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**Institut du Cerveau et de la
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**Université Pierre et Marie Curie
(Paris 6)**

Activity Report 2015

Project-Team ARAMIS

Algorithms, models and methods for images
and signals of the human brain

RESEARCH CENTER
Paris - Rocquencourt

THEME
**Computational Neuroscience and
Medicine**

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Project-Team ARAMIS

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Keywords:

Computer Science and Digital Science:

- 3.4. - Machine learning and statistics
- 5.3. - Image processing and analysis
- 5.9. - Signal processing
- 5.9.4. - Signal processing over graphs

Other Research Topics and Application Domains:

- 2. - Health
- 2.2.6. - Neurodegenerative diseases
- 2.6.1. - Brain imaging

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2. Overall Objectives

2.1. Introduction

Understanding brain function and its alterations requires the integration of multiple levels of organization, operating at different spatial and temporal scales. The integration of such a large variety of data is now possible thanks to the recent emergence of large-scale multimodal datasets (e.g. Alzheimer's disease neuroimaging initiative [ADNI], gene expression atlases from the Allen Institute...). In this context, mathematical and computational approaches are becoming increasingly important because: i) they provide formalized, operational and flexible frameworks for integrating multiple processes and scales; ii) they allow automated processing and analysis of massive datasets. These approaches can then be used to find biomarkers of a disease, for genotype/phenotype correlations, or to characterize functional responses for instance.

3. Research Program

3.1. General aim

The overall aim of our project is to design new computational and mathematical approaches for studying brain structure (based on anatomical and diffusion MRI) and functional connectivity (based on EEG, MEG and intracerebral recordings). The goal is to transform raw unstructured images and signals into formalized, operational models such as geometric models of brain structures, statistical population models, and graph-theoretic models of brain connectivity. This general endeavor is addressed within the three following main objectives.

3.2. Modeling brain structure: from imaging to geometric models

Structural MRI (anatomical or diffusion-weighted) allows studying in vivo the anatomical architecture of the brain. Thanks to the constant advance of these imaging techniques, it is now possible to visualize various anatomical structures and lesions with a high spatial resolution. Computational neuroanatomy aims at building models of the structure of the human brain, based on MRI data. This general endeavor requires addressing the following methodological issues: i) the extraction of geometrical objects (anatomical structures, lesions, white matter tracks...) from anatomical and diffusion-weighted MRI; ii) the design of a coherent mathematical framework to model anatomical shapes and compare them across individuals. Within this context, we pursue the following objectives.

First, we aim to develop new methods to segment anatomical structures and lesions. We are most specifically interested in the hippocampus, a structure playing a crucial role in Alzheimer's disease, and in lesions of vascular origin (such as white matter hyperintensities and microbleeds). We pay particular attention to the robustness of the approaches with respect to normal and pathological anatomical variability and with respect to differences in acquisition protocols, for application to multicenter studies. We dedicate specific efforts to the validation on large populations of coming from patients data acquired in multiple centers.

Then, we develop approaches to estimate templates from populations and compare anatomical shapes, based on a diffeomorphic deformation framework and matching of distributions. These methods allow the estimation of a prototype configuration (called template) that is representative of a collection of anatomical data. The matching of this template to each observation gives a characterization of the anatomical variability within the population, which is used to define statistics. In particular, we aim to design approaches that can integrate multiple objects and modalities, across different spatial scales.

3.3. Modeling dynamical brain networks

Functional imaging techniques (EEG, MEG and fMRI) allow characterizing the statistical interactions between the activities of different brain areas, i.e. functional connectivity. Functional integration of spatially distributed brain regions is a well-known mechanism underlying various cognitive and perceptual tasks. Indeed, mounting evidence suggests that impairment of such mechanisms might be the first step of a chain of events triggering several neurological disorders, such as the abnormal synchronization of epileptic activities. Naturally, neuroimaging studies investigating functional connectivity in the brain have become increasingly prevalent.

Our team develops a framework for the characterization of brain connectivity patterns, based on connectivity descriptors from the theory of complex networks. The description of the connectivity structure of neural networks is able to characterize for instance, the configuration of links associated with rapid/abnormal synchronization and information transfer, wiring costs, resilience to certain types of damage, as well as the balance between local processing and global integration. Furthermore, we propose to extend this framework to study the reconfiguration of networks over time. Indeed, neurophysiological data are often gathered from longitudinal recording sessions of the same subject to study the adaptive reconfiguration of brain connectivity. Finally, connectivity networks are usually extracted from different brain imaging modalities (MEG, EEG, fMRI or DTI) separately. Methods for combining the information carried by these different networks are still missing. We thus propose to combine connectivity patterns extracted from each modality for a more comprehensive characterization of networks.

3.4. Methodologies for large-scale datasets

Until recently, neuroimaging studies were often restricted to series of about 20-30 patients. As a result, such studies had a limited statistical power and could not adequately model the variability of populations. Thanks to wider accessibility of neuroimaging devices and important public and private funding, large-scale studies including several hundreds of patients have emerged in the past years. In the field of Alzheimer's disease (AD) for instance, one can cite the Alzheimer's Disease Neuroimaging Initiative (ADNI) including about 800 subjects (patients with AD or mild cognitive impairment (MCI) and healthy controls) or the French cohort MEMENTO including about 2000 subjects with memory complaint. These are most often multicenter studies in which patients are recruited over different centers and images acquired on different scanners. Moreover, cohort studies include a longitudinal component: for each subject, multiple images are acquired at different time points. Finally, such datasets often include multimodal data: neuroimaging, clinical data, cognitive tests and genomics data. These datasets are complex, high-dimensional and often heterogeneous, and thus require the development of new methodologies to be fully exploited.

In this context, our objectives are:

- to develop methodologies to acquire and standardize multicenter neuroimaging data;
- to develop imaging biomarkers based on machine learning and longitudinal models;
- to design multimodal analysis approaches for bridging anatomical models and genomics.

The first two aspects focus on neuroimaging and are tightly linked with the CATI project. The last one builds on our previous expertise in morphometry and machine learning, but aims at opening new research avenues combining imaging and “omics” data. This is developed in strong collaboration with the new biostatistics/bioinformatics platform of the IHU-A-ICM.

4. Application Domains

4.1. Introduction

We develop different applications of our new methodologies to brain pathologies, mainly neurodegenerative diseases, epilepsy and cerebrovascular disorders. These applications aim at:

- better understanding the pathophysiology of brain disorders;
- designing biomarkers of pathologies for diagnosis, prognosis and assessment of drug efficacy;
- developing brain computer interfaces for clinical applications;
- improving the localisation of stimulation targets in Deep Brain Stimulation protocol.

These applications are developed in close collaboration with biomedical researchers of the ICM and clinicians of the Pitié-Salpêtrière hospital.

4.2. Understanding brain disorders

The approaches that we develop allow to characterize anatomical and functional alterations, thus making it possible to study these alterations in different clinical populations. This can provide provide new insights into the mechanisms and progression of brain diseases. This typically involves the acquisition of neuroimaging data in a group of patients with a given pathology and in a group of healthy controls. Measures of anatomical and functional alterations are then extracted in each subject (for instance using segmentation of anatomical structures, shape models or graph-theoretic measures of functional connectivity). Statistical analyses are then performed to identify: i) significant differences between groups, ii) correlations between anatomical/functional alterations on the one hand, and clinical, cognitive or biological measures on the other hand, iii) progression of alterations over time.

We propose to apply our methodologies to study the pathophysiology of neurodegenerative diseases (mostly Alzheimer’s disease and fronto-temporal dementia), epilepsy, cerebrovascular pathologies and neurodevelopmental disorders (Gilles de la Tourette syndrome). In neurodegenerative diseases, we aim at establishing the progression of alterations, starting from the early and even asymptomatic phases. In Gilles de la Tourette syndrome, we study the atypical anatomical patterns that may contribute to the emergence of symptoms. In epilepsy, we aim at studying the relationships between the different functional and structural components of epileptogenic networks.

4.3. Biomarkers for diagnosis, prognosis and clinical trials

Currently, the routine diagnosis of neurological disorders is mainly based on clinical examinations. This is also true for clinical trials, aiming to assess the efficacy of new treatments. However, clinical diagnoses only partially overlap with pathological processes. For instance, the sensitivity and specificity of clinical diagnosis of Alzheimer’s disease (AD) based on established consensus criteria are of only about 70-80% compared to histopathological confirmation. Furthermore, the pathological processes often begin years before the clinical symptoms. Finally, clinical measures embed subjective aspects and have a limited reproducibility and are thus not ideal to track disease progression. It is thus crucial to supplement clinical examinations with biomarkers that can detect and track the progression of pathological processes in the living patient. This has potentially very important implications for the development of new treatments as it would help: i) identifying patients with a given pathology at the earliest stage of the disease, for inclusion in clinical trials; ii) providing measures to monitor the efficacy of treatments.

The derivation of biomarkers from image analysis approaches requires large-scale validation in well-characterized clinical populations. The ARAMIS team is strongly engaged in such efforts, in particular in the field of neurodegenerative disorders. To that purpose, we collaborate to several national studies (see section Partnerships) that involve multicenter and longitudinal acquisitions. Moreover, ARAMIS is strongly involved in the CATI which manages over 15 multicenter studies, including the national cohort MEMENTO (2000 patients).

4.4. Brain computer interfaces for clinical applications

A brain computer interface (BCI) is a device aiming to decode brain activity, thus creating an alternate communication channel between a person and the external environment. BCI systems can be categorized on the base of the classification of an induced or evoked brain activity. The central tenet of a BCI is the capability to distinguish different patterns of brain activity, each being associated to a particular intention or mental task. Hence adaptation, as well as learning, is a key component of a BCI because users must learn to modulate their brainwaves to generate distinct brain patterns. Usually, a BCI is considered a technology for people to substitute some lost functions. However, a BCI could also help in clinical rehabilitation to recover motor functions. Indeed, in current neuroscience-based rehabilitation it is recognized that protocols based on mental rehearsal of movements (like motor imagery practicing) are a way to access the motor system because they can induce an activation of sensorimotor networks that were affected by lesions. Hence, a BCI based on movement imagery can objectively monitor patients' progress and their compliance with the protocol, monitoring that they are actually imagining movements. It also follows that feedback from such a BCI can provide patients with an early reinforcement in the critical phase when there is not yet an overt sign of movement recovery. The BCI approaches that we develop are based on the characterization of the information contained in the functional connectivity patterns. We expect to significantly increase the performance of the BCI system with respect to the sole use of standard power spectra of the activity generated by single local brain areas. Such an improvement will concretely provide the user with a more precise control of the external environment in open-loop BCI tasks and a more coherent feedback in the closed-loop BCI schemes.

