Department of Clinical Neurosciences

Neuroscience Research Center 2017-2018 Presentation

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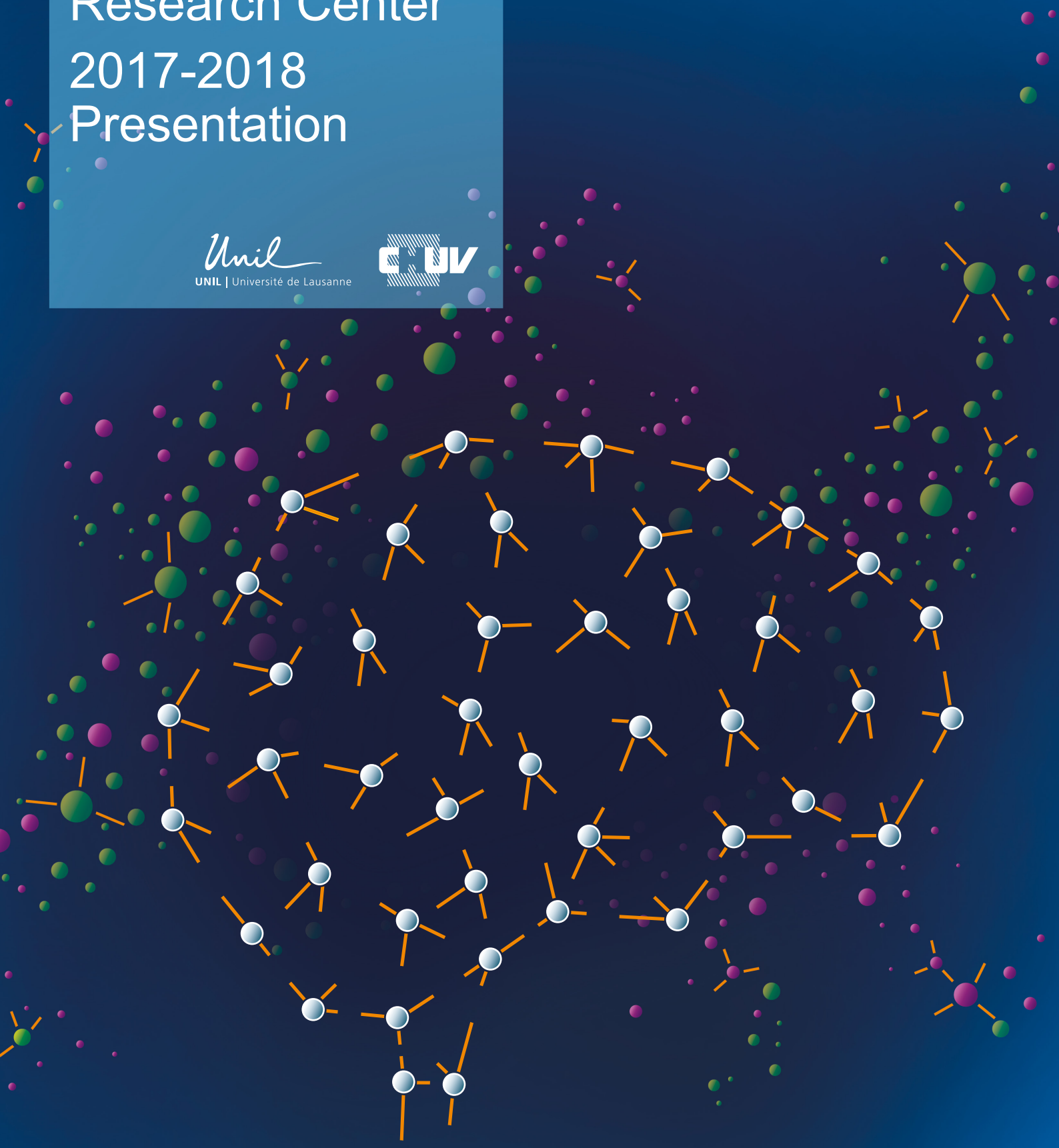

Neuroscience Research Center
2017-2018 Presentation

Content

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Foreword 2017-2018

Excellence

The last two years marked a very successful period for the Neuroscience Research Center (CRN). The excellence of CRN research is highlighted with the opening of the MySpace laboratory of Andrea Serino funded by a Prof. Boursier FNRS grant, the Leenards 2017 Foundation Translational Medical Research Award received by Prof. Pot, the Leenards 2017 Emerging Clinician Award and the Baasch-Medicus Foundation Award received by Dr Sokolov, the Leenards Foundation's award 2018 received by Prof. Draganski, and the Ambizione grant awarded to Dr Eduardo Martin Moraud.

The ever-increasing involvement of CRN members in research projects resulted in numerous funds obtained from the Swiss National Science Foundation, the Horizon2020 EU programs as well as several high impact publications (Table 1), among which, the groundbreaking work on spinal cord injury lead by Prof. Courtine, EPFL in collaboration with Prof. Bloch (STIMO project), CHUV, showing the impressive motor recovery following electrical stimulation of the spinal cord and physical therapy.

Dr Jocelyne Bloch and Andrea Rossetti are to be congratulated for their appointment to the rank of Associate Professors, Prof. Monika Hegi for her promotion to full Professor, Antoine Lutti for his appointment as Assistant Prof. PTC, Prof. Renaud Du Pasquier for his nomination as director of the School of Postgraduate and Continuing Education and finally the election of Prof. Draganski as member of the Faculty Council.

A growing community

New initiatives are underway to ensure optimal environment for state-of-the-art neuroscience research of the faculty members and principal investigators. The SUN project (Service Universitaire de Neuroréhabilitation) will bring together the Service of Neuropsychology and Neurorehabilitation of the CHUV and the Neural Rehabilitation Sector of Lavigny Institution. The governance for the research activities has been established in 2018. The new center proposed initiatives to develop a culture of collaboration which has led to the launch 3 joint projects. In addition, new spaces dedicated to CRN activities as well as the Neurotech, STIMO and Human brain projects have been obtained at Pavillon 4 and Biopôle 3 (300 m^2).

The CRN is pursuing its efforts to share expertise and better mutualize equipment with the development of clinical and research platforms. After the initial development of the Imaging platform (Prof. Bogdan Draganski), the Gamma Knife platform (Dr Marc Levivier), this year, we have seen the implementation of an EEG platform led by Dr Marzia De Lucia, and Neuroscape led by Dr Arseny Sokolov, aiming at sharing the latest innovative advances in electrophysiological projects and implementing novel gamified technological approaches in the department.

