Department of Clinical Neuroscience

Neuroscience Research Center 2021-2022 Presentation

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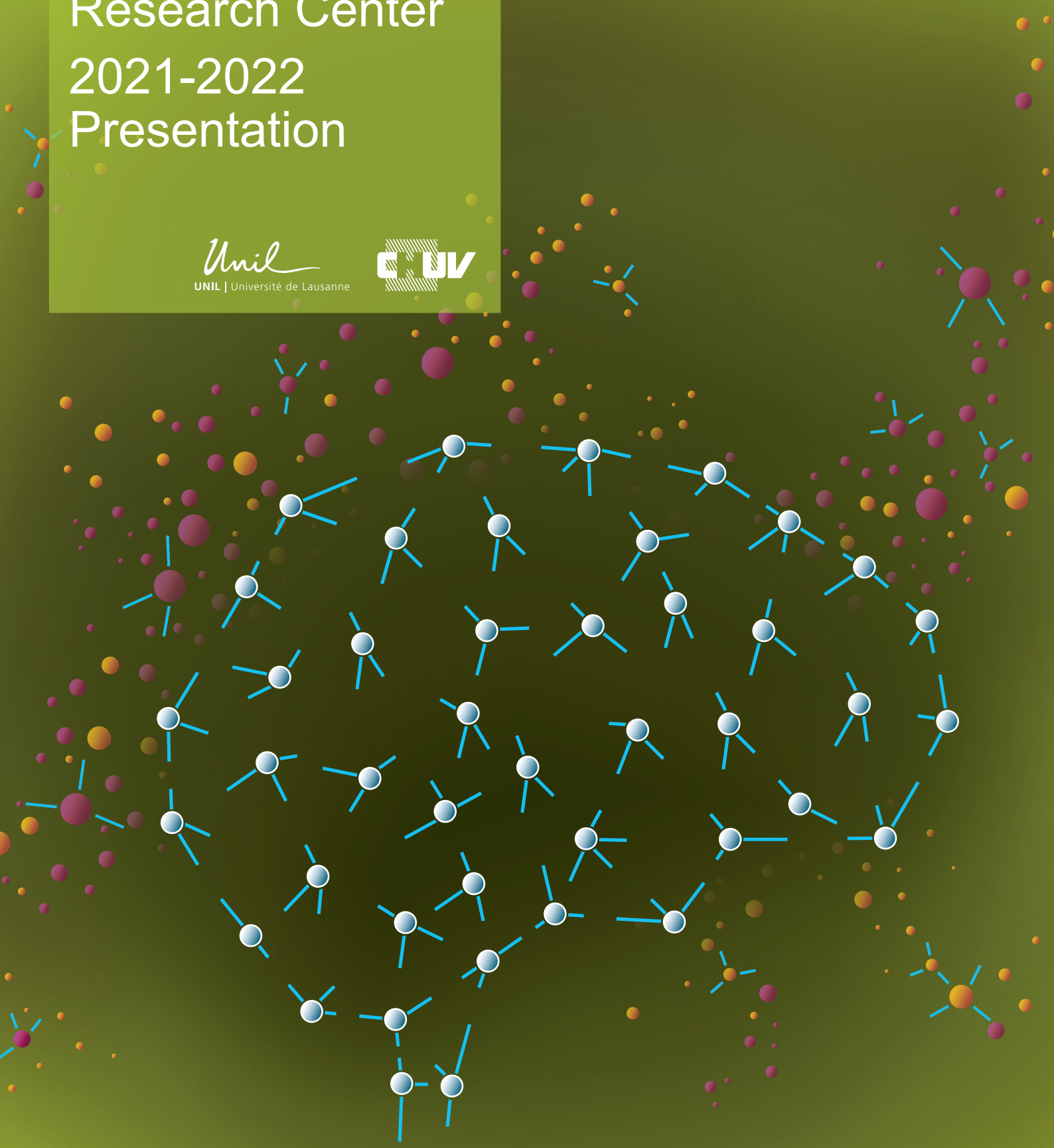

Neuroscience Research Center
2021-2022 Presentation

Content

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Foreword 2021-2022

The years 2021 and 2022 were contrasted with, on the one hand, the end of the COVID-19 crisis and, on the other hand, the dynamism of the CRN teams which resulted in academic appointments/promotions, prestigious funding and the publication of 217 scientific articles. Prof. Gilles Allali, Dominique Rothenfluh and Andrea Serino are to be congratulated for their appointment as head of the Leenaards Memory Center, Spinal Surgery Unit and director of the CRINN, respectively. Prof. Karin Diserens, Arseny Sokolov for their promotion to the rank of Associate Professor. Dr. Sonia Crottaz-Herbette and Constantin Tuleasca, Davide Strambo for their nomination as PD-MERc, Andrea Brioschi Guevara, Daniele Starnoni as MERc and finally Dr. Julien Bally as PD.
CRN members are also very involved in education and training programs to prepare the next generation of MD and PhD for multidisciplinary activities, collaborative networking and diverse career paths. Over the last two years, 15 students obtained their PhD in an attractive, cross-disciplinary environment. The new generation of scientists had the opportunity to present their current projects at the CRN 2022 symposium, whose theme was “gender in neuroscience”.

CRN members have secured 60 funding awards, from the Swiss National Science Foundation, European Horizon2020 programs, granting agencies, foundations, and industrial partners. The budget of the CRN was 14.5 million Swiss francs for 2021-2022. A special mention to Prof. Andrea Serino (PI) and Prof. Arseny Sokolov who have obtained INNOSUISSE Flagship funding for the SwissNeurorehab project. It is one of the 4 flagships financed by the Swiss Confederation in the field of health with a budget of more than 11 million Swiss francs over 5 years. This project brings together 22 Swiss partners, both academic and industrial, and aims to transform the organization of neurorehabilitation of cognitive and motor disorders in Switzerland through the development and implementation of technological innovations, particularly in favor of outpatient care. It will constitute the pillar of the SUN Research Center (CRINN).
Finally, in 2022, CRN launched a new initiative to support researchers. A three-year program was created to provide seed money for projects exploring new scientific approaches, methods, or ideas and to collect preliminary data to support subsequent applications to funding agencies. In addition, a call for support for CRN platforms was launched to develop new tools and to promote access to and use of these facilities. Three research and two platform projects were selected from the 12 applications received.

Additional information

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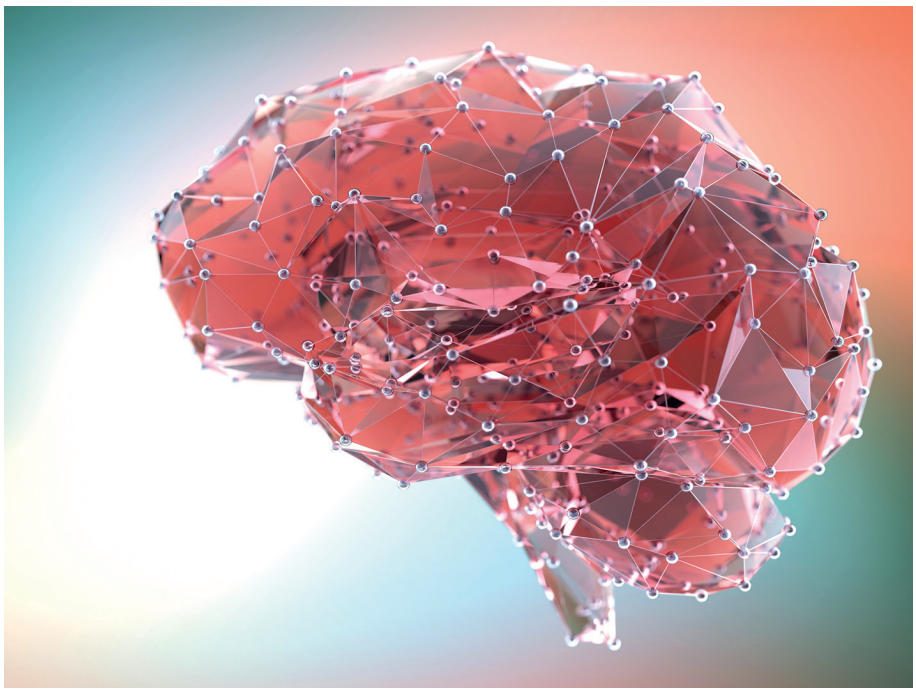
Neuroscience Research Center

Laboratories Presentation

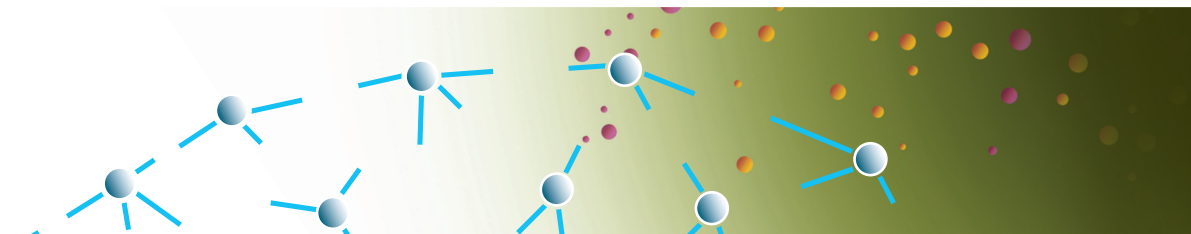
Laboratory for the Exploration of Memory in Neurosciences LEMENS

Professor Gilles Allali, Head of laboratory
Senior Lecturer Andrea Brioschi Guevara
Dr Olivier Rouaud



Laboratory's activity

The Laboratory for the Exploration of Memory in Neurosciences (LEMENS) represents the translational research facet of the Leenaards Memory Centre (www.centrememoire.ch), a Centre devoted to diagnosis and care of patients and their families facing the "Ageing-Brain Cognitive Diseases" (the ABCDs), such as Alzheimer's disease and other associated conditions (fronto-temporal dementias, diffuse Lewy body disease, vascular dementia).



Laboratory for the Exploration of Memory in Neurosciences LEMENS

Professor Gilles Allali
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Affiliations
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Keywords
Memory

Research interests

My research focus on biomarkers of pathological aging among international cooperations implementing digital and clinical data of older adults, with a special interest on the biomarkers of normal pressure hydrocephalus and the impact of COVID-19 on the brain.

Scientific contributions in 2021-2022

> SARS-CoV-2 related encephalopathy: The SARS-CoV-2 related encephalopathy (SACRE) has been reported in more than 60% of patients admitted to intensive care units. With a multimodal neuroimaging and biological approach, and valid clinical assessment, we identified the clinical course; the neurobiological correlates; and the effect of HDG in SACRE.

> Neural correlates of brain changes in normal pressure hydrocephalus: Idiopathic normal pressure hydrocephalus (iNPH) represents the main cause of reversible dementia (reaching 6 % of adults older than 80). Using a multimodal neuroimaging approach, we identified the structural and functional changes found in iiNPH in comparison to non-iiNPH and explored the structural and brain networks associated with reversible changes in iNPH.

> Impact of physiological and pathological ageing on gait control: Gait relates cognitive decline in the elderly population. Recently, gait has been used to define a new pre-dementia syndrome, called the Motoric Cognitive Risk (MCR) syndrome. Poor gait performances and MCR predict incident dementia. We did suggest that amyloid deposition relates to gait in MCI and prodromal AD subjects, but not in MCR.

Main publications in 2021-2022

Griffa A, Bommarito G, Assal F, Preti MG, Goldstein R, Armand S, Herrmann FR, Van De Ville D, **Allali G**. CSF tap test in idiopathic normal pressure hydrocephalus: still a necessary prognostic test? J Neurol. 2022 Sep; 269(9):5114-5126.

Bommarito G, Garibotto V, Frisoni GB, Ribaldi F, Stampacchia S, Assal F, Armand S, **Allali G**, Griffa A. The Biological Substrate of the Motoric Cognitive Risk Syndrome: A Pilot Study Using Amyloid-/Tau-PET and MR Imaging. J Alzheimers Dis. 2022; 87(4): 1483-1490.

Breville G, Adler D, Uginet M, Assal F, Tamisier R, Lalive PH, Pepin JL, **Allali G**. Does Endothelial Vulnerability in OSA Syndrome Promote COVID-19 Encephalopathy? Chest. 2021 Aug; 160(2):e161-e164.

Uginet M, Breville G, Assal F, Lövblad KO, Vargas MI, Pugin J, Serratrice J, Herrmann FR, Lalive PH, **Allali G**. COVID-19 encephalopathy: Clinical and neurobiological features. J Med Virol. 2021 Jul; 93(7):4374-4381.

Griffa A, Bommarito G, Assal F, Herrmann FR, Van De Ville D, **Allali G**. Dynamic functional networks in idiopathic normal pressure hydrocephalus: Alterations and reversibility by CSF tap test. Hum Brain Mapp. 2021 Apr 1; 42(5):1485-1502.

Bommarito G, Van De Ville D, Frisoni GB, Garibotto V, Ribaldi F, Stampacchia S, Assal F, **Allali G**, Griffa A. Alzheimer's Disease Biomarkers in Idiopathic Normal Pressure Hydrocephalus: Linking Functional Connectivity and Clinical Outcome. J Alzheimers Dis. 2021; 83(4):1717-1728.

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Laboratory for the Exploration of Memory in Neurosciences LEMENS

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Keywords
Cognition, assessment and treatment
Brain imaging
Biomarkers
Neurodegenerative diseases
Alzheimer's disease
Diagnosis
Treatment

Research interests
My research focus is on the impact of psycho-social treatments on patients' cognition, quality of life and daily life autonomy. I am also interested in improving neuropsychological assessment of elderly with cognitive decline.

Scientific contributions in 2021-2022
Psychosocial treatment
> In the prevention of a cognitive decline or of the impact of this decline in daily living activities, a great amount of studies showed a significantly positive impact of psychosocial treatments. The kind of treatment, doses and duration have yet to be specified with methodologically stronger studies.

Assessment
> Patients' evaluation has to evolve. For example, the improvement of the assessment of patients with Alzheimer disease, fronto-termporal dementia and depression based on a musical and emotional tests is one of our current goals.

Prevention of cognitive decline and loss of autonomy.

Main publications in 2021-2022

Frisoni GB, Altomare D, Ribaldi F, Villain N, Brayne C, Mukadam N, Abramowicz M, Barkhof F, Berthier M, Bieler-Aeschlimann M, Blennow K, **Brioschi Guevara A**, Carrera E, Chételat G, Csajka C, Demonet JF , Dodich A, Garibotto V, Georges J, Hurst S, Jessen F, Kivipelto M, Llewellyn DJ, McWhirter L, Milne R, Minguillón C, Miniussi C, Molinuevo JL, Nilsson PM, Noyce A, Ranson JM, Grau-Rivera O, Schott JM, Solomon A, Stephen R, van der Flier W, van Duijn C, Vellas B, Visser LNC, Cummings J, Scheltens P, Ritchie C, Dubois B. Dementia prevention in memory clinics: Recommendations from the European Task Force for Brain Health Services. The Lancet Regional Health - Europe, *in press*.

James CE, Stucker C, Junker-Tschopp C, Fernandes AM, Revol A, Mili ID, Kliegel M, Frisoni GB, **Brioschi Guevara A**, Marie D. Musical and psychomotor interventions for cognitive, sensorimotor, and cerebral decline in patients with Mild Cognitive Impairment (COPE): a study protocol for a multicentric randomized controlled study. BMC Geriatrics, *in press*.

Brioschi Guevara A, Bieler M, Altomare D, Berthier M, Csajka C, Dautricourt S, Démonet JF, Dodich A, Frisoni G, Miniussi C, Molinuevo JL, Ribaldi F, Scheltens F, Chételat G. Protocols for cognitive enhancement in persons at risk for dementia. A user manual for Brain Health Services - Part 5 of 5. Alzheimer research and therapy 2021; 13:172 3.

Leidi-Maimone B, Bieler-Aeschlimann M, Bugnon S, Démonet JF, **Brioschi Guevara A**. Télé-réhabilitation neuropsychologique collective de patients avec troubles neurocognitifs débutants dans le contexte de la pandémie Covid-19. Rev Neuropsychol. 2021.

Boccardi M, Monsch AU, Ferrari C, Altomare D, Berres M, Bos I, Buchmann A, Cerami C, [...] **Brioschi Guevara A**, *et al*; Consortium for the Harmonization of Neuropsychological Assessment for Neurocognitive Disorders. Consensus Roadmap to Harmonize N europsychological Assessment for Mild Neurocognitive Disorders in Europe. Alzheimers Dement. 2021; 5.

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Laboratory for the Exploration of Memory in Neurosciences LEMENS

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Keywords
Alzheimer's disease and related disorders

Research interests
My interest focus is on biomarkers and treatment of Alzheimer's disease and related disorders with a special interest on precision diagnostic, young onset dementia and clinical trials.

Scientific contributions in 2021-2022
Increasing precision of diagnosis of Alzheimer's disease and other cause of dementia in memory clinic's daily clinical practice: Validation of a diagnostic method (on going).

A precision diagnosis for neurodegenerative diseases with cognitive and/or behavioral expressions.

Main publications in 2021-2022

Piffer S, Nannoni S, Maulucci F, Beaud V, **Rouaud O**, Cereda CW, Maeder P, Michel P. Acute neurological disease as a trigger or co-occurrence of transient global amnesia: a case series and systematic review. Neurol Sci. 2022 Oct; 43(10):5959-5967.

Lu WH, Giudici KV, Morley JE, Guyonnet S, Parini A, Aggarwal G, Nguyen AD, Li Y, Bateman RJ, Vellas B, de Souto Barreto P; MAPT/DSA Group. Investigating the combination of plasma amyloid-beta and geroscience biomarkers on the incidence of clinically meanin gful cognitive decline in older adults. Geroscience 2022 Jun; 44(3):1489-1503.

He L, Morley JE, Aggarwal G, Nguyen AD, Vellas B, de Souto Barreto P; MAPT/DSA Group. Plasma neurofilament light chain is associated with cognitive decline in non-dementia older adults. Sci Rep. 2021 Jun 28; 11(1):13394.

Frederiksen KS, Nielsen TR, Appollonio I, Andersen BB, Riverol M, Boada M, Ceccaldi M, Dubois B, [...] **Rouaud O**, *et al*. Biomarker counseling, disclosure of diagnosis and follow-up in patients with mild cognitive impairment: A European Alzheimer's disease consortium survey. Int J Geriatr Psychiatry 2021 Feb; 36(2):324-333.

Carlier S, Demonet JF, **Rouaud O**. Aptitude cognitive à la conduite automobile: retour d'expérience du Centre Leenaards de la Mémoire [Cognitive fitness to drive: feedback at Leenaards Memory Centre]. Rev Med Suisse 2021 Jan 27; 17(723):225-229.

Lehingue E, Gueniat J, Jourdaa S, Hardouin JB, Pallardy A, Courtemanche H, Rocher L, Etcharry-Bouyx F, Auriacombe S, Mollion H, Formaglio M, **Rouaud O**, Bretonnière C, Thomas-Antérion C, Boutoleau-Bretonnière C. Improving the Diagnosis of the Frontal Variant of Alzheimer's Disease with the DAPHNE Scale. J Alzheimers Dis. 2021; 79(4): 1735-1745.

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Laboratory of Clinical Neurophysiology and non-Invasive Brain Stimulation

Senior Lecturer David Benninger
Consultant/attending physician

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Keywords
Therapeutic studies for Parkinson
Motor system and movement disorders
Brain stimulation
Neurophysiology
Movement & gait analysis
Nerve-muscle disorders

Laboratory's activity

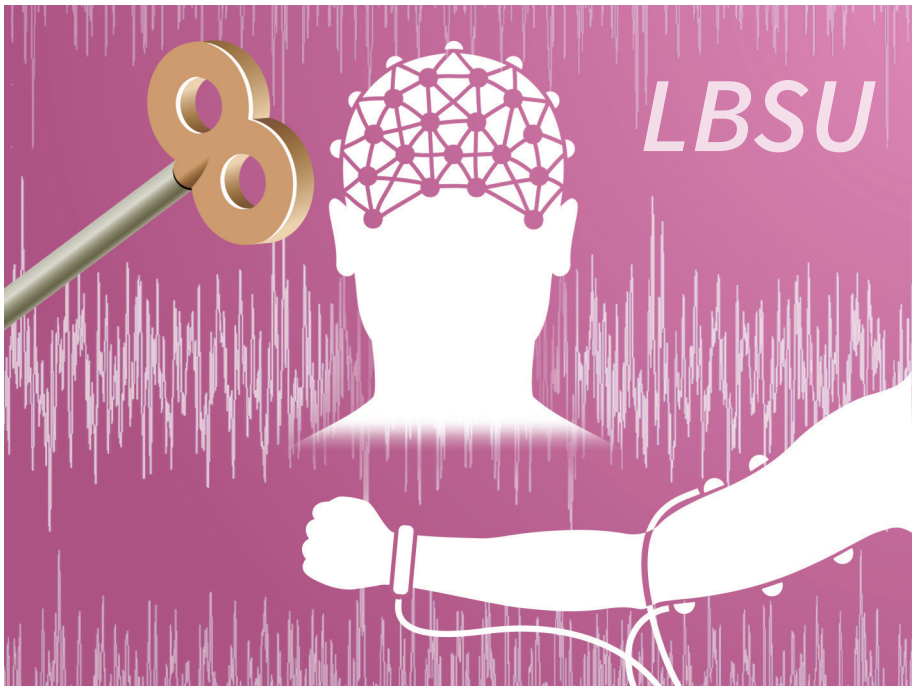
> Randomized controlled therapeutic clinical trial on tDCS for the treatment of the freezing of gait in Parkinson's disease.
> Multicenter randomized controlled therapeutic trial for gait disorder in Parkinson's disease and atypical Parkinsonian disorders (FNS/DACH collaboration CHUV-EPFL with Innsbruck (A), Erlangen (D), Bozen (I), Luxembourg and Nijmegen (NL)).
> Robot-assisted assessment of the rigidity and tremor in Parkinson's disease.
> Investigation of the motor cortex physiology using the triple stimulation technique.
> Investigation of the motor, sensorimotor and plasticity alterations in dystonia associated to a complex regional pain syndrome.

Research interests

Our lab is interested in movement disorders, clinical neurophysiology, brain stimulation and the human motor control. The main research we lead currently concerns Parkinson's disease, dystonia, tremor and normal physiology essentially through transcranial magnetic stimulation (TMS), transcranial direct current stimulation (tDCS), electroneuromyography (ENMG) combined with electroencephalography (EEG), kinematic analysis of movements and gait.