4.5. Deep Brain Stimulation

Deep Brain Stimulation (DBS) is a surgical technique, which consists in sending electrical impulses, through implanted electrodes, to specific parts of the brain for the treatment of movement and affective disorders. The technique has been initially developed for otherwise-treatment-resistant patients with essential tremors or Parkinson's disease. Its benefit in other affections, such as dystonia, obsessive-compulsive disorders, Tourette syndrome is currently investigated. The localisation of the stimulation target in specific nucleus in deep brain regions is key to the success of the surgery. This task is difficult since the target nucleus, or the precise sub-territory of a given nucleus is rarely visible in the Magnetic Resonance Image (MRI) of the patients. To address this issue, a possible technique is to personalize a high-resolution histological atlas of the brain to each patient. This personalization is achieved by registering the histological atlas, which consists of an image and meshes of deep brain structures, to the pre-operative MRI of each patient. The registration is currently done by optimally aligning image intensities in the atlas and patient's MRI using a block-matching algorithm. The linear nature of the transform makes the technique robust at the cost of a lack of precision, especially for elderly patients with expanded ventricles. We investigate the use of non-linear registration techniques to optimally align both image intensities and contours of visible structures surrounding the target. We expect to improve the localisation of the target for patients with large ventricles while keeping the method robust in all cases.

5. Highlights of the Year

5.1. Highlights of the Year

- Stanley Durrleman has been awarded an ERC Starting Grant by the European Research Council

- The team has been awarded the H2020 project EuroPOND, under societal challenge "Personalizing Health and Care"
- The team has been awarded the ANR-NIH project NETBCI, under the "Collaborative Research in Computational Neuroscience" program (CRCNS)

6. New Software and Platforms

6.1. Brain Networks Toolbox

KEYWORDS: Neuroimaging - Medical imaging

FUNCTIONAL DESCRIPTION

Brain Networks Toolbox is a collection of Matlab routines developed to quantify topological metrics of complex brain networks.

- Participants: Mario Chavez and Fabrizio De Vico Fallani
- Contact: Mario Chavez
- URL: <https://sites.google.com/site/fr2eborn/download>

6.2. Deformetrica

KEYWORDS: 3D modeling - C++ - Automatic Learning - Mesh - Anatomy - Image analysis

SCIENTIFIC DESCRIPTION

Deformetrica is a software for the statistical analysis of 2D and 3D shape data. It essentially computes deformations of the 2D or 3D ambient space, which, in turn, warp any object embedded in this space, whether this object is a curve, a surface, a structured or unstructured set of points, or any combination of them.

Deformetrica comes with two applications:

registration, which computes the best possible deformation between two sets of objects, atlas construction, which computes an average object configuration from a collection of object sets, and the deformations from this average to each sample in the collection.

Deformetrica has very little requirements about the data it can deal with. In particular, it does not require point correspondence between objects!

FUNCTIONAL DESCRIPTION

Deformetrica is a software for the statistical analysis of 2D and 3D shape data. It essentially computes deformations of the 2D or 3D ambient space, which, in turn, warp any object embedded in this space, whether this object is a curve, a surface, a structured or unstructured set of points, or any combination of them.

Deformetrica comes with two applications:

- Registration, which computes the optimal deformation between two sets of objects,
- Atlas construction, which computes an average object configuration from a collection of object sets, and the deformations from this average to each sample in the collection.

Deformetrica has very little requirements about the data it can deal with. In particular, it does not require point correspondence between objects!

- Participants: Stanley Durrleman, Alexandre Routier, Pietro Gori, Marcel Prastawa, Ana Fouquier, Joan Alexis Glaunès, Benjamin Charlier, Cédric Doucet and Mauricio Diaz-Melo
- Partners: University of Utah - Université de Montpellier 2 - Université Paris-Descartes
- Contact: Stanley Durrleman
- URL: <http://www.deformetrica.org/>

6.3. SACHA

Segmentation Automatisée Compétitive de l'Hippocampe et de l'Amygdale

KEYWORDS: Neuroimaging - 3D - Hippocampus - Amygdala - Brain scan - Medical imaging

SCIENTIFIC DESCRIPTION

The current stable version is fully automatic and focused on cross-sectional segmentation. The software can be used both as a command-line program or through a graphical user interface (GUI). The core of the program is coded in C++. It has a dependency to the AIMS library and preprocessing steps rely on processes in Matlab from SPM. The GUI is coded in Python and is based on BrainVISA.

FUNCTIONAL DESCRIPTION

SACHA is a software for the fully automatic segmentation of the hippocampus and the amygdala from MRI 3D T1 brain scans. It has been validated in various populations including healthy controls and patients with Alzheimer's disease, epilepsy and depression. It has been successfully applied to over 3,000 subjects, both controls, from adolescents to elderly subjects, and patients with different types of pathologies.

- Participants: Marie Chupin and Ludovic Fillon
- Contact: Marie Chupin
- URL: <http://www.brainvisa.info>

6.4. WHASA

White matter Hyperintensity Automatic Segmentation Algorithm

KEYWORDS: Health - Neuroimaging - Biomedical imaging

SCIENTIFIC DESCRIPTION

The current stable version is fully automatic and focused on cross-sectional segmentation. The software can be used both as a Matlab command-line or through a graphical user interface (GUI). The core of the program is coded in Matlab. It has a dependency to the SPM environment. The GUI is coded in Python and is based on BrainVISA.

FUNCTIONAL DESCRIPTION

WHASA ("White matter Hyperintensity Automatic Segmentation Algorithm") is a software for the fully automatic segmentation of age-related white matter hyperintensities from MRI FLAIR and 3D T1 brain scans. It has been validated on a population showing a wide range of lesion load, and is being further evaluated on elderly subjects with few clinical abnormalities and with different acquisition characteristics.

- Participants: Marie Chupin, Ludovic Fillon and Thomas Samaille
- Contact: Marie Chupin
- URL: <http://www.brainvisa.info/>

6.5. qualiCATI

KEYWORDS: Health - Neuroimaging - Medical imaging

SCIENTIFIC DESCRIPTION

QualiCATI requires training for the visual parts, and is closely linked with a team of clinical research assistants. It has been used to analyse about 5000 subjects from about 15 multi centre research projects initiated before or after the CATI started. Other modules will be added in the future to embed new aspects of the MRI protocol proposed by the CATI. The Aramis team is in charge of the second and third modules and jointly in charge of the first module. The software is centered on a graphical user interface (GUI). The whole program is coded in Python within the pyPTK environment. It has dependencies to SPM and brainVISA environments as well as specific tools for DICOM management.

FUNCTIONAL DESCRIPTION

qualiCATI is a software designed for comprehensive quality control of multimodal MRI data acquisition in large multicentre clinical studies. The software is built as a platform receiving several modules, developed by several CATI engineers. The first module is dedicated to acquisition requirement checking and conversion to nifti format. The second module aims at making 3DT1 acquisition quality check more systematic, and relies both on visual inspection and quantitative indices. The third module allows a simultaneous evaluation of the clinical part of the CATI acquisition protocol. The fourth module embeds automatic indices to evaluate resting state fMRI acquisition. The fifth module is dedicated to first preprocessings and quality indices for dMRI. The sixth module is dedicated to qMRI, with visual and automated quality control together with preprocessings. The last module is dedicated to data and project management.

- Participants: Marie Chupin and Hugo Dary
- Contact: Marie Chupin
- URL: <http://www.fil.ion.ucl.ac.uk/spm/>

7. New Results

7.1. Learning spatiotemporal trajectories from manifold-valued longitudinal data

Participants: Jean-Baptiste Schiratti [Correspondant], Stéphanie Allasonniere, Olivier Colliot, Stanley Durrleman.

We propose a Bayesian mixed-effects model to learn typical scenarios of changes from longitudinal manifold-valued data, namely repeated measurements of the same objects or individuals at several points in time. The model allows the estimation of a group-average trajectory in the space of measurements. Random variations of this trajectory result from spatiotemporal transformations, which allow changes in the direction of the trajectory and in the pace at which trajectories are followed. The use of the tools of Riemannian geometry allows to derive a generic algorithm for any kind of data with smooth constraints, which lie therefore on a Riemannian manifold. Stochastic approximations of the Expectation-Maximization algorithm is used to estimate the model parameters in this highly non-linear setting.

The method is used to estimate a data-driven model of the progressive impairments of cognitive functions during the onset of Alzheimer's disease. Experimental results show that the model correctly put into correspondence the age at which each individual was diagnosed with the disease, thus validating the fact that it effectively estimated a normative scenario of disease progression. Random effects provide unique insights into the variations in the ordering and timing of the succession of cognitive impairments across different individuals.

More details in [30] and [31].

7.2. Joint Morphometry of Fiber Tracts and Gray Matter structures using Double Diffeomorphisms

Participants: Pietro Gori [Correspondant], Olivier Colliot, Linda Marrakchi-Kacem, Yulia Worbe, Alexandre Routier, Cyril Poupon, Andreas Hartmann, Nicholas Ayache, Stanley Durrleman.