To continue the structuration of the research activities, we have seen the creation of the laboratory of epileptology and acute disorders of consciousness, bringing together the activities of Prof. Ryvlin, Rossetti and Dr Novy (LETC). The creation of the laboratory MySpace led by Prof. Serino. The development of the Neuroimmunology Laboratory (LNIS) co-led by Prof. du Pasquier and Prof. Caroline Pot. The integration of Dr Michel's activities into the Cerebrovascular Disease Laboratory (Prof. Hirt, Dr Michel). The integration of the activities of Prof. Bloch and Dr Tenenbaum into the Neurotherapies and Neuromodulation Laboratory (LNTM; Prof. Déglon).

Mission
The mission of the Neuroscience Research Center (CRN) is to promote patient-oriented, interdisciplinary neuroscience research, to strengthen collaborations, partnerships and training, to improve international visibility, to facilitate interactions with basic biomedical and clinical researchers and therefore favor translation of scientific knowledge to clinical practice.

The center is taking advantage of the unique environment at the Lausanne University Hospital (CHUV) as well as major academic institutions in the Lemanic area. Its portfolio offers a large set of platforms and expertise to tackle mechanisms involved in diseases of the central and peripheral nervous system.

The CRN is hosting 12 laboratories, encompassing more than hundred collaborators (>75 FTE). The CRN members are implicated in large national and international initiatives, reflected by >5 millions funding/year.

Table 1: CRN 2014-2018 bibliometric analysis

Publications (WOS)	693
Publications with citations	80,5 %
Number of citations	8378
Citation impact (Average (mean) number of citations/paper)	12
Normalized Citation Impact[1]	1,86
Documents in Top 1%	3,89 %
Documents in Top 10%	22,65 %
International Collaborations	68,97 %
Industry Collaborations	4,90 %

[1]: Citation impact (citations per paper) normalized for subject, year and document type, >1= performance above world average.

Additional information

CHUV
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DNC
www.chuv.ch/neurosciences/en/dnc_home.htm

Uniscience CRN
www.unil.ch/unisciences/crn

Contact
Neuroscience Research Center (CRN)
info.crn@chuv.ch

Neuroscience Research Center

Laboratories Presentation

Laboratory of Clinical Neurophysiology and non-Invasive Brain Stimulation

Senior Lecturer David Benninger, MD
Consultant/attending physician
Head of the Laboratory of Clinical Neurophysiology and non-Invasive Brain Stimulation
Laboratoire de neurophysiologie clinique, stimulation cérébrale et motricité
david.benninger@chuv.ch

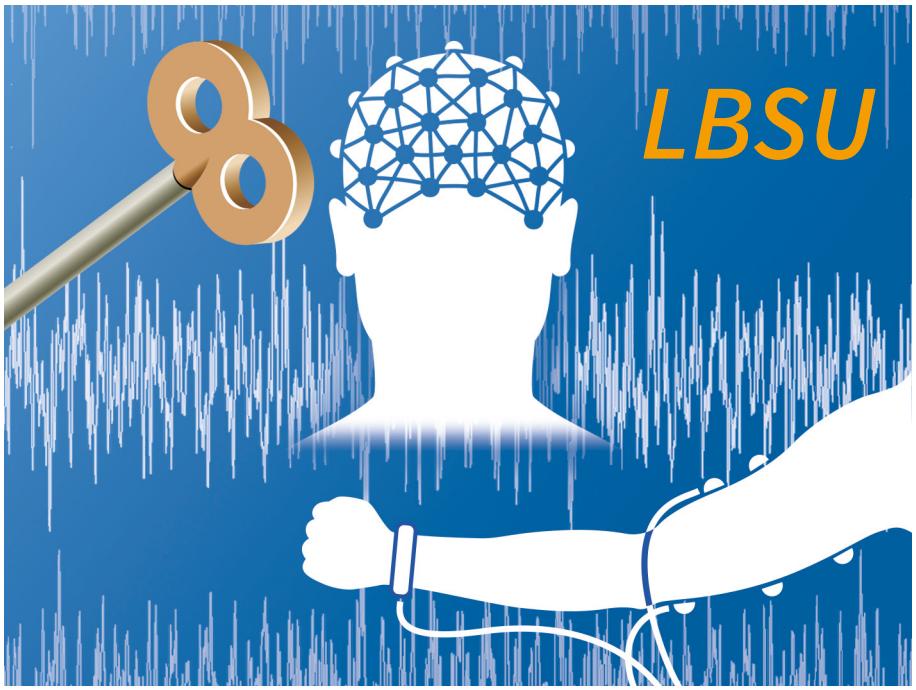
Affiliation
Service of neurology (NLG)

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

Laboratory's activity
> Randomized controlled therapeutic clinical trial on tDCS for the treatment of the freezing of gait in Parkinson's disease.
> Investigation of the contribution of the cerebellum in rest tremor in Parkinson's disease with TMs.
> 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.
> Investigation of motor fatigue with triple stimulation technique.

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 2017-2018
> European Guidelines on Therapeutic Application of Non-invasive Brain Stimulation (rTMS, tDCS).
> Cerebellar stimulation for Parkinson tremor.
> Combined tDCS-behaviour therapy study for freezing of gait in PD.
> CRPS with dystonia.
> Cervical dystonia: contribution of cerebellar dysfunction.



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 2017-2018

Zito GA, Gerber SM, Urwyler P, Shamsollahi J, Pal N, Stephan M, Tarnanas I, Nef T and **Benninger DH**. Development and Pilot Testing of a Novel Electromechanical Device to Measure Wrist Rigidity in Parkinson's Disease. Conf Proc IEEE Eng Med Biol Soc. 2018 Jul; 2018:4885-4888.

Lefaucheur JP, André-Obadia N, Antal A, Ayache SS, Baeken C, **Benninger DH**, *et al*. Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS). Update 2018. in revision for Clin Neurophysiol.

Caranzano L, Stephan M, Herrmann FR, **Benninger DH**. De-synchronization does not contribute to intra-cortical inhibition and facilitation: a paired-pulse paradigm study combined with the triple stimulation technique. J Neurophysiol. 2017.1; 117(3):1052-1056.

Lefaucheur JF, André-Obadia N, Antal A, Ayache SS, Baeken C, **Benninger DH**, *et al*. Evidence-based guidelines on the therapeutic use of transcranial direct current stimulation (tDCS). Clin Neurophysiol. 2017; 128(1):56-92.

