRI functional imaging, EEG-NIRS-MRI, etc.).

- The creation of computational models through the data fusion of molecular, cellular (i.e. through dedicated ligands or nanocarriers), structural and functional image descriptors from group studies of normal and/or pathological subjects.

- The evaluation of these models in relation to acute pathologies, especially for the study of degenerative, psychiatric, traumatic or developmental brain diseases (primarily multiple sclerosis, stroke, traumatic brain injury (TBI) and depression, but applicable with a potential additional impact to epilepsy, Parkinson's disease, dementia, Posttraumatic stress disorder, etc.) within a translational framework.

In terms of new major methodological challenges, we will address the development of models and algorithms to reconstruct, analyze and transform the images, and to manage the mass of data to store, distribute and "semanticize" (i.e. provide a logical division of the model's components according to their meaning). As such, we expect to make methodological contributions in the fields of model inference; statistical analysis and modeling; the application of sparse representation (compressed sensing and dictionary learning) and machine learning (supervised/unsupervised classification and discrete model learning); data fusion (multimodal integration, registration, patch analysis, etc.); high-dimensional optimization; data integration; and brain-computer interfaces. As a team at the frontier between the digital sciences and clinical research in neuroscience, we do not claim to provide theoretical breakthroughs in these domains but rather to provide significant advances in using these algorithms through to the advanced applications we intend to address. In addition, we believe that by providing these significant advances using this set of algorithms, we will also contribute to exhibiting new theoretical problems that will fuel the domains of theoretical computer sciences and applied mathematics.

In summary, we expect to address the following major challenges:

- Developing new information processing methods able to detect imaging biomarkers in the context of mental, neurological, and substance use disorders.
- Providing new computational solutions for our target applications, allowing a more appropriate representation of data for image analysis and the detection of biomarkers specific to a form or grade of pathology, or specific to a population of subjects.
- Providing, for our target applications, new patient-adapted connectivity atlases for the study and characterization of diseases from quantitative MRI.
- Providing, for our target applications, new analytical models of dynamic regional perfusion, and deriving indices of dynamic brain local perfusion from normal and pathological populations.
- Investigating whether the theragnostics paradigm of rehabilitation from hybrid neurofeedback can be effective in some behavioral and disability pathologies.

These major advances will be primarily developed and validated in the context of several priority applications in which we expect to play a leading role: multiple sclerosis, stroke rehabilitation, and the study and treatment of depression.

4. Application Domains

4.1. Population imaging

One major objective of neuroimaging researchers and clinicians is to be able to stratify brain imaging data in order to derive new and more specific population models. In practice this requires to set up large-scale experiments that, due to the lack of resources and capabilities to recruit locally subjects who meet specific inclusion criteria, motivates the need for sharing the load.

But, building and using multi-site large-scale resources poses specific challenges to deal with the huge quantity of data produced and their diversity. Empenn will focus on two challenges in particular:

- Provide computational environments for the computation and use of imaging biomarkers in the targeted brain diseases, a solution to be used by radiologists and neurologists/psychiatrists for the clinical follow-up of a large patient population.
- Modeling analytic variability of image processing pipelines to better understand and predict the behaviour of imaging biomarker detection solutions and improve reproducibility and productivity in clinical neuroimaging research.

4.2. Detection and learning

We intend to make significant contributions with major impacts in learning coupling models between functional recordings during neurofeedback procedures. These advances will provide a breakthrough in brain-computer interfaces for rehabilitation protocols. Our aim is to:

- Provide a computational environment that combines data-driven (machine learning) and Bayesian solutions to improve the detection of abnormal patterns in images through decision or evidence theory data fusion strategies. The major initial application will be for multiple sclerosis. Over the longer term, we also expect to adapt these methods to address a wider range of neurological diseases (epilepsy, stroke, tumors, etc.) in neonate and adult brains.

- Develop solutions for combining brain state measurements from multimodal sensors or sequences (e.g. fMRI, ASL, EEG, NIRS, etc.) with applications in the spatiotemporal reconstruction of brain activity from MRI-EEG or the combined detection of the endogenous hemodynamic and resting state network of the brain from ASL and NIRS. Over the longer term, the advent of new hybrid brain imaging sensors (e.g. PET-MRI) will require these methods to be extended to a larger spectrum of information combining structural, morphological, metabolic, electrophysiological and cellular/molecular information (e.g. through the use of specific ligands/nanocarriers).

4.3. Quantitative imaging

The Empenn research group focuses on the development of several quantitative techniques in magnetic resonance imaging of the brain. These methods allow for a characterization of both the function and the structure of the brain with high precision. Arterial spin labelling (ASL) is a contrast agent-free imaging technique which labels arterial blood water as an endogenous tracer for perfusion and can measure resting-state cerebral blood flow. We are interested in estimating multiparametric hemodynamics using ASL, such as combined cerebral blood flow and arterial transit times, and derive statistical descriptors to represent significant differences between groups. In addition to quantitative perfusion parameters, our contributions on tissue compartment imaging aim at delineating neural circuits and characterize their microstructure properties, using both diffusion MRI and relaxometry. In diffusion MRI, arbitrary gradient waveforms were shown to exhibit higher sensitivity to microstructure parameters than standard pulsed gradients. We work on the optimization of sampling protocols in this domain, with the objective to propose sequences compatible with in vivo acquisition. Complementary to diffusion MRI, we develop methods for the reconstruction of myelin-bound, extra-axonal and cerebrospinal fluid water using multi-compartment modelling of the T2-relaxometry signal. We combine these techniques with tractography to identify trajectories of pathologies associated to the evolution of these microstructural parameters along specific fiber bundles in the brain white matter.

4.4. Behavior

Advances in the field of in vivo imaging offer new opportunities for addressing the management of resistant affective disorders and their consequences (suicide risk and socio-professional impact), and the management of spatial cognition disorders after stroke and their consequences (postural perturbations and the loss of autonomy). Our objective, and the main challenge in this context, will be to introduce medical image computing methods to the multidisciplinary field of behavioral disorders (cognitive disorders, particularly spatial and postural control disorders or anterograde memory impairment, mood disorders, notably resistant depression, schizophrenic disorders, pervasive developmental disorders, attention disorders, etc.) in order to gain a better understanding of the pathology and devise innovative therapeutic approaches.

We also expect to become a major player in the future and make important contributions with significant impacts, primarily in drug-resistant depression in young and old populations. In particular, we expect to provide new image-related metrics combining perfusion, metabolism and microstructural information regarding the brain in order to better characterize pathologies, provide prospective evolution values and potentially provide new brain stimulation targets that could be used in neurofeedback rehabilitation protocols or other types of brain stimulation procedure.

We aim to provide new imaging markers of mental diseases, especially in the context of mood disorders. The new biomarkers will be derived from the metabolic (ASL and later ASL+PET) point of view as well as from the microstructural point of view (multicompartment diffusion MRI and relaxometry). Similarly, we expect to exhibit imaging biomarker regularities combining metabolic and structural information. Over the longer term, we expect these biomarkers to be the target of neurofeedback rehabilitation procedures. Also, over the longer term, we expect to supplement the MRI markers with molecular marker ones coming from new PET tracers, especially those associated with serotonin intake, at one time point or during a rehabilitation protocol under hybrid PET-EEG-MRI neurofeedback procedures.

4.5. Neuroinflammation

Some of the major ongoing research issues in the neuroimaging of neuro-inflammatory diseases concern the definition of new biomarkers for tracking the development of the pathology using high- dimensional data (e.g. nD+t MRI). This includes the use of white matter-specific imaging, such as magnetization transfer MRI, relaxometry and diffusion-weighted imaging (DW-MRI). Our objective is (1) to develop information-processing tools to tag the spatiotemporal evolutions of MS patterns at the brain parenchyma and spinal cord levels from their different signatures (inflammatory cells visible with USPIO or Gd contrast agents on MRI, persistent black holes, eloquent regional atrophy and microstructure signatures); and (2) to test these new tools on new imaging cohorts. In this respect, we for instance conduct studies on brain and spinal cord imaging, continuing on from the PHRC multicentric EMISEP project (PI: G. Edan), as it is very likely that lesions in the spine will directly affect the ambulatory ability of the patient (and thereby the clinical scores). In order to extend this experiment to a larger MS population, based on our expertise from the OFSEP cohort, we also plan to improve the MS therapeutic decision process through the MUSIC project (Multiple Sclerosis Imaging Check out, a public/private project). Our goal is to develop and assess a standardized monitoring tool that provides a robust, long-term computerized MRI follow-up that will become the gold standard in clinical practice for therapeutic decisions in MS treatment. As part of this project, Empenn will share its expertise in data management systems (Shanoir and FLI-IAM) and automatic processing tools (through the medInria and Anima software repositories) to extract quantitative indices from the images.

4.6. Recovery

Mental and neurological disorders are the leading cause of years lived with a disability. Treatment-resistant depression affects approximately 2% of the European population. Meanwhile, in the case of brain disorders, almost 1.5 million Europeans (15 million people worldwide) suffer a stroke event each year. Current recovery methods for brain disorders and traumatic brain injuries remain limited, preventing many from achieving full recuperation. We propose addressing the issue of brain recovery by introducing new advances from recent breakthroughs in computational medical imaging, data processing and human-machine interfaces, and demonstrating how these new concepts can be used, in particular for the treatment of stroke and major depressive disorders.

We ambition to combine advanced instrumental devices (Hybrid EEG, NIRS and MRI platforms), with new hybrid brain computer interface paradigms and new computational models to provide neurofeedback-based therapeutic and neuro-rehabilitation paradigms in some of the major mental and neurological disorders of the developmental and the aging brain.

Neurofeedback involves using a brain-computer interface that provides an individual with real-time biofeedback about his or her brain activity in the form of sensory feedback. It enables individuals to learn to better control their brain activity, which can be measured in real time using various non-invasive sensors as described above. Although EEG is currently the only modality used by clinical practitioners in that context, it lacks specificity due to its low spatial resolution. Dynamic research into fMRI-neurofeedback has held promise for treating depression, chronic pain and stroke, since it offers the prospect of real-time imagery of the activity in deep brain structures with high spatial resolution. However, the low temporal resolution and high cost of fMRI-Neurofeedback has hampered the development of many applications. We believe that the future belongs to hybrid responses that combine multimodal sensors and intend to demonstrate this in the Empenn project.

5. Highlights of the Year

5.1. Highlights of the Year

5.1.1. *New NIRS system at the Neurinfo platform*

An MRI and EEG-compatible functional near-infrared spectroscopy (fNIRS) system was installed at the Neurinfo platform in September 2019.

5.1.2. *Sciences en Cour[t]s*

This event is a festival of short films, which offers doctoral students the opportunity to make short films about their thesis work. Raphael Truffet, Antoine Legouhy and Xavier Rolland won the high school award in science en Cour[t]s event https://www.youtube.com/watch?v=IKgqv-iCwak.

5.1.3. *Second neuroscience hackathon in Rennes*

We organized the second edition of hackathon in the Empenn team, November 14-15 as part of the international event Brainhack Global 2019.

6. New Software and Platforms

6.1. Anima

KEYWORDS: Filtering - Medical imaging - Diffusion imaging - Registration - Relaxometry

SCIENTIFIC DESCRIPTION: Anima is a set of libraries and tools developed by the team as a common repository of research algorithms. As of now, it contains tools for image registration, statistical analysis (group comparison, patient to group comparison), diffusion imaging (model estimation, tractography, etc.), quantitative MRI processing (quantitative relaxation times estimation, MR simulation), image denoising and filtering, and segmentation tools. All of these tools are based on stable libraries (ITK, VTK), making it simple to maintain.

- Participants: Aymeric Stamm, Fang Cao, Florent Leray, Guillaume Pasquier, Laurence Catanese, Olivier Commowick, Renaud Hedouin and René-Paul Debroize
- Contact: Olivier Commowick
- URL: https://github.com/Inria-Visages/Anima-Public/wiki

6.2. autoMRI

KEYWORDS: FMRI - MRI - ASL - FASL - SPM - Automation

SCIENTIFIC DESCRIPTION: This software is highly configurable in order to fit a wide range of needs. Pre-processing includes segmentation of anatomical data, as well as co-registration, spatial normalization and atlas building of all data types. The analysis pipelines perform either within-group analysis or between-group or one subject-versus-group comparison, and produce statistical maps of regions with significant differences. These pipelines can be applied to structural data to exhibit patterns of atrophy or lesions, to ASL (both pulsed or pseudo-continuous sequences) or PET data to detect perfusion or metabolic abnormalities, to relaxometry data to detect deviations from a template, to functional data - either BOLD or ASL - to outline brain activations related to block or event-related paradigms. In addition to the standard General Linear Model approach, the ASL pipelines implement an a contrario approach and, for patient-specific perfusion study, an heteroscedastic variance model. Besides, the vascular pipeline processes 4D MRA data and enables accurate assessment of hemodynamic patterns.

FUNCTIONAL DESCRIPTION: AutoMRI Based on MATLAB and the SPM8 toolbox, autoMRI provides complete pipelines to pre-process and analyze various types of images (anatomical, functional, perfusion, metabolic, relaxometry, vascular).