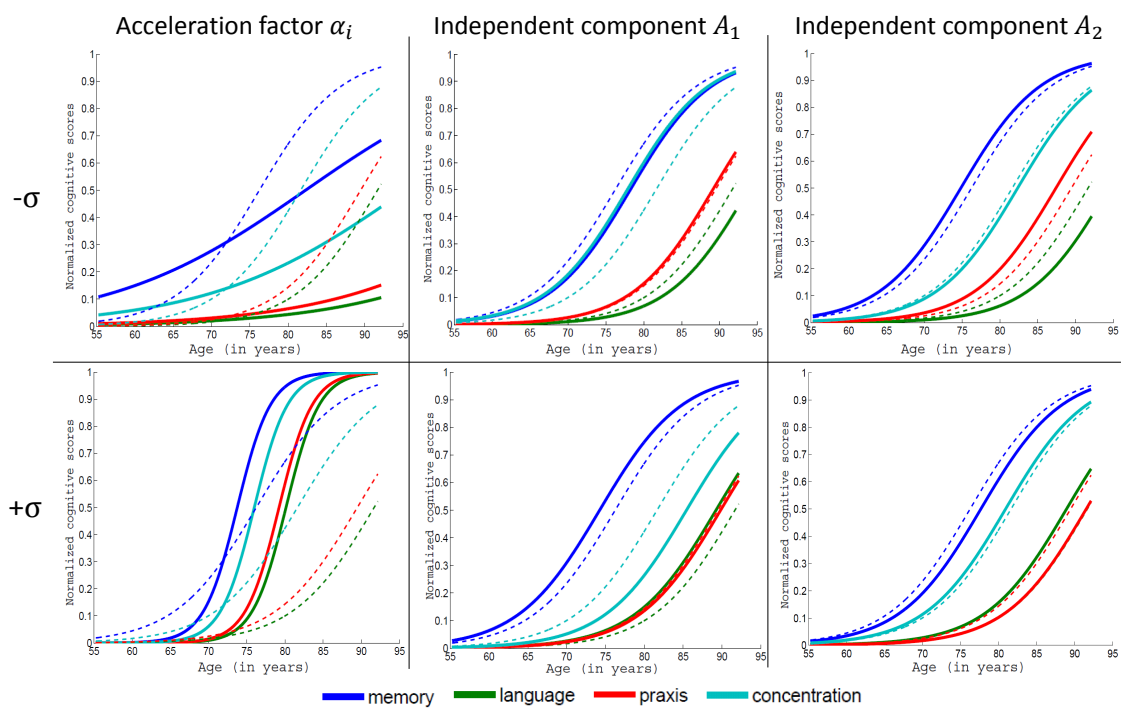


Figure 1. Disease progression model obtained from neuropsychological assessments of 248 patients observed at multiple times (from 3 to 11 times) who converted from Mild Cognitive Impairment stage to Alzheimer's disease during the observation period. Dashed lines represent the average scenario of disease progression (same in all plots). Solid lines represent the variability of this scenario within the observed population in terms of pace of disease progression (left) and relative timing and ordering of the decline of cognitive functions (middle and right).

This work proposes an atlas construction method to jointly analyse the relative position and shape of fiber tracts and gray matter structures. It is based on a double diffeomorphism which is a cascade of two diffeomorphisms. The first deformation acts only on the white matter keeping fixed the gray matter of the atlas. The resulting white matter, together with the gray matter, are then deformed by the second diffeomorphism which puts into correspondence the homologous anatomical structures across subjects. The first diffeomorphism makes the fiber bundles slide on the fixed gray matter revealing the variability in structural connectivity within the population, namely both the changes in the connected areas and in the geometry of the pathway of the tracts. Fiber bundles are approximated with weighted prototypes using the metric of weighted currents. The algorithm is based on a Bayesian framework which allows the automatic estimation of the covariance matrix of deformation parameters and of the noise variance of each structure. This approach is applied to patients with Tourette syndrome and controls showing a variability in the structural connectivity of the left cortico-putamen circuit.

More details in [26].

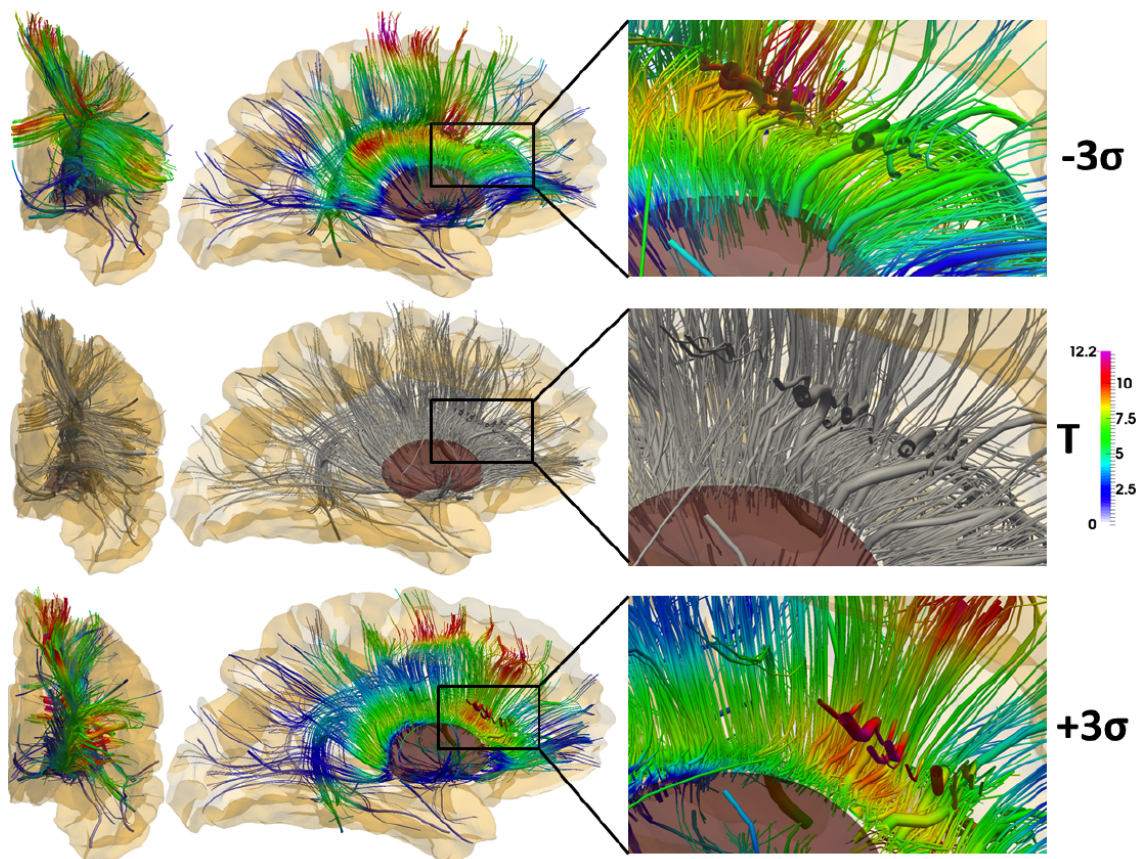


Figure 2. Estimation of a virtual representation of brain structure from anatomical and diffusion images of 3 patients with Gilles de la Tourette syndrome and 2 control subjects. Deformation of the white matter fiber bundle along the first mode of variability is shown while the estimated grey matter frame is kept fixed. Colors refer to the magnitude of displacement during deformation.

7.3. Bayesian Mixed Effect Atlas Estimation with a Diffeomorphic Deformation Model

Participants: Stanley Durrleman [Correspondant], Stéphanie Allasonniere, Estelle Kuhn.

In this work, we introduced a diffeomorphic constraint on the deformations considered in the deformable Bayesian Mixed Effect (BME) Template model. Our approach is built on a generic group of diffeomorphisms, which is parameterized by an arbitrary set of control point positions and momentum vectors. This enables us to estimate the optimal positions of control points together with a template image and parameters of the deformation distribution which compose the atlas. We propose to use a stochastic version of the Expectation-Maximization (EM) algorithm where the simulation is performed using the Anisotropic Metropolis Adjusted Langevin Algorithm (AMALA). We propose also an extension of the model including a sparsity constraint to select an optimal number of control points with relevant positions. Experiments are carried out on the USPS database, on mandibles of mice, and on 3D murine dendrite spine images.

More details in [2].

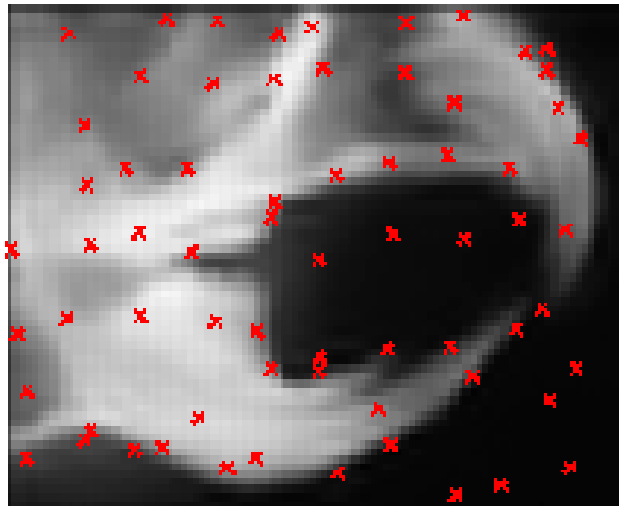


Figure 3. Template image of mouse mandible obtained from 36 X-ray image using 70 control points.

7.4. A sub-Riemannian modular approach for diffeomorphic deformations

Participants: Barbara Gris [Correspondant], Stanley Durrleman, Alain Trouvé.

We develop a generic framework to build large deformations from a combination of base modules. These modules constitute a dynamical dictionary to describe transformations. The method, built on a coherent sub-Riemannian framework, defines a metric on modular deformations and characterises optimal deformations as geodesics for this metric. We present a generic way to build local affine transformations as deformation modules, and display examples.

More details in [27].

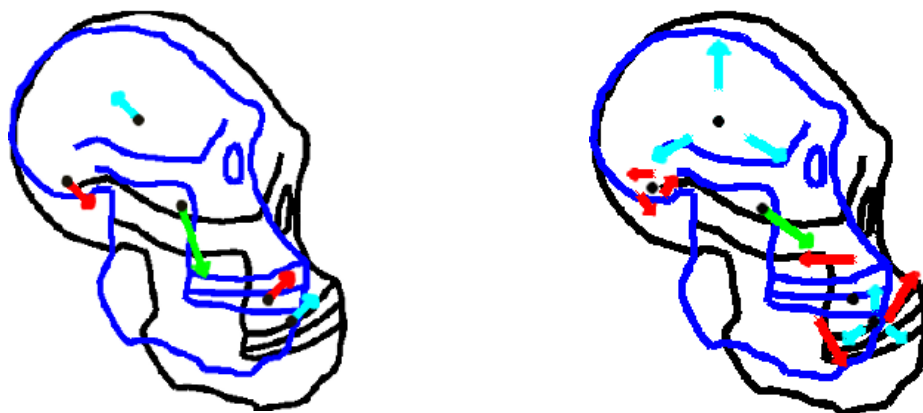


Figure 4. Initial position of deformation modules and their control parameters (left) leads to the construction of local scaling (cyan), rotation (red) and translation (green) (right), which combine together to deform the blue shape into the black one.