ORCID number: 0000-0002-1049-9533

CHUV

www.chuv.ch/crn-neurophysiologie-clinique

Unisciences

www.unil.ch/unisciences/davidbenninger

Laboratory of Cognitive Science

Professor Stephanie Clarke, Head of the laboratory
Professor Brigitte Schurch, Head of the Neurourology Unit

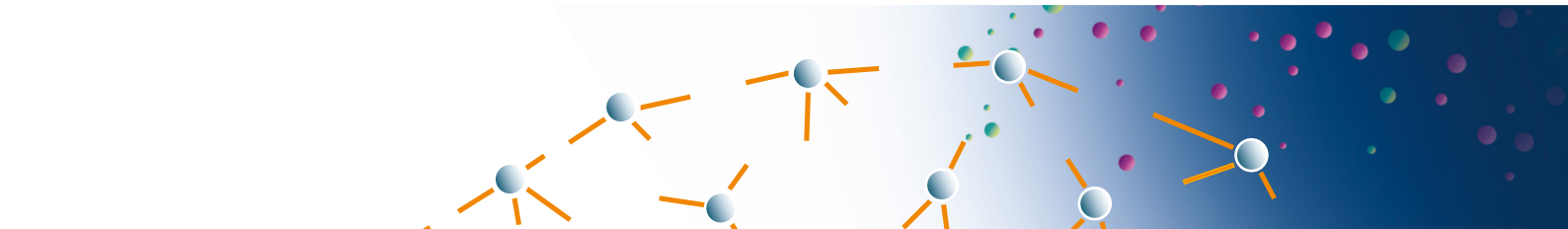
Laboratory's activity

The laboratory works at the interface between clinical neurorehabilitation and basic cognitive neuroscience. Understanding neural mechanisms, which underlie recovery after brain lesion, helps to design innovative therapeutic interventions and to apply them in clinical care. The four principle investigators, Dr Sonia Crottaz-Herbette, Dr Stefano Carda, Dr Jean-Michel Pignat and Prof. Stephanie Clarke, focus on:

> Auditory cognition, investigating representations of sounds, including spatial and temporal aspects, using psychophysical approaches as well as fMRI and EEG. Understanding auditory cognition gives a valuable insight in speech as well as attentional and spatial processing and helps to design new rehabilitation strategies.

> Effects of brief therapeutic interventions and in particular of prismatic adaptation on brain organization, using behavioural and fMRI in normal subjects and in patients with brain damage. These innovative investigations of neural mechanisms underlying therapeutic interventions are essential for their focussed use in clinical practice.

> Neuro-motor rehabilitation, with focus on robotics, brain-machine interfaces and optimization of spasticity care. Carried out with numerous national and international collaborations, this research focuses mainly on hand movement and gait.



Laboratory of Cognitive Science

Professor Stephanie Clarke
Head of the Neuropsychology and Neurorehabilitation Service
Head of the Laboratory of Cognitive Science
Laboratoire des sciences cognitives
stephanie.clarke@chuv.ch

Affiliation
Service of neuropsychology
and neurorehabilitation (NPR)

Keywords
Cognitive functions
Neural plasticity
Recovery from brain lesions
Neuropsychology
Auditory cognition
Cerebral cortex

Laboratory's activity

The laboratory pursues three lines of research to investigate plasticity, which underlies the effectiveness of brief therapeutic interventions in cognitive rehabilitation.

> "Sound objects in space and time", SNSF grant 159708 to S. Clarke (2015-19; CHF834'000) investigates combined representations of sound meaning, location and temporal features, using psychophysical approaches, fMRI and EEG. Understanding how semantic representations are linked to the spatial or temporal characteristics of an object will provide insight into multisensory and object-related representations of space.

> Dr. Sonia Crottaz-Herbette investigates the impacts of brief therapeutic interventions on recovery of cognitive functions using fMRI. After her topical studies on the effect of prismatic adaptation in neglect, she addresses the mechanisms of working memory recovery.

> Dr. Stefano Carda investigates the effects of electrically-assisted movement therapy on motor control of patients with severe upper limb paralysis. He is further involved in a project using fMRI to determine neural substrates of upper limb recovery using this treatment.

A better understanding of the neural mechanisms underlying these effects is likely to focus indications for specific rehabilitation programs and help to design new therapies.

Research interests

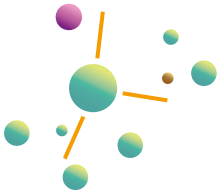
Stephanie Clarke, Sonia Crottaz-Herbette and Stefano Carda investigate cognitive and motor functions in normal subjects and in brain-damaged patients, with particular interest in the organisation and plasticity of the human auditory and motor cortices.

Scientific contributions in 2017-2018

In addition to the dorsal and ventral auditory streams, sounds are encoded in a third, lateral stream, which we investigated. It originates within early-stage auditory areas where the combination of specific objects meaning and position are encoded. Its later stages are left-dominant and underlie implicit uses of spatial cues, in contrast to the right-dominant dorsal stream supporting explicit sound localization.

A brief exposure to rightward prism adaptation switches hemispheric dominance of the ventral attentional system from the right to the left hemisphere, contributing to the alleviation of left neglect. Based on this understanding, responders to this treatment can be identified. We showed that a brief exposure to leftward prism adaptation enhances right hemispheric dominance within the ventral attentional system. In patients with left stroke it may prove useful in treating lateralized and non-lateralized attentional deficits.

Severe chronic upper limb paresis recovered significantly through a 2-week electrically assisted movement therapy, which was controlled by the patient's unaffected hand. Responders to the treatment continued to improve during the follow-up, suggesting that the brief intervention lead to a reorganization of the motor system.



Main publications in 2017-2018

Da Costa S, **Clarke S**, Crottaz-Herbette S. Keeping track of sound objects in space: the contribution of early-stage auditory areas. Hearing Research. 2018; 366:17-31.

Crottaz-Herbette S, Fornari E, Tissieres I, **Clarke S**. A brief exposure to leftward prismatic adaptation enhances the representation of the ipsilateral, right visual field in the right inferior parietal lobule. eNeuro. 2017. DOI: 10.1523/ENEURO.0310-17.

Crottaz-Herbette S, Fornari E, Notter MP, Bindschaedler C, Manzoni L, **Clarke S**. Reshaping the brain after stroke: The effect of prismatic adaptation in patients with right brain damage. Neuropsychologia. 2017; 104: 54-63.

Tissieres I, Elamly M, **Clarke S**, Crottaz-Herbette S. For better or worse: The effect of prismatic adaptation on auditory neglect. Neural Plasticity, Volume 2017, Article ID 8721240.