- Participants: Camille Maumet, Cédric Meurée, Elise Bannier, Fang Cao, Isabelle Corouge, Pierre Maurel, Quentin Duché and Julie Coloigner
- Contact: Isabelle Corouge
- URL: https://team.inria.fr/visages/software/

6.3. MedInria

KEYWORDS: Visualization - DWI - Health - Segmentation - Medical imaging

SCIENTIFIC DESCRIPTION: MedInria aims at creating an easily extensible platform for the distribution of research algorithms developed at Inria for medical image processing. This project has been funded by the D2T (ADT MedInria-NT) in 2010, renewed in 2012. A fast-track ADT was awarded in 2017 to transition the software core to more recent dependencies and study the possibility of a consortium creation.The Empenn team leads this Inria national project and participates in the development of the common core architecture and features of the software as well as in the development of specific plugins for the team's algorithm.

FUNCTIONAL DESCRIPTION: MedInria is a free software platform dedicated to medical data visualization and processing.

- Participants: Maxime Sermesant, Olivier Commowick and Théodore Papadopoulo
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6.4. QtShanoir

KEYWORDS: Qt - Nifti - Medical imaging - Plug-in - DICOM - Health - C++ - Soap - Webservices - Shanoir

SCIENTIFIC DESCRIPTION: QtShanoir is based on Qt/C++ library. It interacts with the Shanoir server using SOAP web services. This application queries the server and displays hierarchical data extracted in tree view. Data could also be easily downloaded or uploaded on the server. In order to extend the Shanoir environment, QtShanoir is developed to contain two shared libraries: - « GUI » that represents all user interfaces. - « DAO » that takes in charge the data model. This library assures the connection to the server and provides all QtShanoir services : search, download and upload of Processed Dataset (NIfTI). QtShanoir dynamic libraries are already reused and integrated in other projects: in the software medInria and in an under development command line program.

FUNCTIONAL DESCRIPTION: QtShanoir is a graphical client application of the medical imaging database Shanoir. This application provides various functionalities to satisfy researchers' needs. It allows users to: - explore neuroimaging data derived from multicenter research trials. Through an intuitive user interface, users could easily visualize voluminous amount of structured data: studies, patients and datasets extracted from Shanoir - download and to upload data from the server. This application is available on Windows, UNIX, MacOs X. It is integrated as a plugin in medInria, a multi-plateform for medical image processing and visualization.

- Participants: Alexandre Abadie, Guillaume Renard, Nicolas Wiest Daessle, Olivier Commowick and Wefa Hakem
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- URL: http://qtshanoir.gforge.inria.fr

6.5. Shanoir

SHAring NeurOImaging Resources

KEYWORDS: Neuroimaging - Medical imaging - PACS - Nifti - Data Sharing - DICOM - Health - Shanoir - Webservices - Data base - Biology - Web Application

FUNCTIONAL DESCRIPTION: SHAring NeurOImaging Resources (Shanoir, Previously InriaNeuroTk) is an open source software platform designed to share, archive, search and visualize neuroimaging data.

It provides a user-friendly secure web access and offers an intuitive workflow to facilitate the collecting and retrieving of neuroimaging data from multiple sources and a wizzard to make the completion of metadata easy. Shanoir comes along many features such as anonymization of data, support for multi-centric clinical studies on subjects or group of subjects.

Shanoir offers an ontology-based data organization (OntoNeuroLOG). Among other things, this facilitates the reuse of data and metadata, the integration of processed data and provides traceability through an evolutionary approach. Shanoir allows researchers, clinicians, PhD students and engineers to undertake quality research projects with an emphasis on remote collaboration. As a secured J2EE web application, it therefore allows safely storing and archiving, with no more requirements than a computer with an internet connection!

Furthermore, Shanoir is not only a web application: it is also a complete neuroinformatics platform in which you can easily integrate your existing processing tools or develop your own ones (see ShanoirTk).

The clinical scores resulting from instrument-based assessments (e.g. neuropsychological tests) can also be entered and easily retrieved and exported in different formats (Excel, CSV, Xml). Scores and image acquisitions are bound together which makes relationship analysis possible. The instrument database is scalable and new measures can be added in order to meet specific project needs, by use of intuitive graphical interfaces.

Using cross-data navigation and advanced search criteria, the users can quickly point to a subset of data of data to be downloaded. Client side applications have as well been developed to illustrate how to locally access and exploit data through the available web services. With regard to security, the system requires authentication and user rights are tunable for each hosted study. The person responsible for the study can define which users are allowed to see, download or import data.

Shanoir serves neuroimaging researchers in organizing efficiently their studies, while cooperating with other laboratories. By managing patient privacy, Shanoir allows the exploitation of clinical data in a research context. It is finally a handy solution to publish and share data with a broader community.

- Participants: Adrien Férial, Anthony Baire, Bernard Gibaud, Christian Barillot, Guillaume Renard, Justine Guillaumont, Michael Kain and Yao Yao
- Partners: Université de Rennes 1 - CNRS - INSERM
- Contact: Christian Barillot
- URL: http://shanoir.gforge.inria.fr

6.6. ShanoirUploader

KEYWORDS: Webservices - PACS - Medical imaging - Neuroimaging - DICOM - Health - Biology - Java - Shanoir

SCIENTIFIC DESCRIPTION: ShanoirUploader is a desktop application on base of JavaWebStart (JWS). The application can be downloaded and installed using an internet browser. It interacts with a PACS to query and retrieve the data stored on it. After this ShanoirUploader sends the data to a Shanoir server instance in order to import these data. This application bypasses the situation, that in most of the clinical network infrastructures a server to server connection is complicated to set up between the PACS and a Shanoir server instance.

FUNCTIONAL DESCRIPTION: ShanoirUploader is a Java desktop application that transfers data securely between a PACS and a Shanoir server instance (e.g., within a hospital). It uses either a DICOM query/retrieve connection or a local CD/DVD access to search and access images from a local PACS or the local CD/DVD. After having retrieved the data, the DICOM files are locally anonymized and then uploaded to the Shanoir server. A possible integration of a hash creation application for patient identifiers is provided as well. The

primary goals of that application are to enable mass data transfers between different remote server instances and therefore reduce the waiting time of the users, when importing data into Shanoir. Most of the time during import is spent with data transfers.

- Participants: Christian Barillot, Inès Fakhfakh, Justine Guillaumont, Michael Kain and Yao Yao
- Contact: Christian Barillot
- URL: http://shanoir.gforge.inria.fr

6.7. Anima medInria plugins

KEYWORDS: IRM - Medical imaging - Diffusion imaging

FUNCTIONAL DESCRIPTION: Plugins for the medInria software based on the open source software Anima developed in the Visages / Empenn team. These plugins are interfaces between anima and medinria allowing to use Anima functionalities within the clinical user interface provided by medInria. The current functionalities included in the plugins are right now: image registration, denoising, quantitative image (relaxometry), and model estimation and visualization from diffusion imaging.

- Participants: Olivier Commowick, René-Paul Debroize and Guillaume Pasquier
- Contact: Olivier Commowick

6.8. Platforms

6.8.1. *The Neurinfo Platform*

Empenn is the founding actor of an experimental research platform which was installed in August 2009 at the University Hospital of Rennes. The University of Rennes 1, Inria, CNRS for the academic side, and the University Hospital of Rennes and the Cancer Institute "Eugene Marquis" for the clinical side, are partners of this neuroinformatics platform called Neurinfo (https://www.neurinfo.org).

Concerning the Neurinfo Platform, the activity domain is a continuum between methodological and technological research built around specific clinical research projects. On the medical field, the translational research domain mainly concerns medical imaging and more specifically the clinical neurosciences. Among them are multiple sclerosis, epilepsy, neurodegenerative, neurodevelopmental and psychiatric diseases, surgical procedures of brain lesions, neuro-oncology and radiotherapy planning. Beyond these central nervous system applications, the platform is also open to alternative applications. Neurinfo ambitions to support the emergence of research projects based on their level of innovation, their pluri-disciplinarity and their ability to foster collaborations between different actors (public and private research entities, different medical specialties, different scientific profiles).

In this context, a research 3T MRI system (Siemens Verio) was acquired in summer 2009 in order to develop the clinical research in the domain of morphological, functional, structural and cellular in-vivo imaging. A new 3T Siemens Prisma MRI scanner was installed at the Neuroinfo platform in February 2018. In 2014, an equipment for simultaneous recording of EEG and MRI images was acquired from Brain Product. In 2015, a mock scanner for experimental set-up was acquired as well as a High Performance Computing environment made of one large computing cluster and a data center that is shared and operated by the Inria center and IRISA (UMR CNRS 6074). The computation cluster (480 cores) and the data center (up to 150 TB) are dedicated to host and process imaging data produced by the Neurinfo platform, but also by other research partners that share their protocols on the Neurinfo neuroinformatics system (currently more than 60 sites). In 2019, an MRI and EEG-compatible fNIRS system was acquired through a co-funding from the INS2I institute of CNRS and FEDER. At the end of 2019, GIS IBISA awarded the Neurinfo platform with a complementary funding that will be dedicated to supplement the current system with additional sensors (from 8x8 optodes to 16x16 optodes).

7. New Results

7.1. Research axis 1: Medical Image Computing in Neuroimaging

Extraction and exploitation of complex imaging biomarkers involve an imaging processing workflow that can be quite complex. This goes from image physics and image acquisition, image processing for quality control and enhancement, image analysis for features extraction and image fusion up to the final application which intends to demonstrate the capability of the image processing workflow to issue sensitive and specific markers of a given pathology. In this context, our objectives in the recent period were directed toward following major methodological topics:

7.1.1. Diffusion imaging

7.1.1.1. Free water estimation using single-shell diffusion-weighted images
Participant: Emmanuel Caruyer.

Free-water estimation requires the fitting of a bi-compartment model, which is an ill-posed problem when using only single-shell data. Its solution requires optimization, which relies on an initialization step. We propose a novel initialization approach, called "Freewater EstimatoR using iNtErpolated iniTialization" (FERNET), which improves the estimation of free water in edematous and infiltrated peritumoral regions, using single-shell diffusion MRI data. The method has been extensively investigated on simulated data and healthy and brain tumor datasets, demonstrating its applicability on clinically acquired data. Additionally, it has been applied to data from brain tumor patients to demonstrate the improvement in tractography in the peritumoral region [57].

7.1.1.2. Multi-dimensional diffusion MRI sampling scheme: B-tensor design and accurate signal reconstruction
Participant: Emmanuel Caruyer.

B-tensor encoding enables the separation of isotropic and anisotropic tensors. However, little consideration has been given as to how to design a B-tensor encoding sampling scheme. In this work, we propose the first 4D basis for representing the diffusion signal acquired with B-tensor encoding. We study the properties of the diffusion signal in this basis to give recommendations for optimally sampling the space of axisymmetric b-tensors. We show, using simulations, that the proposed sampling scheme enables accurate reconstruction of the diffusion signal by expansion in this basis using a clinically feasible number of samples [24].

This work was done in collaboration with A. Bates, Australian National University and Al. Daducci, University of Verona.

7.1.1.3. Optimal selection of diffusion-weighting gradient waveforms using compressed sensing and dictionary learning
Participants: Raphaël Truffet, Emmanuel Caruyer, Christian Barillot.

Acquisition sequences in diffusion MRI rely on the use of time-dependent magnetic field gradients. Each gradient waveform encodes a diffusion-weighted measure; a large number of such measurements are necessary for the in vivo reconstruction of microstructure parameters. We propose here a method to select only a subset of the measurements, while being able to predict the unseen data using compressed sensing. We learn a dictionary using a training dataset generated with Monte-Carlo simulations; we then compare two different heuristics to select the measures to use for the prediction. We found that an undersampling strategy limiting the redundancy of the measures allows for a more accurate reconstruction when compared with random undersampling with similar sampling rate [49].

7.1.1.4. Geometric evaluation of distortion correction methods in diffusion MRI of the spinal cord
Participants: Haykel Snoussi, Emmanuel Caruyer, Olivier Commowick, Benoit Combès, Élise Bannier, Christian Barillot.

Acquiring and processing Diffusion MRI in spinal cord present inherent challenges. Differences in magnetic susceptibility between soft tissues, air and bones make the magnetic field non uniform in spinal cord. In this context, various procedures were proposed for correcting inhomogeneity-induced distortions; in this work, we propose novel geometric statistics to measure the alignment of the reconstructed diffusion model with the apparent centerline of the spine. In parallel of the correlation with an anatomical T2-weighted image, we show the utility of these statistics to study and evaluate the impact of distortion correction by comparing three correction methods using a pair of images acquired with reversed gradient polarity [48].

This work was done in collaboration with Anne Kerbrat, Neuropoly Montréal and Julien Cohen-Adad from NeuroPoly Lab, Institute of Biomedical Engineering, Polytechnique Montreal, Montreal, QC, Canada.

7.1.2. Arterial Spin Labeling

7.1.2.1. Acquisition duration in resting-state arterial spin labeling. How long is enough?
Participants: Corentin Vallée, Pierre Maurel, Isabelle Corouge, Christian Barillot.

Resting-state Arterial Spin Labeling (rs-ASL) is a rather confidential method compared to resting-state BOLD but it drives great prospects with respect to potential clinical applications. By enabling the study of cerebral blood flow maps, rs-ASL can lead to significant clinical subject-scaled applications as CBF is a biomarker in neuropathology. An important parameter to consider in functional imaging is the acquisition duration. Despite directly impacting practicability and functional networks representation, there is no standard for rs-ASL. Our work here focuses on strengthening the confidence in ASL as a rs-fMRI method, and on studying the influence of the acquisition duration. To this end, we acquired a long rs-ASL sequence and assessed the quality of typical functional brain networks quality over time compared to gold-standard networks. Our results show that after 14min of duration acquisition, functional networks representation can be considered as stable [58], [50].