7.5. Results of a multicenter randomized placebo-controlled clinical trial in prodromal Alzheimer's disease

Participants: Bruno Dubois, Marie Chupin, Harald Hampel, Simone Lista, Enrica Cavedo, Bernard Croisille, Guy Louis Tisserand, Jacques Touchon, Alain Bonafé, Pierre-Jean Ousset, Amir Ait Ameer, Olivier Rouaud, Frédéric Ricolfi, Alain Viguetto, Florence Pasquier, Christine Delmaire, Mathieu Ceccaldi, Nadine Girard, Carole Dufouil, Stéphane Lehericy, Isabelle Tonelli, Françoise Duveau, Olivier Colliot, Line Garnerro, Marie Sarazin, Didier Dormont [Correspondant].

Our team coordinated neuroimage acquisition and analysis of a multicenter randomized placebo-controlled clinical trial aiming to assess the efficacy of donepezil in prodromal Alzheimer's disease. Subjects underwent two brain magnetic resonance imaging scans (baseline and final visit). The primary efficacy outcome was the annualized percentage change (APC) of total hippocampal volume (left + right) measured by the software (see Section SACHA 6.3) developed by our team. Two-hundred and sixteen only subjects were randomized across 28 French expert clinical sites. In the per protocol population (placebo = 92 and donepezil = 82), the donepezil group exhibited a significant reduced rate of hippocampal atrophy (APC= -1.89%) compared with the placebo group (APC= -3.47%), $P < .001$. There was no significant difference in neuropsychological performance between treatment groups. A 45% reduction of rate of hippocampal atrophy was observed in prodromal AD following 1 year of treatment with donepezil compared with placebo.

This new approach opens interesting perspectives for the evaluation of treatments in neurodegenerative diseases.

More details in [12].

7.6. Sulcal morphology as a new imaging marker for the diagnosis of early onset Alzheimer's disease

Participants: Lorraine Hamelin, Bruno Dubois, Marie Chupin, Olivier Colliot [Correspondant], Marie Sarazin.

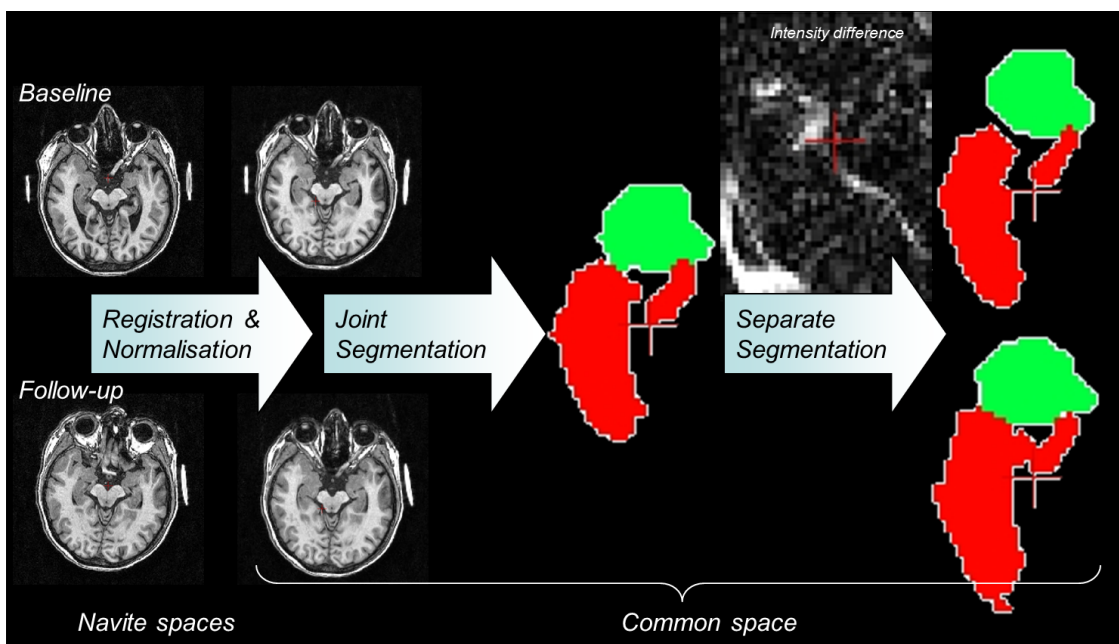


Figure 5. Hippocampus longitudinal segmentation method illustrating preliminary registration of the baseline and final visit magnetic resonance imaging (MRI) scans in a common space followed by normalization of the intensities of both scans. The baseline and final visit MRI scans were then segmented jointly. The resulting segmentation was then used as an initialization of separate segmentations while keeping the two segmentations consistent between the two time-points.

We investigated the utility of sulcal width measures in the diagnosis of Alzheimer's disease (AD). Sixty-six biologically confirmed AD patients (positive amyloid positron emission tomography [PET] and/or AD cerebrospinal fluid profile) were contrasted to 35 controls with negative amyloid PET. Patients were classified into prodromal or dementia stages as well as into late onset (LOAD, $n = 31$) or early onset (EOAD, $n = 35$) subgroups according to their age of onset. An automated method was used to calculate sulcal widths and hippocampal volumes (HV). In EOAD, the greatest ability to differentiate patients from age-matched controls, regardless of severity, was displayed by sulcal width of the temporoparietal cortex. In this region, diagnosis accuracy was better than the HV, especially at prodromal stage. In LOAD, HV provided the best discrimination power from age-matched controls. In conclusion, sulcal width measures are better markers than the HV for identifying prodromal AD in patients aged <65 years. In contrast, in older patients, the risk of over-diagnosis from using only sulcal enlargement is important.

More details in [14].

7.7. Imaging Markers of the Presymptomatic GRN Disease

Participants: Paola Caroppo, Stanley Durrleman, Alexandre Routier, Olivier Colliot [Correspondant], Alexis Brice, Isabelle Le Ber.

The preclinical stage of frontotemporal lobar degeneration (FTLD) is not well characterized. We conducted a brain metabolism (FDG-PET) and structural (cortical thickness) study to detect early changes in asymptomatic GRN mutation carriers (aGRN+) that were evaluated longitudinally over a 20-month period. At baseline, a left lateral temporal lobe hypometabolism was present in aGRN+ without any structural changes. Importantly, this is the first longitudinal study and, across time, the metabolism more rapidly decreased in aGRN+ in lateral temporal and frontal regions. The main structural change observed in the longitudinal study was a reduction of cortical thickness in the left lateral temporal lobe in carriers (Figure 6). A limit of this study is the relatively small sample ($n=16$); nevertheless, it provides important results. First, it evidences that the pathological processes develop a long time before clinical onset, and that early neuroimaging changes might be detected approximately 20 years before the clinical onset of disease. Second, it suggests that metabolic changes are detectable before structural modifications and cognitive deficits. Third, both the baseline and longitudinal studies provide converging results implicating lateral temporal lobe as early involved in GRN disease. Finally, our study demonstrates that structural and metabolic changes could represent possible biomarkers to monitor the progression of disease in the presymptomatic stage toward clinical onset.

More details in [6].

7.8. Incomplete Hippocampal Inversions in healthy subjects: a comprehensive study of over 2000 participants

Participants: Claire Cury [Correspondant], Joan Glaunès, Dominique Hasboun, Fanny Cohen, Jorge Samper-González, Roberto Toro, Vincent Frouin, Gunter Schumann, Olivier Colliot.

The incomplete-hippocampal-inversion (IHI), also known as malrotation, is an atypical anatomical pattern of the hippocampus, which has been reported in healthy subjects in different studies. However, extensive characterization of IHI in a large sample has not yet been performed. Furthermore, it is unclear whether IHI are restricted to the medial-temporal lobe or are associated with more extensive anatomical changes. Here, we studied the characteristics of IHI in a community-based sample of 2008 subjects of the IMAGEN database and their association with extra-hippocampal anatomical variations. The presence of IHI was assessed on T1-weighted anatomical magnetic resonance imaging (MRI) using visual criteria. We assessed the association of IHI with other anatomical changes throughout the brain using automatic morphometry of cortical sulci. We found that IHI were much more frequent in the left hippocampus (left: 17%, right: 6%, χ^2 -test, $p < 10^{-28}$). Compared to subjects without IHI, subjects with IHI displayed morphological changes in several sulci located mainly in the limbic lobe. Our results demonstrate that IHI are a common left-sided phenomenon in normal subjects and that they are associated with morphological changes outside the medial temporal lobe.

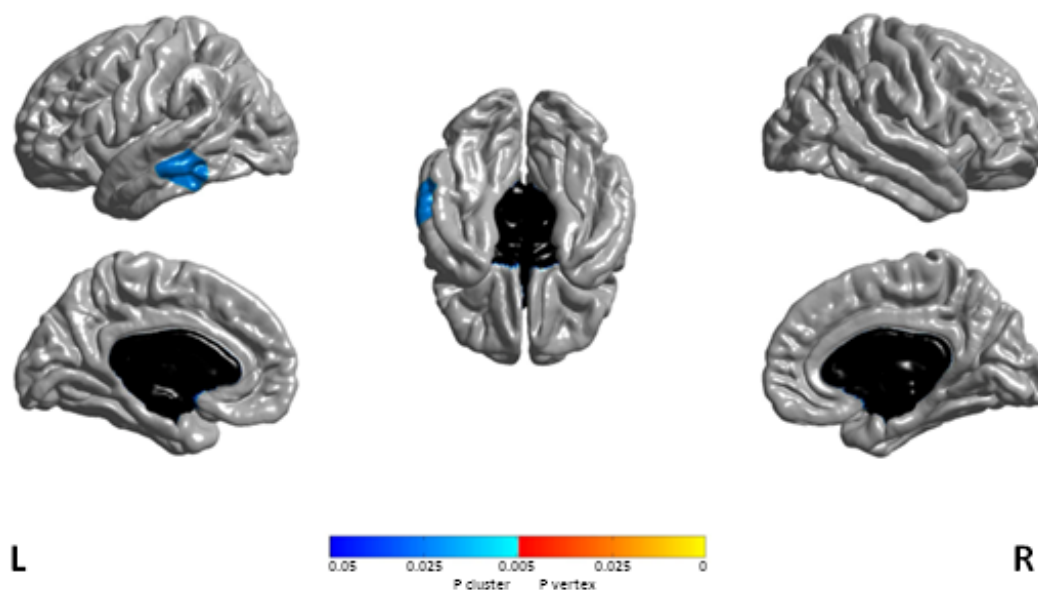


Figure 6. Cluster with significant cortical thickness changes in aGRN+ between the two time-points ($p < 0.05$ corrected). L, left; R, right.

More details in [9].