Scientific contributions in 2021-2022

> Consensus Statement on High-Intensity Focused Ultrasound for Functional Neurosurgery in Switzerland.
> Non-invasive brain stimulation for Parkinson's disease.
> Clinical diagnostic utility of transcranial magnetic stimulation in neurological disorders. Updated report of an IFCN committee.
> Combined tDCS-behavior therapy study for freezing of gait in PD.
> CRPS with dystonia.
> Cervical dystonia: contribution of cerebellar dysfunction.
> Cerebellar stimulation for Parkinson tremor.



Our research team mainly uses electrophysiological techniques. Either to record activity: at the cerebral level with electroencephalography (EEG - cap and recording) and muscle level with electromyography (EMG - electrodes and recording); or to interfere or modify ongoing cerebral activity (TMS - coil).

Main publications in 2021-2022

Vucic S, Chen KS, Kiernan MC, Hallett M, **Benninger DH**, Di Lazzaro V, Rossini PM, Bennussi A, Berardelli A, Curra A, Krieg SM, Lefaucheur JP, Long Ly, Macdonnell RA, Massimini M, Rosanova M, Picht T, Stinear CM, Paulus WP, Ugawa Y, Ziemann U, Chen R. Clinical diagnostic utility of transcranial magnetic stimulation in neurological disorders. Updated report of an IFCN committee.Submitted to Clinical Neurophysiology 2022.

Madrid J, Ulrich B, Santos AN, Jolles BM, Favre J, **Bennninger DH**. Spatiotemporal parameters during turning gait maneuvers of different amplitudes in young and elderly healthy adults: a descriptive and comparative study. Gait & Posture 2022.

Stieglitz LH, Oertel MF, Accola EA, Bally J, Bauer R, Baumann CR, **Benninger DH**, Bohlhalter S, Buchele F, Hagele-Link S, Kaegi G, Krack P, Krueger MT, Mahendran S, Moeller JC, Mylius V, Piroth T, Werner B, Kaelin-Lang A. Consensus Statement on High-Intensity Focused Ultrasound for Functional Neurosurgery in Switzerland. Frontiers Neurology 2021 Sep 22; 12:722762. eCollection 2021.

Good JM, Atallah I, Castro Jimenez M, **Benninger DH**, Kuntzer T, Superti-Furga A, Tran C. NGS-based diagnosis of treatable neurogenetic disorders in adults: opportunities and challenges. Genes 2021 May 6; 12(5):695.

Madrid J, **Benninger DH**. Non-invasive brain stimulation for Parkinson's disease: Clinical evidence, latest concepts and future goals: A systematic review. J Neurosci. Methods 2021 Jan 1; 347:108957.

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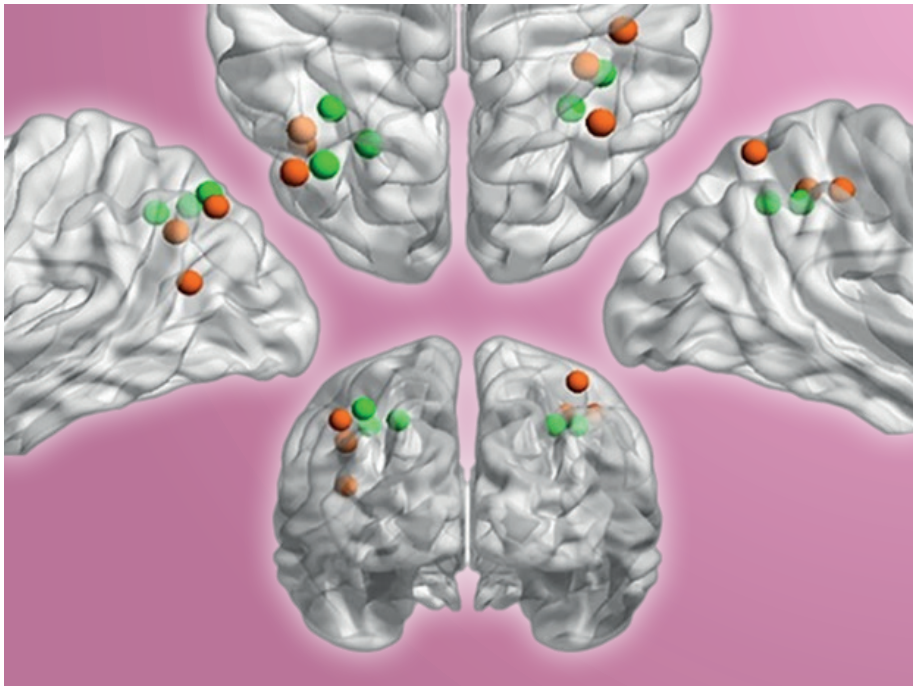
Laboratory of Cognitive Science

Professor Emeritus Stephanie Clarke, Head of the laboratory
Senior Lecturer, Privat-Docent Sonia Crottaz-Herbette



Laboratory's activity
The laboratory works at the interface between clinical neurorehabilitation and basic cognitive neuroscience. The laboratory investigates cognitive functions in normal subjects and in brain-damaged patients, with particular interest in the organisation and plasticity of the human auditory cortex and attentional networks.

Professor Stephanie Clarke pursue innovative studies on auditory cognition showing that knowledge modulates the semantic representations of sounds, highlighting interactions between culture and brain organization.

Dr Sonia Crottaz-Herbette leads several projects that investigate the plasticity and brain reorganization consecutive to cognitive therapeutic interventions. Recent focus is made on the use of new technology, such as virtual-reality, for the cognitive rehabilitation of attention and working memory in stroke patients. Understanding the neural mechanisms, which underlie recovery after brain lesion, helps to design innovative therapeutic interventions and to apply them in clinical care.

Laboratory of Cognitive Science

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Keywords
Auditory cognition
Brain-mind
Neural plasticity
Neuroimaging

Research interests
Prof. Stephanie Clarke focuses on auditory cognition, investigating sound representations, including spatial and temporal aspects, using psychophysical approaches, fMRI and EEG. Recent contributions give new insight to the malleability of semantic and spatial representations, both in health and in disease.

Scientific contributions in 2021-2022
> The fine-tuned neural representations of cognitive functions are disrupted by focal lesions and possibly by general conditions. The group studied the latter in the context of SARS-CoV2, in patients who suffered from severe COVID-19 but who did not present signs of overt brain damage.
> Semantic representations of sounds were shown to be modulated by knowledge, which is acquired by formal education, personal experience and/or social interactions. Work of the group on this topic highlighted some of the mechanisms, which underlie the interactions between culture and brain organisation and are of relevance to the understanding of human nature.

Laboratory of Cognitive Science

Senior Lecturer, Privat-Docent Sonia Crottaz-Herbette
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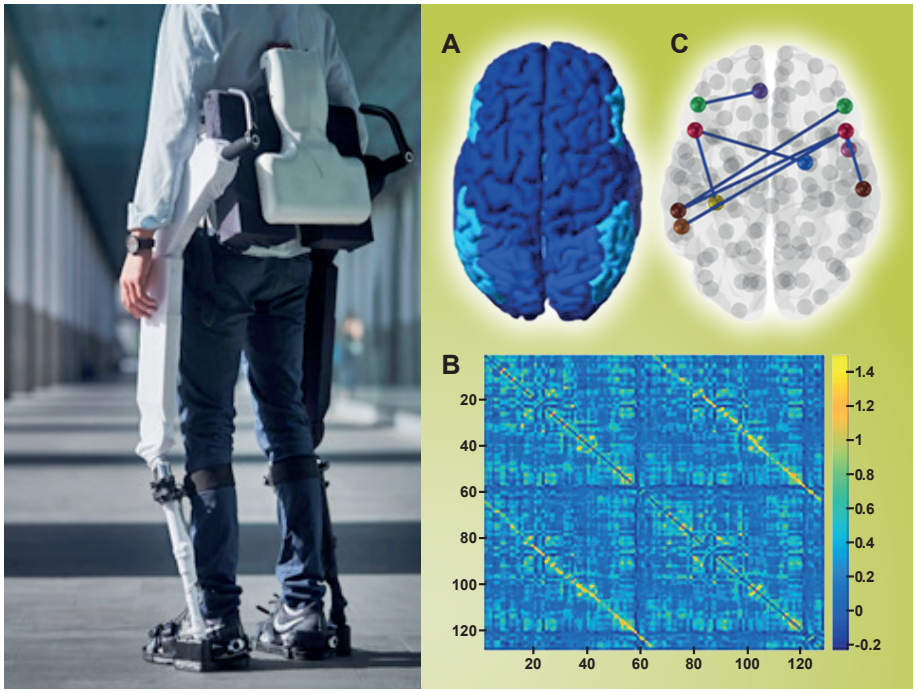
Keywords
Cognitive rehabilitation
Acquired brain injury
Neural plasticity
Neuroimaging
Virtual reality

Research interests
Dr Sonia Crottaz-Herbette focuses on cerebral reorganizations following innovative cognitive interventions on attention and working memory in stroke patients, using task-related and resting-state fMRI. Investigations of the neural mechanisms underlying therapeutic interventions are essential for their impact on clinical practice.

Scientific contributions in 2021-2022
> Prism adaptation is used routinely to treat spatial attention deficits in neglect patients but the underlying mechanisms remain to be understood. In a new study (Farron *et al.* 2022), we showed that the use of right versus left hand during the adaptation modulates the consecutive reshaping of the ventral attentional system. Depending on the patients' conditions, using the right or the left hand during prism adaptation might potentiate the beneficial effects of this intervention.

> Our projects on stroke patients and cognitive rehabilitation is exploring new ways to treat attention deficits using a whole program of gamified activities based on virtual reality, including a new prism adaptation method. Our neuroimaging study (Wilf *et al*, 2021) showed that prism adaptation done in virtual-reality can change large-scale cortical connectivity, such information is crucial to target more precisely the use of this treatment in clinical population.



A. *Regions of the ventral attentional network (cyan), dorsal attentional network (azur blue), and rest of the brain (marine blue).*

B. *Resting state connectivity matrices before and after visuo-motor adaptation for the R-PA group and for the control group.*

C. *Nodes and edges that yielded a significant R-PA-related decrease in connectivity. Adapted from Gundmundsson et al, 2020.*

Main publications in 2021-2022

Clarke S, Farron N, **Crottaz-Herbette S**. Choosing Sides: Impact of Prismatic Adaptation on the Lateralization of the Attentional System. Front Psychol. 2022; 13:909686.

Farron N, **Clarke S**, **Crottaz-Herbette S**. Does hand modulate the reshaping of the attentional system during rightward prism adaptation? An fMRI study. Front Psychol. 2022; 13:909815.

Wilf M, Dupuis C, Nardo D, Huber D, Sander S, Al-Kaar J, Haroud M, Perrin H, Fornari E, **Crottaz-Herbette S**, Serino A. Virtual reality-based sensorimotor adaptation shapes subsequent spontaneous and naturalistic stimulus-driven brain activity. Cereb. Cortex 2022.

Beaud V, **Crottaz-Herbette S**, Dunet V, Vaucher J, Bernard-Valnet R, Du Pasquier R, Bart PA, **Clarke S**. Pattern of cognitive deficits in severe COVID-19. J Neurol. Neurosurg. Psychiatry 2021; 92(5):567-568.

Wilf M, Cerra Cheraka M, Jeanneret M, Ott R, Perrin H, **Crottaz-Herbette S**, Serino A. Combined virtual reality and haptic robotics induce space and movement invariant sensorimotor adaptation. Neuropsychologia 2021; 150:107692.

Kerkhoff G, Rode G, **Clarke S**. Treating neurovisual deficits and spatial neglect. In Platz T (ed) Clinical Pathways in Stroke Rehabilitation. Springer 2021; 191-217.

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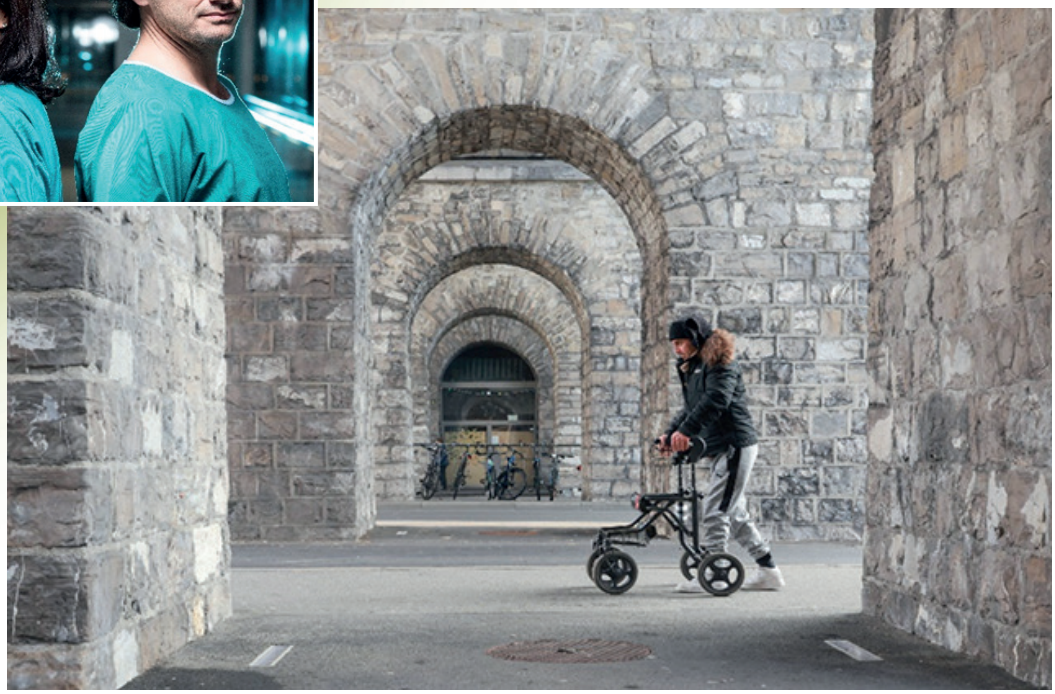

NeuroRestore, Defitech Center for Interventional Neurotherapies

Laboratoire NeuroRestore, Centre Defitech de neurothérapies interventionnelles

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Assoc. Professor Jocelyne Bloch
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Laboratory's activity
NeuroRestore is a research, innovation and treatment center that develops and applies bioengineering strategies involving neurosurgical interventions to restore neurological functions.

The objectives of NeuroRestore are to integrate implantable neurotechnologies and innovative treatments resulting from rigorous preclinical studies that have been conducted during the last two decades in rodent and non-human primate models. These developments have led to breakthroughs for the treatment of paraplegia, tetraplegia, Parkinson's disease, stroke, and traumatic brain injuries.

Research interests

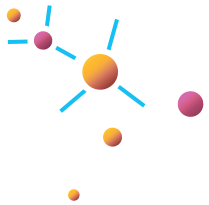
NeuroRestore neurological functions, including the in-depth understanding of their mechanims in preclinical models and implementation in humans.

Scientific contributions in 2021-2022

> Uncovering the neurons that restore walking in patients with spinal cord injury. We established a molecular atlas of the spinal cord that allows us to observe the evolution of the healing process.

> Development of a neuroprosthetic treatment to alleviate hemodynamic instability in a patient with multiple system atrophy.

> Understanding the principles of gait encoding in the subthalamic nucleus of patients with Parkinson's disease to restore gait deficits in the future.



Main publications in 2021-2022

Kathe C, Skinnider MA, Hutson TH, Regazzi N, Gautier M, Demesmaeker R, Komi S, Ceto S, James ND, Cho N, Baud L, Galan K, Matson KJE, Rowald A, Kim K, Wang R, Minassian K, Prior JO, Asboth L, Barraud Q, Lacour SP, Levine AJ, Wagner F, **Bloch J**, Squair JW, **Courtine G**. The neurons that restore walking after paralysis. Nature 2022; 1-8.

Rowald A, Komi S, Demesmaeker R, Baaklini E, Hernandez-Charpak SD, Paoles E, Montanaro H, Cassara A, [...] **Bloch J**, **Courtine G**. Activity-dependent spinal cord neuromodulation rapidly restores trunk and leg motor functions after complete paralysis. Nat Med 2022; 28:260-71.

Squair JW, Berney M, Jimenez MC, Hankov N, Demesmaeker R, Amir S, Paley A, Hernandez-Charpak S, Dumont G, Asboth L, Allenbach G, Becce F, Schoettker P, Wuerzner G, Bally JF, **Courtine G**, **Bloch J**. Implanted System for Orthostatic Hypotension in Multiple-System Atrophy. New Engl J Med 2022; 386:1339-44.

Thenaisie Y, Lee K, Moerman C, Scafa S, Gálvez A, Pirondini E, Burri M, Ravier J, Puiatti A, Accolla E, Wicki B, Zacharia A, Jiménez MC, Bally JF, **Courtine G**, **Bloch J**, Moraud EM. Principles of gait encoding in the subthalamic nucleus of people with Parkinson's disease. Sci Transl Med 2022; 14 eabo1800.

Skinnider MA, Squair JW, Kathe C, Anderson MA, Gautier M, Matson KJE, Milano M, Hutson TH, Barraud Q, Phillips AA, Foster LJ, Manno GL, Levine AJ, **Courtine G**. Cell type prioritization in single-cell data. Nat Biotechnol 2021; 39:30-4.

Kathe C, Michoud F, Schönle P, Rowald A, Brun N, Ravier J, Furfaro I, Paggi V, Kim K, Soloukey S, Asboth L, Hutson TH, Jelescu I, Philippides A, Alwahab N, Gandar J, Huber D, Zeeuw CID, Barraud Q, Huang Q, Lacour SP, **Courtine G**. Wireless closed-loop optogenetics across the entire dorsoventral spinal cord in mice. Nat Biotechnol 2021; 1-11.

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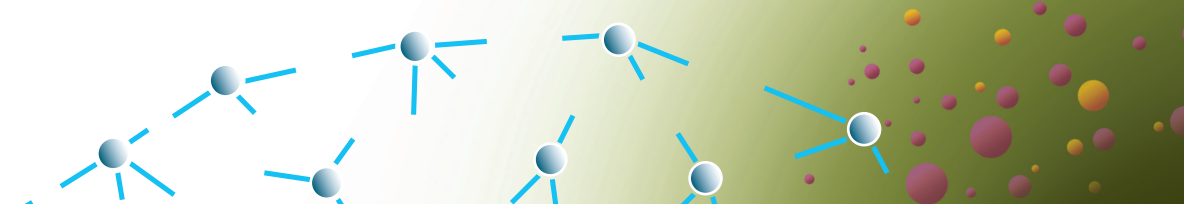
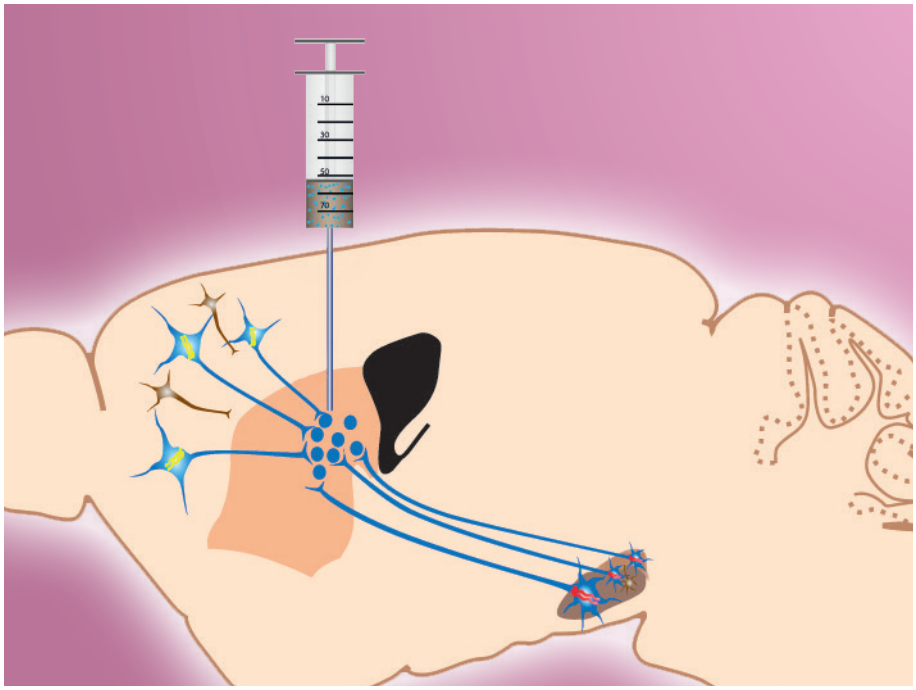


Laboratory of Cellular and Molecular Neurotherapies LNCM

Assoc. Professor Nicole Déglon, Head of laboratory
Privat-Docent Liliane Tenenbaum



Laboratory's activity
The laboratory's activities are focusing on the development and validation of innovative neurotherapies and neuromodulation strategies. The research programs are focusing on:

> Underlying molecular and environmenental mechanisms in Huntington's disease (HD).

> Pre-clinical development of molecular therapies for Huntington's disease (HTT gene editing).

> Modulation of neuroinflammation and drug-inducible gene therapy of Parkinson's disease.

Laboratory of Cellular and Molecular Neurotherapies LNCM

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Keywords
Neurodegenerative diseases
Huntington's disease
Gene therapy
Gene editing

Laboratory's activity

We focus our research on the development of molecular therapies for neurodegenerative disorders and in particular polyglutamines disorders (polyQ). Huntington's disease (HD) and the Spinocerebellar ataxia type 3 (SCA3) are the two most common polyQ diseases worldwide. They primarily affect the central nervous system, with the presence of a neuropathological accumulation of disease protein aggregates, largely in neurons. We have been exploiting the genetic origin of these pathologies to develop gene editing strategies as well as the unique features of various AAV serotypes to deliver therapeutic candidates in affected brain circuits.