7.1.2.2. Patch-based super-resolution of arterial spin labeling magnetic resonance images
Participants: Cédric Meurée, Pierre Maurel, Jean-Christophe Ferré, Christian Barillot.

Arterial spin labeling is a magnetic resonance perfusion imaging technique that, while providing results comparable to methods currently considered as more standard concerning the quantification of the cerebral blood flow, is subject to limitations related to its low signal-to-noise ratio and low resolution. In this work, we investigated the relevance of using a non-local patch-based super-resolution method driven by a high-resolution structural image to increase the level of details in arterial spin labeling images. This method was evaluated by comparison with other image resolution increasing techniques on a simulated dataset, on images of healthy subjects and on images of subjects diagnosed with brain tumors, who had a dynamic susceptibility contrast acquisition. The influence of an increase of ASL images resolution on partial volume effects was also investigated in this work [16].

The development of this super-resolution algorithm in the context of the PhD of Cédric Meurée founded by Siemens Healthineers conducted to a stay of one month of the PhD candidate in Erlangen, during summer 2018. This immersion into the neuro-development team allowed him to integrate the proposed solution with tools in use within this team. Part of the work also consisted in reducing the computation, a factor of 5 being achieved at the end of these four weeks.

7.1.3. Atlases

7.1.3.1. Unbiased longitudinal brain atlas creation using robust linear registration and log-Euclidean framework for diffeomorphisms
Participants: Antoine Legouhy, Olivier Commowick, Christian Barillot.

We have defined a new method to create a diffeomorphic longitudinal (4D) atlas composed of a set of 3D atlases each representing an average model at a given age. This is achieved by generalizing atlasing methods to produce atlases unbiased with respect to the initial reference up to a rigid transformation and ensuring diffeomorphic deformations thanks to the Baker-Campbell-Hausdorff formula and the log-Euclidean framework for diffeomorphisms. Subjects are additionally weighted using an asymmetric function to closely match specified target ages. Creating a longitudinal atlas also implies dealing with subjects with large brain differences that can lead to registration errors. This is overcome by a robust rigid registration based on polar decomposition. We illustrated these techniques for the creation of a 4D pediatric atlas, showing their ability to create a temporally consistent atlas [22].

This work was done in collaboration with François Rousseau, IMT Atlantique, LaTIM U1101 INSERM, Brest, France, under the ANR MAIA project.

7.1.3.2. Online atlasing using an iterative centroid
Participants: Antoine Legouhy, Olivier Commowick, Christian Barillot.

Online atlasing, i.e. incrementing an atlas with new images as they are acquired, is key when performing studies on databases very large or still being gathered. We proposed to this end a new diffeomorphic online atlasing method without having to perform again the atlasing process from scratch. New subjects are integrated following an iterative procedure gradually shifting the centroid of the images to its final position, making it computationally cheap to update regularly an atlas as new images are acquired (only needing a number of registrations equal to the number of new subjects). We evaluated this iterative centroid approach through the analysis of the sharpness and variance of the resulting atlases, and the transformations of images, comparing their deviations from a conventional method using Guimond's method. We demonstrated that the transformations divergence between the two approaches is small and stable, and that both atlases reach equivalent levels of image quality [42].

This work was done in collaboration with François Rousseau, IMT Atlantique, LaTIM U1101 INSERM, Brest, France, under the ANR MAIA project.

7.1.4. Neurofeedback

7.1.4.1. Learning bi-modal EEG-fMRI neurofeedback to improve neurofeedback in EEG only
Participants: Claire Cury, Pierre Maurel, Giulia Lioi, Christian Barillot.

In neurofeedback (NF), a new kind of data are available: electroencephalography (EEG) and functional magnetic resonance imaging (fMRI) acquired simultaneously during bi-modal EEG-fMRI neurofeedback. These two complementary techniques have only recently been integrated in the context of NF for brain rehabilitation protocols. Bi-modal NF (NF-EEG-fMRI) combines information coming from two modalities sensitive to different aspect of brain activity, therefore providing a higher NF quality. However, the use of the MRI scanner is cumbersome and exhausting for patients. We presented, a novel methodological development, able to reduce the use of fMRI while providing to subjects NF-EEG sessions of quality comparable to the bi-modal NF sessions. We proposed an original alternative to the ill-posed problem of source reconstruction. We designed a non-linear model considering different frequency bands, electrodes and temporal delays, with a structured sparse regularisation. Results show that our model is able to significantly improve the quality of NF sessions over what EEG could provide alone. We tested our method on 17 subjects that performed three NF-EEG-fMRI sessions each [30].

7.1.4.2. Can we learn from coupling EEG-fMRI to enhance neuro-feedback in EEG only?
Participants: Claire Cury, Pierre Maurel, Christian Barillot.

Neurofeedback (NF) measures brain activation during a task, and gives back to the subject a score reflecting his/her performance that he/she tries to improve. Among noninvasive functional brain imaging modalities, the most used in NF, are electro-encephalography (EEG) and the functional magnetic resonance imaging (fMRI). EEG measures the electrical activity of the brain through channels located on the scalp, with an excellent temporal resolution (milliseconds), but has a limited spatial resolution due to the well-known ill-posed inverse problem of source reconstruction. Also NF-EEG (NF session with NF scores extracted from EEG) is not easy to control since it comes from mixtures of propagating electric potential fluctuations. Blood oxygenation level dependent (BOLD) fMRI measures neuro-vascular activity, easier to control, with an excellent spatial resolution, making NF-fMRI (NF session with NF scores extracted from BOLD-fMRI) an adequate modality for NF. However its temporal resolution is only of a few seconds, and it is a costly, exhausting for subjects and time consuming modality. Since those modalities are complementary, their combined acquisition is actively investigated, as well as the methodology to extract information from fMRI with EEG which is the easiest modality to use [Abreu et al. 2018]. Our challenge is to learn EEG activation patterns from NF-fMRI scores extracted during a NF session using coupled EEG-fMRI data (NF-EEG-fMRI) to improve NF scores when using EEG only [29].

7.1.5. *Deep learning*

7.1.5.1. Unsupervised domain adaptation with optimal transport in multi-site segmentation of multiple sclerosis lesions from MRI data
Participants: Antoine Ackaouy, Olivier Commowick, Christian Barillot, Francesca Galassi.

Automatic segmentation of Multiple Sclerosis (MS) lesions from Magnetic Resonance Imaging (MRI) images is essential for clinical assessment and treatment planning of MS. Recent years have seen an increasing use of Convolutional Neural Networks (CNNs) for this task. Although these methods provide accurate segmentation, their applicability in clinical settings remains limited due to a reproducibility issue across different image domains. MS images can have highly variable characteristics across patients, MRI scanners and imaging protocols. Retraining a supervised model with data from each new domain is not a feasible solution because it requires manual annotation from expert radiologists. In this work, we explored an unsupervised solution to the problem of domain shift. We presented a framework, Seg-JDOT, which adapts a deep model so that samples from a source domain and samples from a target domain sharing similar representations will be similarly segmented. We evaluated the framework on a multi-site dataset, MICCAI 2016, and showed that the adaptation towards a target site can bring remarkable improvements in a model performance over standard training [54].

This work was done in collaboration with Nicolas Courty, Obelix team, IRISA laboratory from University of Bretagne Sud.

7.1.5.2. Deep learning for multi-site MS lesions segmentation: two-step intensity standardization and generalized loss function.
Participants: Francesca Galassi, Olivier Commowick, Christian Barillot.

We presented an improved CNN framework for the segmentation of Multiple Sclerosis (MS) lesions from multi-modal MRI. It uses a two-step intensity normalization and a cascaded network with cost sensitive learning. Performance was assessed on a public multi-site data-set [35].

7.2. Research axis 2: Applications in Neuroradiology and Neurological Disorders

Our objectives is also to provide new computational solutions for our target clinical applications (radiology, neurology, psychiatry and rehabilitation...), allowing a more appropriate representation of data for image analysis and the detection of biomarkers specific to a form or grade of pathology, or specific to a population of subjects. In this section, we present our contributions in different clinical applications.

7.2.1. Rehabilitation

7.2.1.1. Efficacy of EEG-fMRI Neurofeedback for stroke rehabilitation in relation to the DTI structural damage: a pilot study.
Participants: Giulia Lioi, Mathis Fleury, Christian Barillot, Isabelle Bonan.

Recent studies have shown the potential of neurofeedback (NF) for motor rehabilitation after stroke. The majority of these NF approaches have relied solely on one imaging technique: mostly on EEG recordings. Recent study have gone further, revealing the potential of integrating complementary techniques such as EEG and fMRI to achieve a more specific regulation. In this exploratory work, multisession bimodal EEG-fMRI NF for upper limb motor recovery was tested in four stroke patients.The feasibility of the NF training was investigated with respect to the integrity of the corticospinal tract (CST), a well-established predictor of the potential for clinical improvement. Results indicated that patients exhibiting a high degree of integrity of the ipsilesional CST showed significant increased activation of the ipsilesional M1 at the end of the training (p<<0.001, Wilcoxon test). These preliminary findings confirm the critical role of the CST integrity for stroke motor recovery and indicate that this is importantly related also to functional brain regulation of the ipsilesional motor cortex [43].

7.2.2. Multiple sclerosis

7.2.2.1. Tissue microstructure information from T2 relaxometry and diffusion MRI can identify multiple sclerosis (MS) lesions undergoing blood-brain barrier breakdown (BBB)
Participants: Olivier Commowick, Christian Barillot.

Gadolinium-based contrast agents (GBCA) play a critical role in identifying MS lesions undergoing BBB which is of high clinical importance. However, repeated use of GBCAs over a long period of time and the risks associated with administering it to patients with renal complications has mandated for greater caution in its usage. In this work we explored the plausibility of identifying MS lesions undergoing BBB from tissue microstructure information obtained from T2 relaxometry and dMRI data. We also proposed a framework to predict MS lesions undergoing BBB using the tissue microstructure information and demonstrated its potential on a test case [26].

7.2.2.2. Neural basis of irony in patients with Multiple Sclerosis: an exploratory fMRI study
Participants: Quentin Duché, Élise Bannier.

Irony is a form of non-literal language that is characterized by the opposition between the literal meaning of a statement and the message that the speaker wishes to convey. Knowledge about the neural bases of non-literal language has largely developed in recent years from injury studies or more recently through data from functional imaging studies. Multiple sclerosis (MS) is a neurodegenerative disease that, in addition to cognitive dysfunction, results in variable impairment of theory of mind and non-literal language skills. This work aims at exploring neural basis underpinning the comprehension of irony in MS patients compared to a group of healthy subjects. The results suggest that multiple sclerosis patients require higher left hemisphere resources than healthy controls to understand irony [32].

This work is done in collaboration with by Florian Chapelain (Pôle Saint Hélier), Philippe Gallien (Pôle Saint Hélier) and Virginie Dardier (Université Rennes 2).

7.2.2.3. Joint assessment of brain and spinal cord motor tract damage in patients with early relapsing remitting multiple sclerosis (RRMS): predominant impact of spinal cord lesions on motor function
Participants: Benoit Combès, Élise Bannier, Haykel Snoussi, Jean-Christophe Ferré, Christian Barillot.

The effect of structural multiple sclerosis damage to the corticospinal tract (CST) has been separately evaluated in the brain and spinal cord (SC), even though a cumulative impact is suspected. In this work, we evaluated CST damages on both the cortex and cervical SC, and examine their relative associations with motor function, measured both clinically and by electrophysiology. This study highlights the major contribution of SC lesions to CST damage and motor function abnormalities [8].

This work was done in collaboration with Anne Kerbrat (Neuropoly Montréal) and Raphael Chouteau (CHU Rennes).

7.2.2.4. Spatial distribution of multiple sclerosis lesions in the cervical spinal cord
Participants: Élise Bannier, Gilles Edan.

Spinal cord lesions detected on MRI hold important diagnostic and prognostic value for multiple sclerosis. Our aim was to explore the spatial distribution of multiple sclerosis lesions in the cervical spinal cord, with respect to clinical status. We included 642 suspected or confirmed multiple sclerosis patients (31 clinically isolated syndrome, and 416 relapsing-remitting, 84 secondary progressive, and 73 primary progressive multiple sclerosis) from 13 clinical sites. With an automatic publicly-available analysis pipeline we produced voxelwise lesion frequency maps to identify predilection sites in various patient groups characterized by clinical subtype, Expanded Disability Status Scale score and disease duration. We also measured absolute and normalized lesion volumes in several regions of interest using an atlas-based approach, and evaluated differences within and between groups. The lateral funiculi were more frequently affected by lesions in progressive subtypes than in relapsing in voxelwise analysis ($P < 0.001$), which was further confirmed by absolute and normalized lesion volumes ($P < 0.01$). The central cord area was more often affected by lesions in primary progressive than relapse-remitting patients ($P < 0.001$). Between white and grey matter, the absolute lesion volume in the white matter was greater than in the grey matter in all phenotypes ($P < 0.001$); however when normalizing by each region, normalized lesion volumes were comparable between white and grey matter in primary progressive patients. Lesions appearing in the lateral funiculi and central cord area were significantly correlated with Expanded Disability Status Scale score ($P < 0.001$). High lesion frequencies were observed in patients with a more aggressive disease course, rather than long disease duration. Lesions located in the lateral funiculi and central cord area of the cervical spine may influence clinical status in multiple sclerosis. This work shows the added value of cervical spine lesions, and provides an avenue for evaluating the distribution of spinal cord lesions in various patient groups [14].