7.9. Analysis of anatomical variability using diffeomorphic iterative centroid in patients with Alzheimer’s disease

Participants: Claire Cury [Correspondant], Joan Glaunès, Marie Chupin, Olivier Colliot.

We proposed a new approach for template-based analysis of anatomical variability in populations, in the framework of Large Deformation Diffeomorphic Metric Mappings and mathematical currents. We propose a fast approach in which the template is computed using an diffeomorphic iterative centroid method. Statistical analysis is then performed on the initial momenta that define the deformations between the centroid and each individual subject. We applied the approach to study the variability of the hippocampus in 134 patients with Alzheimer’s disease (AD) and 160 elderly control subjects. We show that this approach can describe the main modes of variability of the two populations and can predict the performance to a memory test in AD patients.

More details in [8].

7.10. Innovation-based sparse estimation of functional connectivity from multivariate autoregressive models

Participants: Fabrizio de Vico Fallani [Correspondant], Stéphanie Allasonniere [Correspondant], Francois Deloche.

One of the main limitations of functional connectivity estimators of brain networks is that they can suffer from statistical reliability when the number of areas is large and the available time series are short. To estimate directed functional connectivity with multivariate autoregressive (MVAR) model on sparse connectivity assumption, we propose a modified Group Lasso procedure with an adapted penalty. Our procedure includes

the innovation estimates as explaining variables. This approach is inspired by two criteria that are used to interpret the coefficients of the MVAR model, the Directed Transfer Function (DTF) and the Partial Directed Coherence (PDC). A causality measure can be deduced from the output coefficients which can be understood as a synthesis of PDC and DTF. We demonstrate the potential of our method and compare our results with the standard Group Lasso on simulated data.

More details in [25]

7.11. Lucid Dreaming in Narcolepsy

Participants: Pauline Daudet, Mario Chavez [Correspondant], Smaranda Leu-Semenescu, Jean-Louis Golmard, Isabelle Arnulf.

Lucid dreaming is the experience of being aware of dreaming while asleep and continuing to dream. Lucid dreams generally arise in REM sleep. Compared to non-lucid REM sleep, lucid REM sleep is associated with local frontal lobe EEG changes in the 40 Hz band, increased brain coherence, and increased activity on functional MRI in the bilateral precuneus, cuneus, parietal lobules, and prefrontal and occipito-temporal cortices, which may correspond to restored reflective consciousness. We decided to study the frequency and determinants of lucid dreaming in narcolepsy and to challenge patients' alleged ability to achieve lucid dreaming using sleep monitoring during nighttime and daytime sleep. Compared to 53 healthy controls, the 53 narcolepsy patients reported more frequent dream recall, nightmares and recurrent dreams. The frequency of cataplexy, hallucinations, sleep paralysis, dyssomnia, positivity, and the severity of sleepiness were similar in narcolepsy with and without lucid dreaming. The delta power in the electrode average, in delta, theta, and alpha powers in C4, and coherences between frontal electrodes were lower in lucid than non-lucid REM sleep in spectral EEG analysis. The duration of REM sleep was longer, the REM sleep onset latency tended to be shorter, and the percentage of atonia tended to be higher in lucid vs. non-lucid REM sleep; the arousal index and REM density and amplitude were unchanged. Our results suggest that narcoleptics have a high propensity for lucid dreaming without differing in REM sleep characteristics from people without narcolepsy. This also suggests that narcolepsy patients may provide useful information in future studies on the nature of lucid dreaming.

More details in [11]

7.12. An Algebraic Topological Method for Multimodal Brain Networks Comparisons

Participants: Tiago Simas, Mario Chavez [Correspondant], Pablo Rodriguez, Albert Diaz-Guilera.

Understanding brain connectivity is one of the most important issues in neuroscience. Nonetheless, connectivity data can reflect either functional relationships of brain activities or anatomical connections between brain areas. Although both representations should be related, this relationship is not straightforward. We have devised a powerful method that allows different operations between networks that share the same set of nodes, by embedding them in a common metric space, enforcing transitivity to the graph topology. Here, we apply this method to construct an aggregated network from a set of functional graphs, each one from a different subject. Once this aggregated functional network is constructed, we use again our method to compare it with the structural connectivity to identify particular brain regions that differ in both modalities (anatomical and functional). Remarkably, these brain regions include functional areas that form part of the classical resting state networks. We conclude that our method -based on the comparison of the aggregated functional network- reveals some emerging features that could not be observed when the comparison is performed with the classical averaged functional network.

More details in [23]

7.13. Steady state visual evoked potentials-based patient interface under breathing constraints

Participants: Xavier Navarro [Correspondant], Sebastien Champion, Fabrizio de Vico Fallani [Correspondant], Pierre Pouget, Thomas Similowski, Mathieu Raux, Mario Chavez.

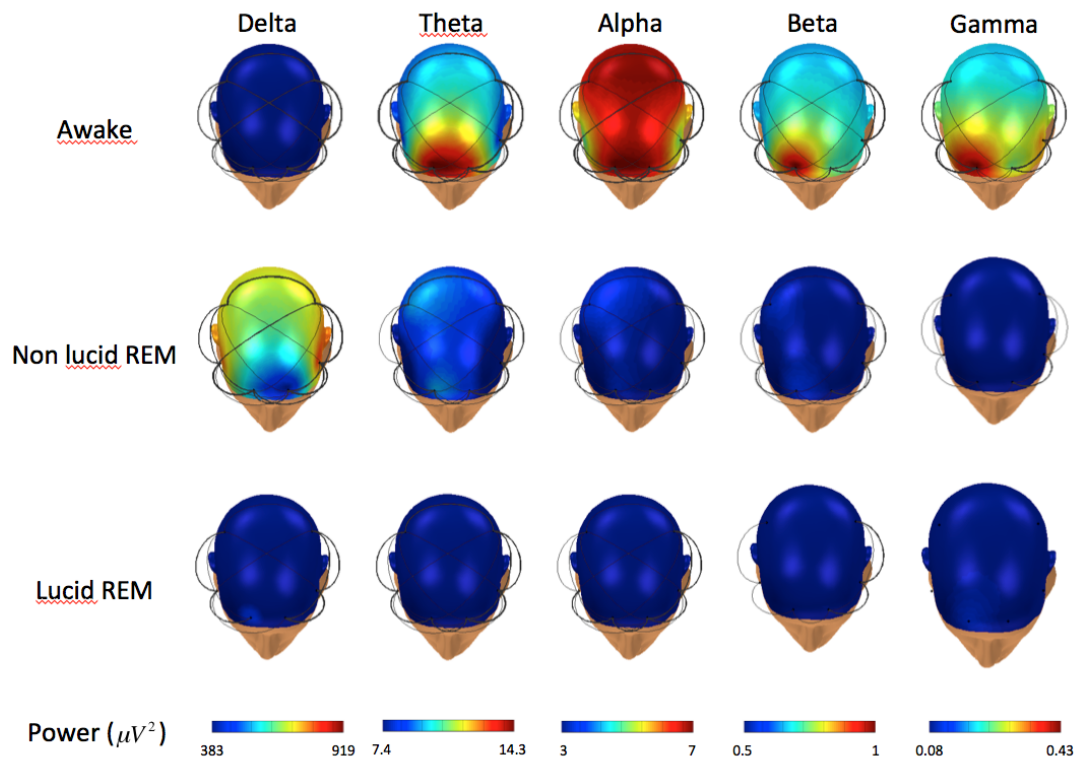


Figure 7. Topographical distribution (obtained by a spherical spline interpolation) of EEG spectral power during wakefulness (top row), non-lucid (middle row) and lucid (bottom row) REM sleep for different frequency bands. Significant couplings between the electrodes are indicated by the black links (the thickness is proportional to the coherence value). Colors from dark blue (lower EEG power) to dark red (higher EEG power) indicated for each EEG band in the Power line (bottom row).

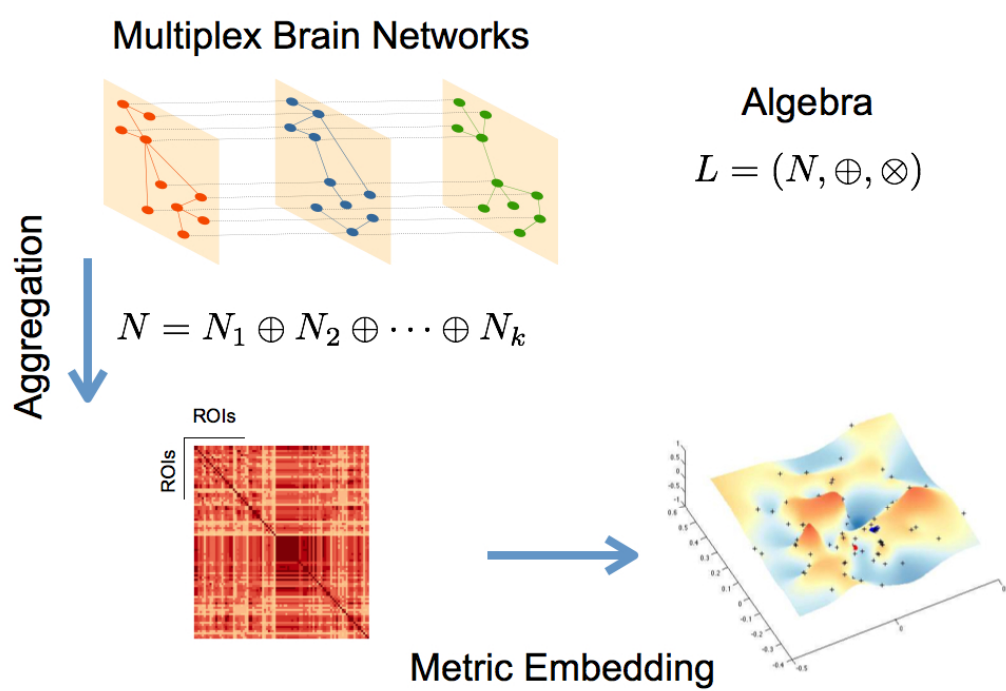


Figure 8. Schematic representation of the main steps for the described networks aggregation and metric embedding (defined here for the algebra L)

Steady state visual evoked potentials (SSVEP) have been widely utilized in brain computer interfacing (BCI) in last years. In this paper, we present a study exploring the possibilities of SSVEP to manage the communication between patients suffering respiratory disorders and health care providers. By imposing different breathing constraints, five healthy subjects communicated their breathing sensations (breathing well/breathing bad) using a visual frequency tagging paradigm: two visual stimuli with different flickering frequencies (15 and 20 Hz) were simultaneously presented on a screen. Using electroencephalographic (EEG) signals from only three EEG electrodes, two spectral features were extracted by a spatial filter in a sliding window, then classified by an unsupervised algorithm based on k-medians. Average detection success rates were of 70% during breathing discomfort, and of 83% when subjects breathed comfortably. Results suggest that SSVEP-based BCI may be a promising choice to improve patient-caregiver communication in situations of breathing discomfort when verbal communication is difficult.