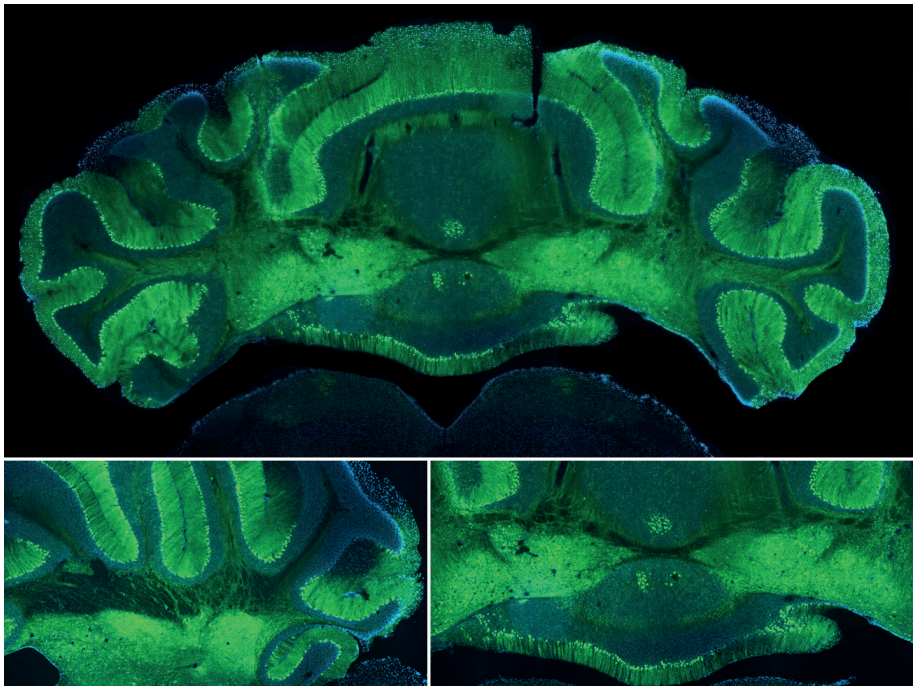
Research interests

The group has a long-standing experience and expertise in viral gene transfer technology to deliver therapeutic candidates in the brain and in particular gene silencing or gene editing strategies for autosomal dominant disorders.

Scientific contributions in 2021-2022

> To better decipher the contributions of the various cell populations in the CNS, we have developed cell-type specific gene delivery platforms based on lentiviral (LV) and adeno-associated vectors (AAV). In two collaborative studies, astrocyte-specific vectors were used to investigate the role of lactate transporters in the barrel cortex and the contribution of mitochondrial biogenesis in astrocyte maturation and synapse formation.

> A second line of research aims at deciphering the mechanism of propagation of the Tau protein in the brain. In collaboration with Dr. Buee's group, France, we have shown that brain-derived enriched extracellular vesicles contain pathological species that can induce tau damage *in vivo*.



Visualization of the green fluorescent protein in the cerebellum of the mouse brain.

Main publications in 2021-2022

Rybarikova M, Almacellas Barbanoj A, Schorge S, **Déglon N**. CNS gene therapy: present developments and emerging trends accelerating industry-academia pathways. Hum. Gene Ther. 2022; 33:913-922.

Leroux E, Perbet R, Caillerez R, Richetin K, Lieger S, Espourteille J, Bouillet T, Bégard S, Danis C, Loyens A, Toni N, **Déglon N**, Deramecourt V, Schraen-Maschke S, Buée L, Colin M. Extracellular vesicles: major actors of heterogeneity in tau spreading among human tauopathies. Mol. Ther. 2022; 30:782-797.

Thiebaut AM, Buendia I, Ginet V, Lemarchand E, Boudjadja MB, Hommet Y, Lebouvier L, Lechevallier C, Maillasson M, Hedou E, **Déglon N**, Oury F, Rubio M, Montaner J, Puyal J, Vivien D, Roussel BD. Thrombolysis by tPA increases serum free IGF-1 leading to a decrease of deleterious autophagy following brain ischemia. Autophagy 2022; 18(6):1297-1317.

Roumes H, Jollé C, Blanc J, Benkhaled I, Chatain C, Massot P, Raffard G, Bouchaud V, Biran M, Pythoud C, **Déglon N**, Zimmer ER, Pellerin L, Bouzier-Sore AC. Lactate transporters in the rat barrel cortex sustain whisker-dependent BOLD fMRI signal and behavioral performance. PNAS 2021; 118(47):e2112466118.

Zehnder T, Petrelli F, Romanos J, De Oliveira Figueiredo EC, Lewis TL, **Déglon N**, Polleux F, Santello M, Bezzi P. Mitochondrial biogenesis in developing astrocytes regulates astrocyte maturation and synapse formation. Cell Reports 2021; 35(2): 108952.

Humbel M, Ramosaj M, Zimmer V, Aeby L, Moser S, Sipion M, Boizot A, Rey M, **Déglon N**. Maximizing gene transfer and therapeutic efficacy in the CNS. Gene Ther. 2021; 28:75-88.

ORCID number: 0000-0003-4475-9476

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Laboratory of Cellular and Molecular Neurotherapies LNCM

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Keywords
Parkinson's disease
Neuroprotection
Targeted viral vectors
Gene transfer
GDNF
Neuroinflammation

Laboratory's activity

Current treatments for Parkinson's disease are symptomatic. Neurotrophic factors could halt disease progression. AAV vectors deliver GDNF in the brain, protecting dopaminergic neurons and reducing motor symptoms. However, long-term or off-target delivery induce side effects. Currently used AAVs i) do not allow to adjust the dose and period of treatment; ii) express GDNF into all types of neurons, mainly projection neurons. In contrast, endogenous GDNF is expressed by interneurons. We are developing inducible and targeted AAVs in order to optimize neuroprotective gene therapy.

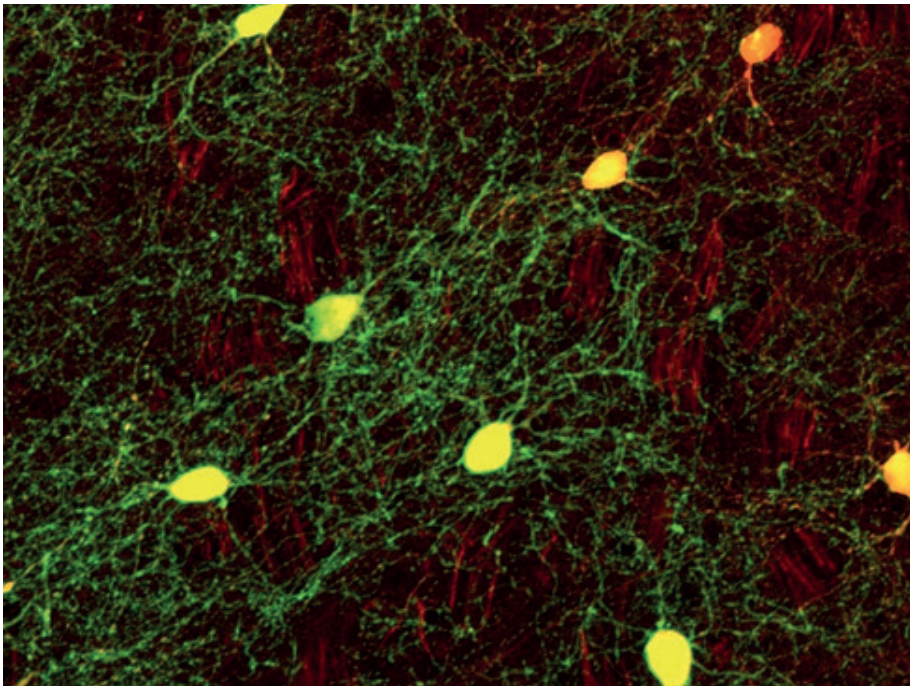
Research interests

Neuroprotective gene therapy for Parkinson's disease
> Mechanism of GDNF neuroprotective effects *in vivo*.
> Drug-inducible and targeted AAV vectors.

Brain inflammatory responses
> Modulators of neuroinflammatory signalling.

Scientific contributions in 2021-2022

> We have targeted AAV-mediated transgene expression in striatal parvalbumin-expressing (PV^+) interneurons using genetic tools (PV-cre driver mice) with a high efficiency and specificity.
> We have demonstrated that PV-cre mice are however not an adequate tool to study neuroprotective paradigms since the expression of CRE protein induces a decrease of the number of PV^+ interneurons.
> We are developing novel AAV tools to target striatal interneurons.



Striatal injections of AAV-FLEx-GFP vectors in PVcre mice leads to a specific GFP expression (green) in parvalbumine-positive interneurons (red).

Main publications in 2021-2022

Duarte Azevedo M, Sander S, Jeanneret C, Olfat S, **Tenenbaum L**. Selective targeting of striatal parvalbumin-expressing interneurons for transgene delivery. J Neurosci Meth. 2021; 354:109105.

Tenenbaum L. CDNF: an innovative actor in disease-modifying approaches for Parkinson's disease. Commentary. Molecular Therapy 2021; 29(9):2634-2636.

ORCID number: 0000-0003-4619-9660

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Laboratory of Acute Neurorehabilitation - LNRA

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Senior staff member
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Keywords
Coma
Disorders of Consciousness (DOC)
Cognitive Motor Dissociation (CMD)
Prognosis
Acute neurorehabilitation
Neurosensorial approach
Brain Computer Interface
PeriPersonal Space
Robotic neurovegetative disorders
Virtual reality
Spasticity
Early mobilization

Laboratory's activity

> To present a new approach to classification of unresponsive patients.
> To provide accurate identification of Clinical Cognitive Motor Dissociation (cCMD) among Disorders of Consciousness (DOC) in the acute phase by means of the refinement of the clinical diagnosis.
> To investigate the functional/cognitive recovery in patients with cCMD.
> To implement an EEG motor imagery paradigm coupled with functional electrical stimulation, and an EEG task-free paradigm to differentiate patients evidencing intention without being able to implement it.
> To characterize the diagnostic and prognostic value of PET and MRI imaging patterns in the acute stage in terms of identification of strong biomarkers of covert awareness.

Research interests

Overall our research aims to develop a coordinated multimodal approach involving several experts, integrating information from complementary sources to increase detection accuracy of covert awareness/Cognitive Motor Dissociation among Disorders of Consciousness in the acute stage, to inform better the decision-making process and prognosis and to improve early therapeutic interventions for severely neurolesioned patients.

Scientific contributions in 2021-2022

> Clinical diagnostic refinement of DOC/CMD in the acute phase.
> Detangling the percepts of illusory movement and sensory stimulation during tendon vibration in the EEG.
> Description of the early neurorehabilitation care pathway during COVID-19.
> Description of a new MRI-based score assessing brain damage and accurately detecting patients with residual consciousness.
> Demonstration of embodied mirror visual feedback during movement preparation and execution.

Vibramoov research project investigating neural correlates of illusory movement induced by functional proprioceptive stimulation.

Vibramoov project's team.

Main publications in 2021-2022

Diserens K, Meyer I, Jöhr J, Pincherle A, Dunet V, Pozeg P, Ryvlin P, Muresanu DF, Stevens RD, Schiff ND. The Importance of Being Clinical: A Focus on Subtle Signs and Motor Behavior to Unveil Awareness in Unresponsive Brain-Impaired Patients. Neurology 2022 Dec, *ahead of print*.

Jöhr J, Aureli V, Meyer I, Cossu G, **Diserens K**. Clinical Cognitive Motor Dissociation: A Case Report Showing How Pitfalls Can Hinder Early Clinical Detection of Awareness. Brain sciences 2022 Jan 25; 12(2):157.

Schneider C, Marquis R, Jöhr J, Lopes da Silva M, Ryvlin P, Serino A, De Lucia M, **Diserens K**. Disentangling the percepts of illusory movement and sensory stimulation during tendon vibration in the EEG. NeuroImage 2021 Nov 1; 241:118431.

Garipelli G, Rossy T, Perez-Marcos D, Jöhr J, **Diserens K**. Movement-Related Cortical Potentials in Embodied Virtual Mirror Visual Feedback. Front Neurol. 2021 Jun 15; 12:646886.

Diserens K, Carda S, Epiney JB, Meyer I, Jöhr J. Neurorééducation en phases aiguë et postaiguë: qu'avons-nous appris de la première vague de Covid-19 ? [Neurorehabilitation in the acute and post-acute phase: what did we learn from the first wave of COVID-19?] Rev Med Suisse 2021 Apr 28; 17(736):835-840.

Pozeg P, Jöhr J, Pincherle A, Marie G, Ryvlin P, Meuli R, Hagmann P, **Diserens K**, Dunet V. Discriminating cognitive motor dissociation from disorders of consciousness using structural MRI. NeuroImage Clinical 2021; 30:102651.

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Laboratory for Research in Neuroimaging - LREN

Assoc. Professor Bogdan Draganski, Head of laboratory
Senior Lecturer Ferath Kherif
Senior Lecturer Marzia De Lucia
Assist. Professor Antoine Lutti
Dr Ann-Marie de Lange

Laboratory's activity

LREN is an imaging neuroscience laboratory dedicated to the study of brain structure and function relevant to the endogenous and environmental effects on human behaviour and cognition across the lifespan. We develop and apply non-invasive neuroimaging methods - magnetic resonance imaging and electro-encephalography that help advancing our knowledge in brain health maintenance, early diagnosis of neurodegeneration and mechanisms governing brain plasticity. Our research has a specific focus on sex and gender differences.

LREN is responsible for a state-of-the-art neuroimaging platform featuring high-end research-only Siemens Prisma 3T MRI scanner, sophisticated MRI compatible neurophysiological equipment and high-density EEG machines.

LRENs main goal is to translate research findings into clinical applications for prevention, early diagnosis of disease and for prediction of clinical outcome. We provide the neuroimaging expertise and infrastructure for large-scale initiatives supported by the Swiss National Science Foundation and the Swiss Academy of Medical Sciences – the longitudinal CoLaus|PsyCoLaus and the SPHN SACR cohorts.

LRENs research is supported by competitive national (SNSF, SAMS, InnoSuisse, Bertarelli) and EU grants additionally to generous funding from the charitable Roger De Spoelberch and Partridge foundations.

Laboratory for Research in Neuroimaging - LREN

Assoc. Professor Bogdan Draganski
Consultant/attending physician

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Keywords
Imaging neuroscience
In vivo histology

Research interests

One of my main research directions is the investigation of inter-individual heterogeneity of brain health outcomes in a lifespan perspective additionally to probing the brain plasticity potential of electro-convulsive therapy. Our most recent developments in quantitative MRI mapping of brain microstructure properties combined with sophisticated multivariate classification techniques and bio-physical modelling strengthen this research direction.

Scientific contributions in 2021-2022

Intramural funding

> CRN seed grant for effects of "long COVID" on the brain.
> CLIMACT UNIL-EPFL on the impact of climate change on brain and behaviour.

Funding obtained from the Swiss National Science Foundation

> Personal project grant on the neuroplasticity effects of electro-convulsive therapy for major depression.
> Co-applicant of Synergia grant on the genetic basis of micro- and macro-vascular anatomy (Coordinator Pr Sven Bergmann CIG UNIL).
> Co-applicant of InnoSuisse grant HeadFirst on the mechanisms of head trauma and associated behavioural effects.
> EU Funding - ERA-NET Neuron on prosthesis for visually impaired individuals (together with McGill - Canada, University Bremen - Germany, EPFL).

Main publications in 2021-2022

Manfredi-Lozano M, Leysen V, Adamo M, Paiva I, Rovera R, Pignat JM, Timzoura FE, Candlish M, [...] **Draganski B**, *et al*. GnRH replacement rescues cognition in Down syndrome. Science 2022 Sep 2; 377(6610):eabq4515.

Grosu C, Trofimova O, Gholam-Rezaee M, Strippoli MF, Kherif F, Lutti A, Preisig M, **Draganski B**, Eap CB. CYP2C19 expression modulates affective functioning and hippocampal subiculum volume-a large single-center community-dwelling cohort study. Transl Psychiatry 2022 Aug 5; 12(1):316.

Loued-Khenissi L, Trofimova O, Vollenweider P, Marques-Vidal P, Preisig M, Lutti A, Kliegel M, Sandi C, Kherif F, Stringhini S, **Draganski B**. Signatures of life course socioeconomic conditions in brain anatomy. Hum Brain Mapp. 2022 Jun 1; 43(8):2582-2606.

Roggenhofer E, Toumpouli E, Seeck M, Wiest R, Lutti A, Kherif F, Novy J, Rossetti AO, **Draganski B**. Clinical phenotype modulates brain's myelin and iron content in temporal lobe epilepsy. Brain Struct Funct. 2022 Apr; 227(3):901-11.

Trofimova O, Loued-Khenissi L, DiDomenicantonio G, Lutti A, Kliegel M, Stringhini S, Marques-Vidal P, Vollenweider P, [...] **Draganski B**. Brain tissue properties link cardio-vascular risk factors, mood and cognitive performance in the CoLaus|PsyCoLaus epidemiological cohort. Neurobiol. Aging 2021 Jun; 102:50-63.

Gyger L, Regen F, Ramponi C, Marquis R, Mall JF, Swierkosz-Lenart K, von Gunten A, Toni N, Kherif F, Heuser F, **Draganski B**. Gradient of electro-convulsive therapy's antidepressant effects along the longitudinal hippocampal axis. Transl Psychiatry. 2021 Mar 29; 11(1):191.

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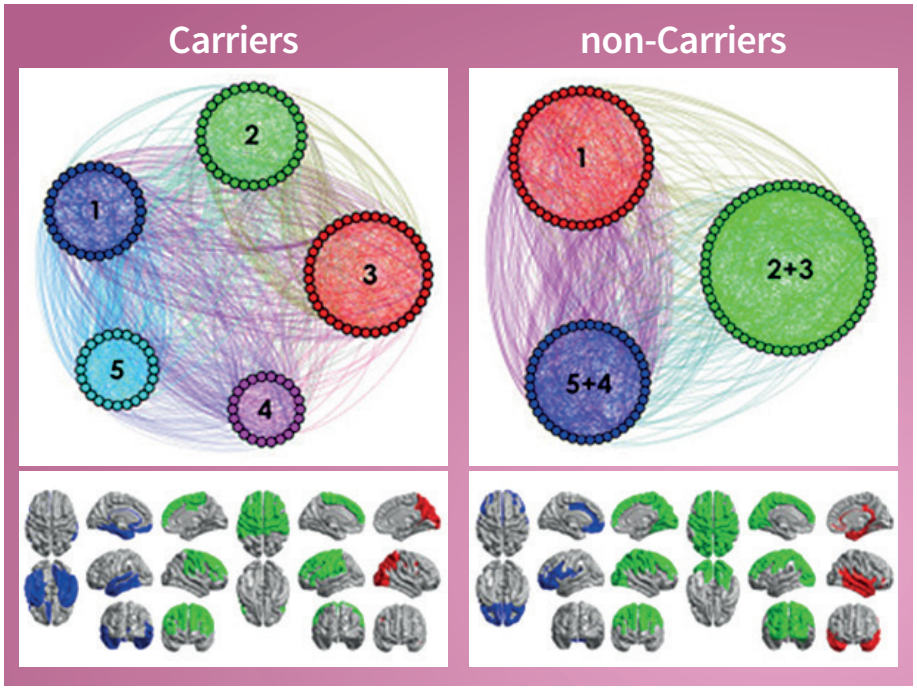
Keywords
Neurosciences
Neuroimaging
Clinical neurology & psychiatry
Psychology experimental
Artificial intelligence
Mathematical computational cognitive anatomy
Brain systems

Laboratory's activity
Neuroscience's contribution to people's quality of life extends beyond traditional approaches like neurology and psychiatry, and is a fundamental question. Our goal is to develop new Multivariate methods for understanding how the human brain works, how it interacts with the environment, how the function of the brain relates to its anatomy and development over time, as well as how it is altered in disease. Our research focuses on topics such as language, memory, and individual differences in dementia and mental illness using mathematical formalisms, statistical models, and deep neural networks.

Research interests
Modelling and identifying dynamic neuroclinical signatures in language, memory and learning in health and disease using multivariate models and large-scale data. Incorporating informatics into a theoretical framework for mapping structure and function.

Scientific contributions in 2021-2022
As a result of our research, large amounts of data (hospital data, databases, medical informatics platform MIP, etc.) can be federated to identify biological signatures of diseases in the brain (imaging, tissue and blood samples, clinical records, medical history, genomics, etc.).
> Benchmark deep learning systems against multivariate predictive models and more traditional techniques.
By disseminating our open source code and testing implementations in clinical settings, we contribute to the diffusion of these innovations.
> Identify brain algorithms for visual perception, memory and learning. Improve current neural networks to predict participants' behaviour and brain activity. A multivariate model that predicts brain activity and time-dependent neural connections between different brain regions is compared with conventional to-pological maps in our study.
> Analyse the relationship between a spatio-temporal dynamic model of the hippocamus and other brain regions based on a computational model of memory.
> Contribute to the MOPRHMIC project, a case study showing how cloud computing can optimise neuroscience workflows.
> Participation in the development of international standards for artificial intelligence in healthcare.



Mathematics, psychology and neuroscience in Multivariate Brain Research: as leader of the group, Dr Kherif pioneered innovative techniques for modelling the complex interplay of genetics, environment, and pathology in shaping the dynamics of the brain and its impact on mental health, memory and learning.

Main publications in 2021-2022

Paunova R, Kandilarova S, Todeva-Radneva A, Latypova A, **Kherif F,** Stoyanov D. Application of Mass Multivariate Analysis on Neuroimaging Data Sets for Precision Diagnostics of Depression. Diagnostics (Basel) 2022 Feb 12; 12(2):469.

Oala L, Murchison AG, Balachandran P, Choudhary S, Fehr J, Leite AW, Goldschmidt PG, Johner C, [...] **Kherif F**, *et al*. Machine Learning for Health: Algorithm Auditing & Quality Control. J Med Syst. 2021 Nov 2; 45(12):105.

Gyger L, Ramponi C, Mall JF, Swierkosz-Lenart K, Stoyanov D, Lutti A, Gunten A, **Kherif F**, Draganski B. Temporal trajectory of brain tissue property changes induced by electroconvulsive therapy. Neuroimage 2021 May 15; 232:117895.

Weitnauer L, Frisch S, Melie-Garcia L, Preisig M, Schroeter M, Sajfutdinow I, **Kherif F**, Draganski B. Mapping grip force to motor networks. Neuroimage 2021 Apr 1; 229:117735.

Sanabria-Diaz G, Melie-Garcia L, Draganski B, Demonet JF, **Kherif F**. Apolipoprotein E4 effects on topological brain network organization in mild cognitive impairment. Sci Rep. 2021 Jan 12; 11(1):845.