This work was done in collaboration with Julien Cohen-Adad (Neuropoly, Montreal) and Anne Kerbrat (Neuropoly Montréal).

7.2.2.5. Automatic segmentation of the spinal cord and intramedullary multiple sclerosis lesions with convolutional neural networks
Participants: Élise Bannier, Gilles Edan.

The goal of this study was to develop a fully-automatic framework - robust to variability in both image parameters and clinical condition - for segmentation of the spinal cord and intramedullary MS lesions from conventional MRI data of MS and non-MS cases. Scans of 1042 subjects (459 healthy controls, 471 MS patients, and 112 with other spinal pathologies) were included in this multi-site study (n=30). Data spanned three contrasts (T1-, T2-, and T2$_*$-weighted) for a total of 1943vol and featured large heterogeneity in terms of resolution, orientation, coverage, and clinical conditions. The proposed cord and lesion automatic segmentation approach is based on a sequence of two Convolutional Neural Networks (CNNs). CNNs were trained independently with the Dice loss. When compared against manual segmentation, our CNN-based approach showed a median Dice of 95% vs. 88% for PropSeg ($p \leq 0.05$), a state-of-the-art spinal cord segmentation method. Regarding lesion segmentation on MS data, our framework provided a Dice of 60%, a relative volume difference of -15%, and a lesion-wise detection sensitivity and precision of 83% and 77%, respectively. In this study, we introduce a robust method to segment the spinal cord and intramedullary MS lesions on a variety of MRI contrasts. The proposed framework is open-source and readily available in the Spinal Cord Toolbox.

This work was done in collaboration with Julien Cohen-Adad (Neuropoly, Montreal) and Anne Kerbrat (Neuropoly Montréal).

7.2.3. Arterial Spin Labeling in pediatric populations

7.2.3.1. Changes in brain perfusion in successive arterial spin labeling MRI scans in neonates with hypoxic-ischemic encephalopathy
Participants: Maia Proisy, Isabelle Corouge, Antoine Legouhy, Christian Barillot, Jean-Christophe Ferré.

The primary objective of this study was to evaluate changes in cerebral blood flow (CBF) using arterial spin labeling MRI between day 4 of life (DOL4) and day 11 of life (DOL11) in neonates with hypoxic-ischemic encephalopathy (HIE) treated with hypothermia. The secondary objectives were to compare CBF values between the different regions of interest (ROIs) and between infants with ischemic lesions on MRI and infants with normal MRI findings. We prospectively included all consecutive neonates with HIE admitted to the neonatal intensive care unit of our institution who were eligible for therapeutic hypothermia. Each neonate systematically underwent two MRI examinations as close as possible to day 4 (early MRI) and day 11 (late MRI) of life. We proposed an innovative processing pipeline for morphological and ASL data suited to neonates that enable automated segmentation to obtain CBF values over ROIs. We evaluated CBF on two successive scanswithin thefirst 15 days of life in the same subjects. ASL imaging in asphyxiated neonates seems more relevant when used relatively early, in the first days of life. The correlation of intra-subject changes in cerebral perfusion between early and late MRI with neurodevelopmental outcome warrants investigation in a larger cohort, to determine whether the CBF pattern change can provide prognostic information beyond that provided by visible structural abnormalities on conventional MRI [18], [47].

7.2.4. Cerebral blood flow in sickle cell populations

7.2.4.1. White matter has impaired resting oxygen delivery in sickle cell patients
Participant: Julie Coloigner.

Although modern medical management has lowered overt stroke occurrence in patients with sickle cell disease (SCD), progressive white matter (WM) damage remains common. It is known that cerebral blood flow (CBF) increases to compensate for anemia, but sufficiency of cerebral oxygen delivery, especially in the WM, has not been systematically investigated. Cerebral perfusion was measured by arterial spin labeling in 32 SCD patients (age range: 10-42 years old, 14 males, 7 with hemoglobin SC, 25 hemoglobin SS) and 25 age and race-matched healthy controls (age range: 15-45 years old, 10 males, 12 with hemoglobin AS, 13 hemoglobin AA); 8/24 SCD patients were receiving regular blood transfusions and 14/24 non-transfused SCD patients were taking hydroxyurea. Imaging data from control subjects were used to calculate maps for CBF and oxygen delivery in SCD patients and their T-score maps. Whole brain CBF was increased in SCD patients with a mean T-score of 0.5 and correlated with lactate dehydrogenase (r2 $= 0.58$, P < 0.0001). When corrected for oxygen content and arterial saturation, whole brain and gray matter (GM) oxygen delivery were normal in SCD, but WM oxygen delivery was 35% lower than in controls. Age and hematocrit were the strongest predictors for WM CBF and oxygen delivery in patients with SCD. There was spatial co-localization between regions of low oxygen delivery and WM hyperintensities on T2 FLAIR imaging. To conclude, oxygen delivery is preserved in the GM of SCD patients, but is decreased throughout the WM, particularly in areas prone to WM silent strokes [7].

This work was done in collaboration with Natasha Leporé and her team, Children's hospital Los Angeles, University of Southern California, USA.

7.2.5. Alzheimer disease

7.2.5.1. Abnormal fMRI response in sub-hippocampal structures: how prior knowledge impairs memory in AD
Participants: Quentin Duché, Pierre-Yves Jonin.

Early Alzheimer's disease typically impairs associative learning abilities, up to 18 years before dementia. Importantly, patients' concerns refer to their daily routine, meaning that they lack associative memory for highly familiar stimuli. However, most of the tests involve much less familiar stimuli (e.g. isolated words). It follows that we ignore whether prior knowledge about memoranda alters memory formation and its neural correlates in Alzheimer's Disease. Here, we aimed at manipulating prior knowledge available at encoding and repetition to investigate whether prior knowledge could alter the neural underpinnings of associative encoding, in a way sensitive to early AD. The results suggest that distinct forms of prior knowledge may drive partly non-overlapping brain networks at encoding, and in turn these regions differentially contribute to successful memory formation. Thus, our finding that sub-hippocampal, not hippocampal, activation underlie the inability of the patients to benefit remote prior knowledge in new learning opens perspectives for further diagnostic and prognostic markers development [37].

7.2.5.2. Learning what you know: how prior knowledge impairs new associative learning in early AD.
  Participants: Pierre-Yves Jonin, Quentin Duché, Élise Bannier, Isabelle Corouge, Jean-Christophe Ferré, Christian Barillot.

While associative memory impairment is a core feature of prodromal Alzheimer's Disease (AD), whether prior knowledge affects associative learning is largely overlooked. Stimuli repetition yields suppression or enhancement of the BOLD signal, allowing the functional mapping of brain networks. We addressed the role of prior knowledge in associative encoding by manipulating repetition and familiarity of the memoranda in a subsequent memory fMRI study design. 17 patients with prodromal AD (AD-MCI) and 19 Controls learned face-scene associations presented twice in the scanner. Pre-experimental knowledge trials (PEK) involved famous faces while in Experimental Knowledge trials (EK), unknown faces familiarized before scanning were used. Study events were sorted as associative hits, associative misses or misses after a recognition test outside the scanner. We computed the Repetition X Prior knowledge interaction contrast to test whether the encoding networks differed along with prior knowledge, then looked for subsequent associative memory effects in the resulting clusters. PEK and EK yielded similar associative memory performance in AD-MCI, while PEK increased associative memory by 28% in Controls. Repetition effects were modulated by Prior knowledge in Controls, but AD-MCI showed aberrant repetition effects. Subsequent memory effects were observed only in Controls for PEK in the right subhippocampal structures. By contrast, in both groups, EK triggered a subsequent memory effect in the right hippocampus. Provided that tau pathology starts within anterior subhippocampal regions in early AD, our findings that subhippocampal, not hippocampal, involvement underlies the inability of the patients to benefit from PEK open innovative clinical and research perspectives [38].

7.2.6. Depression

7.2.6.1. White matter abnormalities in depression: a categorical and phenotypic diffusion MRI study.
  Participants: Julie Coloigner, Olivier Commowick, Isabelle Corouge, Christian Barillot.

Mood depressive disorder is one of the most disabling chronic diseases with a high rate of everyday life disability that affects 350 million people around the world. Recent advances in neuroimaging have reported widespread structural abnormalities, suggesting a dysfunctional frontal-limbic circuit involved in the pathophysiological mechanisms of depression. However, a variety of different white matter regions has been highlighted and these results lack reproducibility of such categorical-based biomarkers. These inconsistent results might be attributed to various factors: actual categorical definition of depression as well as clinical phenotype variability. In this study, we 1/ examined WM changes in a large cohort (114 patients) compared to a healthy control group and 2/ sought to identify specific WM alterations in relation to specific depressive phenotypes such as anhedonia (i.e. lack of pleasure), anxiety and psychomotor retardation –three core symptoms involved in depression. Consistent with previous studies, reduced white matter was observed in the genu of the corpus callosum extending to the inferior fasciculus and posterior thalamic radiation, confirming a frontal-limbic circuit abnormality. Our analysis also reported other patterns of increased fractional anisotropy and axial diffusivity as well as decreased apparent diffusion coefficient and radial diffusivity in the splenium of the corpus callosum and posterior limb of the internal capsule. Moreover, a positive correlation between FA and anhedonia was found in the superior longitudinal fasciculus as well as a negative correlation in the cingulum. Then, the analysis of the anxiety and diffusion metric revealed that increased anxiety was associated with greater FA values in genu and splenium of corpus callosum, anterior corona radiata and posterior thalamic radiation. Finally, the motor retardation analysis showed a correlation between increased Widlöcher depressive retardation scale scores and reduced FA in the body and genu of the corpus callosum, fornix, and superior striatum. Through this twofold approach (categorical and phenotypic), this study has underlined the need to move forward to a symptom-based research area of biomarkers, which help to understand the pathophysiology of mood depressive disorders and to stratify precise phenotypes of depression with targeted therapeutic strategies [9]. This work was done with Centre Hospitalier Guillaume Régnier, Academic Psychiatry Department, 35703 Rennes, France.

7.2.6.2. Structural connectivity analysis in treatment-resistant depression
  Participants: Julie Coloigner, Isabelle Corouge, Christian Barillot.

Depressive disorder is characterized by a profound dysregulation of affect and mood as well as additional abnormalities including cognitive dysfunction, insomnia, fatigue and emotional disturbance. Converging evidence shows that a dysfunction in prefrontal-subcortical circuits is associated with depressive state. However, the process of treatment resistance was poorly studied. One study of functional magnetic resonance imaging has reported more disrupted connectivity in prefrontal areas and in thalamus for resistant (R) group (Lui et al., 2011). These observations suggest a modification of functional connectivity in the prefrontal-subcortical circuits in the R patients. Using graph theory-based analysis, we examined white matter changes in the organization of networks in R patients compared with non-resistant (NR) group. We revealed 15 areas with significant density differences in R patients compared to NR subjects. The NR depression seems associated with decreased connectivity among distributed limbic areas, particularly in the ACC and in basal ganglia. However, the R patients exhibit a reduced connectivity in anterior limb of internal capsule and genu of corpus callosum compared with NR patients. Combined with previous studies, which described a widespread disruption in prefrontal-subcortical networks, this result suggests a more important connectivity decrease in the frontal cortex, as well as a smaller reduction in the limbic circuit for the patients with pejorative outcome. These results were consistent with connectivity studies, which suggested that the degree of disruption could influence the resistance severity and that two distinct networks could be implicated in NR end R depression. [27].

7.2.7. Prenatal exposure

7.2.7.1. *Prenatal exposure to glycol ethers and motor inhibition function evaluated by functional MRI at the age of 10 to 12years in the PELAGIE mother-child cohort*
Participants: Élise Bannier, Christian Barillot.

Pregnant women are ubiquitously exposed to organic solvents, such as glycol ethers. Several studies suggest potential developmental neurotoxicity following exposure to glycol ethers with a lack of clarity of possible brain mechanisms. We investigated the association between urinary levels of glycol ethers of women during early pregnancy and motor inhibition function of their 10- to 12-year-old children by behavioral assessment and brain MR imaging. Prenatal urinary levels of two glycol ether metabolites were associated with poorer Go/No-Go task performance. Differential activations were observed in the brain motor inhibition network in relation with successful inhibition, but not with cognitive demand. Nevertheless, there is no consistence between performance indicators and cerebral activity results. Other studies are highly necessary given the ubiquity of glycol ether exposure [5].

This work is done in collaboration with Fabienne Pelé and Cécile Chevrier (IRSET). Anne Claire Binter defended her PhD in December 2019 supervised by Fabienne Pelé, Cécile Chevrier and Élise Bannier. t

7.2.7.2. *Effect of prenatal organic solvent exposure on structural connectivity at childhood*
Participants: Julie Coloigner, Élise Bannier, Jean-Christophe Ferré, Christian Barillot.