More details in [29]

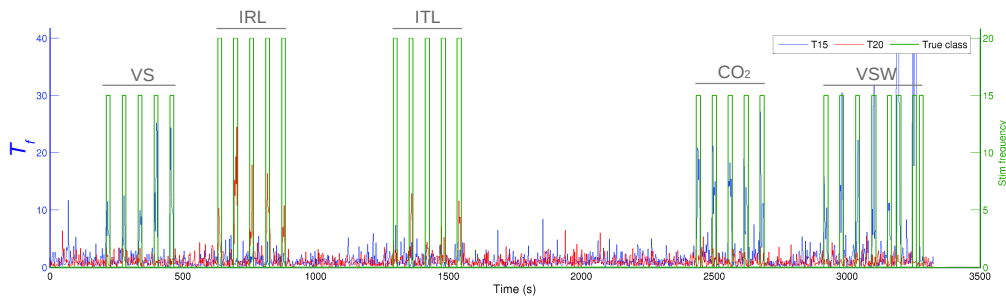


Figure 9. An example of T_f obtained after applying the spatial filters on 15 Hz (blue curve) and 20 Hz (red curve) during the experiment in subject 3. The statistics T_f reflects the signal-to-noise ratio at frequency f with respect to the no-stimulus power.

8. Bilateral Contracts and Grants with Industry

8.1. Bilateral Contracts with Industry

8.1.1. Air-Liquide Medical Systems

Participants: Mario Chavez [Correspondant], Xavier Navarro.

Project title: Real-time characterisation of respiratory states from EEG

Founded in 2014

Amount: 370 K€

Coordinator: Thomas Similowski

Other partners: UPMC, Inserm UMR 1158

Abstract: The project aims at developing a real-time brain computer interface (BCI) for the monitoring of respiratory states from scalp EEG data of healthy volunteers and patients, recorded at the laboratory, hospital ward, operating room or intensive care units..

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. ANR

9.1.1.1. ANR PREV-DEMALS

Participants: Olivier Colliot [Correspondant], Marie Chupin, Stanley Durrleman, Anne Bertrand.

Project acronym: PREV-DEMALS

Project title: Predict to prevent frontotemporal lobar degeneration (FTLD) and amyotrophic lateral sclerosis (ALS)

Duration: Avr 2015 - Avr 2019

Amount: 487k€

Coordinator: Isabelle Le Ber

Other partners: ICM, AP-HP, CHR de Lille, CHU Limoges, CHU Rouen, Laboratory of Biomedical Imaging

Abstract: The project focuses on C9ORF72, the most frequent genetic form of frontotemporal lobar degeneration (FTLD) and amyotrophic lateral sclerosis (ALS). Since 2006, major discoveries have helped elucidate the pathological bases and linked FTLD and ALS: 1) TDP-43 aggregates in neurons and 2) C9ORF72 mutations in both disorders. Two major pathological subtypes are now defined in FTLD, FTLD-TDP and FTLD-TAU. C9ORF72 mutations (associated to FTLD-TDP) are the most frequent genetic causes of FTLD (15%), FTLD-ALS (65%) and ALS (40%). No curative treatment actually exists, but therapeutics emerged against tau aggregation. The objectives of the project are to develop appropriate cognitive, brain imaging markers and peripheral biomarkers of the early phase of FTLD, to follow disease progression and to guide future targeted therapeutic trials. To address this questions, we will conduct a multimodal study (cognition, brain structural MRI, brain metabolism - FDG-PET) in C9ORF72 families. The cohort will be followed at 3-time points (M0, M18, M36). Longitudinal analyses will aim at characterizing the trajectory of decline across time. Brain structural changes will be evaluated by 1) morphometric analysis to assess global brain atrophy, cortical thickness and study of the cortical sulci; 2) functional connectivity analysis of resting-state MR data; 3) structural connectivity analysis of diffusion-weighted MRI. Brain metabolism will be evaluated with FDG-PET. We will use the most recent RNA sequencing technology to detect gene expression and RNA splicing alterations in lymphocytes of patients and presymptomatic carriers. The discovery of new markers involved in FTLD will have practical consequences for early and accurate diagnosis of FLD and ALS disease.

9.1.2. IHU

9.1.2.1. General program

Participants: Olivier Colliot, Mario Chavez, Stanley Durrleman, Marie Chupin, Didier Dormont, Dominique Hasboun, Damien Galanaud, Fabrizio de Vico Fallani.

Project acronym: IHU-A-ICM

Project title: Institute of Translational Neuroscience

Founded in 2011

General Director: Bertrand Fontaine

The IHU-A-ICM program was selected, in 2011, in a highly competitive national call for projects. A 10-year, 55M€ program, has been implemented by a recently created foundation for scientific cooperation. Based on the clinical and scientific strenghts of the ICM and the hospital Department of Nervous System Diseases, it mainly supports neuroscience research, but is also invested in improving care and teaching. ARAMIS is strongly involved in the IHU-A-ICM project, in particular in WP6 (neuroimaging and electrophysiology), WP7 (biostatistics), WP2 (Alzheimer) and WP5 (epilepsy). We have started collaborations with the new bioinformatics/biostatistics platform (IHU WP7, head: Ivan Moszer), in particular through a joint project on the integration of imaging and genomics data.

9.1.2.2. ICM-Internal Research projects

Participants: Mario Chavez [Correspondant], Fabrizio de Vico Fallani [Correspondant].

Project title: Non-invasive manipulation of brain synchrony to enhance brain function and rehabilitate faulty cognition in humans: A proof of concept

Founded in 2014

Coordinator: Antoni Valero Cabre (ICM-team “Dynamiques Cérébrales, Plasticité et Rééducation”)

Other partners: Service des Urgences Cérébro-Vasculaires de l’Hôpital Pitié-Salpêtrière, Paris.

The long-term goal of this project is to develop the use of non-invasive manipulation of abnormal cerebral oscillations underlying cognitive activity to restore brain function in neurological patients. Cognitive functions emerge from large distributed networks organized in space and time. The short-term goal of this application is to study the causal role played by oscillatory activity in visual awareness and test whether their manipulation by non-invasive brain stimulation has the potential to restore its function in stroke patients.

9.1.2.3. IFR49-Internal Research projects

Participants: Mario Chavez [Correspondant], Fabrizio de Vico Fallani [Correspondant].

Project title: Exploring the impact and time frequency signature of rhythmic patterns of Transcranial Magnetic Stimulation (TMS) on network activity by Magneto-Encephalography (MEG)

Founded in 2014

Coordinator: Antoni Valero Cabre (ICM-team “Dynamiques Cérébrales, Plasticité et Rééducation”)

Other partners: TMS, EEG and MEG technical platforms of the ICM at the Hopital Pitié-Salpêtrière; and Service des Urgences Cérébro-Vasculaires de l’Hôpital Pitié-Salpêtrière, Paris.

The long-term goal of this project is to better understand the ability of non invasive neurostimulation to induce lasting local and distributed reorganization effects in the human brain to better plan and document therapies for patients. The short-term goal of this application is to develop a new mapping procedure to be able to capture and characterize in terms of oscillatory activity the lasting impact of repetitive Transcranial Magnetic Stimulation (TMS) on specific brain regions and associated networks.

9.1.3. CATI (Alzheimer Plan)

Participants: Olivier Colliot [Correspondant], Marie Chupin [Correspondant], Stanley Durrleman, Didier Dormont, Chabha Azouani, Ali Bouyahia, Johanne Germain, Kelly Martineau, Sonia Djobeir, Hugo Dary, Ludovic Fillon, Takoua Kaaouana, Alexandre Routier, Mathieu Dubois.

Project acronym: CATI

Project title: Centre d’Acquisition et de Traitement des Images

Founded in 2011

Amount: 9M€

Coordinator: Jean-François Mangin

Other partners: Neurospin, CENIR, Inserm U678, IM2A

Abstract: The CATI project (funded by the National Alzheimer Plan for 9M€, 2.1M€ for ARAMIS) aims at creating a national platform for multicenter neuroimaging studies. CATI aims to be a national resource for the scientific, medical and industrial research community and will provide a wide range of services: access to a national acquisition network, standardization of acquisitions, image quality control, image analysis, databasing/archiving, meta-analyses. Through CATI, our team coordinates a large network composed of over 30 image acquisition centers. CATI already supports over 15 multicenter projects including the national cohort MEMENTO (2300 subjects). CATI is integrated with France Life Imaging (PI: F. Lethimonnier) and the Neugrid for you (N4U, PI: G. Frisoni) network.

9.1.4. National Networks

- GdR Statistics and Medicine - <http://gdr.statsante.fr/Accueil.html>

9.1.5. Other National Programs

9.1.5.1. Programme Hospitalier de Recherche Clinique (PHRC)

Participants: Olivier Colliot, Marie Chupin, Stanley Durrleman, Didier Dormont, Damien Galanaud.

- PHRC PredictPGRN, co-funding by Alzheimer Plan, *Caractérisation multimodale prospective de la démence frontotemporale due à des mutations du gène PGRN à un stade symptomatique et présymptomatique.* (Coordinator : A. Brice)
- PHRC ImaBio3, co-funding by Roche (pharmaceutical industry), *Rôle des réactions cellulaires sanguines, inflammatoires et immunitaires anti-amyloïde centrales et périphériques dans la maladie d'Alzheimer débutante.* (Coordinator : M. Sarazin)
- PHRC CAPP, *Caractérisation linguistique, anatomique/métabolique et biologique des différentes formes d'aphasie primaire progressive : vers le rationnel pour des essais pharmacologiques et des rééducations du langage ciblées.* (Coordinator: M. Teichmann)

9.1.5.2. Institut Universitaire d'Ingénierie pour la Santé (IUIS)

Participants: Mario Chavez, Xavier Navarro.