Sanabria-Diaz G, Demonet JF, Rodriguez-Herreros B, Draganski B, **Kherif F**, Melie-Garcia L. Apolipoprotein E allele 4 effects on Single-Subject Gray Matter Networks in Mild Cognitive Impairment. Neuroimage Clin. 2021; 32:102799.

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Laboratory for Research in Neuroimaging - LREN

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Keyword
Electrophysiology
Consciousness

Laboratory's activity

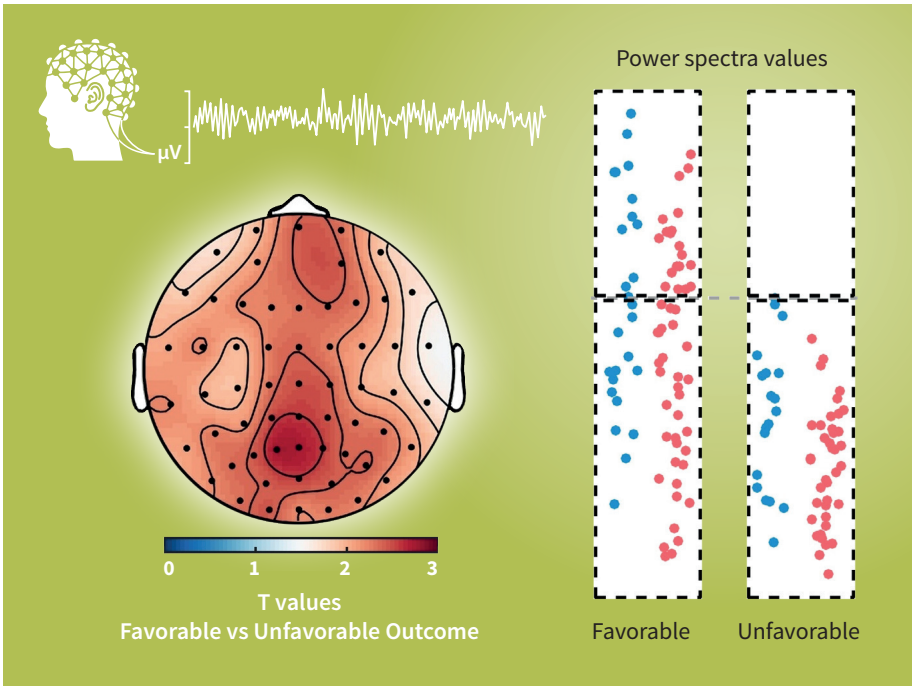
Loss of consciousness involves dramatic changes in neural activity and is accompanied by a drastic reduction in the responsiveness to sensory stimuli. My research work aims at shedding light on common principles underlying preserved brain responses to sensory stimuli across different varieties of unconscious states including coma and deep sleep. This knowledge informs the development of quantitative markers revealing covert consciousness in unresponsive patients. We acquire data through intracranial and scalp electrophysiological recordings, diffusion tensor and magnetic resonance imaging. We employ machine learning techniques, network analysis and signal processing methods for combining functional and structural data.

Research interests

> Coma
> Disorders of consciousness
> Statistical regularities
> Interoception.

Scientific contributions in 2021-2022

> Implementation of a novel experimental and methodological framework for studying the cardiac and neural correlates of cardio-audio regularities during sleep in humans.
> Implementation of a novel experimental and methodological framework for measuring the interemispheric transfer time in humans.
> Identification of a new marker for measuring preserved cardio-audio regularity processing in humans, during wakefulness, sleep and coma.
> MDL is PI of the project "The impact of heartbeat signals on auditory regularity processing in humans" funded by the Swiss National Science Foundation.
> MDL is PI of the project "Neural responses to cardio-audio sequences as a marker of consciousness in health and disease" funded by the Bertarelli Catalyst Foundation in collaboration with Prof. Sophie Schwartz of the University of Geneva.
> MDL is awarded the platform grant for the project "The installation of a new shared facility for EEG-based research" from the Center of Research in Neuroscience, Lausanne University Hospital.
> MDL receives support from the Center for Open Science and Templeton World Charity for her project "Encoding of global auditory regularities in unconscious states".



EEG resting state analysis predicts favorable outcome in comatose patients.

Main publications in 2021-2022

Aellen FM, Alnes SL, Fabian Loosli F, Rossetti AO, Zubler F, **De Lucia M**, Tzovara A. Auditory stimulation and deep learning predict awakening from coma after cardiac arrest. Brain 2022, *in press*.

Oliveira R, Pelentritou A, Di Domenicantonio G, **De Lucia M**, Lutti A. *In vivo* Estimation of Axonal Morphology From Magnetic Resonance Imaging and Electroencephalography Data. Front Neurosci. 2022 Apr 21; 16:874023.

Riganello F, Zubler F, Haenggi M, **De Lucia M**. Heart rate complexity: An early prognostic marker of patient outcome after cardiac arrest. Clin Neurophysiol. 2022 Feb; 134:27-33.

Alnes SL, **De Lucia M**, Rossetti AO, Tzovara A. Complementary roles of neural synchrony and complexity for indexing consciousness and chances of surviving in acute coma. Neuroimage 2021 Dec 15; 245:118638.

Schneider C, Marquis R, Jöhr J, Lopes da Silva M, Ryvlin P, Serino A, **De Lucia M***, Diserens K*. Disentangling the percepts of illusory movement and sensory stimulation during tendon vibration in the EEG. Neuroimage 2021 Nov 1; 241:118431. *equal contribution.

Lasaponara S, D'Onofrio M, Pinto M, Aiello M, Pellegrino M, Scozia G, **De Lucia M**, Doricchi F. Individual EEG profiling of attention deficits in left spatial neglect: A pilot study. Neurosci Lett. 2021 Sep 14; 761:136097.

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https://sites.google.com/view/marziadelucia/home

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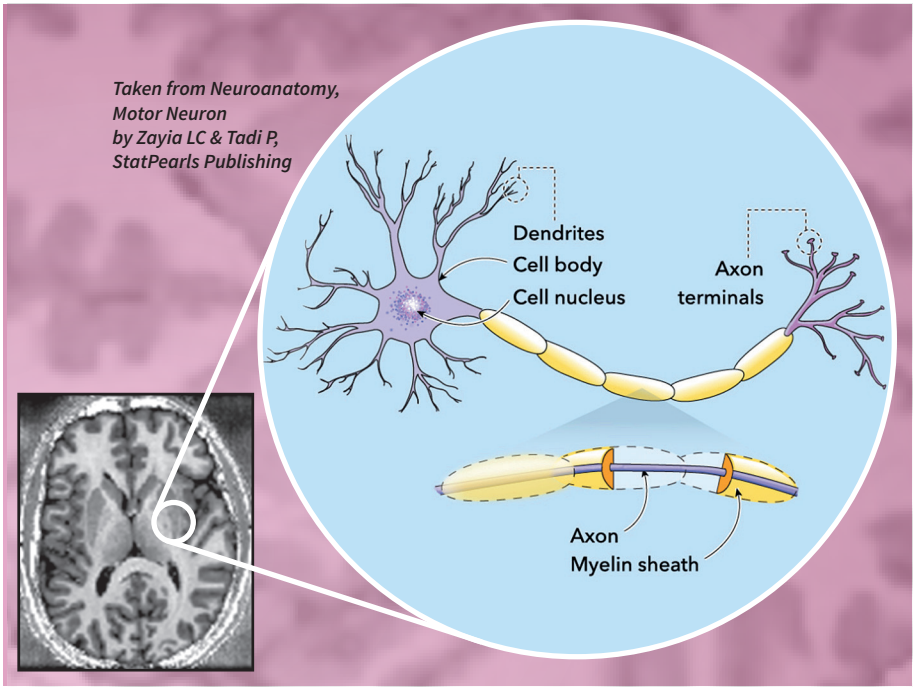
Keywords
MRI physics
Quantitative MRI
In vivo histology
Imaging neuroscience

Laboratory's activity
Magnetic Resonance Imaging (MRI) is a technology of primary importance to study brain disease *in vivo* in patient populations. However, many disease-related changes take place at the microscopic scale within the brain and cannot be detected with standard MRI techniques. Our group focuses on the development of quantitative MRI (qMRI) technologies that provide measures of microscopic brain tissue properties from *in vivo* data ("*in vivo* histology") and improve the monitoring of disease evolution in patient populations.

Research interests
> MRI techniques for neuroscience
> Motion correction
> Biophysical modelling of the MRI signal
> MRI biomarkers of brain tissue.

Scientific contributions in 2021-2022
> PI of the SNF project "Advanced quantitative MRI biomarkers of Parkinsons's Disease - towards *in vivo* histology".
> PI of the CRN platform project "On-site manufacturing of tooth clips for the correction of patient motion in the MRI scanner".
> Technical supervision of the MRI platform of the Department for Clinical Neuroscience - CHUV.
> MRI platform of the DNC-CHUV achieved the examination of its 6000th research participant.



Our group focuses on the development of MRI technologies that allow the measurement of microscopic properties of the brain from data acquired in vivo in patients ("in vivo histology").

Main publications in 2021-2022

Loued-Khenissi L, Trofimova O, Vollenweider P, Marques-Vidal P, Preisig M, **Lutti A**, Kliegel M, Sandi C, Kherif F, Stringhini S, Draganski B. Signatures of life course socioeconomic conditions in brain anatomy. Hum Brain Mapp. 2022 Jun 1; 43(8):2582-2606.

Oliveira R, Pelentritou A, Di Domenicantonio G, De Lucia M, **Lutti A**. *In vivo* Estimation of Axonal Morphology From Magnetic Resonance Imaging and Electroencephalography Data. Front Neurosci. 2022 Apr 21; 16:874023.

Lutti A, Corbin N, Ashburner J, Ziegler G, Draganski B, Phillips C, Kherif F, Callaghan MF, Di Domenicantonio G. Restoring statistical validity in group analyses of motion-corrupted MRI data. Hum Brain Mapp. 2022 Apr 15; 43(6):1973-1983.

Manfredi-Lozano M, Leysen V, Adamo M, Paiva I, Rovera R, Pignat JM, Timzoura FE, Candlish M, Eddarkaoui S, Malone SA, Silva MSB, Trova S, Imbernon M, Decoster L, Cotellessa L, Tena-Sempere M, Claret M, Paoloni-Giacobino A, Plassard D, Paccou E, Vionnet N, Acierno J, Maceski AM, **Lutti A**, *et al.* Cognitive and olfactory defects in Down Syndrome are caused by GnRH deficiency. Science 2022.

Trofimova O, Loued-Khenissi L, DiDomenicantonio G, **Lutti A**, Kliegel M, Stringhini S, Marques-Vidal P, Vollenweider P, Waeber G, Preisig M, Kherif F, Draganski B. Brain tissue properties link cardio-vascular risk factors, mood and cognitive performance in the CoLaus|PsyCoLaus epidemiological cohort. Neurobiol. Aging 2021 Jun; 102:50-63.

Gyger L, Ramponi C, Mall JF, Swierkosz-Lenart K, Stoyanov D, **Lutti A**, Gunten A, Kherif F, Draganski B. Temporal trajectory of brain tissue property changes induced by electroconvulsive therapy. Neuroimage 2021 May 15; 232:117895.

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https://sites.google.com/view/antoinelutti/home

Laboratory for Research in Neuroimaging - LREN

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Keywords
Brain health and ageing
Women's health
Mental health
Neuroimaging
Big-data analysis
Machine learning

Laboratory's activity

Women are at greater risk of developing Alzheimer's disease relative to men, and have higher prevalence of autoimmune diseases and depression. As women's health is historically understudied, little is known about mechanisms underlying epidemiological sex differences in disease, and how factors such as sex-hormones influence brain health across the female lifespan.

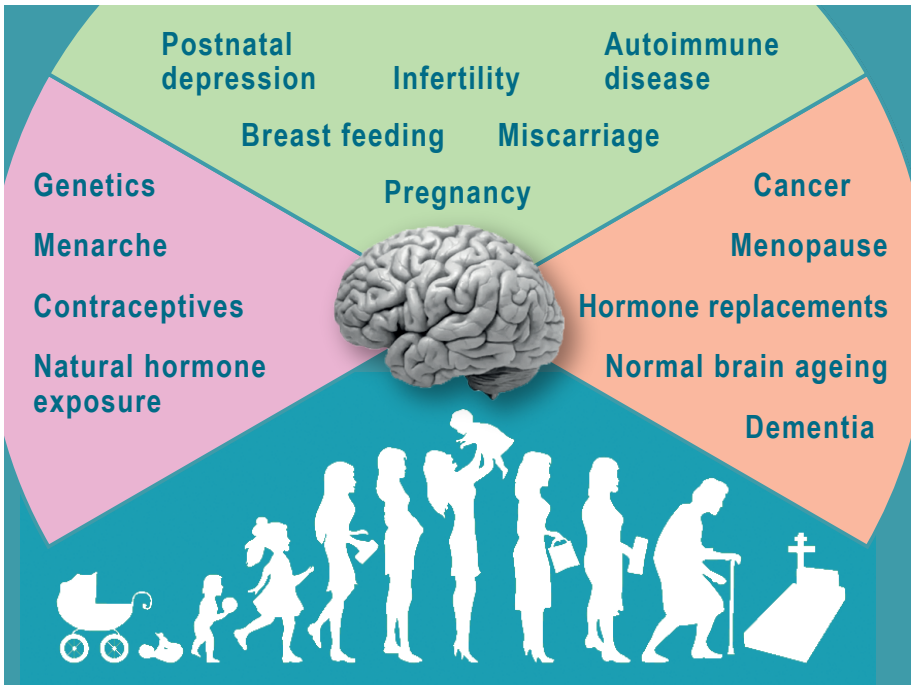
FemiLab aims to increase the understanding of transitional life phases including puberty, pregnancy, and menopause, and how biological and psychosocial factors related to these events influence brain health. To investigate this, we analyse brain imaging, clinical, genetic, biological, and psychosocial data from large population-based studies.

Research interests

> Menopause and brain ageing
> Cardiometabolic health and lifestyle
> Brain plasticity in pregnancy
> Mental health and depression
> Sex-hormones and neuroendocrinology.

Scientific contributions in 2021-2022

> PI of "FemiLab: Women's Brain Health Across the Lifespan" (SNSF Ambizione).
> >20 papers published as main author/co-author, including pioneering studies on relationships between structural brain integrity, cardiometabolic risk, and sex-hormone exposure.
> Authored/co-authored multiple methods papers on Machine Learning for neuroimaging data (e.g., Leonardsen *et al.* 2022, de Lange *et al.* 2021, Beck *et al.* 2021).
> ~10 invited scientific talks across Europe and abroad.
> Science communication activities including media interviews, podcast, and TV appearance in the BBC documentary film "A Mother's Brain".
> Co-lead of Women's NeuroNetwork, organising events for women in neuroscience.



Research addressing women's health is not only necessary to obtain a more complete understanding of brain ageing and disease, but also to approach gender equity in health care. By combining large datasets including neuroimaging and genetic data, FemiLab aims to identify factors that influence women's brain health across the lifespan - including risk factors for neurodegeneration and mental health problems.

Main publications in 2021-2022

Subramaniapillai S, Suri S, Barth C, Maximov II, Voldsbekk I, van der Meer D, Gurholt TP, Beck D, Andreassen OA, Draganski B, Ebmeier KP, Westlye LT, **de Lange AMG**. Sex- and age-specific associations between cardiometabolic risk and white matter brain age in the UK Biobank cohort. Hum Brain Mapp. 2022 Aug 15; 43(12):3759-3774.

de Lange AMG, Anatürk M, Rokicki J, Han LKM, Franke K, Alnæs D, Ebmeier KP, Draganski B, Kaufmann T, Westlye LT, Hahn T, Cole JH. Mind the gap: performance metric evaluation in brain-age prediction. Hum Brain Mapp. 2022 Jul; 43(10):3113-3129.

Schindler LS, Subramaniapillai S, Barth C, Pedersen ML, van der Meer D, Kaufmann K, Maximov II, Linge J, Leinhard OD, Beck D, Gurholt TP, Voldsbekk I, Suri S, Ebmeier KP, Draganski B, Andreassen OA, Westlye LT, **de Lange AMG**. Associations between abdominal adipose tissue, reproductive span, and brain characteristics in post-menopausal women. Neuroimage Clin. 2022; 36:103239.

de Lange AMG, Kaufmann T, Quintana DS, Winterton A, Andreassen OA, Westlye LT, Ebmeier KP. Prominent health problems, socioeconomic deprivation, and higher brain age in lonely and isolated individuals: A population-based study. Behav Brain Res. 2021 Sep 24; 414:113510.

Voldsbekk I, Barth C, Maximov II, Kaufmann T, Beck D, Richard G, Moberget T, Westlye LT, **de Lange AMG**. A history of previous childbirths is linked to women's white matter brain age in midlife and older age. Hum Brain Mapp. 2021 Sep; 42(13):4372-4386.

Beck D, **de Lange AMG**, Maximov II, Andreassen OA, Nordvik JE, Westlye LT. White matter microstructure across the adult lifespan: A mixed longitudinal and cross-sectional study using advanced diffusion models and brain-age prediction. Neuroimage 2021 Jan 1; 224:117441.

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FemiLab
https://www.femi-lab.com/

Women's NeuroNetwork
https://www.womensneuronet.com/

Laboratories of Neuroimmunology

Laboratory of Neuroimmunology/Multiple Sclerosis - LNIS
Professor Renaud Du Pasquier, Head of laboratory

Laboratory of Experimental Neuroimmunology - LNIE
Assoc. Professor Caroline Pot Kreis, Head of laboratory

Laboratory's activity
Multiple sclerosis (MS) is an auto-inflammatory disease of the central nervous system, where all components of the immune system, innate and adaptive, are involved. In addition to genetic factors, environmental ones play a crucial role in triggering this complex disease. In the Laboratories of neuroimmunology, we examine how environmental factors, among which Epstein-Barr virus, gut microbiome or cholesterol metabolites support autoreactivity of B and T cells. To tackle our hypothesis, we use different approaches, including animal models, namely the experimental autoimmune encephalomyelitis, human samples analysis (blood, cerebrospinal fluid, urine, soon stools) of MS patients and a human *in vitro* model of MS brain, using induced pluripotent stem cells (iPSC).

Laboratory of Neuroimmunology/Multiple Sclerosis LNIS

Professor Renaud Du Pasquier
Head of the Neurology Service

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Keywords
Neuroimmunology
Multiple sclerosis
$CD8^+$ T cells
Induced pluripotent stem cells (iPSC)
Progressive multifocal leukoencephalopathy

Laboratory's activity

Primarily devoted to research in Multiple Sclerosis (MS), our Laboratory studies the interaction between the immune response - with a focus on $CD8^+$ T cells - and environmental factors. In particular, we have investigated the mechanism by which Epstein-Barr virus (EBV) might be implicated in the pathogenesis of MS. We have found that EBV-specific $CD8^+$ T cells are dysregulated in the blood and the cerebrospinal fluid (CSF) of MS patients. In order to examine whether EBV-specific $CD8^+$ T cells would cross-react with central nervous system (CNS) cells, we have established a program of human induced pluripotent stem cells (hiPSC). We have thus set up an *in vitro* human model allowing to study in a fully autologous way the interaction between peripheral immune cells and CNS cells. Thanks to this potent tool, several opportunities opened to us and are leading to fruitful collaborations.

We also have a long-standing interest in the immunopathogenesis of progressive multifocal leukoencephalopathy (PML), a disease mediated by the polyomavirus JC (JCV). Our hiPSC model allows to elucidate how JCV spreads from one CNS cell to the other.

Research interests

The research of Prof. Renaud Du Pasquier is driven by the willingness to better understand the pathogenesis of inflammation in the brain, in particular in the field multiple sclerosis. Only such an understanding will lead to breakthrough treatments.

Scientific contributions in 2021-2022

> Jones S, Perriot S, Begarie D, Canales M, Oberholster L, Theaudin M, Pot C, Mathias A, Du Pasquier R. An autologous human stem cell-derived CNS model for unbiased assessment of autoreactive $CD8^+$ T cells in multiple sclerosis. CRN symposium, October 3 2022, Lausanne, Switzerland. Award: Best oral presentation.

> Oberholster L, Perriot S, Canales M, Jones S, Mathias A, Du Pasquier R. Human iPSC-derived astrocytes as a model to understand JCV infection in the brain. 15th International Congress of Neuroimmunology (ISNI), November 8-12 2021, France. (virtual) Oral presentation.

> Perriot S, Jones S, Bégarie D, Canales M, Oberholster L, Théaudin M, Pot C, Mathias A, Du Pasquier R. Using hiPSC-derived CNS cells as antigen presenting cells for unbiased identification of CNS autoreactive $CD8^+$ T cells. 15th ISNI Congress, Nov 8-12 2021, Nice, France. (virtual) Oral presentation.

> Mathias A, Perriot S, Bernard-Valnet R, Canales M, Jones S, Oberholster L, Deffert C, Lalive P, Theaudin M, Pot C, Du Pasquier R. Human induced pluripotent stem cells-derived neurons to study CNS-reactive autoantibodies in COVID-19-mediated neurological syndromes. ISNI, November 8-12 2021, Nice, France. (virtual) Oral presentation.

> Mathias A, Pantazou V, Perriot S, Canales M, Jones S, Oberholster L, Bernard-Valnet R, Theaudin M, Pot C, Du Pasquier R. Multiparametric phenotyping of immune cell dynamics under ocrelizumab: a one-year longitudinal study in MS patients. ECTRIMS, October 13-21 2021, Vienna, Austria. (virtual) ePoster presentation.