Tissieres I, Fornari E, **Clarke S**, Crottaz-Herbette S. Supramodal effect of rightward prismatic adaptation on spatial representation within the ventral attentional system. Brain Structure and Function. 2017, epub.

Carda S, Biasiucci A, Maesani A, Ionta S, Montcharmont J, **Clarke S**, Murray MM, Milan JD. Electrically assisted movement therapy in chronic stroke patients with severe upper limb paresis: A pilot, single-blind, randomized crossover study. Archives of Physical Medicine and Rehabilitation. 2017; 98: 1628-1635.

ORCID number: 0000-0001-9393-5718

CHUV

www.chuv.ch/crn-sciences-cognitives

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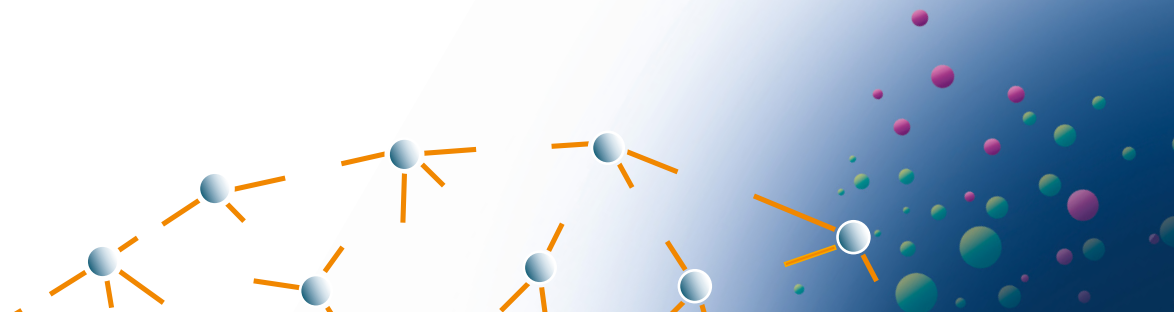
http://wp.unil.ch/lsc/en/

Unisciences

www.unil.ch/unisciences/stephanieclarkehosek



Laboratory of Cognitive Science

Professor Brigitte Schurch
Head of the Neurourology Unit
Laboratory of Cognitive Science
Laboratoire des sciences cognitives
brigitte.schurch@chuv.ch

Affiliation
Service of neuropsychology and neurorehabilitation (NPR)

Keywords
Neurourology
Neurogenic bladder
Urodynamic
Botulinum toxin
Sacral neuromodulation
Brain imaging
Neural plasticity
Spinal cord injury
Multiple sclerosis
Parkinson

Laboratory's activity

The Neurourology center in CHUV has been created in May 2012, after the arrival of Prof. Brigitte Schurch, who was nominated to achieve this task and on a regular basis treat. The Neurourology center is a co-venture between the Department of Urology and the Department of Neuroscience.

It takes care of patients with a large spectrum of non-neurogenic and neurogenic urological conditions.

Nature of referrals can be very diverse and the neuro-urological diagnosis involve complex instrumental evaluations with the aim of identifying optimal treatment for each patient. Around 1000 patients are evaluated per year.

Research interests

The research activity is an integrated part of the Neuro-urology center usual activities.

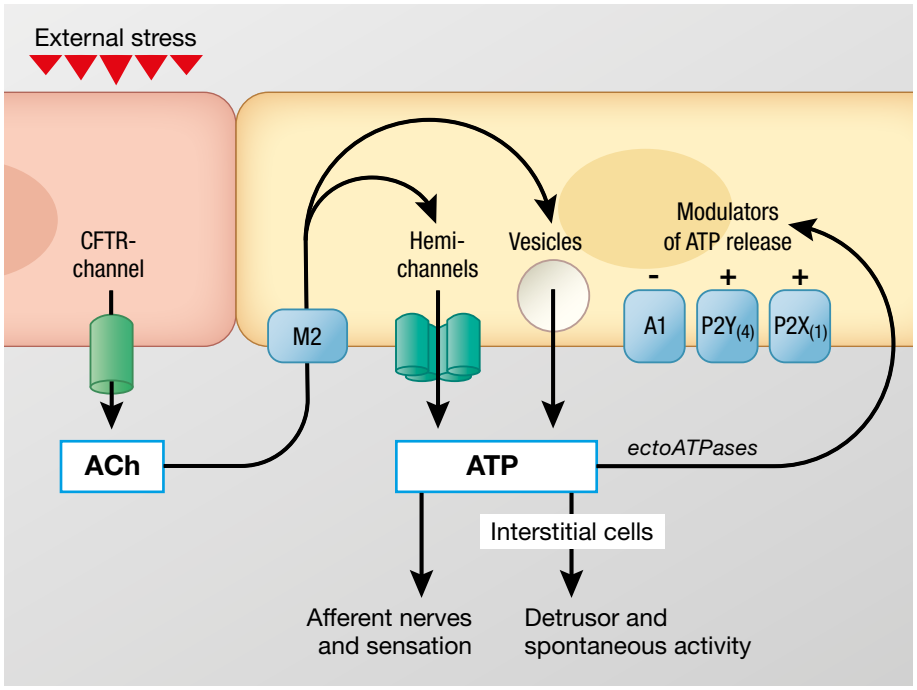
The research activity is divided into two main categories:
> Clinical: in partnership with all the units of the Department of Neuroscience (Neurology, Neurorehabilitation, Neurosurgery as well as with the Department of Urology, the Department of Interventional Radiology, the Department of Internal Medicine (Geriatrics Unit) in CHUV, but also with other university hospitals, including those from Zurich, Marseille, Paris, Montreal and London.
> Fundamental: mainly in partnership with the Swiss Federal Institute of Technology, EPFL, Prof. Courtine.

Our clinical research focuses on the study of new therapies used in the management of voiding disorders and their clinical outcomes. Assessing functional reorganization of the spine and the brain after lesions of the spinal cord is another of our centers of interest. In collaboration with the University of Paris, the Internal Continence Society and the European Board of Rehabilitation we are currently working in a full program of basic educational videos dedicated to rehabilitation physicians. The aim of this task is to provide high quality courses based on evidence based medicine to all rehabilitation physicians interested in neurogenic lower urinary tract diseases or having patients who suffer from neurogenic pelvic disorders. The complete diagnostic instrumentation as well as therapeutic armamentarium will be taught.

Our fundamental research focuses on the study of structural and functional change of the spinal cord and brain after peripheral nerves and spinal cord stimulation.
In collaboration with the Internal Consultation on Incontinence, we are also researching on the mechanism of action of botulinum toxin A and sacral nerve stimulation in the treatment of overactive bladder/detrusor overactivity as well as interstitial cystitis.