Project acronym: DYSPEV

Project title: Dépistage de la dyspnée par potentiels évoqués visuels

Founded in 2014

Amount: 38K€

Coordinator: Thomas Similowski

Other partners: UPMC, Inserm UMR 1158

Abstract: Steady state visual evoked potentials (SSVEP) have been widely utilized in brain computer interfacing (BCI) in last years. In this project, we explore the possibilities of SSVEP to manage the communication between patients suffering from respiratory disorders and health care providers. By imposing different breathing constraints, we use a SSVEP-based brain computer interface to help those subjects to communicate their breathing sensations (breathing well/breathing bad).

9.2. European Initiatives

9.2.1. FP7 & H2020 Projects

Participants: Stefan Thurner, Vito Latora, Albert Diaz-Guilera, Maxi San Miguel, Cecilia Mascolo, Mirco Murolesi, Mario Chavez [Correspondant].

Project acronym: LASAGNE

Project title: multi-LAyer SpAtiotemporal Generalized NEtworks

Dates: 2012-2015

Amount: 1.6M€

Coordinator: Stefan Thurner

Other partners: Medical University of Vienna, Queen Mary University of London, Universitat de Barcelona, Universitat de les Illes Balears, University of Cambridge, University of Birmingham.

Abstract: The aim of the LASAGNE project is to provide a novel and coherent theoretical framework for analyzing and modelling dynamic and multi-layer networks in terms of multi-graphs embedded in space and time. To do this, we will treat time, space and the nature of interactions not as additional dimensions of the problem, but as natural, inherent components of the very same generalized network description. The theory will be validated on real-world applications involving large and heterogeneous data sets of brain networks, on- and off-line social systems, healthcare systems, and transportation flows in cities. The LASAGNE project will provide new quantitative opportunities in different fields, ranging from the prediction of pathologies to the diffusion of ideas and trends in societies, and for the management of socio-technological systems.

9.3. International Initiatives

9.3.1. Inria International Partners

9.3.1.1. Informal International Partners

S. Durrleman has an enduring collaboration with the Scientific Computing and Imaging (SCI) Institute at the University of Utah (USA). He is consultant for NIH Grant "4D shape analysis for modeling spatiotemporal change trajectories in Huntington's Disease "predict-HD". He is part of the PhD committees of J. Fishbaugh and A. Sharma supervised by professor Guido Gerig.

M. Chupin and O. Colliot have an enduring collaboration with the Center for Magnetic Resonance Research, University of Minnesota, USA (P-F Van de Moortele, T. Henry, M. Marjanska, K. Ugurbil) a leading center in 7T MRI.

S. Durrleman and O. Colliot have a collaboration with the Center for Medical Image Computing (CMIC) at University College London (UCL), London, UK (S. Ourselin, D. Alexander, M. Modat).

D. Galanaud has an enduring collaboration with the Massachusetts General Hospital, Harvard University, USA (R. Gupta).

M. Chavez has different collaborations with the Mathematics Departement of the Queen Mary University of London, UK (Prof. V. Latora); and the Physics Department of the Universitat de Barcelona, Spain (Prof. Albert Diaz-Guilera)

F. De Vico Fallani has a collaboration with the University Sapienza, Rome, Italy (Profs. Fabio and Claudio Babiloni) and with the IRCCS Fondazione Santa Lucia, Rome, Italy (M. Molinari and D. Mattia).

10. Dissemination

10.1. Promoting Scientific Activities

10.1.1. Scientific events organisation

10.1.1.1. General chair, scientific chair

S. Durrleman was co-chair of the 5th Workshop on "Mathematical Foundations of Computational Anatomy" held in Munich on October 5, 2015 in conjunction with the MICCAI conference.

F. De Vico Fallani was co-chair of the satellite on "Brain Networks" during the International School and Conference on Network Science (NETSCI15) in Zaragoza, Spain, 2015.

F. De Vico Fallani was co-chair of the satellite on "Graph Models in Neuroimaging " in conjunction with the annual conference Wavelets and Sparsity (SPIE), San Diego, US, 2015.

M. Chavez was co-chair of the Minisymposia "Graph analysis of functional brain networks: theory, applications and issues" during the 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society that took place in Milano, Italy, 2015.

10.1.1.2. Member of the organizing committees

F. De Vico Fallani was technical member of the symposium on "Human brain connectomics " in conjunction with IEEE Global SIP conference, Orlando, US, 2015

10.1.2. Scientific events selection

10.1.2.1. Member of the conference program committees

O. Colliot was a member of program committee of the Workshop on Patch-based Techniques in Medical Imaging (Patch-MI) held in Munich in October 2015 in conjunction with the MICCAI conference.

10.1.2.2. Reviewer

O. Colliot acted as a reviewer for the annual meeting of the Organization for Human Brain Mapping (OHBM).

S. Durrleman acted as a reviewer for the conferences Information Processing in Medical Imaging (IPMI) and International Conference on Computer Vision (ICCV).

F. De Vico Fallani acted as a reviewer for the annual conference of the IEEE Engineering in Medical and Biology Society (EMBS).

10.1.3. Journal

10.1.3.1. Member of the editorial boards

O. Colliot is a member of the Editorial Board of Medical Image Analysis (Elsevier).

10.1.3.2. Reviewer - Reviewing activities

During the past year the members of the team acted as reviewers for numerous journals:

O. Colliot acted as a reviewer for NeuroImage, NeuroImage: Clinical, IEEE Trans Medical Imaging, Medical Image Analysis and Neurobiology of Aging.

S. Durrleman acted as a reviewer for NeuroImage, IEEE Trans Medical Imaging, Medical Image Analysis, IEEE Trans Pattern Analysis and Machine Intelligence, IEEE Trans Biomedical Engineering.

F. De Vico Fallani acted as a reviewer for NeuroImage, IEEE Trans Biomedical Engineering, IEEE Trans Neural Systems Rehabilitation Engineering, Brain Topography, Plos One, Human Brain Mapping, Nature Scientific Reports, Journal of neuroscience methods, PLoS Computational Biology.

M. Chavez acted as a reviewer for the Imperial College Press and the following journals: PLoS Comput Biol; PLoS One; J. Neurosci Methods; Phil. Trans. R. Soc. B; J. R. Soc. Interface; Human Brain Mapping; IEEE Proceedings; Neurosci. Biobehav. Rev. and Clin Neurophys;

10.1.4. Invited talks

S. Durrleman was invited lecturer at:

- Erwin Schrodinger International Institute for Mathematical Physics in Vienna for the program "Infinite-dimensional Riemannian Geometry with Applications to Image Matching and Shape Analysis",
- First congress of the Trisomy 21 Research Society at the ICM in Paris,
- "Shape Symposium" in Délemont, Switzerland,
- Colloquium "Horizon-Math" of the Mathematical Foundation of Paris.

F. De Vico Fallani was invited lecturer at:

- Conference of the IEEE Engineering in Medicine and Biology Society", Milan, Italy
- Conference on Wavelets and Sparsity (SPIE), San Diego, US
- Workshop on computational methods in system neuroscience, Tenerife, Spain
- Symposium on Magnetoencephalography, Lyon, France

M. Chavez was invited lecturer at:

- Seminario de Biofísica, Instituto de Física, Universidad de San Luis Potosi, Mexico (10/12/2015)
- Mediterranean School of Complex Networks, Salina, Italy (09/2015)
- Satellite Physics of Multiplex Networks, International School and Conference on Network Science (NetSci15), Zaragoza, Spain, (06/2015).
- Scientific sessions of the Centro de Tecnología Biomédica (CTB), Madrid, Spain, (05/2015)

10.1.5. Scientific expertise

O. Colliot acted as an expert for the HCERES (Haut-Conseil de l'Evaluation de la Recherche et de l'Enseignement Supérieur).

F. De Vico Fallani acted as an expert for the NIH-NSF CRCNS program, US; the Research Foundation (FWO), Flanders; the Organization for research (NWO), Netherlands.

M. Chavez acted as an expert for the Fond National Suisse de la Recherche Scientifique.

10.2. Teaching - Supervision - Juries

10.2.1. Teaching

Master: Olivier Colliot coordinates the module "Méthodes d'imagerie médicale" of the Master 2 in Computer Science of Université Pierre et Marie Curie.

Master: Olivier Colliot, Master in Computer Science, 4.5 hours (eqTD), Université Pierre et Marie Curie

Master: Stanley Durrleman, Master in Computer Science, 9 hours (eqTD), Université Pierre et Marie Curie

Master: Olivier Colliot, Master in Cognitive Science, 4.5 hours (eqTD), Ecole Normale Supérieure (Ulm)

Master: Stanley Durrleman, Master in Applied Mathematics, 2 hours (eqTD), Ecole Normale Supérieure (Cachan)

Master: Marie Chupin, Master in Computer Science, 3 hours (eqTD), Université Pierre et Marie Curie

Master: Dominique Hasboun, Master in Biology, 4 hours, Ecole Normale Supérieure (Ulm)

Master: Dominique Hasboun, Master in Cognitive Science, 12 hours, Ecole Normale Supérieure (Ulm)

Master: Dominique Hasboun, Master in Biology, 15 hours, Université Pierre et Marie Curie

Master: Dominique Hasboun, Master in Medical Physics, 7 hours, Université Paris-Sud

Master: Fabrizio De Vico Fallani, Master in "Méthodologies et applications en imagerie médicale", 3 hours (eqTD), Université Pierre et Marie Curie

Master: Damien Galanaud, Master in Medical Physics, 4 hours, Université Paris-Sud

Engineering school: Olivier Colliot, 4.5 hours (eqTD), Telecom ParisTech

Engineering school: Dominique Hasboun, 3 hours, ENSEA

Medical school: Didier Dormont is the Director of the University Diploma (DIU) "Diagnostic and Therapeutic Neuroradiology", Université Pierre et Marie Curie

Medical school: Didier Dormont, Courses for Medical Students, Université Pierre et Marie Curie

Medical school: Dominique Hasboun, Courses for Medical Students, Université Pierre et Marie Curie

Medical school: Damien Galanaud, Courses for Medical Students, Université Pierre et Marie Curie

Medical school: Didier Dormont organizes and participates in the practical teaching of Neuroradiology for Medical Students in the Department of Diagnostic Neuroradiology of Pitié Salpêtrière University Hospital

Medical school: Didier Dormont organizes and participates in the practical teaching of Neuroradiology for Radiology Specializing Residents in the Department of Diagnostic Neuroradiology of Pitié Salpêtrière University Hospital

Medical school: Didier Dormont, Courses to the university diplomas (DU) : "Maladie d'Alzheimer", and "Imagerie Vasculaire non Invasive"