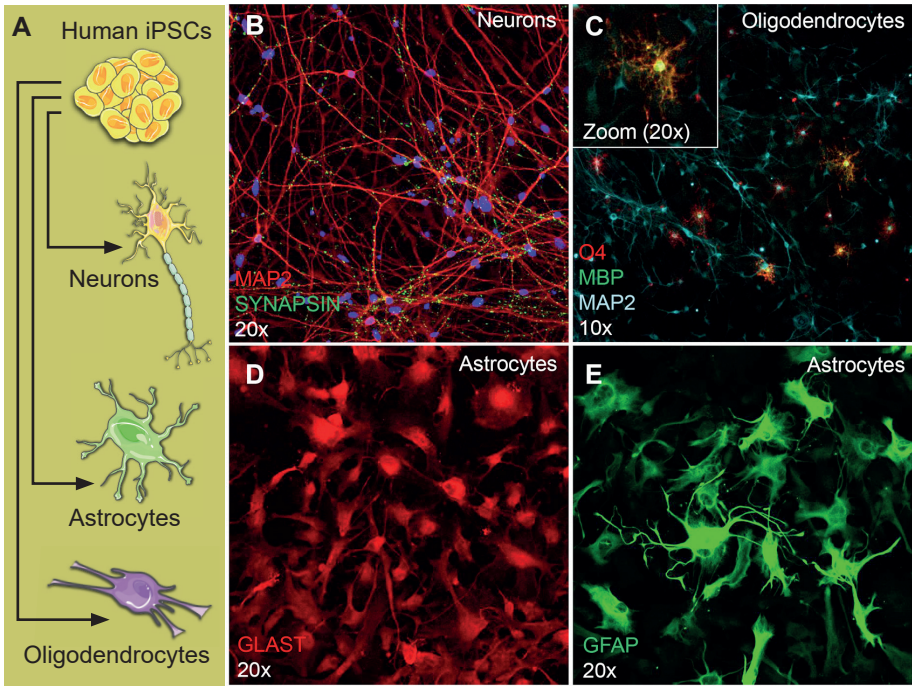
Selected invited lectures:

> How COVID-19 could affect the brain? - Plenary session, SFCNS, Basel, September 29 2022.

> The nervous system manifestations of COVID-19: pathogenic mechanisms - Special session, EAN, Vienna, June 19 2021.

> Immunology and virology, Hot topic : COVID-19 and MS, ECTRIMS, Vienna, October 21 2021.

> Opportunistic infections under disease-modifying therapies - Educational session 6, Infections and MS, ECTRIMS, Vienna, October 14 2021.



Differentiation of CNS cells from human iPSCs.
10 ml of blood was drawn from a patient with multiple sclerosis. Erythroblasts were isolated, then reprogrammed into human induced pluripotent stem cells (hiPSCs) (A), and finally differentiated into CNS cells, including neurons (B), oligodendrocytes (C), and astrocytes (D, E).

Main publications in 2021-2022

Mathias A, Pantazou V, Perriot S, Canales M, Jones S, Oberholster L, Moulin M, Fenwick C, Bernard-Valnet R, Théaudin M, Pot C, **Du Pasquier R**. Ocrelizumab impairs the phenotype and function of memory $CD8^+$ T cells: a one-year longitudinal study in multiple sclerosis patients. Neurol. Neuroimmunol. Neuroinflamm. *In press*.

Nishihara H, Perriot S, Gastfriend BD, Steinfort M, Cibien C, Soldati S, Matsuo K, Guimbal S, Mathias A, Palecek SP, Shusta EV, **Du Pasquier R**, Engelhardt B. Intrinsic blood-brain barrier dysfunction contributes to multiple sclerosis pathogenesis. Brain 2022 Jan 27:awac019. *Online ahead of print*.

Perriot S, Canales M, Mathias A, **Du Pasquier R**. Generation of transgene-free human induced pluripotent stem cells from erythroblasts in feeder-free conditions. STAR Protoc. 2022 Aug 17; 3(3):101620.

Perriot S, Mathias A, Canales M, **Du Pasquier R**. Differentiation of functional astrocytes from human induced pluripotent stem cells in chemically defined media. STAR Protoc. 2021 Oct 20; 2(4):100902. eCollection 2021 Dec 17.

Bernard-Valnet R, Perriot S, Canales M, Pizzarotti B, Caranzano L, Castro-Jiménez M, Epiney JB, Vijiala S, Salvioni-Chiabotti P, Anichini A, Salerno A, Jaton K, Vaucher J, Perreau M, Greub G, Pantaleo G, **Du Pasquier R**. Encephalopathies associated with severe COVID-19 present neurovascular unit alterations without evidence for strong neuroinflammation. Neurol. Neuroimmunol. Neuroinflamm. 2021; 8(5):e1029.

Vicino A, Loser V, Salvioni P, Brouland JP, **Du Pasquier R**. Anti-AK 5 encephalitis with histological evidence of central nervous system vasculitis. Neurol. Neuroimmunol. Neuroinflamm. 2021; 8(4).

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Laboratory of Experimental Neuroimmunology - LNIE

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Service of immunology and allergy (LIA)

Keywords
Neuroimmunology
Experimental autoimmune encephalomyelitis
Multiple sclerosis
Immunometabolism
Lipidic pathways
Gut-brain axis

Laboratory's activity

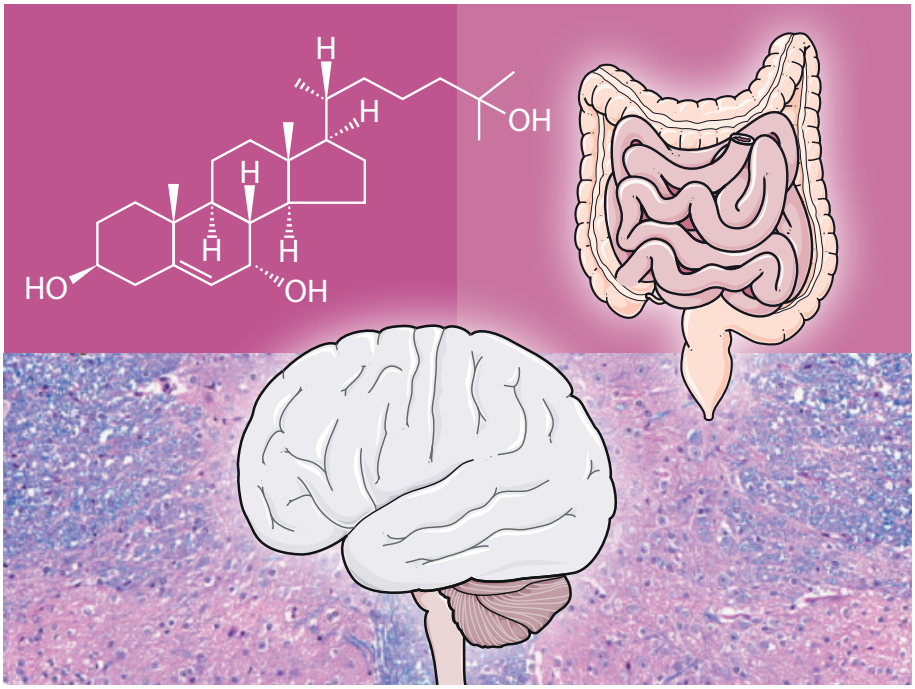
Multiple sclerosis (MS) is an autoimmune disorder affecting young patients. MS and its animal model, the experimental autoimmune encephalomyelitis (EAE), are characterized by inflammatory cell infiltrates and demyelination of the central nervous system. While risk factors such as viral infections and smoking are established, the role of cholesterol metabolism, mucosal immunology and nutrition remains unclear.
In our laboratory, we study the role of the gut-brain axis and lipid metabolism during neuroinflammation. We propose that the gut is a reservoir for immune cells and showed that blocking encephalitogenic T cell entry into the gut dampens EAE. Furthermore, perturbation of steroids pathways promote inflammation. We show that oxysterols, oxidized forms of cholesterol, shape the immune responses during inflammatory diseases including colitis and MS. However the sole hypercholesterolemia is not sufficient to promote EAE and lowering cholesterol levels with PCSK9-inhibitors does not modify EAE disease course. We finally translate our murine results to human MS research and conduct translational studies to understand how nutrition and gut flora as well as lipid metabolism affect MS.

Research interests

The aims of Caroline Pot's research is to fine-tune immune responses in regards to environmental factors or metabolic pathways. This could lead to novel therapeutics and contribute to scientific re-evaluations of life-changes thus promoting personalized medical approaches for MS patients.

Scientific contributions in 2021-2022

> October 26-28th 2022, 38th European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS). Location: Amsterdam, The Netherlands. Poster presentations.
> September 28-30th 2022, 5th SFCNS meeting. Congress Swiss Federation of Clinical Neuro-Societies. Location: Basel, Switzerland. Poster and oral presentations.
> June 25-28th 2022, 8th Hybrid Congress of the European Academy of Neurology (EAN), Vienna, Austria. Posters and oral invited presentation.
> November 8-12th 2021. 15th International Society of Neuroimmunology (ISNI). Nice, France, virtual meeting. Congress Oral and Poster presentations. Best poster presentation award to Solenne Vigne.
> October 13-15th 2021, 37th European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS). Location: virtual. Poster presentations.
> June 18-21th 2021, 7th Congress of the European Academy of Neurology (EAN). Poster presentations.



Schematic drawing illustrating the interplay between lipid metabolism, gut immune response and inflammation of the central nervous system during multiple sclerosis.
We study the interactions between oxysterols, oxidized forms of cholesterol (depicted on the left) and gut homeostasis/ gut flora (right) to assess their contributions in driving autoimmunity in the central nervous system (bottom).

Main publications in 2021-2022

Rebeaud J, Peter B, **Pot C**. How Microbiota-Derived Metabolites Link the Gut to the Brain during Neuroinflammation. Int J Mol Sci. 2022 Sep 4; 23(17):10128.

Borrelli S, Mathias A, Goff GL, Pasquier RD, Théaudin M, **Pot C**. Delayed and recurrent dimethyl fumarate induced lymphopenia in patients with multiple sclerosis. Mult Scler Relat Disord. 2022 Jul; 63:103887.

Renaud CO, Ziros PG, Mathias A, **Pot C**, Sykiotis GP. Thyroid Disorders in Patients treated with Dimethyl Fumurate for Multiple Sclerosis: A Retrospective Observational Study. Antioxidants 2022 May 21; 11(5):1015.

Vigne S, Duc D, Peter B, Rebeaud J, Yersin Y, Ruiz F, Bressoud V, Collet TH, **Pot C**. Lowering blood cholesterol does not affect neuroinflammation in experimental autoimmune encephalomyelitis. J Neuroinflam. 2022 Feb 7; 19(1):42.

Misselwitz B, Wyss A, Raselli T, Cerovic V, Sailer AW, Krupka N, Ruiz F, **Pot C**, Pabst O. The oxysterol receptor GPR183 in inflammatory bowel diseases. Br J Pharmacol. 2021 Aug; 178(16):3140-3156.

Ruiz F, Wyss A, Rossel JB, Sulz MC, Brand S, Moncsek A, Mertens JC, Roth R, Clottu A, Burri E, Juillerat P, Biedermann L, Greuter T, Rogler G, **Pot C***, Misselwitz B*. A SNP within the gene locus of the oxysterol receptor EBI2 is associated with EBI2 expression on blood lymphocytes in patients with IBD. Br J Pharmacol. 2021 Jan 28. *These authors equally contributed to this work.

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Laboratory of Brain Tumour Biology and Genetics LBGT

Professor Monika E. Hegi, Head of laboratory

Senior Lecturer, Privat-Docent Andreas F. Hottinger, Head of the Neurooncology Unit

Laboratory's activity

Taking advantage of the clinical setting of the laboratory, we aim at integrating clinical and basic cancer research in neuro-oncology at the CHUV. Joint efforts integrating research databases, including the brain tumor bank, foster research collaborations and have yielded collaborative translational research projects. We investigate mechanisms of treatment resistance and use perturbation studies to uncover the "achilles heel" of the tumors in order to identify novel promising treatment combinations. Multidimensional OMICs datasets of clinically well defined glioma datasets have yielded predictive factors and potential new targets that we are further investigating in the laboratory. We aim at bridging this knowledge with the new opportunities that will open with the new "Lucas Lundin Center for Research in Neuro-Oncology" headed by PD Dr Andreas Hottinger, for improvement of patient management and development of future studies and trials.

Laboratory of Brain Tumour Biology and Genetics - LBGT

Professor Monika E. Hegi
Head research laboratory

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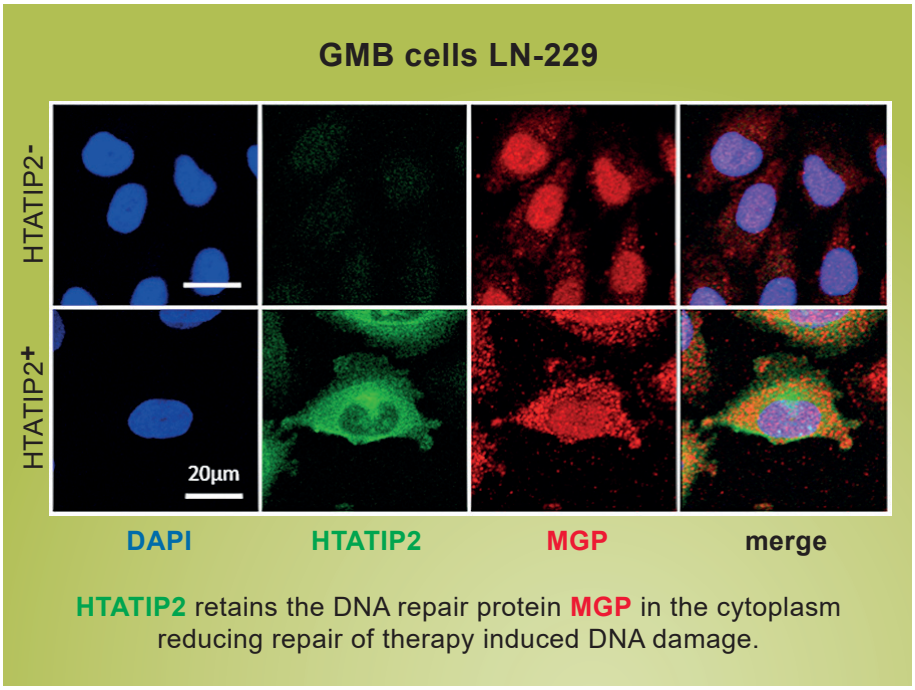
Keywords
Brain tumors
Tumor genetics and epigenetics
Translational research
Predictive biomarkers
PDX-mouse models
High resolution magnetic resonance spectroscopy

Research interests
> (Epi)genomics of glioma, their relevance for tumor biology, classification, and novel therapeutic strategies.
> Molecular mechanisms and biomarkers of resistance.
> Translational research.
> Longiitudinal modeling of tumor invasion using spectroscopy.

Scientific contributions in 2021-2022
> GBM of elderly patients are not molecularly different from other age groups, falling into the same subtypes (RTK I & II, MES), advocating for similar treatments if frailty and co-morbidities permit.
> Age acceleration of GBM (epigenetic age minus chronologic age of the patient, Horvath clock) was revealed as integrative part explaining methylation-based classification of GBM.
> Contributions to investigations of the tumor microenvironment of primary brain tumors and brain metastasis revealed disease-specific differences.
> Perturbation studies in GBM derived spheres uncovered pathway vulnerabilities targetable with mechanistically informed combination therapies.
> Metabolic and transcriptional profiles of glioblastoma invasion characterized by 1H Magnetic Resonance Spectroscopy (7T/14T) of patients' tumors and corresponding orthotopic mouse xenografts provided insights into underlying pathways and revealing similarities.



Main publications in 2021-2022

Bady P, Marosi C, Weller M, Grønberg BH, Schultz H, Taphoorn MJB, Gijtenbeek JMM, van den Bent MJ, [...] **Hegi ME**. DNA methylation-based age acceleration observed in IDH wild-type glioblastoma is associated with better outcome - including in elderly patients. Acta Neuropathol Commun. 2022; 10(1):39.

Beltzig L, Schwarzenbach C, Leukel P, Frauenknecht KBM, Sommer C, Tancredi A, **Hegi ME**, Christmann M, Kaina B. Senescence is the main trait induced by temozolomide in glioblastoma cells. Cancers 2022; 14(9):2233.

Klemm F, Möckl A, Salamero-Boix A, Alekseeva T, Schäffer A, Schulz M, Niesel K, Maas RR, Groth M, Elie BT, Bowman RL, **Hegi ME**, *et al*. Compensatory CSF2-driven macrophage activation promotes adaptive resistance to CSF1R inhibition in breast-to-brain metastasis. Nat Cancer 2021; 2(10):1086-1101.

Cudalbu C, Bady P, Lai M, Xin L, Gusyatiner O, Hamou MF, Lepore M, Brouland JP, Daniel RT, *Hottinger AF, ***Hegi ME**. Metabolic and transcriptomic profiles of glioblastoma invasion revealed by comparisons between patients and corresponding orthotopic xenografts in mice. Acta Neuropathol Commun. 2021; 9(1):133. *co-senior authorship.

Maas RR, Soukup K, Klemm F, Kornete M, Bowman RL, Bedel R, Marie DN, Álvarez-Prado ÁF, [...] **Hegi ME**, *et al*. An integrated pipeline for comprehensive analysis of immune cells in human brain tumour clinical samples. Nat Protoc. 2021; 16(10):4692-4721.

Gusyatiner O, Bady P, Pham MDT, Lei Y, Park J, Daniel RT, Delorenzi M, **Hegi ME**. BET inhibitors repress expression of Interferon-stimulated genes and synergize with HDAC inhibitors in glioblastoma. Neuro Oncol. 2021; 23(10):1680-1692.

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Laboratory of Brain Tumour Biology and Genetics - LBGT

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Affiliations
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Keywords
Neuro-oncology
Primary brain tumors
Glioblastoma
Astrocytoma
Oligodendroglioma
Familial brain tumors
Neurologic complications of cancer
Clinical trial

Laboratory's activity

Primary brain tumors
We focus on the development of novel and innovative treatment strategies for patients with primary brain tumors including glioblastoma, astrocytomas, oligodendrogliomas and other rare forms of cancers of the nervous system.

Neurologic complications of cancer and cancer therapies
Our group has gained an expertise in the management of neurological complications of novel oncologic immune therapies including checkpoint inhibitors.

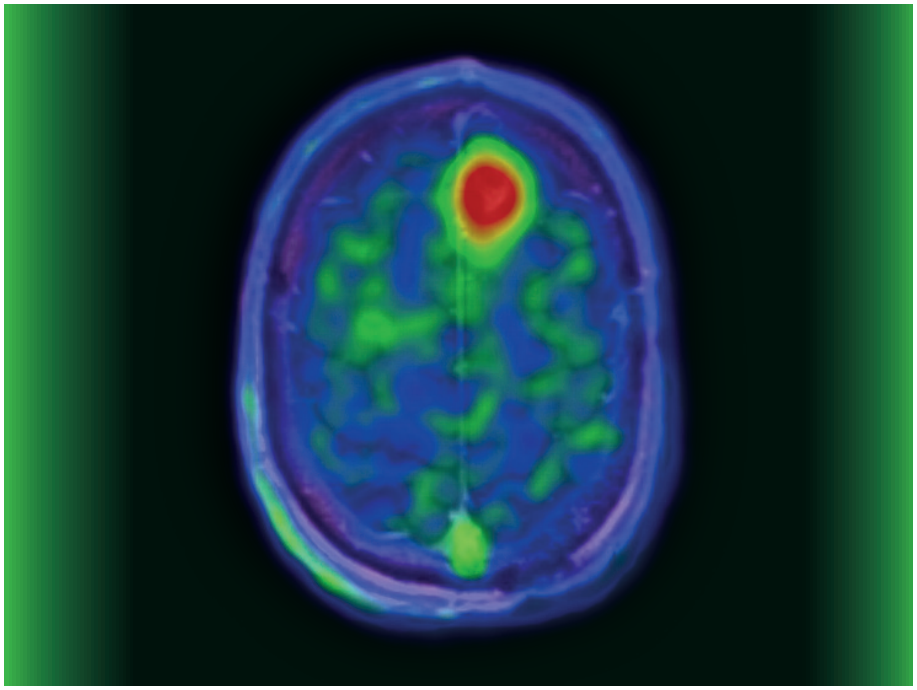
Translational research
A first area of focus is the development and evaluation of xenograft models of glioblastoma - collaboration work with the laboratory of brain tumor biology and genetics (LBGT) and the Center of Biomedical Imaging (CIBM, CHUV).
In a collaboration with the Laboratory for Research in Neuroimaging (LREN) we are also interested in better characterizing the modifications induced by glioblastoma and treatment with alternating electrical fields on the brain parenchyma.

Research interests

Our group has a long-standing experience and expertise in clinical trials. We are involved in a number of international clinical trials with several organizations, including the Swiss Neurooncology Society, the European Organization for Research and Treatment of Cancer (EORTC) as well as a number of pharmacological companies.

Scientific contributions in 2021-2022

> Collaboration with the laboratory of biology and genetics of brain tumors and the Center for biomedicine imaging to evaluate patient-derived xenograft models of glioblastoma.
> Evaluation of the effects of tumor treating fields in patients with newly diagnosed GBM.
> Participated in several international treatment guidelines for gliomas and primary CNS lymphoma.
> During 2022 and 2023, thanks to an important donation, we will set up the Lundin Family Brain Tumor research center with the aim to boost translational and clinical research on brain tumors with the aim to improve the outcome and quality of life of patients with brain tumors.



Brain FET-PET showing a high grade glioma in the left frontal lobe.

Main publications in 2021-2022

Hoang-Xuan K, Deckert M, Ferreri AJM, Furtner J, Perez-Larraya JG, Henriksson R, **Hottinger AF**, *et al.* European Association of Neuro-Oncology (EANO) Guidelines for Treatment of Primary Central Nervous System lymphoma (PCNSL). Neuro Oncol. 2023 Jan 5; 25(1):37-53.

Glas M, Ballo MT, Bomzon Z, Urman N, Levi S, Lavy-Shahaf G, Jeyapalan S, Sio TT , [...] **Hottinger AF**, *et al*. The Impact of Tumor Treating Fields on Glioblastoma Progression Patterns. Int J Radiat Oncol Biol Phys. 2022 Apr 1; 112(5):1269-1278.

Mohile NA, Messersmith H, Gatson NT, **Hottinger AF**, *et al*. Therapy for Diffuse Astrocytic and Oligodendroglial Tumors in Adults: ASCO-SNO Guideline. J Clin Oncol. 2022 Feb 1; 40(4):403-426.

Frappaz D, Barritault M, Montané L, Laigle-Donadey F, Chinot O, Le Rhun E, Bonneville-Levard A, **Hottinger AF**, *et al*. MEVITEM - A Phase I/II trial of vismodegib + temozolomide *vs* temozolomide in patients with recurrent/refractory medulloblastoma with Sonic Hedgehog pathway activation. Neuro Oncol. 2021 Nov 2; 23(11):1949-1960.