Scientific contributions in 2017-2018

> Progress in research in different fields leading to 12 publications.
> Obtained four industry grants with national and international collaborations.
> One person obtained a Lemanic Neuroscience PhD in the lab.
> Established a large retrospective urodynamic database.
> Several invitations for lectures and symposia, both national and international.



Proposed pathways for stretch-evoked urothelial ATP and acetylcholine (ACh) release according to current experimental data. ACh is importantly (but not exclusively) released via CFTR channels under much lower stresses compared to ATP release. ATP release is increased by muscarinic (M2) receptor activation via routes that include vesicular exocytosis and through connexion hemichannels. ATP may than exert autocrine effects, either directly or via its breakdown products from ectoATPase activity, through purinergic (P2Y or P2X receptors) or adenosine (A1) receptors to modulate further ATP release. ATP may also signal to sensory nerves or interstitial cells in the suburothelium, or even directly to detrusor myocytes.

Main publications in 2017-2018

Wagner FB, Mignardot JB, Le Goff-Mignardot CG, Demesmaeker R, Komi S, Capogrosso M, Rowald A, Seáñez I, Caban M, Pirondini E, Vat M, McCracken LA, Heimgartner R, Fodor I, Watrin A, Seguin P, Paoles E, Van Den Keybus K, Eberle G, **Schurch B**, Pralong E, Becce F, Prior J, Buse N, Buschman R, Neufeld E, Kuster N, Carda S, von Zitzewitz J, Delattre V, Denison T, Lambert H, Minassian K, Bloch J, Courtine G. Targeted neurotechnology restores walking in humans with spinal cord injury. Nature 2018 Nov; 563(7729):65-71.

Peyronnet B, Even A, Capon G, De Seze M, Hascoet J, Biardeau X, Baron M, Perrouin-Verbe MA, Boutin JM, Saussine C, Phé V, Lenormand L, Chartier-Kastler E, Cornu JN, Karsenty G, Manunta A, **Schurch B**, Denys P, Amarenco G, Game X; GENULF and the AFU Committee of NeuroUrology. Intradetrusor Injections of Botulinum Toxin A in Adults with Spinal Dysraphism. J Urol. 2018 Oct; 200(4):875-880.

Malde S, Fry C, **Schurch B**, Marcelissen T, Averbeck M, Digesu A, Sahai A. What is the exact working mechanism of botulinum toxin A and sacral nerve stimulation in the treatment of overactive bladder/detrusor overactivity? ICI-RS 2017. Neurourol Urodyn. 2018 Jun; 37(S4):S108-S11.

Rahnama'i MS, Marcelissen T, Apostolidis A, Veit-Rubin N, **Schurch B**, Cardozo L, Dmochowski R. The efficacy of botulinum toxin A and sacral neuromodulation in the management of interstitial cystitis (IC)/bladder pain syndrome (BPS), what do we know? ICI-RS 2017 think thank, Bristol. Neurourol Urodyn. 2018 Jun; 37(S4):S99-S107.

Gajewski JB, **Schurch B**, Hamid R, Averbeck M, Sakakibara R, Agrò EF, Dickinson T, Payne CK, Drake MJ, Haylen BT. An International Continence Society (ICS) report on the terminology for adult neurogenic lower urinary tract dysfunction (ANLUTD). Neurourol Urodyn. 2018 Mar; 37(3):1152-1161.

Schurch B, Iacovelli V, Averbeck MA, Stefano C, Altaweel W, Finazzi Agrò E. Urodynamics in patients with spinal cord injury: A clinical review and best practice paper by a working group of The International Continence Society Urodynamics Committee. Neurourol Urodyn. 2018 Feb; 37(2):581-591.

Rahnama'i MS, Marcelissen TAT, Brierley B, **Schurch B**, de Vries P. Long-term compliance and results of intravesical botulinum toxin A injections in male patients. Neurourol Urodyn. 2017 Sep; 36(7):1855-1859.

Mignardot JB, Le Goff CG, van den Brand R, Capogrosso M, Fumeaux N, Vallery H, Anil S, Lanini J, Fodor I, Eberle G, Ijspeert A, **Schurch B**, Curt A, Carda S, Bloch J, von Zitzewitz J, Courtine G. A multidirectional gravity-assist algorithm that enhances locomotor control in patients with stroke or spinal cord injury. Sci Transl Med. 2017; Jul 19;9(399).

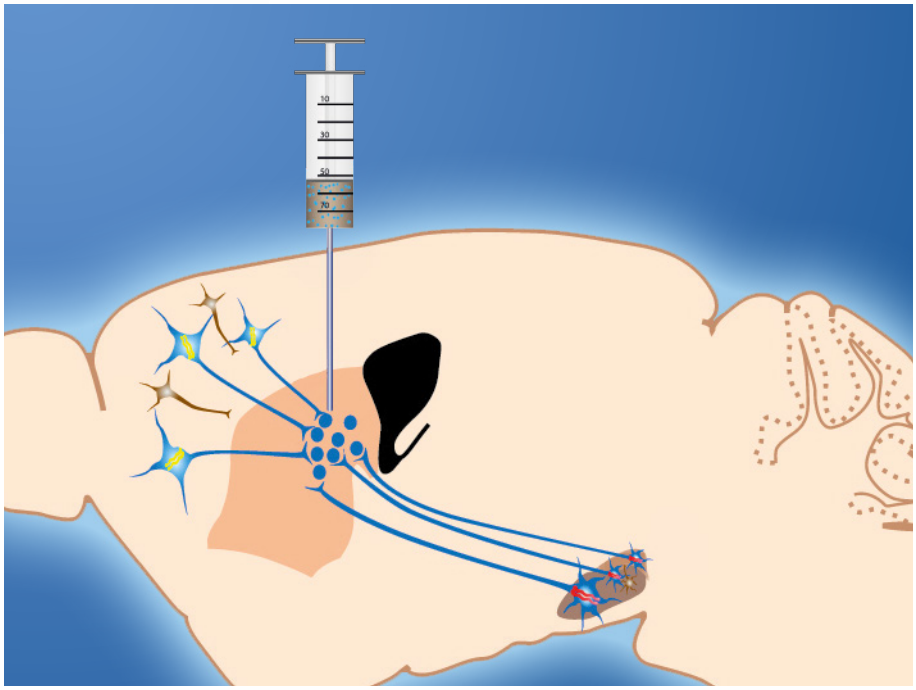
ORCID number: 0000-0003-4965-6898

Unisciences

www.unil.ch/unisciences/brigitteschurch

Laboratory of Neurotherapies and Neuromodulation LNTM

Assoc. Professor Nicole Déglon, Head of laboratory
Assoc. Professor Jocelyne Bloch
Senior Lecturer Liliane Tenenbaum



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

> Brain and spinal cord interface and stimulation.
> Autologous cell transplantation for stroke, Parkinson's disease and spinal cord injury.
> Modulation of neuroinflammation and drug-inducible gene therapy of Parkinson's disease.
> Underlying molecular and environmenental mechanisms in Huntington's disease (HD).
> Pre-clinical development of molecular therapies for Huntington's disease (HTT gene editing).