Medical school: Damien Galanaud, courses to the University Diploma (DIU) "Diagnostic and Therapeutic Neuroradiology", Université Pierre et Marie Curie

Medical school: Dominique Hasboun, courses to the University Diploma (DIU) "Diagnostic and Therapeutic Neuroradiology", Université Pierre et Marie Curie

Paramedical studies: Dominique Hasboun, Psychomotricity, 50 hours, Université Pierre et Marie Curie

10.2.2. Supervision

Post-doc in progress : Xavier Navarro, "Analyse des interactions entre les activités corticales et la respiration", UPMC, started in 2014, advisor: Mario Chavez

PhD in progress : "Catalina Obando-Forero, Graph models of cortical plasticity in temporal brain networks", Inria, started in 2015, advisor: Fabrizio De Vico Fallani

PhD in progress : Jeremy Guillon, "Méthode d'analyse multimodale de connectivités neuronales basée sur la théorie des réseaux complexes multicouches", EDITE Université Pierre et Marie Curie, started in 2015, advisors: Fabrizio De Vico Fallani and Mario Chavez

PhD in progress : Wen Junhao, "Cortical morphometry for discovering new biomarkers of neurodegenerative diseases", Université Pierre et Marie Curie, Started in 2015, advisors: Olivier Colliot and Stanley Durrleman

PhD in progress : Jorge Samper-Gonzalez, "Learning from heterogeneous data for prediction of Alzheimer's disease", Université Pierre et Marie Curie, Started in 2015, advisors: Olivier Colliot and Theodoros Evgeniou

PhD in progress : Alexandre Routier, "Multimodal neuroimaging for characterization of primary progressive aphasia", Université Pierre et Marie Curie, Started in 2015, advisors: Marc Teichmann, Olivier Colliot and Marie-Odile Habert

PhD in progress: Jean-Baptiste Schiratti, "Méthodes et algorithmes pour l'analyse statistique de données anatomiques longitudinales – application à la caractérisation des phases pré-symptomatiques des maladies neurodégénératives", Ecole Polytechnique, Started in 2013, advisors: S. Allassonnière and S. Durrleman

PhD in progress: Barbara Gris, "Approche modulaire des méthodes de grandes déformations pour l'appariement de formes", Ecole Normale Supérieure de Cachan, Started 2013, advisors: A. Trounev and S. Durrleman

Engineer: Fanny Grosslin, "Implementation of a Brain Computer Interface for the MEG platform", ICM, started in January 2015, advisor: Mario Chavez

Master 2: Francois Deloche, "Sparse estimation of Granger-causality with MVAR models", Ecole Polytechnique, Mar-Aug 2015, advisor: Fabrizio De Vico Fallani and Stephanie Allassonniere

Master 2: Jorge Samper-Gonzalez, Master in data mining and knowledge management – Erasmus Mundus, Mar-Sept 2015, advisor: Olivier Colliot

Master 2: Alexandre Pron, Master in BioMedical Engineering – ParisTech Université Paris Descartes, Mar-Sept 2015, advisor: Marie Chupin

Summer internship: Daniela Ganelin, Massachusetts Institute of Technology, June-Aug 2015, advisor: Olivier Colliot

Summer internship: Regis Pierrard, Supelec, July-Aug 2015, advisor: Olivier Colliot

10.2.3. Juries

Olivier Colliot participated, as referee, to the PhD committee of Yogesh Karpate (Inria Rennes), 2015 (supervisors: Christian Barillot and Olivier Commowick).

Olivier Colliot participated, as examiner, to the PhD committee of Claudia Cioli (Université Pierre et Marie Curie), 2015 (supervisor: Yves Burnod and Habib Benali).

Marie Chupin participated, as examiner, to the PhD committee of Elise Blandin (Université Pierre et Marie Curie), 2015 (supervisor: Philip Gorwood).

Marie Chupin participated, as examiner, to the PhD committee of Quentin Duché (Université de Rennes 1), 2015 (supervisor: Hervé Saint-James, Oscar Acosta, Olivier Salvado).

Fabrizio De Vico Fallani participated, as referee, to the PhD committee of Yoann Isaac (Univ. Paris Sud), 2015 (supervisors: Michele Sebag).

10.3. Popularization

Fabrizio De Vico Fallani was interviewed for the French TV program “Zone Interdite” (M6) about the project on Brain Computer Interfaces. The video of the interview is available at <https://www.youtube.com/watch?v=BmGiaPG9cnA>

11. Bibliography

Publications of the year

Articles in International Peer-Reviewed Journals

- [1] L. G. ABUD, L. THIVARD, T. G. ABUD, G. S. NAKIRI, A. C. DOS SANTOS, D. DORMONT. *Partial epilepsy: A pictorial review of 3 TESLA magnetic resonance imaging features*, in "Clinics (São Paulo, Brazil)", August 2015, vol. 70, n^o 9, pp. 654-61 [DOI : 10.6061/CLINICS/2015(09)10], <https://hal.inria.fr/hal-01251490>
- [2] S. ALLASSONNIÈRE, S. DURRLEMAN, E. KUHN. *Bayesian Mixed Effect Atlas Estimation with a Diffeomorphic Deformation Model*, in "SIAM Journal of Imaging Sciences", July 2015, vol. 8, n^o 3, 29 p. [DOI : 10.1137/140971762], <https://hal.inria.fr/hal-01246570>
- [3] F. AMEUR, O. COLLIOT, P. CAROPPO, S. STROER, D. DORMONT, A. BRICE, C. AZUAR, B. DUBOIS, I. LE BER, A. BERTRAND. *White matter lesions in FTL: distinct phenotypes characterize GRN and C9ORF72 mutations*, in "Neurology: Genetics", 2016, vol. 2, n^o 1 [DOI : 10.1212/NXG.0000000000000047], <https://hal.inria.fr/hal-01266596>
- [4] A. BERTRAND, C. VIGNAL, F. LAFITTE, P. KOSKAS, O. BERGÈS, F. HÉRAN. *Open-angle glaucoma and paraoptic cyst: first description of a series of 11 patients*, in "AJNR. American journal of neuroradiology", March 2015, vol. 36, n^o 4, pp. 779-82, <https://hal.inria.fr/hal-01252635>
- [5] E. E. BRON, M. SMITS, W. M. VAN DER FLIER, H. VRENKEN, F. BARKHOF, P. SCHELTENS, J. M. PAPMA, R. M. E. STEKETEE, C. MÉNDEZ ORELLANA, R. MEIJBOOM, M. PINTO, J. R. MEIRELES, C. GARRETT, A. J. BASTOS-LEITE, A. ABDULKADIR, O. RONNEBERGER, N. AMOROSO, R. BELLOTTI, D. CÁRDENAS-PEÑA, A. M. ÁLVAREZ-MEZA, C. V. DOLPH, K. M. IFTEKHARUDDIN, S. F. ESKILDSEN, P. COUPÉ, V. S. FONOV, K. FRANKE, C. GASER, C. LEDIG, R. GUERRERO, T. TONG, K. R. GRAY, E. MORADI, J. TOHKA, A. ROUTIER, S. DURRLEMAN, A. SARICA, G. DI FATTA, F. SENSI, A. CHINCARINI, G. M. SMITH, Z. V. STOYANOV, L. SØRENSEN, M. NIELSEN, S. TANGARO, P. INGLESE, C. WACHINGER, M. REUTER, J. C. VAN SWIETEN, W. J. NIESSEN, S. KLEIN. *Standardized evaluation of algorithms for computer-aided diagnosis of dementia based on structural MRI: the CADDementia challenge*, in "NeuroImage", May 2015, vol. 111, pp. 562-79 [DOI : 10.1016/J.NEUROIMAGE.2015.01.048], <https://hal.archives-ouvertes.fr/hal-01220123>

- [6] P. CAROPPO, M.-O. HABERT, S. DURRLEMAN, A. FUNKIEWIEZ, V. PERLBARG, V. HAHN, H. BERTIN, M. GAUBERT, A. ROUTIER, D. HANNEQUIN, V. DERAMECOURT, F. PASQUIER, S. RIVAUD-PECHOUX, M. VERCELLETTO, G. EDOUART, R. VALABREGUE, P. LEJEUNE, M. DIDIC, J.-C. CORVOL, H. BENALI, S. LEHERICY, B. DUBOIS, O. COLLIOT, A. BRICE, I. LE BER. *Lateral Temporal Lobe: An Early Imaging Marker of the Presymptomatic GRN Disease?*, in "Journal of Alzheimer's Disease", August 2015, vol. 47, n^o 3, pp. 751-9 [DOI : 10.3233/JAD-150270], <https://hal.inria.fr/hal-01220380>
- [7] R. COLLE, M. CHUPIN, C. CURY, C. VANDENDRIE, F. GRESSIER, P. HARDY, B. FALISSARD, O. COLLIOT, D. DUCREUX, E. CORRUBLE. *Depressed suicide attempters have smaller hippocampus than depressed patients without suicide attempts*, in "Journal of Psychiatric Research", February 2015, vol. 61, 6 p. [DOI : 10.1016/J.JPSYCHIRES.2014.12.010], <https://hal.inria.fr/hal-01108928>
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- [10] R. DEBS, E. MAILLART, R. FAHED, C. PAPEIX, C. DUYCKAERTS, C. STADELMANN, D. GALANAUD, C. LUBETZKI. *Extensive brain demyelinating lesions under natalizumab: The role of anti-natalizumab antibodies*, in "Neurology", November 2015, vol. 85, n^o 18, pp. 1630-2, <https://hal.inria.fr/hal-01251509>
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- [20] P. MESEJO, A. VALSECCHI, L. MARRAKCHI-KACEM, S. CAGNONI, S. DAMAS. *Biomedical image segmentation using geometric deformable models and metaheuristics*, in "Computerized Medical Imaging and Graphics", July 2015, vol. 43, pp. 167-178 [DOI : 10.1016/J.COMPMEDIMAG.2013.12.005], <https://hal.inria.fr/hal-01221316>
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International Conferences with Proceedings

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International Publishing, Cambridge, United States, January 2015, vol. 8682, 89 p. [DOI : 10.1007/978-3-319-14905-9], <https://hal.inria.fr/hal-01114150>

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Other Publications

- [45] J.-B. SCHIRATTI, S. ALLASSONNIERE, O. COLLIOT, S. DURRLEMAN. *Learning spatio-temporal trajectories from manifold-valued longitudinal data*, December 2015, Neural Information Processing Systems, Poster, <https://hal.archives-ouvertes.fr/hal-01245909>