Cudalbu C, Bady P, Lai M, Xin L, Gusyatiner O, Hamou MF, Lepore M, Brouland JP, Daniel RT, Hegi ME, **Hottinger AF**. Metabolic and transcriptomic profiles of glioblastoma invasion revealed by comparisons between patients and corresponding orthotopic xenografts in mice. Acta Neuropathol Commun. 2021 Aug 4; 9(1):133.

Desbaillets N, **Hottinger AF**. Immunotherapy in Glioblastoma: A Clinical Perspective. Cancers (Basel) 2021 Jul 24; 13(15):3721.

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Unisciences

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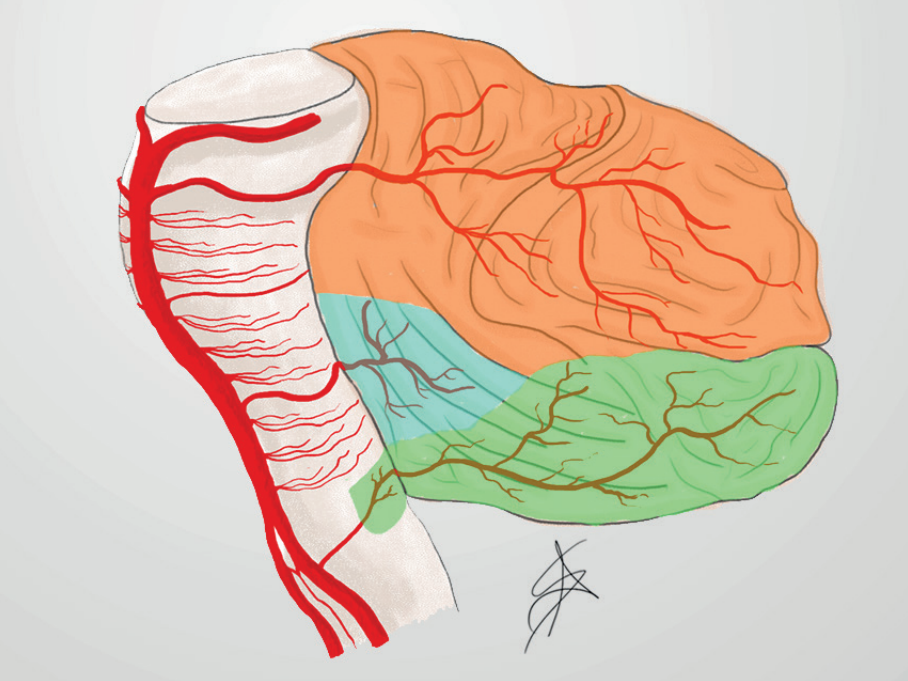
Laboratories of Stroke Research - LMCV

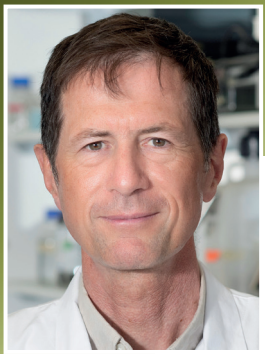
Experimental Stroke Research Laboratory
Assoc. Professor Lorenz Hirt, Head of laboratory

Laboratory of Clinical Stroke Research Unit
Assoc. Professor Patrik Michel, Head of laboratory



Schematical drawing of normal blood supply of the brainstem and cerebellum. Drawing by A. Salerno, MD.
Ref: Salerno A, Strambo D, Nannoni S, Dunet V, Michel P. Patterns of ischemic posterior circulation strokes: A clinical, anatomical and radiological review. Int J Stroke 2022; 17(7):714-722.

The Stroke Research branch in the CRN has a wide fundamental research activity including neuroprotection, neuroradiological analyses, and clinical stroke research. It is well known that experimental lab and clinical registries contribute to the understanding of stroke mechanisms as well as to the advancement of acute and chronic treatment of stroke victims. Both the Stroke Laboratory and the Clinical Stroke Research teams are well connected through local, national and international collaborations and welcome international researchers.



Experimental Stroke Research Laboratory

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Affiliation
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Keywords
Stroke
Cerebral ischemia
Experimental stroke
Lactate

Laboratory's activity

The stroke laboratory is studying mechanisms of cell death after cerebral ischemia using an experimental model (mouse middle cerebral artery occlusion, MCAO). We are studying lactate as an agent for repair and protection as well as its neuroprotective mechanisms involving its receptor and transporters. We have shown that the mode of action lactate *in vivo* is predominantly metabolic, as receptor agonists failed to induce protection and as lack of receptor did not lead to enhanced susceptility to stroke in receptor deficient mice. In an SNF-funded project analysing hyperpolarized substrate administration after MCAO by magnetic resonance spectroscopy, we have shown a rapid metabolism in the ischemic brain of both 13C-lactate and 13C-pyruvate. These preclinical results led us to initiate a clinical trial in acute stroke patients testing lactate against placebo (10 patients included so far). Lab members are Lara Buscemi, PhD; Melanie Price, PhD and Julia Castillo Gonzalez, MSc.

Research interests

Our research aims at finding additional options to improve the outcome of stroke patients. Experimentally, we are investigating the neurovascular unit, neuroinflammation, angiogenesis and metabolism after stroke. We are running a double blind randomised controlled clinical trial on lactate administration in ischemic stroke patients, thereby translating our project on lactate from bench to bedside, in collaboration with the clinical stroke research team of Pr. Patrik Michel. In clinical research, we are also exploring our large retrospective Doppler US database.

Scientific contributions in 2021-2022

We have shown that:

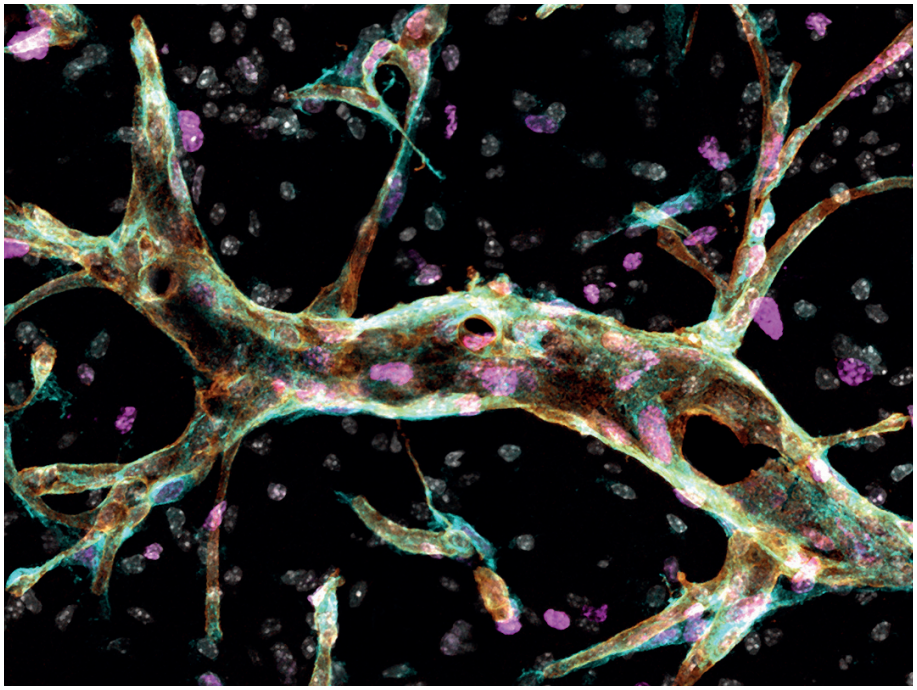
> HCAR1 is not involved in the beneficial effect of lactate after MCAO .

> The free radical TEMPOL used in DNP influences the MRS data after MCAO in mice.

> Diabetes influences the hemodynamic and arterial wall parameters in acute ischemic stroke patients.

> Low echogenicity at the surface of carotid plaques is associated with increased stroke risk.

> We have obtained new FNS and ERA-NET neuron grants for the next period.



The image illustrates the attempt of brain cells to repair the damage caused by experimental ischemia. It shows cell proliferation (ki67, magenta) occurring in and around a blood vessel (collagen IV, brown) in the lesion area, which is enveloped by pericytes (PDGFRbeta1, cyan), three days after surgery. Cell nuclei are shown in gray.

Main publications in 2021-2022

Bill O, Mazya MV, Michel P, Prazeres Moreira T, Lambrou D, Meyer IA, **Hirt L**. Intima-media thickness and pulsatility index of common carotid arteries in acute ischaemic stroke patients with diabetes mellitus. J Clin Med. 2022 Dec 29; 12(1):246.

Sztajzel RF, Engelter ST, Bonati LH, Mono ML, Slezak A, Kurmann R, Nedeltchev K, Gensicke H, Traenka C, Baumgartner RW, Bonvin C, **Hirt L**, Medlin F, Burow A, Kagi G, Kapauer M, Vehoff J, Lovblad KO, Curtin F, Lyrer PA. Carotid plaque surface echogenicity predicts cerebrovascular events: An echographic multicentric swiss study. J Neuroimaging 2022 Nov; 32(6):1142-1152.

Buscemi L, Price M, Castillo-Gonzalez J, Chatton JY, **Hirt L**. Lactate neuroprotection against transient ischemic brain injury in mice appears independent of hcar1 activation. Metabolites 2022 May 21; 12(5):465.

Correia PN, Meyer IA, Eskandari A, Amiguet M, **Hirt L**, Michel P. Preconditioning by preceding ischemic cerebrovascular events. J Am Heart Assoc. 2021 Aug 17; 10(16):e020129.

Buscemi L, Blochet C, Magistretti PJ, **Hirt L**. Hydroxycarboxylic acid receptor 1 and neuroprotection in a mouse model of cerebral ischemia-reperfusion. Front Physiol. 2021 May 21; 12:689239.

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CHUV

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Unisciences

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Laboratory of Clinical Stroke Research Unit

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Affiliation
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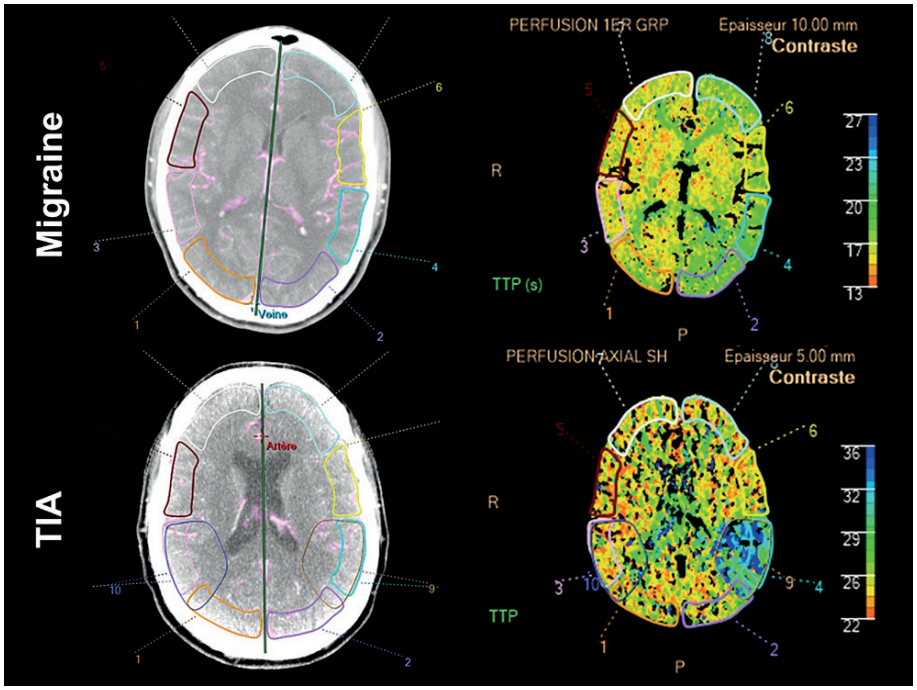
Keywords
Stroke
Thrombolysis
Thrombectomy
Neuroimaging
ASTRAL registry

Laboratory's activity
The Clinical Stroke Research team maintains since 2003 the ASTRAL registry (Acute STroke Registry and Analysis of Lausanne). It contains >7'000 acute stroke patients, each with >300 variables including demographic, clinical, comorbidity, multimodal imaging, etiological, metabolic and outcome data. CT and more recently MRI-based angiographic and perfusion data are collected and analysed in a detailed manner. We also study the influence of acute revascularization treatments in different situations, frequent and rare stroke mechanisms, and prognostic markers of long-term outcome. The team participates in multiple national and international randomized trials for acute stroke treatment and secondary prevention.

Research interests
Our team's research interests concern clinical stroke syndromes, acute stroke imaging, acute stroke management and stroke prognosis, and secondary stroke prevention. Beside participation in multiple randomized trials, we recently published on stroke syndromes and causes (posterior circulation stroke/basilar artery occlusion, COVID-19 and stroke, PFO-related stroke, rare stroke mechanisms), acute imaging of ischemic stroke (perfusion imaging, collaterals, posterior circulation), acute revascularization treatments (effect of thrombolysis and thrombectomy in different situations, complications of thrombectomy), stroke management (Stroke-unit strokes; palliative predictors) and secondary stroke prevention (PFO-closure).

Scientific contributions in 2021-2022
> Participation in several randomized clinical trials (BASICS, SWIFT-DIRECT, ESTREL, ELAN, DISTAL and others).
> 56 peer-reviewed publications.
> Grant from UNIL as main applicant. Grants from Swiss Heart Foundation as main and as co-applicant.
> One MD thesis terminated, two ongoing. One PhD thesis terminated (co-supervisor), two ongoing (one as co-supervisor).
> Organiser, speaker and chairman of multiple national and international conferences.
> Multiple collaborations nationally (Swiss Stroke Registry) and internationally (TRISP/EVATRISP; Prof. M. Wintermark, Houston; Dr P. Seners, Stanford; Prof. Th. Nguyen, Boston; and others).



Focal hypoperfusion in the left hemisphere on perfusion-CT analysis in a patient with migrainous aura (upper panels) and in a patient with a TIA (lower panels).

Left: regions of interest
Right: time-to-peak perfusion-CT.

Strambo D, Nannoni S, Rebordao L, Dunet V, Michel P. Computed Tomographic Perfusion abnormalities in acute migraine with aura: Characteristics and comparison with Transient Ischemic Attack. Eur Stroke J, 2022; 7(4): 431-438.

Main publications in 2021-2022

Marto JP, Strambo D, Ntaios G, Nguyen TN, Herzig R, Czlonkowska A, Demeestere J, Mansour OY, [...] **Michel P** and the The Global COVID-19 Stroke Registry Collaborators. Safety and outcome of revascularization treatment in patients with acute ischemic stroke and COVID-19: The Global COVID-19 Stroke Registry. Neurology, accepted.

Marto JP, Salerno A, Maslias E, Lambrou D, Eskandari A, Strambo D, **Michel P**. Stroke in the Stroke Unit - Recognition, treatment and outcomes in a single-center cohort. Eur J Neurol. 2022 Sept; 29(9):2674-2682.

Salerno A, Strambo D, Nannoni S, Dunet V, **Michel P**. Patterns of ischemic posterior circulation strokes: A clinical, anatomical and radiological review. Int J Stroke 2022 Aug; 17(7):714-722.

Nannoni S, Kaesmacher J, Ricciardi F, Strambo D, Dunet V, Hajdu S, Saliou G, Gralla J, Fischer U, **Michel P**. ASPECTS-based selection for late endovascular treatment: a retrospective two-site cohort study. Int J Stroke 2022 Apr; 17(4):434-443.

Langezaal LCM, van der Hoeven EJRJ, Mont'Alverne FJA, de Carvalho JJF, Lima FO, Dippel DWJ, van der Lugt A, Lo RTH, [...] **Michel P,** Puetz V, Audebert HJ, Pontes-Neto OM, Vos JA, Jaap Kappelle L, Algra A, Schonewille WJ; BASICS study group. Endovascular Therapy for Stroke Due to Basilar-Artery Occlusion. New Engl J Med. 2021 May 20; 384(20):1910-1920.

Strambo D, Sirimarco G, Nannoni S, Kalliopi P, Ntaios G, Vemmos K, **Michel P**. Embolic stroke of undetermined source and patent foramen ovale: RoPE score validation and atrial fibrillation prediction. Stroke 2021 May; 52(5):1643-1652.

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Laboratory of Clinical Neurosurgery Research

Assoc. Professor Roy Thomas Daniel, Head of laboratory
Senior Lecturer, Privat-Docent Mahmoud Messerer
Senior Lecturer Daniele Starnoni
Senior Lecturer Giulia Cossu
Dr Lorenzo Giammattei

The Neurosurgery Education and Training laboratory (NET-lab) activities explore new surgical approaches. Our theme is "From the Lab to the OR" as a reflection of a true translational effort to introduce novel anatomical concepts and innovative surgical technique into real surgical practice.

Laboratory's activity

The laboratory research is based on cohort studies (institutional or multicentric) with a view to improve neurological outcomes following surgery. This led to publication of several european guidelines on behalf of the European Association of Neurosurgical Societies for treatment of complex skull base pathologies. The Neurosurgery Education and Training laboratory (NET-lab) activities explore new surgical approaches in order to limit neurological morbidity. We also pioneered the strategy of combined surgery with radiosurgery and implemented combined endoscopic and open surgical approaches for complex skull base pathologies. The lab contributes data to the Swiss SOS registry on aneurysmal subarachnoid hemorrhage allowing several multicentric cohort studies on epidemiology and treatment outcomes. The clinical and NET lab research studies is also focused on new surgical strategies for disconnective epilepsy surgery. Surgical strategies for pituitary tumors that favor endocrine functional preservation are explored through combination of large cohort studies, newer surgical approaches and molecular markers analysis. New paradigms for the treatment of severe brain trauma have also been developed with promising outcomes that have challenged traditional concepts of treatment care.

Laboratory of Clinical Neurosurgery Research

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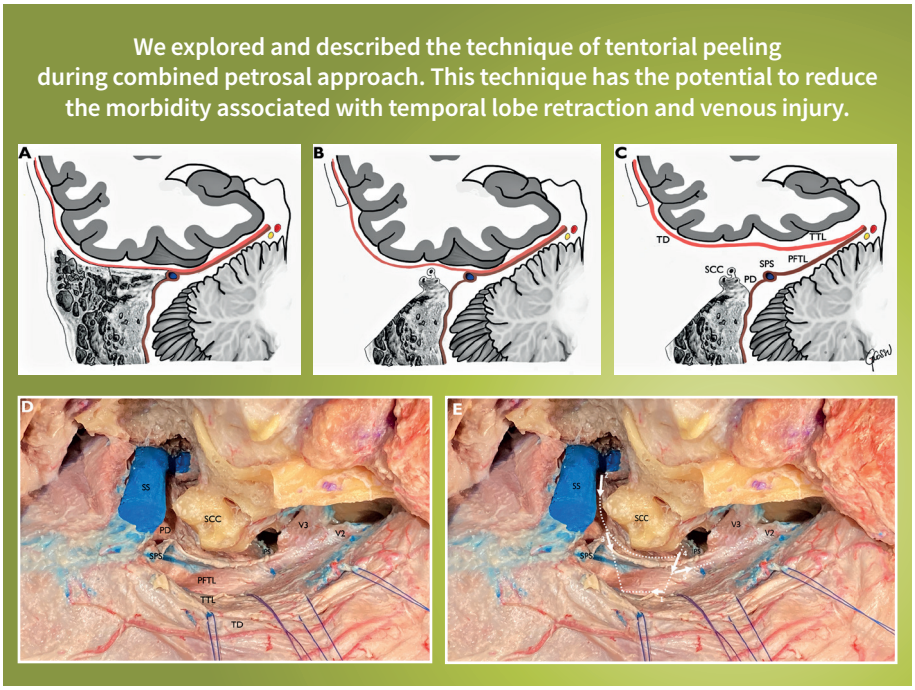
Keywords
Skull base
Skull base endoscopic approach
Vascular neurosurgery
sos registry, pituitary

Research interests

The primary focus of this team centers on the tumors and vascular lesions of the brain. The lab focuses on innovative surgical strategies that combine surgical (endoscopic and open) and radiosurgical treatment. We also focus on comparing outcomes of surgical and interventional neuroradiological procedures for the aneurysm treatment especially in relation to DCI and its treatment.

Scientific contributions in 2021-2022

> Progress in research and clinical trials leading to 40 peer-reviewed publications.
> One Brihaye EANS research grant.
> Two MD obtained and a PhD.
> Participation in 2 national/international randomized clinical trials.
> Organiser, speaker and chairman of multiple national and international conferences.
> Multiple collaborations nationally and internationally (Swiss SOS registry, EANS, WFNS).



A) Coronal view of the temporal lobe, tentorium, petrous bone, and cerebellum. The pink line indicates the temporal dura (TD), which is in continuity with the temporal tentorial leaf (TTL). The brown line indicates the presigmoid dura (PD), which is in continuity with the posterior fossa tentorial leaf (PFTL).

B) Exposure after mastoidectomy and petrosectomy has been performed, with preservation of the semicircular canals (SCC).

C) The plane between the TTL and PFTL that is created by tentorial peeling, superior to the superior petrosal sinus (SPS).

D) Cadaveric image after tentorial peeling showing the development of the PFTL and TTL. The PD and TD are also visible.

E) Representation of the dural cuts.

Main publications in 2021-2022

Giammattei L, Starnoni D, Ronconi D, Camara B, George M, Cossu G, **Messerer M**, Peters D, **Daniel RT**. Tentorial peeling during combined petrosal approach: a cadaveric dissection. Acta Neurochir (Wien) 2022 Nov; 164(11):2833-2839.

Harel E, Cossu G, **Daniel RT**, **Messerer M**. Relationship with the diaphragm to predict the surgical outcome in large and giant pituitary adenomas. Front Surg. 2022 Sep 1; 9:962709. eCollection 2022.

Starnoni D, Cossu G, Maduri R, Tuleasca C, George M, Maire R, **Messerer M**, Levivier M, Pralong E, **Daniel RT**. Direct cochlear nerve stimulation monitoring through evoked muscle responses during retrosigmoid vestibular schwannoma resection surgery: technical note. J Neurosurg. 2022 Jun 17;1-6. *Online ahead of print*.

González-López P, Cossu G, Thomas CM, Marston JS, Gómez C, Pralong E, **Messerer M**, **Daniel RT**. Cadaveric White Matter Dissection Study of the Telencephalic Flexure: Surgical Implications. Front Neurol. 2022 Feb 15; 13:757757. eCollection 2022.