Laboratory of Neurotherapies and Neuromodulation LNTM

Assoc. Professor Nicole Déglon
Head of laboratory, Head of CRN

Head of the Laboratory of Neurotherapies and Neuromodulation - LNTM
Laboratoire de neurothérapies et neuromodulation - LNTM
nicole.deglon@chuv.ch

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 huntingtin (HTT) gene editing for Huntington's disease (HD). We have been exploiting the unique features and targeting specificities of viral vectors to deliver therapeutic candidates, generate new models of CNS pathologies or improve our understanding of the pathological mechanisms. In parallel, we are taking advantage of local and cell-type specific overexpression of transgenes in the CNS to investigate spreading of wild-type Tau protein in sporadic tauopathies as well as the contribution of mitochondrial dysfunctions in early AD.

Research interests
The group has a long-standing experience and expertise in viral gene transfer technology to deliver therapeutic candidates in the brain or to model CNS pathologies by overexpressing disease-causing proteins.

Scientific contributions in 2017-2018
Development a self-inactivating CRISPR/Cas9 system for HTT gene editing. We showed that mutant huntingtin was efficiently inactivated in mouse models of HD, leading to an improvement in key markers of the disease.

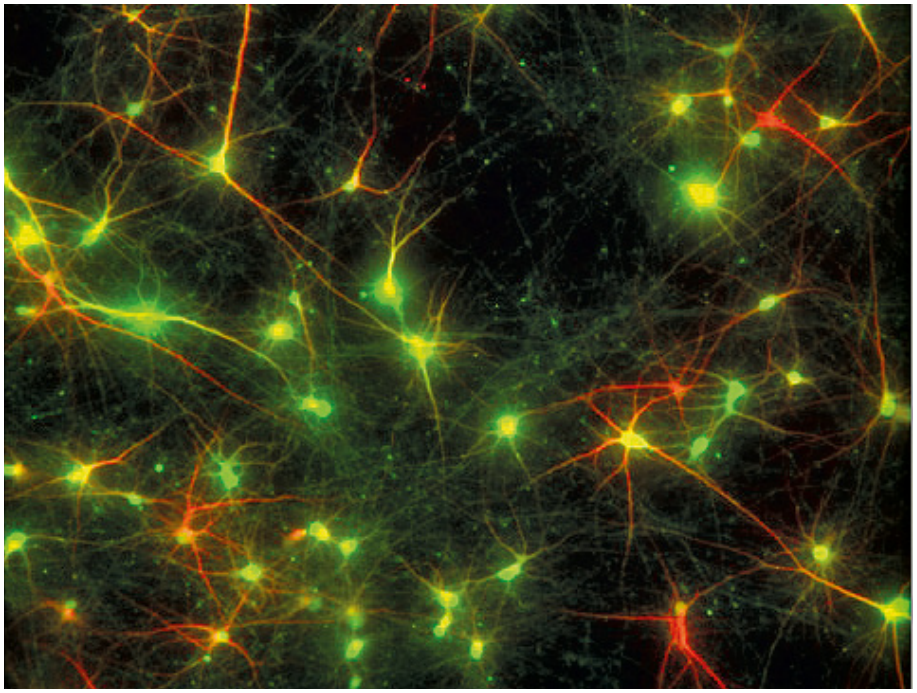
Adeno-associated virus (AAV) vectors are currently among the most commonly applied for *in vivo* gene therapy approaches. we set up a scalable process for AAV production, using orbitally shaken bioreactors and a fully characterized suspension-adapted cell line.

Gene therapy is currently an irreversible approach, without possibilities to fine-tune or halt the expression of a therapeutic gene product. We developed an advanced single-genome inducible AAV vector for regulated expression of therapeutic genes, under control of the approved small molecule drug mifepristone.

In Huntington's disease, the underlying mechanisms integrating environmental cues into the gene regulatory program have remained largely unclear. We employed RNA-seq to examine effects of maternal separation (MS) and environmental enrichment (EE) on striatal gene expression during development of BACHD rats.

We discovered that doublecortin like kinase 3 (DCLK3) in striatal neurons may play a key role in transcription regulation and chromatin remodelling in these brain cells, and show that reduced expression of the kinase in Huntington's disease could render the striatum highly vulnerable to neurodegeneration.

There is currently no cure for Huntington's disease, but recent studies suggest that RNAi to downregulate the expression of both normal and mutant HTT is a promising therapeutic approach. We perforemed a preclinical evaluation of a lentiviral vector for huntingtin silencing.



Neurones derived from induced pluripotent stem cells (iPSC) and transduced with a GFP-expressing lentiviral vector.

Main publications in 2017-2018

Cheng S, Tereshchenko J, Zimmer V, Vachey G, Pythoud C, Rey M, Liefhebber J, Raina A, Streit F, Mazur A, Bähr M, Konstantinova P, **Déglon N**, Kügler S. Therapeutic efficacy of regulable GDNF expression for Huntington's and Parkinson's disease by a high-induction, background-free «GeneSwitch» vector. Exp. Neurol. 2018; 309:79-90.

Novati A, Hentrich T, Wassouf Z, Weber JJ, Yu-Taeger L, **Déglon N**, Nguyen HP, Schultze-Hentrich JM. Environment-dependent striatal gene expression in the BACHD rat model for Huntington's disease. Sci Rep. 2018; 8:5803.

Galvan L, Francelle L, Gaillard MC, de Longprez L, Carrillo-de Sauvage MA, Liot G, Cambon K, Stimmer L, Luccantoni S, Flament J, Valette J, de Chaldee M, Auregan G, Guillermier M, Josephine C, Petit F, Jan C, Jarrige M, Dufour N, Bonvento G, Humbert S, Saudou F, Hantraye P, Merienne K, Bemelmans AP, Perrier AL, **Déglon N**, Brouillet E. The striatal kinase DCLK3 produces neuroprotection against mutant huntingtin. Brain 2018; 141:1434-1454.