Glycol ethers are part of organic solvents. They are used in industry and at home during manufacturing or usage of products such as paints, cleaning agents and cosmetics. The specific detection of subtle, low-dose effects of early-life exposure to these solvents on neuropsychological performance in children is a trendy subject of investigation. Neuroimaging allows looking into brain function and identifying different cerebral connections that may be affected by these neurotoxicants. In this paper, we investigated the specific effects of prenatal low-level exposure to different glycol ethers, on brain development of children between 10 and 12 years old. Based on previous studies suggesting cognitive disabilities in the attention, inhibition and working memory, we proposed a structural connectivity analysis using graph theory restricted to the regions involved in these functions. Our results suggest a possible relationship between the attention, working memory and inhibition and prenatal exposure to specific glycol ethers, such as ethoxyacetic acid, ethoxyethoxyacetic acid and 2-butoxyacetic acid [28].

7.2.8. Cognitive food-choice task

7.2.8.1. *Implemention of a new food picture database in the context of fMRI and visual cognitive food-choice task in healthy volunteers*
Participant: Élise Bannier.

This pilot study aimed at implementing a new food picture database in the context of functional magnetic resonance imaging (fMRI) cognitive food-choice task, with an internal conflict or not, in healthy normal-weight adults. The fMRI analyses showed that the different liking foods (i.e. foods with different hedonic appraisals) condition elicited the activation of dorsal anterior cingulate cortex, involved in internal conflict monitoring, whereas similar liking (ie, foods with similar hedonic appraisals) condition did not, and that low-energy (LE) food choice involved high-level cognitive processes with higher activation of the hippocampus (HPC) and fusiform gyrus compared to high-energy (HE) food choice. Overall, this pilot study validated the use of the food picture database and fMRI-based procedure assessing decision-making processing during a food choice cognitive task with and without internal conflict[15].

This work was done in collaboration with Yentl Gautier, Paul Meurice, Yann Serrand, Nicolas Coquery Romain Moirand and David Val-Laillet from the NuMeCan Institute (Nutrition Metabolisms Cancer, UMR 1241, Inserm - Université de Rennes 1) and INRA.

7.3. Research axis 3: Management of Information in Neuroimaging

In the context of population imaging, we have made progress in three main areas this year. First we were involved in the development of infrastructures for open science with OpenAIRE, we also participated in the collaborative definition of standards that will ensure that infrastructures remain interoperable. Finally, we started a research new axis looking at how variations in analytical pipelines impact neuroimaging results (i.e. analytic variability).

7.3.1. Infrastructures

7.3.1.1. Open research: linking the bits and pieces with OpenAIRE-connect
Participants: Camille Maumet, Christian Barillot, Xavier Rolland.

Open research is growing in neuroimaging. The community — supported by funders who want best use of public funding but also by the general public who wants more transparent and participatory research practices — is constantly expanding online resources including: data, code, materials , tutorials, etc. This trend will likely amplify in the future and is also observed in other areas of experimental sciences. Open resources are typically deposited in dedicated repositories that are tailored to a particular type of artefact. While this is best practice, it makes it difficult to get the big picture: artefacts are scattered across the web in a multitude of databases. Although one could claim that the publication is here to link all related artefacts together, it is not machine-readable and does not me toallow searching for artefacts using filters (e.g. all datasets created in relation with a given funder). We presented OpenAIRE-connect, an overlay platform that links together research resources stored on the web: https://beta.ni.openaire.eu/ [45].

This work was done in collaboration with Dr. Sorina Caramasu-Pop and Axel Bonnet from Creatis in Lyon and with collaborators of the OpenAIRE-Connect project.

7.3.2. Standardisation and interoperability

7.3.2.1. The best of both worlds: using semantic web with JSON-LD. An example with NIDM-Results & Datalad
Participant: Camille Maumet.

The Neuroimaging data model (NIDM-Results) provides a harmonised representation for fMRI results reporting using Semantic Web technologies. While those technologies are particularly well suited for aggregation across complex datasets, using them can be costly in terms of initial development time to generate and read the corresponding serialisations. While the technology is machine accessible, it can be difficult to comprehend by humans. This hinders adoption by scientific communities and by software developers used to more-lightweight data-exchange formats, such as JSON. JSON-LD: a JSON representation for semantic graphs ("JSON-LD 1.1" n.d.) was created to address this limitation and recent extensions to the specification allow creating JSON-LD documents that are structured more similar to simple JSON. This representation is simultaneously readable by a large number of JSON-based applications and by Semantic Web tools. Here we review our work on building a JSON-LD representation for NIDM-Results data and exposing it to Datalad, a data-management tool suitable for neuroimaging datasets with built-in support for metadata extraction and search [44].

This work was done in collaboration with Prof. Michael Hanke from Institute of Neuroscience and Medicine in Julich and with members of the INCF.

7.3.2.2. Tools for FAIR Neuroimaging Experiment Metadata Annotation with NIDM Experiment
Participant: Camille Maumet.

Acceleration of scientific discovery relies on our ability to effectively use data acquired by consortiums and/or across multiple domains to generate robust and replicable findings. Efficient use of existing data relies on metadata being FAIR1 - Findable, Accessible, Interoperable and Reusable. Typically, data are shared using formats appropriate for the specific data types with little contextual information. Therefore, scientists looking to reuse data must contend with data originating from multiple sources, lacking complete acquisition information and often basic participant information (e.g. sex, age). What is required is a rich metadata standard that allows annotation of participant and data information throughout the experiment workflow, thereby allowing consumers easy discovery of suitable data. The Neuroimaging Data Model (NIDM)2 is an ongoing effort to represent, in a single core technology, the different components of a research activity, their relations, and derived data provenance3. NIDM-Experiment (NIDM-E) is focused on experiment design, source data descriptions, and information on the participants and acquisition information. In this work we report on annotation tools developed as part of the PyNIDM4 application programming interface (API) and their application to annotating and extending the BIDS5 versions of ADHD2006 and ABIDE7 datasets hosted in DataLad[40].

This work was led by Dr David Keator from UCI Irvine and done in collaboration with members of the INCF.

7.3.3. *Quantifying analytic variability*

7.3.3.1. Exploring the impact of analysis software on task fMRI results
Participant: Camille Maumet.

A wealth of analysis tools are available to fMRI researchers in order to extract patterns of task variation and, ultimately, understand cognitive function. However, this 'methodological plurality' comes with a drawback. While conceptually similar, two different analysis pipelines applied on the same dataset may not produce the same scientific results. Differences in methods, implementations across software packages, and even operating systems or software versions all contribute to this variability. Consequently, attention in the field has recently been directed to reproducibility and data sharing. Neuroimaging is currently experiencing a surge in initiatives to improve research practices and ensure that all conclusions inferred from an fMRI study are replicable. In this work, our goal is to understand how choice of software package impacts on analysis results. We use publically shared data from three published task fMRI neuroimaging studies, reanalyzing each study using the three main neuroimaging software packages, AFNI, FSL and SPM, using parametric and nonparametric inference. We obtain all information on how to process, analyze, and model each dataset from the publications. We make quantitative and qualitative comparisons between our replications to gauge the scale of variability in our results and assess the fundamental differences between each software package. While qualitatively we find broad similarities between packages, we also discover marked differences, such as Dice similarity coefficients ranging from 0.000-0.743 in comparisons of thresholded statistic maps between software. We discuss the challenges involved in trying to reanalyse the published studies, and highlight our own efforts to make this research reproducible [6].

This work was done in collaboration with Alexander Bowring and Prof. Thomas Nichols from the Oxford Big Data Institute in the UK.

8. Bilateral Contracts and Grants with Industry

8.1. Bilateral Contracts with Industry

8.1.1. *Siemens*
Participants: Elise Bannier, Christian Barillot, Emmanuel Caruyer, Olivier Commowick, Isabelle Corouge, Jean-Christophe Ferré, Jean-Yves Gauvrit.

In the context of the Neurinfo imaging platform, a master research agreement between Siemens SAS - Healthcare and University of Rennes 1 defines the terms of the collaboration between Siemens, Empenn and the Neurinfo platform. Relying on this research agreement contract, Neurinfo has received work in progress (WIP) sequences from Siemens in the form of object code for evaluation in the context of clinical research. The Neurinfo platform has also received source code of selected MRI sequences. As an example, the diffusion sequence code was modified to load arbitrary diffusion gradient waveforms for the FastMicroDiff project led by E. Caruyer. This is crucial in the collaboration since it enables the development of MRI sequences on site. The MR Diffusion pulse sequence source code was modified in collaboration with our Siemens clinical scientist as part of our Master Research Agreement, Marc Lapert, in order to play arbitrary gradient waveforms. This was done on the Syngo VB17 software version and again VE11C (nearly finished).

9. Partnerships and Cooperations

9.1. Regional Initiatives

9.1.1. *Défis scientifiques 2019 of University of Rennes 1: Compensating analytic variability for a better use of open data (2019, 6500€).*

Participant: Camille Maumet.

In neuroimaging, open data are now well developed with hundred of thousands of images available for the research community. However, those data are still mainly studied in isolation, limiting the potential for new discoveries. Here we focus our efforts on developing neuroinformatics standards and algorithms that will support publication and combination of open datasets.

9.1.2. *Region Bretagne: project VARANASI*

Participants: Christian Barillot, Camille Maumet, Xavier Rolland.

Thanks to the development of open science practices, more and more public datasets are available to the research community. In the field of brain imaging, these data, combined, bring a critical increase in sample size, necessary to build robust models of the typical and atypical brain. However, in order to build valid inferences on these data, we need to take into account their heterogeneity. Variability can arise due to multiple factors such as: differences in imaging instruments, in acquisitions protocols and even, in post-processing pipelines. In particular, the expansion of open source machine learning workflows creates a multitude of possible outputs out of the same dataset. The variations induced by this methodological plurality can be reFerréd to as 'analytic variability' which will be the focus of the thesis funded in half by region Bretagne. The thesis of Xavier Rolland (2018-2021) will address two challenges: 1) How to combine neuroimaging data generated by different analysis pipelines? 2) How to publish neuroimages with an adequate level of metadata to enable their reuse? Methodological developments will combine machine learning techniques with methods from knowledge representation.

9.2. National Initiatives

9.2.1. *Projet Fondation de France: PERINE: 99k€ (33 k€ for IRM acquisition and 22 k€ for image analysis) for 2011-2021*

Participants: Élise Bannier, Isabelle Corouge, Julie Coloigner, Maia Proisy, Jean-Christophe Ferré, Christian Barillot.

The PELAGIE cohort evaluates the effect of prenatal exposure to neurotoxicants on child development. Following previous studies, the PERINE study focuses on the assessment of brain developement at 10-12 years old using MRI (ASL, Diffusion imaging, Working memory as well as motor inhibition BOLD fMRI together with neuropsychological tests). A total of 101 children were included. A PhD of Anne-Claire Binter was defended in December 2019 linking epidemiology with functional imaging during a GoNoGo task and neuropsychological scores. This work is done in collaboration with Fabienne Pele´ and Ce´cile Chevrier (IRSET).

9.2.2. *Fondation de l'Avenir: EPMR-MA*

Participants: Pierre-Yves Jonin, Élise Bannier, Christian Barillot, Quentin Duché.

Recognition memory refers to our ability to discriminate between previously experienced vs. unexperienced stimuli. It is impaired very early in the course of Alzheimer's Disease (AD), both regarding behavioural performance and related brain activity. When the memoranda is associated or with existing knowledge, subsequent memory increases in healthy subjects. Moreover, existing knowledge related to prior exposures may alter the brain network underlying successful memory formation. While much is known regarding the brain substrates of recognition memory in early AD, little is known about the impact of prior exposure. Yet, this factor could both enhance memory formation in patients, and highlight a pattern of memory impairments and related brain activity that might accurately discriminates between early AD, before dementia, and healthy aging. The present task-based fMRI study aims at assessing the influence of prior exposures on recognition memory and its neural underpinnings in patients with Mild Cognitive Impairment due to AD. Inclusions were performed between 2016 and 2017 and data analysis is ongoing.

9.2.3. *Projet Fondation de France: Connectivity of the amygdala in depression: (PI: M.-L. Paillère Martinot, Paris Descartes University), €200k for 2018-2021*

Participants: Christian Barillot, Olivier Commowick, Emmanuel Caruyer, Julie Coloigner.

The onset of depression in teenagers and young adults increases the risk to develop a drug-resistant depression in the adulthood. This project aims at evaluating the role of early changes in the microstructure and connectivity of the amygdala. Using a cohort of drug-resistant patients (N=30), non drug-resistant patients (N=30) and controls (N=30), the aim is to identify imaging biomarkers of the pathology and to compare these with emotional and cognitive phenotypes in this population, searching for early differences in the development of the amygdala connectivity.

9.2.4. *CNRS-Inserm Défi Santé numérique – AAP 2019: Imagerie Multimodale de l'Amygdale limbiquE pour le pronostic de la Dépression (IMpAirED): 19k€ for 2019*

Participants: Julie Coloigner, Olivier Commowick, Élise Bannier, Emmanuel Caruyer, Christian Barillot.

This grant is an extension of the Projet Fondation de France: Connectivity of the amygdala in depression.

In order to identify early features of this depression disease, the aim of this project is to develop multimodal modeling of the limb amygdala and its network from MR imaging combining activation and rest functional imaging and MR brain microstructure imaging quantitative (diffusion and relaxometry). The development of this model will allow us to define three imaging biotypes corresponding to depressed adult patients responding to antidepressant treatments, depressed resistant patients and controls. These multimodal imaging biomarkers will be used to stratifie a large longitudinal cohort of young adults into three sub-groupsgroups, in order to retrospectively identify early differences in development trajectories of amygdala.

Inclusions of the patients will begin in early 2020.