Starnoni D, Tuleasca C, Giammattei L, Cossu G, Bruneau M, Berhouma M, Cornelius JF, Cavallo L, [...] **Messerer M**, **Daniel RT**. Surgical management of anterior clinoidal meningiomas: consensus statement on behalf of the EANS skull base section. Acta Neurochir (Wien) 2021 Dec; 163(12):3387-3400.

Schatlo B, Fung C, Stienen MN, Fathi AR, Fandino J, Smoll NR, Zumofen D, **Daniel RT**, *et al.* Incidence and Outcome of Aneurysmal Subarachnoid Hemorrhage: The Swiss Study on Subarachnoid Hemorrhage (Swiss SOS). Stroke 2021 Jan; 52(1):344-347.

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CHUV

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Unisciences

https://www.unil.ch/unisciences/nch

Laboratory of Cortical Excitability and Arousal Disorders - LE²C

Professor Philippe Ryvlin, Head of laboratory
Assoc. Professor Andrea Rossetti
Senior Lecturer, Privat-Docent Jan Novy

Laboratory's activity

Our laboratory's activities are focusing on clinical research in patients with epilepsy, migraine or disorders of consciousness, including status-epilepticus and post-anoxic coma.

In epilepsy, we pursue five main research objectives:

> Pathophysiology and prevention of Sudden Unexpected Death in Epilepsy Patients.
> Seizure detection in ambulatory patients using mobile health technology.
> Point-of-care testing of antiepileptic drugs plasma dosage.
> Pharmacogenomic and other biological biomarkers.
> Epidemiology and management of status-epilepticus.

In disorders of consciousness, our current research primarily focuses on outcome prognostication of acute coma, particularly after cardiac arrest.

In migraine, our current research focuses on the detection of neurovegetative biomarkers that would precede or accompany migraine attacks, using wrist-worn wearable devices.

We are also coordinating the development of the Medical Informatics Platform (MIP) and the Human Intracerebral EEG Platform (HIP) of the Human Brain Project. The MIP offers a unique solution for performing federated analyses of datasets distributed across hospitals. The HIP provides the scientific community access to the largest and most advanced solution worldwide for storing, curating, sharing, and analyzing data directly recorded from the Human brain during SEEG in patients with epilepsy.

Laboratory of Cortical Excitability and Arousal Disorders - LE²C

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Head of the Laboratory of Cortical Excitability and Arousal Disorders - LE²C
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Affiliation
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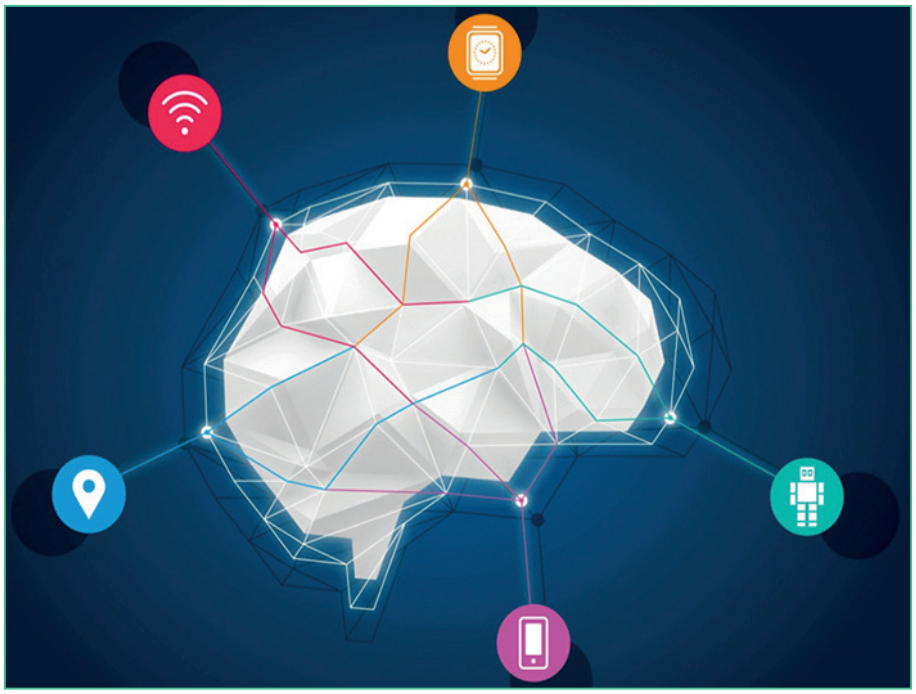
Keywords
Epilepsy
Coma
Cardiac arrest
Sudden unexpected death in epilepsy (SUDEP)
Status-epilepticus
Seizure detection
Drug monitoring
Biomarkers
Intracerebral EEG
Medical Informatics Platform (MIP)
Human Intracerebral EEG Platform (HIP)
Federated analyses

Research interests
Biomarkers and prevention of SUDEP, seizure detection, large scale data sharing.

Scientific contributions in 2021-2022
> Clinical partner for the Neurosense Horizon Project (NEUROendocrine SENSor for sudden unexpected death in Epilepsy prediction and prevention).
- Development of methodology within our platform.
- Brainstem fMRI in breath-holding in patients with epilepsy *vs* controls (1st study).
> Advancing the deployment and usage of the HBP funded Medical Informatics Platform (MIP) with use-cases in TBI, mental health, dementia, stroke and epilepsy.
> Developing the HBP-funded Human intracerebral EEG platform (HIP) with 10 centers performing closed beta testing of the platform.



The NeuroTech Platform provides an infrastructure dedicated to the evaluation of the medical and medico-economic impact of novel technologies in clinical neurosciences.

Main publications in 2021-2022

Ciumas C, Rheims S, **Ryvlin P**. fMRI studies evaluating central respiratory control in humans. Front Neural Circuits 2022 Sep 23; 16:982963. (IF 3.5)

Ryvlin P, Dimova S, Elmoufti S, Floricel F, Laloyaux C, Nondonfaz X, Biton V. Tolerability and efficacy of adjunctive brivaracetam in adults with focal seizures by concomitant antiseizure medication use: Pooled results from three phase 3 trials. Epilepsia 2022 Aug; 63(8):2024-2036. (IF 6.4)

Sopic D, Teijeiro T, Atienza D, Aminifar A, **Ryvlin P**. Personalized seizure signature: An interpretable approach to false alarm reduction for long-term epileptic seizure detection. Epilepsia 2022 Feb 3. (IF 6.4)

Ryvlin P, Rheims S, Hirsch LJ, Sokolov A, Jehi L. Neuromodulation in epilepsy: state-of-the-art approved therapies. Lancet Neurol. 2021 Dec; 20(12):1038-1047. (IF 59.9)

Ryvlin P, Jehi LE. Neuromodulation for Refractory Epilepsy. Epilepsy Curr. 2021 Dec 15; 22(1):11-17. (IF 7.9)

Beniczky S, Wiebe S, Jeppesen J, Tatum WO, Brazdil M, Wang Y, Herman ST, **Ryvlin P**. Automated seizure detection using wearable devices: A clinical practice guideline of the International League Against Epilepsy and the International Federation of Clinical Neurophysiology. Epilepsia 2021 Mar; 62(3):632-646. (IF 6.4)

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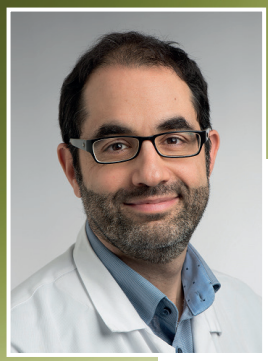

Laboratory of Cortical Excitability and Arousal Disorders - LE²C

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Affiliation
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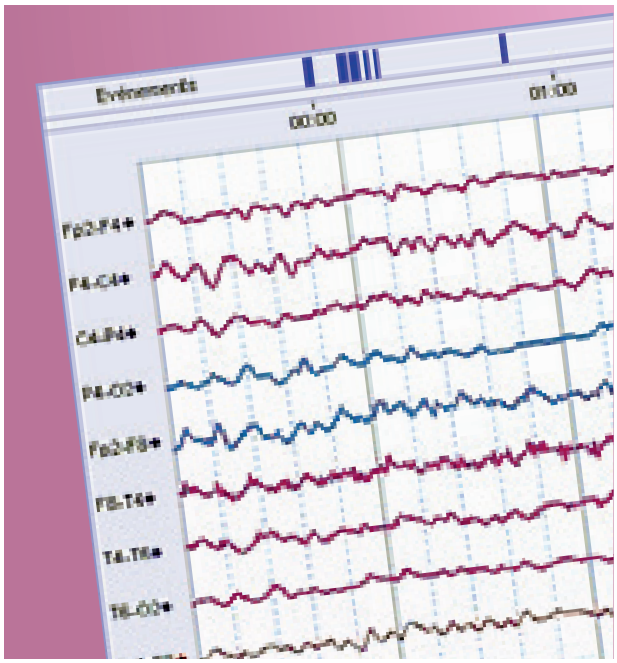
Keywords
Epilepsy
Status epilepticus
Coma prognostication
EEG
Evoked potentials



Laboratory's activity

Studies on nosology and treatment of status epilepticus prognostication of acute coma; EEG monitoring in intensive care unit.

Research interests

Prognostication of coma after cardiac arrest, status epilepticus.

Scientific contributions in 2021-2022

> In depth analyses of the CERTA trial, focusing on the cEEG role in prognostication of comatose patients.
> Participation to the NORSE (new-onset refractory status epilepticus) Consensus Group.
> Completion of the case-control study on delirium in COVID patients.

Main publications in 2021-2022

Bernard-Valnet R, Favre E, Bernini A, Oddo M, Chiche JD, Du Pasquier R, **Rossetti AO**; CORO-NEURO-ICU study group. Delirium in Adults With COVID-19-related ARDS: Comparison With Other Etiologies. Neurology 2022 Aug 25:10.1212/WNL.0000000000201162.

Wickstrom R, Taraschenko O, Dilena R, Payne ET, Specchio N, Nabbout R, Koh S, Gaspard N, Hirsch LJ; International NORSE Consensus Group. International consensus recommendations for management of New Onset Refractory Status Epilepticus (NORSE) including Febrile Infection-Related Epilepsy Syndrome (FIRES): Summary and Clinical Tools. Epilepsia 2022 Aug 11; 63(11):2827-39.

Urbano V, Novy J, Alvarez V, Schindler K, Rüegg S, **Rossetti AO**. EEG recording latency in critically ill patients: Impact on outcome. An analysis of a randomized controlled trial (CERTA). Clin Neurophysiol. 2022 Jul; 139:23-27.

Urbano V, Alvarez V, Schindler K, Rüegg S, Ben-Hamouda N, Novy J, **Rossetti AO**. Continuous *versus* routine EEG in patients after cardiac arrest: Analysis of a randomized controlled trial (CERTA). Resuscitation 2022 Jul; 176:68-73.

Beuchat I, Rosenow F, Kellinghaus C, Trinka E, Unterberger I, Rüegg S, Sutter R, Tilz C, Uzelac Z, **Rossetti AO**, *et al.* Refractory Status Epilepticus: Risk Factors and Analysis of Intubation in the Multicenter SENSE Registry. Neurology 2022; 99:e1824-e1834.

Vassallo P, Novy J, Zubler F, Schindler K, Alvarez V, Rüegg S, **Rossetti AO**. EEG spindles integrity in critical care adults. Analysis of a randomized trial. Acta Neurol Scand. 2021 Dec; 144(6):655-662.

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Unisciences

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Laboratory of Cortical Excitability and Arousal Disorders - LE²C

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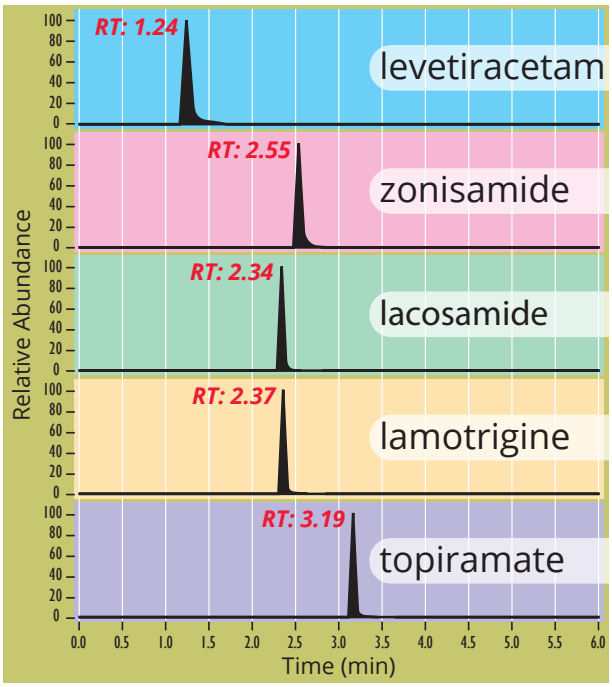
Keywords
Epilepsy
Sudden unexpected death in epilepsy
Neuroimaging
Intracerebral EEG
Seizure detection
Neurotechnologies
Pharmacology
Epidemiology
Biomarkers
Genetic



Laboratory's activity
Assess the ways to improve the pharmacological treatment of epilepsy and identify biomarkers of the disease to guide the therapy. Establish a closed-loop therapy assessing on the one hand the treatment exposure and on the other hand markers of the disease activity. This closed loop therapy will allow a more efficient proactive rather than reactive treatment of epilepsy.

Research interests
Therapeutic monitoring and biomarkers of epileptic seizures.

Scientific contributions in 2021-2022
> Correlation between efficacy and medications plasma levels.
> Setting medications levels associated with need to switch medication.
> Assessing the use of therapeutic drug monitoring at treatment failure.
> Assessing drug load effects in term of adverse events.

Main publications in 2021-2022
Pretat T, Aícua-Rapún I, André P, Lebon S, Rossetti AO, Decosterd LA, Buclin T, **Novy J**. Treatment emergent adverse events and antiseizure medication actual drug load. Epilepsy & Behavior 2022 Dec; 137(Pt A):108980.
Vijiala S, André P, Buclin T, Decosterd LA, Rossetti AO, **Novy J**. Valproate in status epilepticus: Correlation between loading dose, serum levels, and clinical response. Eur J Neurol. 2022 Sep; 29(9):2607-2611.
Fluckiger P, Aícua-Rapún I, André P, Rossetti AO, Decosterd LA, Buclin T, **Novy J**. Therapeutic drug monitoring of newer generation antiseizure medications at the point of treatment failure. Seizure 2022 Jan; 94:66-69.
Rajakulendran S, Belluzzo M, **Novy J**, Sisodiya SM, Koepp MJ, Duncan JS, Sander JW. Late-life terminal seizure freedom in drug-resistant epilepsy: "Burned-out epilepsy". J Neurol Sci. 2021 Dec 15; 431:120043.
Aícua-Rapún I, André P, Rossetti AO, Décosterd LA, Buclin T, **Novy J**. Seizure freedom and plasma levels of newer generation antiseizure medications. Acta Neurol Scand. 2021 Aug; 144(2):202-208.

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Unisciences
www.unil.ch/unisciences/jannovy

Laboratory MySpace

Assist. Professor Andrea Serino
Head of laboratory

Head of the Laboratory MySpace
Laboratoire MySpace
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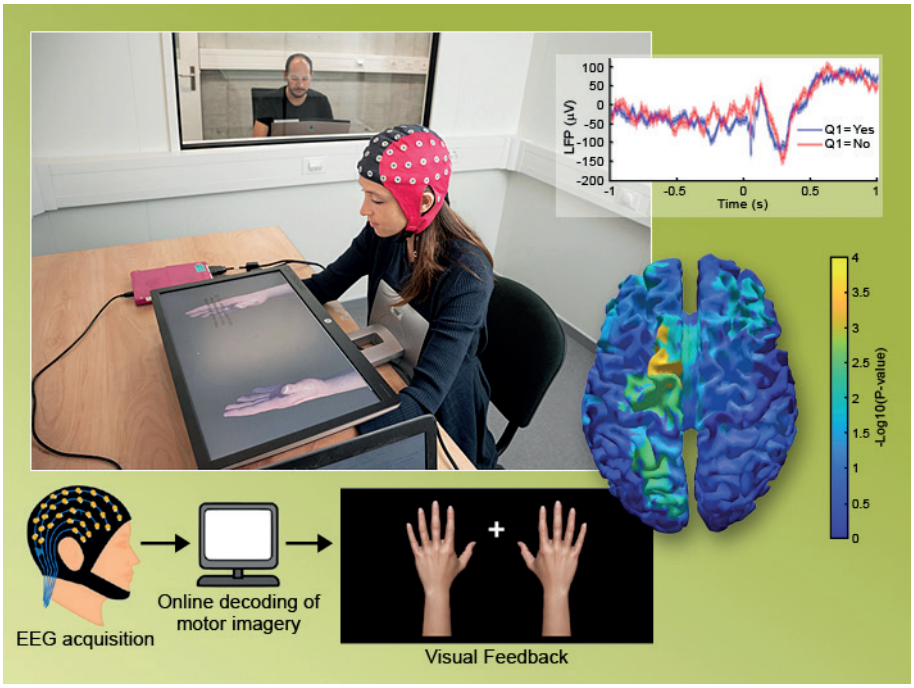
Affiliation
Service of neuropsychology and neurorehabilitation (NPR)

Keywords
Peripersonal space
Body representations
Multisensory integration
Virtual reality & robotics
Embodiment
Cognitive assessment and rehabilitation

Laboratory's activity
The main goal of the lab is understanding how the human brain builds a representation of the body in space, important for action, perception and consciousness. To this aim, we use different techniques from cognitive neuroscience, including psychophysics, fMRI, intracranial and scalp EEG recording, neuropsychology and neural network modeling to study the multisensory mechanisms underlying Body Representations (BR) and Peripersonal Space (PPS) in the human brain. This knowledge is applied to develop novel neurotechnology-based approaches, using e.g., virtual reality, robotics and brain machine inferfaces, to study and help patients suffering physical (e.g., amputees) or neurlogical (e.g., stroke) impariments.

Research interests
Thanks to his multidisciplinary group, Andrea Serino carries out research to unravel the neural and cognitive basis of body and self experience in space. MySpace Lab's approach combines basic research, translational work and novel neurotechnology solutions.

Scientific contributions in 2021-2022
> Discovering a novel form of interaction between the brain and the immune system, leading to the concept of Cognitive Immunity - funded by a SNSF Sinergia project.
> Investigating the neural bases of the sense of agency for brain machine interfaces.
> Validating novel combined clinical, computational and imaging tools to study body and space representations in healthy individuals, brain damaged and amputee patients.
> Describing a neurophysiological marker of multisensory integration within the Peripersonal Space (PPS) and assessing it during development (newborns), alterations (sleep and dreams) and disorders of (self-)consciousness.
> Developing, testing and implementing together in collaboration with neurotechnology companies, novel solutions for neurorehabilitation, leading to projects funded by innovation funds, such as the flagship Innosuisse Project SwissNeuroRehab.



Participants control a virtual hand through a Brain Computer Interface. Brain signals are translated to the movement of the virtual hand to study the sense of agency, i.e., the feeling of being in control of movements of our own body, a virtual body or a prosthesis.

Main publications in 2021-2022

Wilf M, Dupuis C, Nardo D, Huber D, Sander S, Al-Kaar J, Haroud M, Perrin H, Fornari E, Crottaz-Herbette S, **Serino A**. Virtual reality-based sensorimotor adaptation shapes subsequent spontaneous and naturalistic stimulus-driven brain activity. Cereb Cortex 2022 Oct 26:bhac407.

Bassolino M, Franza M, Guanziroli E, Sorrentino G, Canzoneri E, Colombo M, Crema A, Bertoni T, Mastria G, Vissani M, Sokolov AA, Micera S, Molteni F, Blanke O, **Serino A**. Body and peripersonal space representations in chronic stroke patients with upper limb motor deficits. Brain Commun. 2022 Aug 5; 4(4):fcac179.

Serino A, Bockbrader M, Bertoni T, Colachis Iv S, Solcà M, Dunlap C, Eipel K, Ganzer P, Annetta N, Sharma G, Orepic P, Friedenberg D, Sederberg P, Faivre N, Rezai A, Blanke O. Sense of agency for intracortical brain-machine interfaces. Nat Hum Behav. 2022 Apr; 6(4): 565-578.

Serino S, Trabanelli S, Jandus C, Fellrath J, Grivaz P, Paladino MP, **Serino A**. Sharpening of peripersonal space during the COVID-19 pandemic. Curr Biol. 2021 Jul 26; 31(14):R889-R890.

Akselrod M, Martuzzi R, van der Zwaag W, Blanke O, **Serino A**. Relation between palm and finger cortical representations in primary somatosensory cortex: A 7T fMRI study. Hum Brain Mapp. 2021 May; 42(7): 2262-2277.

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CHUV
www.chuv.ch/crn-myspace

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https://wp.unil.ch/myspacelab/

Unisciences
www.unil.ch/unisciences/andreaserino

Laboratory of Nerve-Muscle Unit - NMUL

Senior Lecturer Marie Théaudin
Neurologist
Head of the Laboratory of Nerve-Muscle Unit - NMUL
Laboratoire de l'unité nerf-muscle - LUNM
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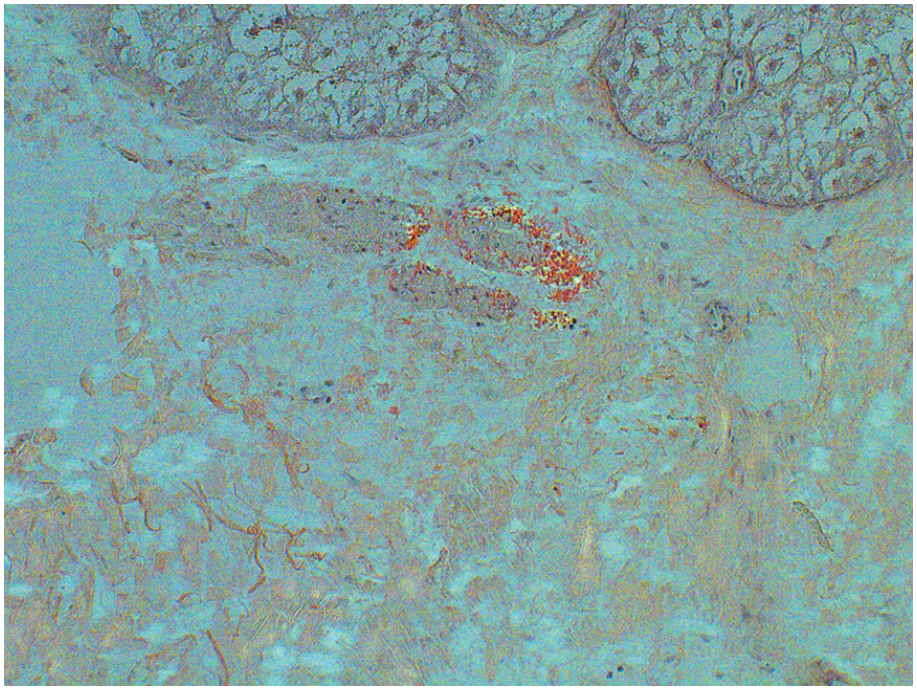
Affiliation
Service of neurology (NLG)

Keywords
Peripheral neuropathy
Hereditary amyloidosis
Neuroimmunology
Multiple sclerosis

Laboratory's activity
The Lab is specialized in studying characteristics of patients with hATTR amyloidosis, including MRI nerve studies and small nerve fiber quantification in the cornea. Other activities include studying gene expression from skin in inflammatory nerve or degenerative disorders.