Cambon K, Zimmer V, Martineau S, Gaillard,MC, Jarrige M, Bugi A, Miniarikova J, Rey M, Hassig R, Dufour N, Auregan G, Hantraye P, Perrier AL and **Déglon N**. Preclinical evaluation of a lentiviral vector for huntingtin silencing. Mol. Ther. Methods Clin. Dev. 2017; 5:259-276.

Merienne N, Vachey G, de Longprez L, Meunier C, Zimmer V, Perriard G, Canales M, Mathias A, Hergott L, Beltraminelli T, Maulet A, Dequesne T, Pythoud C, Rey M, Pellerin L, Brouillet E, Perrier A, du Pasquier R, **Déglon N**. The self-inactivating KamiCas9 system for the editing of CNS disease genes. Cell Reports 2017; 20:2980-2991.

ORCID number: 0000-0003-4475-9476

CHUV
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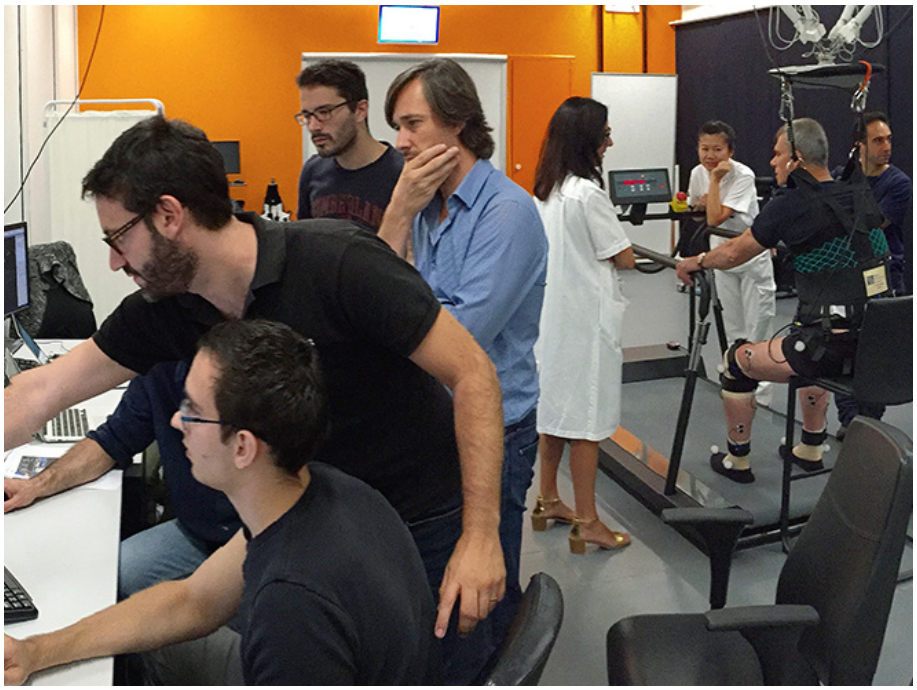
Laboratory of Neurotherapies and Neuromodulation LNTM

Assoc. Professor Jocelyne Bloch
Neurosurgeon

Laboratory of Neurotherapies and Neuromodulation - LNTM
Laboratoire de neurothérapies et neuromodulation - LNTM
jocelyne.bloch@chuv.ch

Affiliation
Service of neurosurgery (NCH)

Keywords
Cell therapy
Neuroprosthetics



Rehabilitation session in patients with spinal cord injury

Laboratory's activity

Cell therapy:

> Application of autologous brain cell transplantation in animal models of stroke, Parkinson's disease and Spinal cord injury.

> Collaborative work with the group of Eric Rouiller Physiology Institute of Fribourg, as well as with the EPFL.

Neuroprosthetics:

> Projects with the EPFL groups of Grégoire Courtine and Stéphanie Lacour on spinal cord stimulation and brain spinal interface for spinal cord injury.

> Projects with the EPFL group of José Millan on closed loop deep brain stimulation in Parkinson's disease and brain machine interface.

Research interests

> Cell therapy

> Neuroprosthetics

Autologous brain cell transplantation in an ischemic brain.

Main publications in 2017-2018

Formento E, Minassian K, Wagner F, Mignardot JB, Le Goff-Mignardot CG, Rowald A, **Bloch J**, Micera S, Capogrosso M, Courtine G. Electrical spinal cord stimulation must preserve proprioception to enable locomotion in humans with spinal cord injury. Nat Neurosci. 2018 Dec; 21(12):1728-1741.

Martin S, Iturrate I, Chavarriaga R, Leeb R, Sobolewski A, Li AM, Zaldivar J, Peciu-Florianu I, Pralong E, Castro-Jiménez M, Benninger D, Vingerhoets F, Knight RT, **Bloch J**, Millán JDR. Differential contributions of subthalamic beta rhythms and 1/f broadband activity to motor symptoms in Parkinson's disease. NPJ Parkinsons Dis. 2018 Nov 5; 4:32.

Wagner FB, Mignardot JB, Le Goff-Mignardot CG, Demesmaeker R, Komi S, Capogrosso M, Rowald A, Seáñez I, Caban M, Pirondini E, Vat M, McCracken LA, Heimgartner R, Fodor I, Watrin A, Seguin P, Paoles E, Van Den Keybus K, Eberle G, Schurch B, Pralong E, Becce F, Prior J, Buse N, Buschman R, Neufeld E, Kuster N, Carda S, von Zitzewitz J, Delattre V, Denison T, Lambert H, Minassian K, **Bloch J**, Courtine G. Targeted neurotechnology restores walking in humans with spinal cord injury. Nature 2018 Nov; 563(7729):65-71.

Capogrosso M, Wagner FB, Gandar J, Moraud EM, Wenger N, Milekovic T, Shkorbatova P, Pavlova N, Musienko P, Bezard E, **Bloch J**, Courtine G. Configuration of electrical spinal cord stimulation through real-time processing of gait kinematics. Nat Protoc. 2018 Sep; 13(9):2031-2061.

Tuleasca C, Pralong E, Najdenovska E, Cuadra MB, Marques JRF, Vingerhoets F, Régis J, **Bloch J**, Levivier M. Deep brain stimulation after previous gamma knife thalamotomy of the Vim for essential tremor is feasible! Clinical, electrophysiological and radiological findings. Acta Neurochir. 2017 Jul; 159(7):1371-1373.

Bloch J, Lacour SP, Courtine G. Electronic Dura Mater Meddling in the Central Nervous System. JAMA Neurol. 2017 Apr 1; 74(4):470-475.