9.2.5. *ANR "MAIA", generic projects program: €150k for 2016-2019 (PI: F. Rousseau, IMT Atlantique, Brest)*

Participants: Maia Proisy, Pierre Maurel, Antoine Legouhy, Olivier Commowick, Isabelle Corouge, Jean-Christophe Ferré, Christian Barillot.

Each year in France, 55 000 children are born prematurely, i.e., before the 37th week of gestation. Long-term studies of the outcome of prematurely born infants have clearly documented that the majority of such infants may have significant motor, cognitive, and behavioral deficits.

However, there is a limited understanding of the nature of the cerebral abnormality underlying these adverse neurologic outcomes. In this context, the emergence of new modalities of 3D functional MRI, e.g., Arterial Spin Labeling (ASL), or optical imaging technologies, e.g., Near InfraRed Spectroscopy (NIRS), brings new perspectives for extracting cognitive information, via metabolic activity measures. Other classical techniques devoted to cerebral signal measurement, such as ElectroEncephaloGraphy (EEG), provide cognitive information at the cortical level. Each of these various non-invasive imaging technologies brings substantial and specific information for the understanding of newborn brain development.

This project is developing innovative approaches for multi-image / multi-signal analysis, in order to improve neurodevelopment understanding methods. From a fundamental point of view, mathematics and computer science have to be considered in association with imaging physics and medicine, to deal with open issues of signal and image analysis from heterogeneous data (image, signal), considered in the multiphysics contexts related to data acquisition (magnetic, optic, electric signals) and biophysics modeling of the newborn brain. A sustained synergy between all these scientific domains is then necessary.

Finally, the sine qua non condition to reach a better understanding of the coupled morphological cognitive development of premature newborns, is the development of effective software tools, and their distribution to the whole medical community. The very target of this project is the design of such software tools for medical image / signal analysis, actually operational in clinical routine, and freely available. Academic researchers and industrial partners are working in close collaboration to reach that ambitious goal.
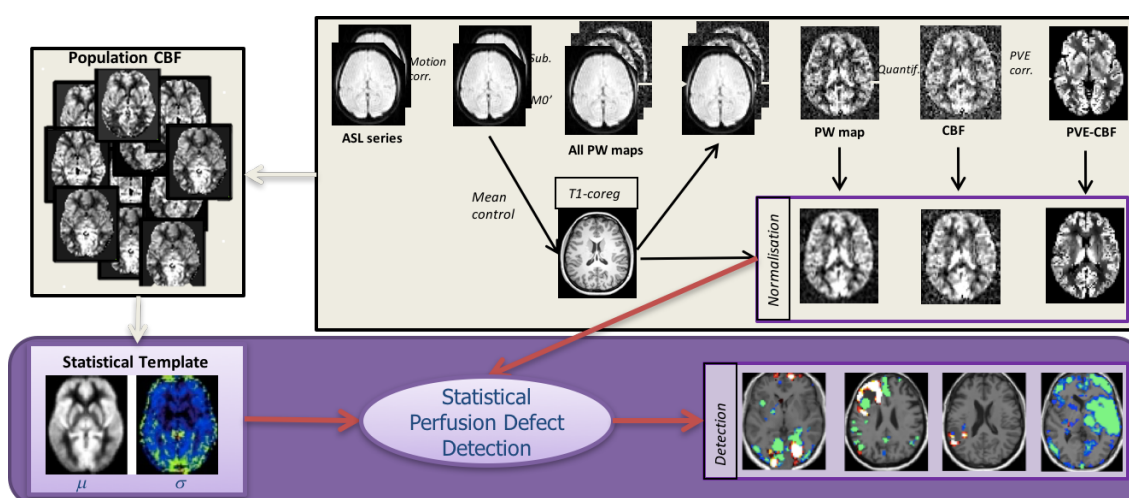
Figure 2. Processing workflow for quantification of Arterial Spin Labelling Cerebral Blood Flow with detection of abnormal perfusion

9.2.6. *Fondation pour la recherche médicale (FRM) - Project Hybrid EEG/IRM Neurofeedback for rehabilitation of brain pathologies: 370k€ (2017-2021)*

Participants: Élise Bannier, Isabelle Bonan, Isabelle Corouge, Jean-Christophe Ferré, Jean-Yves Gauvrit, Pierre Maurel, Mathis Fleury, Giulia Lioi, Christian Barillot.

The goal of this project is to make full use of neurofeedback (NF) paradigm in the context of brain rehabilitation. The major breakthrough will come from the coupling associating functional and metabolic information from Magnetic Resonance Imaging (fMRI) to Electro-encephalography (EEG) to "optimize" the neurofeedback protocol. We propose to combine advanced instrumental devices (Hybrid EEG and MRI

platforms), with new hybrid Brain computer interface (BCI) paradigms and new computational models to provide novel therapeutic and neuro-rehabilitation paradigms in some of the major mental and neurological disorders of the developmental and the aging brain (stroke, language disorders, Mood Depressive Disorder (MDD), . . .). Though the concept of using neurofeedback paradigms for brain therapy has somehow been experimented recently (mostly through case studies), performing neurofeedback through simultaneous fMRI and EEG has almost never been done before so far (two teams in the world including us within the HEMISFER CominLabs project). This project will be conducted through a very complementary set of competences over the different involved teams: Empenn U1228, HYBRID and PANAMA Teams from Inria/Irisa Rennes and EA 4712 team from University of Rennes I.

9.2.7. *PHRC EMISEP: Evaluation of early spinal cord injury and late physical disability in Relapsing Remitting Multiple Sclerosis: €200k for 2016-2019*

Participants: Élise Bannier, Christian Barillot, Emmanuel Caruyer, Benoit Combès, Olivier Commowick, Gilles Edan, Jean-Christophe Ferré, Haykel Snoussi.

Multiple Sclerosis (MS) is the most frequent acquired neurological disease affecting young adults (1 over 1000 inhabitants in France) and leading to impairment. Early and well adapted treatment is essential for patients presenting aggressive forms of MS. This PHRC (Programme hospitalier de recherche clinique) project focuses on physical impairment and especially on the ability to walk. Several studies, whether epidemiologic or based on brain MRI, have shown that several factors are likely to announce aggressive development of the disease, such as age, number of focal lesions on baseline MRI, clinical activity. However, these factors only partially explain physical impairment progression, preventing their use at the individual level. Spinal cord is often affected in MS, as demonstrated in postmortem or imaging studies. Yet, early radiological depiction of spinal cord lesions is not always correlated with clinical symptoms. Preliminary data, on reduced number of patients, and only investigating the cervical spinal cord, have shown that diffuse spinal cord injury, observed via diffusion or magnetisation transfer imaging, would be correlated with physical impairment as evaluated by the (EDSS) Expanded Disability Status Scale score. Besides, the role of early spinal cord affection (first two years) in the evolution of physical impairment remains unknown.

In this project, we propose to address these different issues and perform a longitudinal study on Relapsing Remitting Multiple Sclerosis (RRMS) patients, recruited in the first year of the disease. Our goal is to show that diffuse and focal lesions detected spinal cord MRI in the first two years can be used to predict disease evolution and physical impairment at 5 years. Twelve centers are involved in the study to include 80 patients.

To date, all subjects have been included. Haykel Snoussi defended his PhD Thesis on diffusion imaging in the spinal cord starting with distortion correction.

B. Combe`s started as a post-doc in November 2016 to process the EMISEP imaging data, starting with morphological data processing (registration, segmentation) and magnetization transfer data processing.

9.2.8. *MS-TRACTS (ARSEP and COREC funding): Estimating the impact of multiple sclerosis lesions in motor and proprioceptive tracts, from the brain to the thoracic spinal cord, on their functions, assessed from clinical tests and electrophysiological measurements: 45k€ (2019-2021).*

Participants: Élise Bannier, Benoit Combès.

Previous studies, whether epidemiologic or based on brain MRI, have shown that several factors were likely to announce aggressive development of the disease, such as age, clinical relapses, number of focal lesions on baseline MRI. However, these factors only partially explain physical disability progression, preventing their use at the individual level. The access to advanced brain and cord MR images, the development of associated processing tools combined. We hypothesize that a fine assessment of damage on specific networks, from the brain to the thoracic cord, offers a relevant biomarker of disability progression in MS. Such damage assessments must take into account both lesion location, assessed on structural brain and cord MR images and lesion severity, assessed using quantitative MR images. We propose to test this hypothesis by combining

assessments of lesion location and severity on corticospinal and proprioceptive tracts from the brain to the thoracic cord with clinical and electrophysiological measurements. This study includes two French centers (Rennes, Marseille) and includes a total of 60 patients. The expected outcome is to obtain early biomarkers of physical impairment evolution in RRMS patients, first treated with immunomodulatory treatment. The long-term goal is to provide the clinician with biomarkers able to anticipate therapeutic decisions and support the switch to alternative more aggressive treatment.

9.2.9. PIA projects

9.2.9.1. The HEMISFER Project: (€400k for 2017-2019)
Participants: Élise Bannier, Isabelle Bonan, Isabelle Corouge, Claire Cury, Jean-Christophe Ferré, Jean-Yves Gauvrit, Pierre Maurel, Christian Barillot.

The HEMISFER project ("Hybrid Eeg-MrI and Simultaneous neuro-FEedback for brain Rehabilitation") is conducted at Inria Rennes with the support of the Labex "CominLabs" [1]. The goal of HEMISFER is to make full use of the neurofeedback paradigm in the context of rehabilitation and psychiatric disorders. The major breakthrough will come from the use of a coupling model associating functional and metabolic information from Magnetic Resonance Imaging (fMRI) to Electro-encephalography (EEG) to "enhance" the neurofeedback protocol. We combine advanced instrumental devices (Hybrid EEG and MRI platforms), with new man-machine interface paradigms (Brain computer interface and serious gaming) and new computational models (source separation, sparse representations and machine learning) to provide novel therapeutic and neuro-rehabilitation paradigms in some of the major neurological and psychiatric disorders of the developmental and the aging brain (stroke, attention-deficit disorder, language disorders, treatment-resistant mood disorders, etc.). This project involves with the HYBRID and PANAMA Teams from Inria Rennes, the EA 4712 team from University of Rennes I and the ATHENA team from Inria Sophia-Antipolis. This work benefits from the research 3T MRI and MRI-compatible EEG systems provided by the NeurInfo in-vivo neuroimaging platform on which these new research protocols aree set up. A budget of 500K€ is provided by CominLabs to support this project (through experimental designs, PhDs, post-docs and expert engineers).

9.2.9.2. France Life Imaging (FLI): 2012-2023, €2000k (phase 1) + €1200k (phase 2)
Participants: Christian Barillot, Olivier Commowick.

France Life Imaging (FLI) is a large-scale research infrastructure project to establish a coordinated and harmonized network of biomedical imaging in France. This project was selected by the call "Investissements d'Avenir - Infrastructure en Biologie et Santé". One node of this project is the node Information Analysis and Management (IAM), a transversal node built by a consortium of teams that contribute to the construction of a network for data storage and information processing. Instead of building yet other dedicated facilities, the IAM node use already existing data storage and information processing facilities (LaTIM Brest; CREATIS Lyon; CIC-IT Nancy; Empenn U1228 Inria Rennes; CATI CEA Saclay; ICube Strasbourg) that increase their capacities for the FLI infrastructure. Inter-connections and access to services are achieved through a dedicated software platform that is developed based on the expertise gained through successful existing developments. The IAM node has several goals. It is building a versatile facility for data management that inter-connects the data production sites and data processing for which state-of-the-art solutions, hardware and software, are available to infrastructure users. Modular solutions are preferred to accommodate the large variety of modalities acquisitions, scientific problems, data size, and to be adapted for future challenges. Second, it offers the latest development that are made available to image processing research teams. The team Empenn fulfills multiple roles in this nation-wide project. Christian Barillot is the chair of the node IAM, Olivier Commowick is participating in the working group workflow and image processing and Michael Kain is the technical manager. Apart from the team members, software solutions like MedInria and Shanoir are part of the software platform.

9.2.9.3. OFSEP: €175k for 2017-2019
Participants: Élise Bannier, Christian Barillot, Olivier Commowick, Gilles Edan, Jean-Christophe Ferré, Francesca Galassi.

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[1] https://iww.inria.fr/cominlabs-newsletter/april-2013-four-projects-selected/#hemisfer
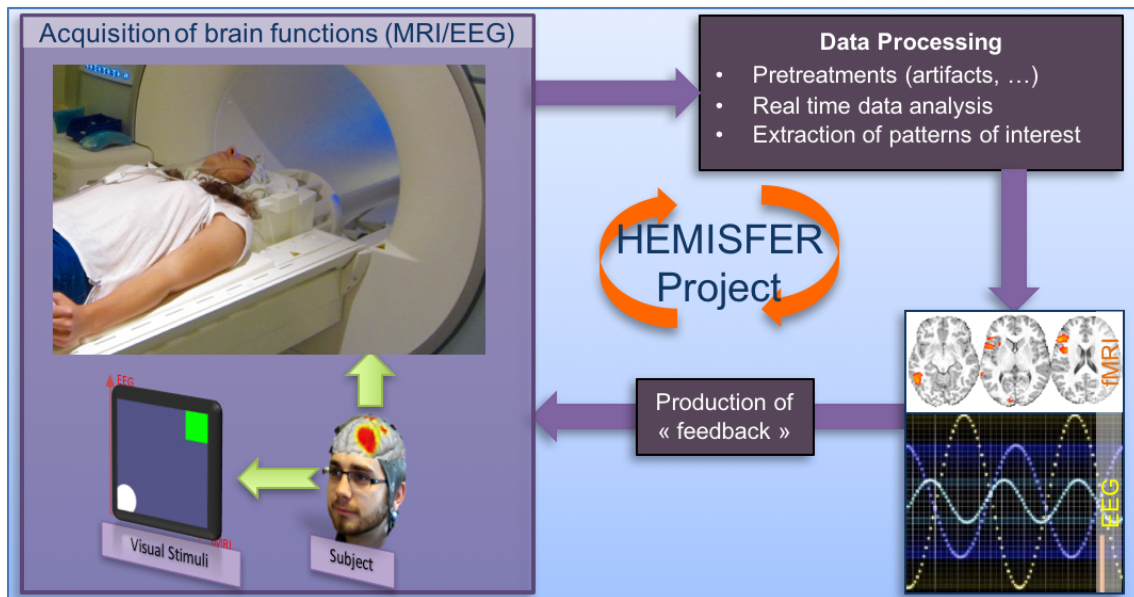
Figure 3. Principle of the Hemisfer project.