Research interests
The research of Dr Marie Théaudin has 2 centers of interest:
> To describe characteristics of the Swiss hATTR patients and identify biomarkers of disease progression.
> To identify imaging biomarkers in multiple sclerosis and describe response to treatment in this disease.

Scientific contributions in 2021-2022
> Value of sNLF dosage in the follow-up of hATTR patients.
> Description of induced lymphopenia on dimethyl fumarate in MS.



Congo red positive amyloid deposits in a salivary gland biopsy.

Main publications in 2021-2022

Borrelli S, Mathias A, Goff GL, Pasquier RD, **Théaudin M**, Pot C. Delayed and recurrent dimethyl fumarate induced-lymphopenia in patients with multiple sclerosis. Mult Scler Relat Disord. 2022 Jul; 63:103887.

Papeix C, Castelnovo G, Leray E, Coustans M, Levy P, Visy JM, Kobelt G, Lamy F, Allaf B, Heintzmann F, Chouette I, Raponi E, Durand B, Grevat E, Kamar D, Debouverie M, Lebrun-Frenay C; Virgile Study Group. Long-Term Effectiveness, Safety and Tolerability of Fingolimod in Patients with Multiple Sclerosis in Real-World Treatment Settings in France: The VIRGILE Study. Neurol Ther. 2022 Jun; 11(2):633-658. Free PMC article.

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Théaudin M, Ochsner F, Adam C, Echaniz-Laguna A, Magy L, Fayolle D, Vicino A, Hübers A, Pereon Y. Small fiber neuropathy diagnosis. Rev Med Suisse 2022 Apr 27; 18(779):803-807.

Magy L, Echaniz-Laguna A, Fayolle D, Hübers A, Ochsner F, Vicino A, **Théaudin M**. What have we learned about chronic inflammatory demyelinating polyradiculoneuropathy in the last twenty years ? Rev Med Suisse 2022 Apr 27; 18(779):808-812. French.

Echaniz-Laguna A, Magy L, Vicino A, Fayolle D, Hübers A, Ochsner F, **Théaudin M**. Treating hereditary neuropathies: a dream come true ? Rev Med Suisse 2022 Apr 27; 18(779):813-816.

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CHUV
www.chuv.ch/crn-maladies-neuromusculaires

Unisciences
www.unil.ch/unisciences/marietheaudin

Neuroscience Research Center

Platforms Presentation

Magnetic Resonance Imaging Platform (MRI)

Assoc. Professor Bogdan Draganski, MD
Head of the MRI Platform

The MRI platform of the Department of Clinical Neurosciences, CHUV, was established in 2013 thanks to the generous support from the charitable foundations Roger De Spoelberg and Partridge. Pr Bogdan Draganski is the Director of the platform, the technical and methodological support is ensured by the expertise of LRENs Principal Investigators - Pr Antoine Lutti and Dr Ferah Kherif.

Equipment & Expertise
The platform consists of a high-end 3T MR system offering optimal signal-to-noise ratio, speed and stability, additionally to equipment for real-time assessment of study participants' behaviour during data acquisition.

Mission & Services
The mission of the MRI platform is to provide the needed research infrastructure for clinical and basic neuroscientists to study human brain structure and function relevant to health and disease.

LRENs MRI physics group offers in-house developed brain imaging acquisition sequences for optimal sensitivity in cross-sectional and longitudinal studies alongside a full range of customized protocols for assessment of brain anatomy and function. The support team includes an MRI engineer and experienced radiographer for optimal data acquisition.

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Electrophysiology Platform (EEG Platform)

Senior Lecturer Marzia De Lucia
Head of the EEG Platform

The EEG platform at the Department of Clinical Neuroscience (https://eegplatformdnc.com/) is coordinated by Dr Marzia De Lucia since November 2017. The platform supports collaborative initiatives for sharing available equipments and advanced techniques for the analysis of electroencephalography and stereo electroencephalography recordings in humans.

Equipment & Expertise
The Department of Clinical Neuroscience is equipped with several EEG systems hosted across different laboratories and research units. A non-comprehensive list of available equipments includes:
> 63 channels g.tec sytem (De Lucia's laboratory)
> 64 channels ANT (Démonet's laboratory)
> 128 channels g.tec system (Diserens' laboratory)
> 128 Micromed system for scalp and intracranial recordings (Ryvlin's lab and EEG unit)
> EG electrode digitizer - ANT xensor™ for electrode digitization with infrared camera (Ryvlin's lab and EEG unit).

Mission & Services
The mission of the EEG platforms are sharing a comprehensive set of user-friendly tools for the analysis of electrophysiological recordings (https://github.com/DNC-EEGplatform), providing support for designing and implementing EEG experiments, developing tools that can support the development of common scientific topics, promoting discussions about ongoing and future projects.

EEG platform website
https://eegplatformdnc.com/

EEG analysis repository
https://github.com/DNC-EEG-platform

Unisciences
www.unil.ch/unisciences/marziadelucia

Neuroscape Facility

Assoc. Professor Arseny Sokolov
Head of the Neuroscape Facility

The Neuroscape Facility implements serious video games for cognitive neurology, neuropsychology and neurorehabilitation. The Facility has been established in January 2018, is co-directed by Professors Arseny Sokolov and Andrea Serino, and located in the Pavillon 4 at the CHUV. The Facility is a founding member of the Neuroscape Alliance (https://neuroscape.ucsf.edu/alliance/), spear-headed by the Neuroscape Center at the University of California San Francisco.

Equipment & Expertise
The Neuroscape Facility is equipped with virtual reality devices, a driving simulator, an immersive giant screen, high-end computers, whole-body tracking and wearable physiological sensors. Research staff and collaborators consist of engineers, neuroscientists, neuropsychologists, physical therapists and neurologists with expertise in neurological rehabilitation.

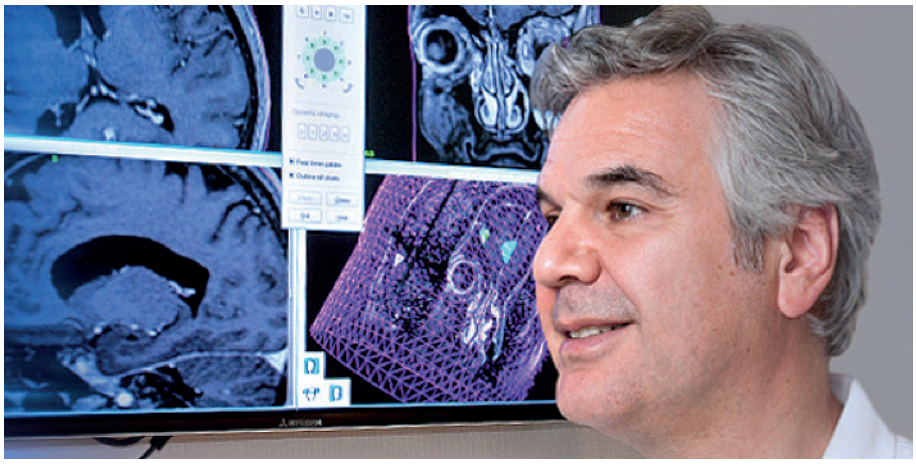
Mission & Services
The mission of the Neuroscape Facility is to design, assess, validate and implement novel gamified technological approaches for the assessment and rehabilitation of cognitive function and behavior in neurological patients. To this end, the Facility initiates projects itself, but is also available to colleagues interested in performing fundamental research or clinical trials using gamified and immersive technology for cognitive assessment and/or neurorehabilitation.

Unisciences
www.unil.ch/unisciences/arsenysokolov

https://neuroscape.ucsf.edu/alliance/

Gamma Knife Center

Professor Marc Levivier
Head of the Neurosurgery Service - Head of the Gamma Knife Center



In the 1960s, Swedish neurosurgeon Lars Leksell created the Gamma Knife, a technique to focus high dose radiation focused in intracranial targets with submillimeter accuracy. Gamma Knife is a radio-neurosurgical approach used as an alternative to open microsurgical procedures in many neurosurgical conditions, combining stereotactic image guidance with high-precision robotic beam delivery.

Equipment & Expertise
The Gamma Knife radio-neurosurgery platform was established in CHUV in June 2010. The first model used was Leksell Gamma Knife Perfexion. Since 2016, our hospital is equipped with the latest model, Leksell Gamma Knife ICON. The Gamma Knife Center is directed and coordinated by Professor Marc Levivier, who is the current President of the International Stereotactic Radiosurgery Society.

Mission & Services
Gamma Knife radio-neurosurgery is an ambulatory procedure, which includes frame attachment or mask immobilisation (allowing for hypo-fractionated procedures), acquisition of imaging, target determination and further treatment planning, stereotactic radiation and clinical and radiological follow-up. The clinical applications of Gamma Knife radio-neurosurgery include benign and malignant conditions of the brain and skull-base, vascular malformations and functional procedures. Our Gamma Knife Center serves as a source for clinical and translational research. During the past 12 years, more than 130 peer-reviewed papers have been published. Internal collaborations are primarily with the Neuroradiology, Radiotherapy or ENT departments, as well as with EPFL (Prof. Jean-Philippe Thiran, Prof. Van de Ville). International collaborations include the CHU Timone in Marseille (France), Oxford University (United Kingdom), and Roger Salengro Hospital in Lille (France). Numerous prizes have rewarded our projects, including, among others, the Excellence Prize of the University of Lausanne in 2019 (Dr Tuleasca, PD&MERc for his MD-PhD project related to the radiobiology of radiosurgical thalamotomy for tremor).

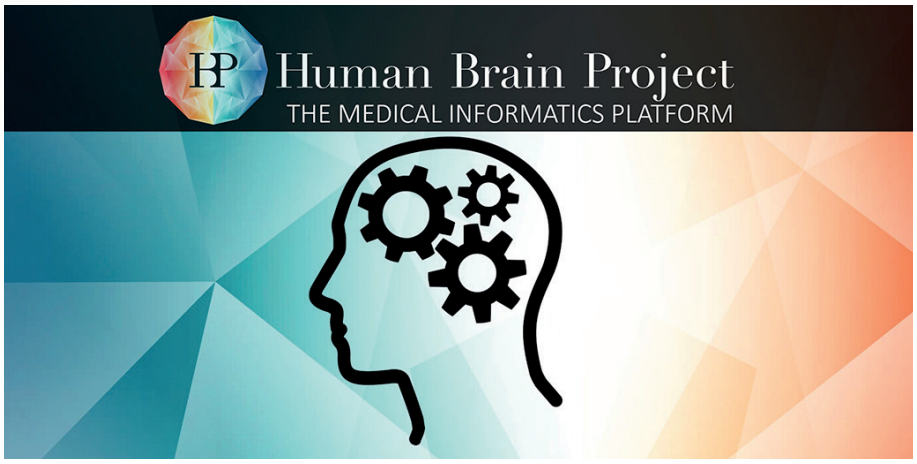
CHUV
www.chuv.ch/gamma-knife

Unisciences
www.unil.ch/unisciences/marclevivier

https://www.isrsy.org/en/

Medical Informatics Platform of HBP (Subproject 8)

Professor Philippe Ryvlin
Head of the Medical Informatics Platform of HBP



The Medical Informatics Platform (MIP) is a digital platform dedicated to the federation and federated analyses of health datasets distributed across different institutions and countries. It enables sharing such data without requiring individual data to be moved away from their original site of storage and being centralized. The MIP web-based front-end provides a user-friendly interface to launch queries that will be executed on the data in each participating hospital on their federated datasets, simultaneously, to retrieve and aggregate the findings. Thanks to this framework, the MIP offers an ideal solution to federate de-centralised data and develop novel predictive models, while ensuring data privacy and GDPR compliance. Anonymised data of any research area of interest can be analysed with the MIP.

Equipment & Expertise
The MIP is an open-source free-of-use software, developed within the framework of the Human Brain Project (HBP), which is currently installed in more than 40 European Hospitals, and used to run health data federations in the fields of dementia, traumatic brain injury, epilepsy, mental health and soon on stroke. Platform activities are supported by an IT and data management team.

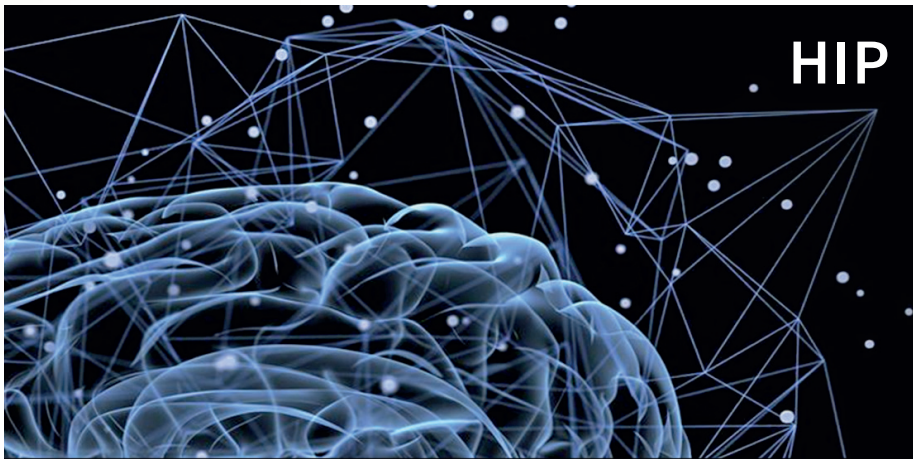
Mission & Services
The MIP team @ NeuroTech, with Prof. Ryvlin being the product owner of the MIP, is committed to help health stakeholders federating new datasets and creating new federations on any topics of interest. This is particularly relevant for DNC researchers who would like to develop ambitious data sharing projects in their field of interest or to participate in ongoing federations.
We aim at promoting the development and validation of predictive models in clinical neurosciences, including for rare diseases.

CHUV
https://www.chuv.ch/fr/neurosciences/dnc-home/recherche/human-brain-project

MIP
https://ebrains.eu/service/medical-informatics-platform

Human Intracerebral EEG Platform (HIP)

Professor Philippe Ryvlin
Head of the Human Intracerebral EEG Platform (HIP)



The Human Intracerebral EEG Platform (HIP) is a digital platform dedicated to the collection, storage, sharing and analysis of Human intracerebral EEG data recorded from patients with drug resistant epilepsy undergoing pre-surgical evaluation using stereo-EEG (SEEG). It provides unique facilities to transfer such data from hospitals to the HIP, convert EEG files into BIDS-SEEG format, access workflows to precisely locate each recording SEEG contact on patient's MRI, and run state-of-the-art SEEG analytical tools. **73** European, Asian and Australian centers have committed to share SEEG data on HIP, representing up to **1000 patients per year**. Such data are being used to investigate scientific issues in the fields of epilepsy but also cognition at large.

Equipment & Expertise
The HIP is being developed by the NeuroTech team within the framework of the Human Brain Project (HBP). In September 2022, a HIP closed-beta version was opened to 10 European Health Centers for exploration and testing of the provided functionalities. The platform is supported by an IT and scientific team.

Mission & Services
The HIP team @ NeuroTech is committed to promote the usage of the HIP by investigators interested in using SEEG data for epilepsy or cognition-driven research. In particular, novel cognitive paradigms are welcome to enrich the list of research protocols run by the HIP consortium.

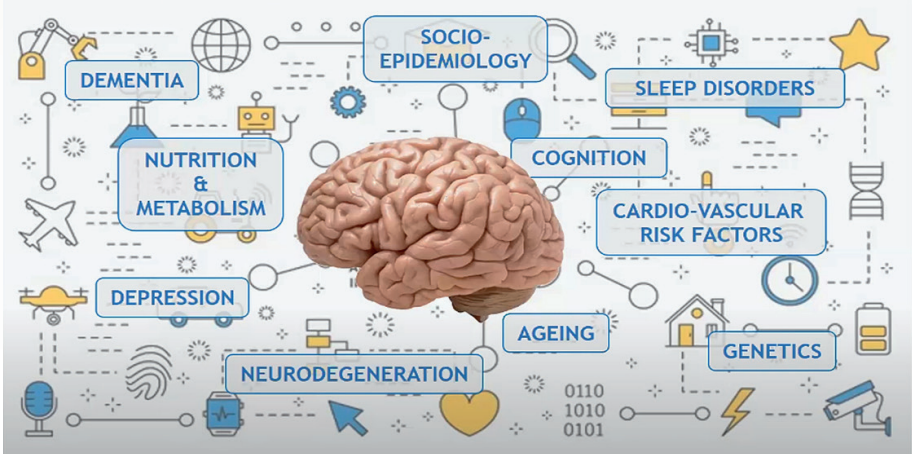
CHUV
https://www.chuv.ch/fr/neurosciences/dnc-home/recherche/human-brain-project

HIP
https://www.humanbrainproject.eu/en/science-development/focus-areas/medical-data-analytics/

https://hip-infrastructure.github.io/build/html/index.html

BrainSystem: integrated redcap and datascience

Senior Lecturer Ferath Kherif
Head of the BrainSystem Platform



The platform was first developed and installed in 2010 by PI F. Kherif for the Stroke Study and Neuro-Geno Project with charitable support from Pharnext. With the help of Pharnext, the platform was expanded in 2011 to provide free access and support to researchers at CHUV and other institutions. There are currently more than 80 projects and 250 active users. Unlike other RedCap instances at the CHUV, we offer free support and extended services beyond data collection, including all the tools needed for a neuroscience project (metadata, collection, curation and analysis).

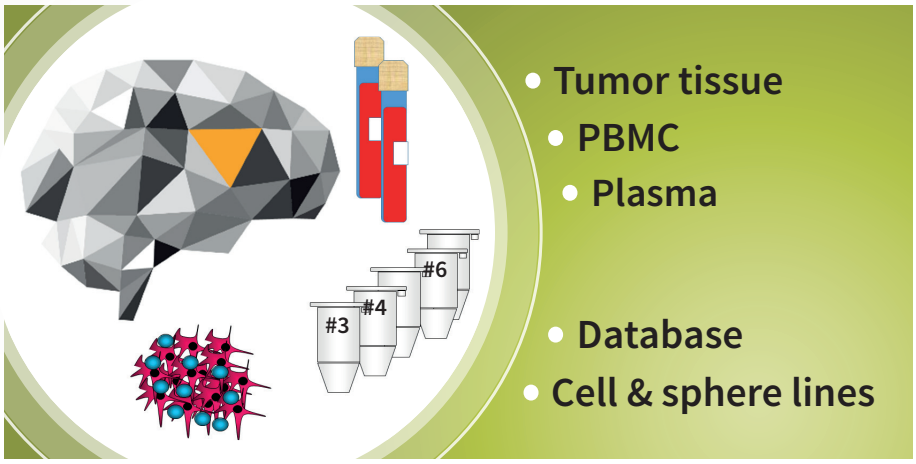
Equipment & Expertise
Brainsystem is a web-based platform with tools and resources for neuroscience projects, including REDCap and custom-built science platforms. By using the Redcap platform, users can create and manage online surveys and databases, and the data science component streamlines the process of designing AI-based neuroscience project. F. Kherif oversees user and data management, surveys and statistics, and AI experiments for the platform. He is supported by an IT technician.

Mission & Services
Users' management, data capture projects, APIs for loading data, data curation, data science tools (descriptive of advanced statistical or AI-based techniques).

CHUV
https://lren.chuv.ch/redcap/

Brain Tumor Biobank Platform

Professor Monika E. Hegi
Head of the Brain Tumor Biobank Platform



The Brain Tumor Bank of the Laboratory of Brain Tumor Biology and Genetics (LBGT) and the Service of Neurosurgery is a prospective collection of brain and spine tumor samples associated with a clinical database since 1983. It is directed and coordinated by Prof. Monika Hegi and is located at the CHUV campus in Epalinges (CLE). The BTbiobank of the LBGT is accredited by the CHUV (BB_031_BBLBGT), has received the certificate VITA from the Swiss Biobanking Platform, and has been approved by the local ethics committee (CER-VD, F25/99).

Biobank & Expertise
The BT-biobanque of the LBGT comprises over 5100 entries and represents a valuable research tool of the Brain and Spine Tumor Center of the CHUV. This prospective collection comprises brain and spine tumors operated by the service of neurosurgery and the spine center at the CHUV, and corresponding blood samples (PBMC and plasma), with informed consent of the patients. For a subset of the patients, CSF is available. A panel of glioblastoma derived cell-lines and/or sphere lines (isolated and kept under stem cell conditions) have been established and characterized. Research staff consists of biologists with expertise in experimental neuro-oncology (*in vitro* and *in vivo*) and molecular biology, and a biostatistician/bioinformatician with expertise in multi-OMICS data analyses.

Mission & Services
The BB serves as resource for translational and basic research projects within the institution, shares resources in local and international academic collaborations, and collects tissue for translational research in clinical trials.
> Resource to study different molecular aspects of brain tumor biology and (epi-)genetics in association with the clinical course and response to therapy, including, but not limited to, interaction with the immune system.
> Biomarker development (diagnostic, predictive).
> Target discovery for novel treatments.

Neuroscience Research Center

Centre de recherche en neurosciences, CHUV

Prof. Nicole Déglon, Head of CRN

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Lausanne, avril 2023

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