The French Observatory of Multiple Sclerosis (OFSEP) is one of ten projects selected in January 2011 in response to the call for proposal in the "Investissements d'Avenir - Cohorts 2010" program launched by the French Government. It allows support from the National Agency for Research (ANR) of approximately 10 million € for 10 years. It is coordinated by the Department of Neurology at the Neurological Hospital Pierre Wertheimer in Lyon (Professor Christian Confavreux), and it is supported by the EDMUS Foundation against multiple sclerosis, the University Claude Bernard Lyon 1 and the Hospices Civils de Lyon. OFSEP is based on a network of neurologists and radiologists distributed throughout the French territory and linked to 61 centers. OFSEP national cohort includes more than 50,000 people with Multiple Sclerosis, approximately half of the patients residing in France. The generalization of longitudinal monitoring and systematic association of clinical data and neuroimaging data is one of the objectives of OFSEP in order to improve the quality, efficiency and safety of care and promote clinical, basic and translational research in MS. For the concern of data management, the Shanoir platform of Inria has been retained to manage the imaging data of the National OFSEP cohort in multiple sclerosis.

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

9.3.1.1. OpenAire-Connect

Participants: Christian Barillot, Camille Maumet, Xavier Rolland.

Project title: **OpenAire-Connect**

Partners: PI: CNR, Italy; Athena Research And Innovation Center In Information Communication & Knowledge Technologies, Greece; Uniwersytet Warszawski, Poland; JISC LBG, UK; Universitaet Bremen, Germany; Universidade Do Minho, Portugal; CNRS (Empenn, Creatis), France; Universita Di Firenze, Italy; Institut De Recherche Pour Le Developpement (IRD), France; European Organization For Nuclear Research (CERN), Switzerland; International Center For Research On The Environment And The Economy, Greece

Budget: 2M € (120k€ for CNRS)

The OpenAire-Connect H2020 project introduces and implements the concept of Open Science as a Service (OSaaS) on top of the existing OpenAIRE infrastructure, delivering out-of-the-box, on-demand deployable tools. OpenAIRE-Connect adopts an end-user driven approach (via the involvement of five prominent research communities), and enriches the portfolio of OpenAIRE infrastructure production services with a Research Community Dashboard Service and a Catch-All Notification Broker Service. The first offers publishing, interlinking, packaging functionalities to enable them to share and re-use their research artifacts (introducing methods, e.g., data, software, protocols). This effort, supported by the harvesting and mining "intelligence" of the OpenAIRE infrastructure, provides communities with the content and tools they need to effectively evaluate and reproduce science. OpenAIRE-Connect combines dissemination and training with OpenAIRE's powerful NOAD network engaging research communities and content providers in adopting such services. These combined actions bring immediate and long-term benefits to scholarly communication stakeholders by affecting the way research results are disseminated, exchanged, evaluated, and re-used. In this project Empenn is acting, through CNRS, as the French coordinator to develop the link with the Neuroimaging research community. This is performed in the context of the FLI-IAM national infrastructure.

9.3.1.2. EIT-Health

Participant: Christian Barillot.

EIT Health aims to promote entrepreneurship and develop innovations in healthy living and active ageing, providing Europe with new opportunities and resources. EIT Health will enable citizens to lead healthier and more productive lives by delivering products, services and concepts that will improve quality of life and contribute to the sustainability of healthcare across Europe. EIT Health is a strong, diverse and balanced partnership of best-in-class organisations in education, research, technology, business creation and corporate and social innovation. EIT Health intends to foster cooperation and unlock Europe's innovation and growth potential – developing and retaining the best talents, creating high-quality jobs and boosting the global competitiveness of European industry. Empenn is involved in this project through the Inserm and Inria institutions. Christian Barillot is representing Inria as one expert in the dedicated WG "Healthy Brain". Empenn is also concerned by the WG "big data".

9.4. International Initiatives

9.4.1. Inria International Labs

9.4.1.1. MMINCARAV

EPFL-Inria

Associate Team involved in the International Lab:

Title: Multimodal Microstructure-Informed Neuronal Connectivity: Acquisition, Reconstruction, Analysis and Validation

International Partner (Institution - Laboratory - Researcher):

Ecole Polytechnique Fédérale de Lausanne (Switzerland) - Laboratoire de Traitement du Signal 5 - Jean-Philippe Thiran

Start year: 2019

See also: https://team.inria.fr/empenn/research/mmincarav-inria-epfl/

Participants: Emmanuel Caruyer, Olivier Commowick, Julie Coloigner, Élise Bannier and Christian Barillot.

The objectives of this associate team will be to address new scientific challenges related to the use of multimodal magnetic resonance imaging (MRI) to derive microstructure indices and apply them to the measure of brain connectivity. We will focus on 4 aspects of this: first we will develop novel sampling techniques, with the objective to reduce acquisition time for the accurate reconstruction of microstructure indices using diffusion MRI; next we will propose joint T2 relaxometry and diffusion models for the description of microstructure, to take advantage of the complementarity of both modalities in the estimation of microstructure indices; in continuation, we will propose new statistical and network analysis methods using the microstructure-informed connectome, and evaluate its potential to reduce bias and false positives; last we will develop a realistic simulation tool combining a fine macroscopic description of fiber bundles, with a fast and realistic simulator at the mesoscopic scale developed by LTS5.

9.4.1.2. Other projects
Participants: Pierre Maurel, Christian Barillot, Claire Cury.

Gundishapur Program (Partenariat Hubert Curien franco-iranien)

This project is a collaboration between the Empenn team and the Institute of medical science and technologies (Shahid Beheshti university, Iran).

Combining EEG (Electroencephalogram) and fMRI (functional Magnetic Resonance Imaging) shows great promise in helping scientists to better understand the complex function of the brain. It can also be used in understanding the brain dysfunctions or specific behaviors. The integration of these two modalities can provide a good spatio-temporal resolution of the neuronal activities, and therefore, it can bring a good insight on the brain function. EEG is the recording of the electrical activity of the brain through scalp surface electrodes. We are already working in this area through the HEMISFER project, whose goal is to make full use of neurofeedback paradigm by using a coupling model associating functional and metabolic information from Magnetic Resonance Imaging (fMRI) and Electro-encephalography (EEG) to "enhance" the neurofeedback protocol. A former member of our team, Dr. Noorzadeh, has already worked on a part of this project, and is now in IMSAT (Iran). He is our main contact for this collaboration.

This project works on the integration methods, in order to first acquire the simultaneous data of high quality with the minimum possible artifacts, and also on biomedical applications in this regard. One of these applications is the source localization using the multi-modal data. Identifying neuronal sources in both high spatial and temporal resolution can open up a bright way to understand lots of diseases, among which epilepsy is the main one. The epileptic seizures or the inter-ictal discharges are nowadays only detected by EEG, but the origin of the activity is only inferred in terms of brain lobes. This spatial precision can be augmented and the method can be used in the precise detection of the focal points of epilepsy for the pre-surgical evaluations.

9.4.1.3. Informal International Collaborations
- Emmanuel Caruyer collaborates with Alice Bates, research fellow at Australian National University, Canberra, on "Dimensionality sampling for B-tensor encoding in diffusion MRI".
- Camille Maumet collaborates with Prof. Thomas Nichols and his group, NISOx at the Oxford Big Data Institute, with Prof. Jean-Baptiste Poline and his group at McGill University, with Prof. Satrajit Ghosh and his group at MIT, with Dr David Keator at UCI Irvine, with Dr. Karl Helmer at MGH, with Dr Tristan Glatard and his group at Concordia University and with international members of the INCF on neuroimaging data sharing.
- Julie Coloigner collaborates with Prof. Natasha Leporé and Dr. John Wood, Children's hospital Los Angeles, University Southern California.

9.5. International Research Visitors

9.5.1. *Visits of International Scientists*
- David Kennedy, Professor at University of Massachusetts Medical School, US visited the team on Feb 27 and gave a talk on Repronim: a center for reproducible neuroimaging.

- Natasha Leporé, Professor at Children's hospital Los Angeles, University of Southern California, US visited the team on April 4-5. She gave a talk on "Understanding pediatric brain anatomy through MRI".
- Jan Petr, Researcher at the HZDR in Dresden visited the team in March 1st, 2019 and give a talk on "Processing ASL data with ExploreASL - technical improvement and clinical applications".

9.5.2. Visits to International Teams

9.5.2.1. Research Stays Abroad

- Corentin Vallée visited Brainnetome center, Institute of Automation, Chinese Academy of Science, Beijing from June 1, 2019 to July 31, 2019; he was awarded a grant for international mobility from the MathSTIC doctoral school.

10. Dissemination

10.1. Promoting Scientific Activities

10.1.1. Scientific Events: Organisation

10.1.1.1. General Chair, Scientific Chair

- Camille Maumet was chair of the Open Science Special Interst Group of the Organisation of Human Brain Mapping. https://www.humanbrainmapping.org/m/pages.cfm?pageid=3712
- Giulia Lioi was chair of a Scientific Symposium during the conference of Organisation of Human Brain Mapping, 2019 : "Multimodal Neurofeedback: The next generation of neurofeedback for advanced brain self-regulation"
- Brainhack Global Rennes 2019: https://brainhack.irisa.fr, November 14-15, Rennes, France (Julie Coloigner, Emmanuel Caruyer and Raphael Truffet).
- Christian Barillot is member of the Board of Directors of IPMI conference series (Information Processing in Medical Imaging)
- Camille Maumet is a member of the "Comité national pour la Science Ouverte (CoSO)" Working group of open software led by Roberto Di Cosmo.
- Camille Maumet is a member of Aperture, a new publishing plateform, working group "workflows" led by Peter Bandettini.

10.1.1.2. Member of the Organizing Committees

- Brainhack Global Rennes 2018: https://brainhack.irisa.fr, May 25-26, Rennes, France (Julie Coloigner, Emmanuel Caruyer and Raphael Truffet).
- ARSEP workshop on multiple sclerosis, Feb 2, ICM (Élise Bannier).
- Élise Bannier is founding member of the REMI network for mutual aid in MRI studies (https://remi.network/) to facilitate setup and quality control of multicenter studies and share expertise between centers, with two meetings organized this year in Strasbourg and Paris.

10.1.2. Scientific Events: Selection

10.1.2.1. Member of the Conference Program Committees

- Emmanuel Caruyer has been a program committee member of the MICCAI CDMRI workshop since 2013.
- Camille Maumet is a member of programm committee of INCF Neuroinformatics 2019 https://www.neuroinformatics2019.org/, September 1-2, Warsaw, Poland.
- Camille Maumet is member of Program Commitee: GEANT workshop: https://neuroinfo.fr/#!/workshops/geant2019, May 21, Marseille, France

10.1.2.2. Reviewer

- IEEE International Symposium on Biomedical Imaging (Emmanuel Caruyer, Olivier Commowick, Julie Coloigner)
- MICCAI (Olivier Commowick, Francesca Galassi)
- Workshop on Biomedical Image Registration (Olivier Commowick)
- Annual congress of the Organisation of Human Brain Mapping (Camille Maumet)
- ESMRMB (Élise Bannier)

10.1.3. Journal

10.1.3.1. Member of the Editorial Boards

- Camille Maumet is member of Editorial Boards of Neuroinformatics
- Christian Barillot is Chief editor of Frontier in Computer science.

10.1.3.2. Reviewer - Reviewing Activities

- NeuroImage (Emmanuel Caruyer, Camille Maumet, Pierre Maurel)
- Medical Image Analysis (Emmanuel Caruyer)
- IEEE TMI (Olivier Commowick)
- Neuroinformatics (Julie Coloigner)
- Med Image Anal (Olivier Commowick, Emmanuel Caruyer, Christian Barillot)
- Scientific Data (Camille Maumet)

10.1.4. Invited Talks

- Emmanuel Caruyer,"Nouveaux enjeux pour l'acquisition d'IRM de diffusion pour la microstructure" ; Journée Nouvelles Imageries INS2I ; December 2019; Lyon."
- Corentin Vallée, "Arterial Spin Labeling, Resting-State and Acquisition duration", Brainnetome center, Institute of Automation, Chinese Academy of Science, Beijing; June 11, 2019
- Corentin Vallée, "Arterial Spin Labeling, Resting-State and Acquisition duration", Brainnetome center, Institute of biophysics, Chinese Academy of Science, Beijing; June 25, 2019
- Giulia Lioi, "EEG-fMRI integration for Neurofeedback", Diagnosis and International Adaptive Imaging (IADI) Laboratory, Nancy, France; September 2019.
- Giulia Lioi, "Multimodal Neurofeedback for Stroke Rehabilitation", 4eme Journee Nationale Neurofeedback Evaluation and Training (NEXT),Bordeaux, France, May 2019.
- Giulia Lioi "Integrating EEG and fMRI for Neurofeedback", Conference Gen2Bio, Biogenouest, Angers, France, May 2019.
- Pierre-Yves Jonin, "Statistiques appliquées en psychométrie. Journées scientifiques de rééducation cognitive chez l'enfant", Lyon, June 14, 2019.
- Pierre-Yves Jonin, "Les méthodes psychométriques pour le cas unique:", Journée de formation de l'Association des Neuropsychologues en Drôme & Ardèche; Valence, France, November 22, 2019.
- Pierre Maurel, "Medical Image Processing: MRI and Brain", seminar at the Mechatronics Department of ENS-Rennes.
- Élise Bannier, "Multi-center (mono-vendor) longitudinal conventional and quantitative spinal cord MRI at 3 Tesla", Spinal Cord Workshop, UCL, London, January 21, 2019.

10.1.5. Leadership within the Scientific Community

- Emmanuel Caruyer: Member (by selection) of the "Bio Imaging and Signal Processing" (BISP) Technical Committee of the IEEE Signal Processing Society (Emmanuel Caruyer).

- Élise Bannier: Elected Member of the French Society for MRI (SFRMBM), starting in Jan 2020 for 6 years.

10.1.6. *Scientific Expertise*

- Expertise as a reviewer for "Agence Nationale de la Recherche" (ANR) (Emmanuel Caruyer)
- Élise Bannier: HCERES Evaluation Committees of the CERCO and TONIC units in Toulouse as expert, representing the research support staff.

10.2. Teaching - Supervision - Juries

10.2.1. *Teaching*

L2 informatique: Raphaël Truffet, Génie Logiciel, 24h and Complexity, 18h, L2, ISTIC, France,

L2 informatique: Raphaël Truffet, Génie Logiciel, 40h, L2, ISTIC, France

ENS Rennes: Raphaël Truffet, Algorithmic (20h)

L2 biologie: Antoine Legouhy, Bio-statistques 34h, L2, Univ. Rennes 1, France.

M1 mathématiques: Antoine Legouhy, Optimisation 12h, M1, Univ. Rennes 1, France.

M1 biologie: Antoine Legouhy, statistiscs 12h, M1, Univ. Rennes 1, France.

Master SIBM, M2, University of Angers-Brest-Rennes, France.

L1 INF1: Francesca Galassi, Functional and Immutable Programming (Scala) (TP : 40h), L1, ISTIC University of Rennes 1, France.

L3 bioinformatique: Corentin Vallée, Statistics, 32h, University of Rennes 1, France.

Master SIBM: Benoit Combès, Statistics (TD, TP: 12h), University of Angers-Brest-Rennes:

- Emmanuel Caruyer, "Introduction to diffusion MRI" (Plenary: 3h).
- Benoit Combès, "Méthodes de recalage linéaire et non-linéaires" (Plenary: 6h)
- Quentin Duché, "Traitements des données d'IRM fonctionnelle" (Plenary: 1h).
- Isabelle Corouge, "Bio-marqueurs d'imagerie et IRM metabolique et fonctionnelle" (Plenary: 3h).
- Camille Maumet, "Imaging processing pipelines" (Plenary: 3h).
- Élise Bannier, "IRM fonctionnelle BOLD" (Plenary: 1h).
- Benoit Combès, "Méthodes statistiques pour le traitement d'image" (Plenary: 3h).
- Claire Cury, "Evaluation des performances en imagerie me´dicale" (Plenary: 3h). item Julie Coloigner, "Méthodes d'analyse de la connectivité cérébrale" (Plenary: 3h).

Master 2 "Langage Cognition et Apprentissage: Pierre-Yves Jonin,"Méthodologie clinique & psychométrique de l'étude de cas" (4h); Université de Poitiers, February 2019

DIU Sémiologie des démences: Pierre-Yves Jonin, "Diagnostic précoce de la maladie d'Alzheimer: contribution neuropsychologique" (4h); Université de Caen Basse Normandie, March 2019

Master 2 Neuropsychologie: Pierre-Yves Jonin, "Apports et limites du bilan neuropsychologique à visée diagnostic dans les syndromes démentiels" (3,5h); Université de Savoie à Chambéry, March 2019

Licence 3 Psychologie, UES Handicap: Pierre-Yves Jonin "Déficit mnésique et handicap invisible. Détection en neuropsychologie" (8 h); Université de Rennes 2, February 2019

Master 2 Psychologie spécialité handicap: Pierre-Yves Jonin "Neuropsychologie clinique du sujet âgé" (10 h); Université de Rennes 2, January-April 2019

Medicine (4th & 5th year) UE Psychologie et Neurobiologie: Pierre-Yves Jonin,L'exploration neuropsychologique des maladies neurologiques et psychiatriques. 4ème & 5ème année de médecine (4h), Université de Brest, France.

Licence 3 de Psychologie: Pierre-Yves Jonin, Les syndromes neuropsychologiques. L3, (16h); Université de Rennes 2, France

Master 2 "Troubles de la Cognition et du Langage": Pierre-Yves Jonin, Evaluation neuropsychologique à visée diagnostique. Le cas des syndromes démentiels. Master 2 (2 x 6h) Université de Poitiers, France.

Master 2 Neurosciences Cliniques: Pierre-Yves Jonin, "La mémoire humaine" (3h); Université de Rennes 1, novembre 2019

IUT St-Malo: Mathis Fleury, statistics (64); 2019

Licences 2 & 3 Biologie: Xavier Rolland, "Introduction aux Biostatistiques" 1 (TP sur R: 64h), Université de Rennes 1

ESIR: Pierre Maurel, General image processing (60h), Algorithmics and complexity (60h), Medical imaging (60h), École Supérieure d'Ingénieur de Rennes (ESIR).

ENS Rennes: Pierre Maurel, Introduction to image processing (24h)

10.2.2. Supervision

10.2.2.1. PhD & HdR

HDR: Olivier Commowick, "Compartments imaging for the characterization of brain diseases from quantitative MRI", Univ. Rennes 1, defended on June 19, 2019, jury: Isabelle Bloch - Professeur, Telecom Paristech, Sébastien Ourselin - Professeur, King's College London, Jean-Philippe Thiran - Professeur, Ecole Polytechnique Fédérale de Lausanne, Christian Barillot - DR CNRS, Equipe Empenn, Alexander Leemans - Associate Professor, UMC Utrecht and Xavier Pennec - DR Inria, Equipe Epione[1].

PhD: Anne-Claire Binter, "Effects of prenatal exposure to neurotoxicants on the child's brain function evaluated by cerebral imaging", defended on December 4, 2019, Univ. Rennes, Élise Bannier.

PhD: Cédric Meurée, "Arterial spin labelling : quality control and super-resolution", defended on March 25, 2019, Univ. Rennes, Pierre Maurel, Christian Barillot.

PhD: Haykel Snoussi, "Population imaging and diffusion MRI for characterizing multiple sclerosis in the human spinal cord.", defended on May 2, 2019, Univ. Rennes, Christian Barillot and Emmanuel Caruyer[3].

PhD in progress: Antoine Legouhy, "Longitudinal brain altas creation, application to development studies", CNRS, from Nov 2016, Defence planned for February 2020, Christian Barillot, François Rousseau, Olivier Commowick.

PhD in progress: Corentin Vallée, "Joint estimation of neuronal activation, resting-state and basal metabolism from Arterial Spin Labeling", Univ. Rennes, from Nov 2016, Christian Barillot, Isabelle Corouge, Pierre Maurel.

PhD in progress: Xavier Rolland, "Modeling analytic variability in brain imaging", CNRS, from Oct 2018, Christian Barillot, Camille Maumet.

PhD in progress: Raphaël Truffet, "Compressed sensing for microstructure-enabled diffusion MRI", Univ. Rennes / ENS Rennes, from Oct 2018, Christian Barillot, Emmanuel Caruyer.

PhD in progress: Giovanna Orrù, "Modeling brain structural and functional connectivity ", Univ. Rennes, from Oct 2019, Julie Coloigner and Christian Barillot.

PhD in progress: Stéphanie Leplaideur, "Equilibre de la rééducation par vibrations cervicales, adaptation prismatique et association aux deux techniques, chez des patients cérébro-lésés droits– Protocole AVC POSTIM " , started in October 2018, Isabelle Bonan, Élise Bannier.

10.2.2.2. Other supervisions

Master student SIF (Master mention Informatique, parcours Science informatique): Antoine Ackaouy, "Deep learning for segmentation of MS lesions from multimodal MRI", Apr-Oct 2018, Francesca Galassi.

3-months visit: Gregory Kiar, PhD student, "Analytical Stability in fMRI" April-June 2019, Camille Maumet in collaboration with Elisa Fromont (LACODAM, Inria Rennes / IRISA).

Co-supervised project : Alexander Bowring, "Exploring the Impact of Analysis Software on Task fMRI Results" 2019, Camille Maumet in collaboration with Thomas Nichols (LACODAM, Inria Rennes / IRISA).

Co-supervised project : Freya Acar, Best practices reporting for fMRI meta-analysis 2019, Camille Maumet in collaboration with Beatrijs Moerkerke (LACODAM, Inria Rennes / IRISA).

M1 Physique Médicale student: Marion Boulanger, "Evaluation of QC procedures at Neurinfo and optimisation".

L3 ESIR Ingénierie Biomédicale student: Chloé Mercier, "Implementation of a Java tool to perform MR Quality Control on a Eurospin test object".

10.2.3. Juries

- Emmanuel Caruyer. PhD committee: Yann Bihan-Poudec, Université Claude Bernard Lyon 1; December 17, 2019.

- Olivier Commowick. PhD committee: Junhao Wen, "Structural and microstructural neuroimaging for diagnosis and tracking of neurodegenerative diseases", Sorbonne Université; July 4, 2019, PhD supervisors: Olivier Colliot et Stanley Durrleman.

- Olivier Commowick. MD thesis committee: Charlotte Laurent "Intérêt pronostique de l'IRM en tenseur de diffusion dans les neuropathies optiques inflammatoires", Université de Rennes 1; Octobre 25, 2019.

- Olivier Commowick. PhD committee: Christian El Hajj "Estimation et classification des temps de relaxation multi-exponentiels en IRM. Application aux tissus ve´ge´taux.", Ecole centrale Nantes; December 16, 2019, PhD supervisors: Guylaine Collewet and Maja Musse.

10.3. Popularization

10.3.1. Brain awareness week: "Semaine du Cerveau"

Empenn team took part in Brain awareness week 2019. Giulia Lioi, Claire Cury and Élise Bannier coordinated this event for Empenn/Neurinfo.

- Camille Maumet and Christian Barillot: Talk "" Le cerveau numérique: explorons-le!"". March 2019, Rennes, France.

- Quiz on brain imaging, March 2019, Rennes, France.

- Lab visits for students (3e and 1ere S) about MRI, functional MRI, EEG and neurofeedback, and image processing.

- Pierre-Yves Jonin: Talk "Entre connaissances et souvenirs : voyage en terre mnésique", March 2019, Rennes, France

10.3.2. Journée Science et Musique (JSM)

This event was initiated in 2010 by IRISA. The idea is to offer a scientific and festive immersion in the research and new technologies of the music of neurosciences and sounds to the general public. Free workshops, conferences, demonstrations and concerts are available to all throughout the day (for more detail see https://jsm.irisa.fr/). Claire Cury organized the event this year with Nancy Bertin, PANAMA team.

10.3.3. Sciences en Cour[t]s

This event is a festival of short movies, which offers doctoral students the opportunity to make short films about their thesis work. Raphael Truffet, Antoine Legouhy and Xavier Rolland won the high school award https://www.youtube.com/watch?v=IKgqv-iCwak.

10.3.4. "J'peux pas j'ai informatique"

"J'peux pas j'ai informatique" is an outreach program to welcome secondary school students for a day at Inria Rennes / IRISA and introduce them to the various facets of computer science. Camille Maumet and Pierre Maurel helped out to run the hands-on tutorials in which students could learn how a computer works without computers.

10.3.5. Other interventions

- Pierre-Yves Jonin: Series of 2 talks on neuropsychology, Universités du Temps Libre de Bretagne, Jan-Dec, Rennes, France.

10.3.6. Education

- L codent L créent - An outreach program to send PhD students to teach Python to middle school students in 8 sessions of 45 minutes. Camille Maumet is a co-organizer of the local version of this program, initiated in Lille. The program is currently supported by: Fondation Blaise Pascal, ED MathSTIC, Inria and Fondation Rennes 1.

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Publications of the year

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[2] C. MEURÉE. *Arterial spin labelling : quality control and super-resolution*, Université Rennes 1, March 2019, https://tel.archives-ouvertes.fr/tel-02281778

[3] H. SNOUSSI. *Imagerie de population et IRM de diffusion pour caractériser la sclérose en plaques pour la moélle épinière humaine*, Université Rennes 1, May 2019, https://tel.archives-ouvertes.fr/tel-02285896

Articles in International Peer-Reviewed Journals

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