ORCID number: 0000-0002-6405-1590

Unisciences

www.unil.ch/unisciences/jocelynebloch

Laboratory of Neurotherapies and Neuromodulation LNTM

Senior Lecturer Liliane Tenenbaum
Group leader

Laboratory of Neurotherapies and Neuromodulation - LNTM
Laboratoire de neurothérapies et neuromodulation - LNTM
liliane.tenenbaum@chuv.ch

Keywords
Parkinson's disease
Neuroprotection
Targeted and inducible gene transfer
GDNF
Neuroinflammation
Tollip

Laboratory's activity

Drug-inducible neuroprotective gene therapy for Parkinson's disease (PD)

On-going gene therapy clinical trials offer efficient but uncontrolled expression of therapeutic transgenes. However, long-term, high-dose or off-target neurotrophic factors administration induces adverse effects. Our laboratory develops inducible adeno-associated viral (AAV) vectors allowing to administer glial cell line-derived neurotrophic factor (GDNF) intracerebrally, following a time- and dose-dependent regimen. Our current project consists in targeting GDNF transgene expression in specific neuronal subpopulations in order to avoid off-target effects.

Modulation of neuroinflammation

Increasing evidence suggests that chronic neuroinflammation as well as misfolded alpha-synuclein accumulation both play important roles in PD. Toll-interacting protein (Tollip) is a modulator of inflammatory cascades. Interestingly, it also acts as an adaptor in complexes that mediate autophagy of aggregated proteins.
We have shown that Tollip was particularly abundant in *substantia nigra* dopaminergic neurons. In addition, the response to an inflammatory challenge in the midbrain was exacerbated in tollip-deficient mice. Our hypothesis is that Tollip, by reducing neuroinflammation and preventing alpha-synuclein oligomerization, could be neuroprotective for dopaminergic neurons.

Research interests

Neuroprotective gene therapy for Parkinson's disease

> Drug-inducible AAV vectors.
> Mechanism of GDNF neuroprotective *versus* neurochemical effects.

Sensing and reducing brain inflammatory responses

> Modulators of neuroinflammatory signalling.

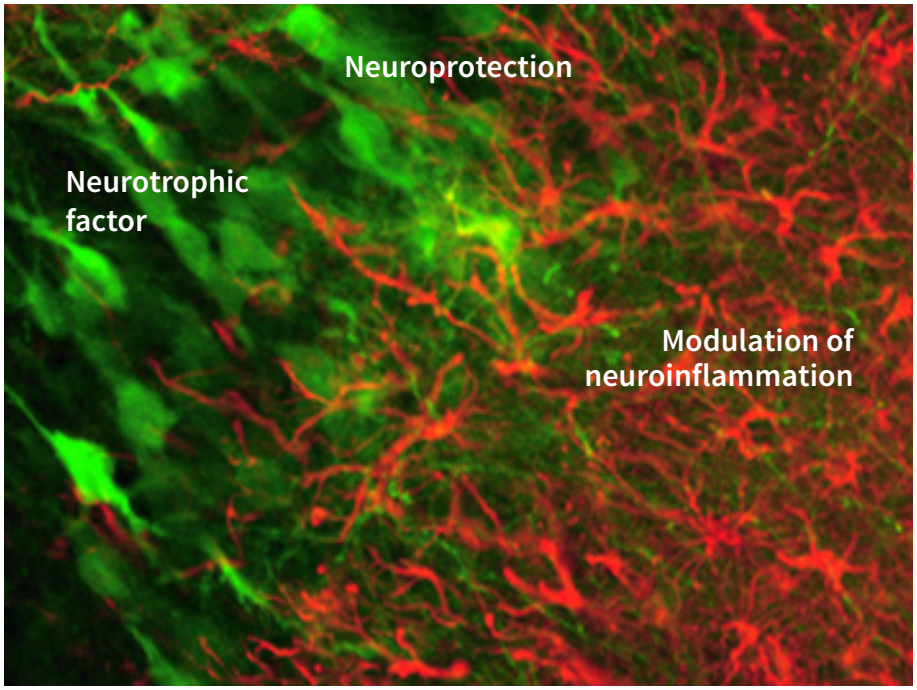
Scientific contributions in 2017-2018

Modulation of neuroinflammation in the substantia nigra pars compacta

We have discovered that the Tollip protein, a modulator of NFκB signalling, was unexpectedly abundant in dopaminergic neurons of the mice *substantia nigra*. We have demonstrated that Tollip deficiency resulted in increased susceptibility to lipopolysaccharide characterized by increased NFκB activation, oxidative and nitrosative stress. Our hypothesis is that Tollip may be a target for neuroprotection in Parkinson's disease.

Drug-inducible neuroprotective gene therapy for Parkinson's disease (PD)

Using a sensitive doxycycline (dox)-inducible AAV vector to administer the GDNF neurotrophic factor in the brain in a controlled manner, we have shown that a prolonged treatment at high-dose induces deleterious effects reducing the clinical benefit (manuscript in preparation). Similar conclusions have been obtained in a rodent model of spinal cord injury using the BDNF neurotrophic factor. These data support the use of regulated viral vectors for neuroprotective and neurorestorative gene therapies.



Our group adresses neurodegeneration in Parkinson's disease by two complementary approaches: protecting dopaminergic neurons using neurotrophic factors and reducing exaggerated inflammation in their environment.

Main publications in 2017-2018

Mestre-Francés N, Lasbleiz Ch, Devau G, Luquin R, **Tenenbaum L**, Kremer EJ, Verdier JM. Combining gene transfer and nonhuman primates to better understand and treat Parkinson's disease. Front. Mol Neurosci, accepted.

Tenenbaum L, Humbert-Claude M. Glial cell line-Derived Neurotrophic Factor gene delivery in Parkinson's disease: a delicate balance between neuroprotection, trophic effects and unwanted compensatory mechanisms. Front. Neuroanat. 2017; doi:10.3389/fnana.00029.

Liu S, Sandner B, Schackel T, Nicholson L, Chtarto A, **Tenenbaum L**, Puttagunta R, Müller R, Weidner N, Blesch A. Regulated Viral BDNF Delivery in Combination with Schwann Cells Promotes Axonal Regeneration through Capillary Alginate Hydrogels after Spinal Cord Injury. Acta Biomaterialia 2017; doi: 10.1016/j.actbio.07.024.

Dwir D, Cabungcal J-H, **Tenenbaum L**, Steullet P, Cuenod M, Do K. 59.2 Matrix Metalloproteinase Inhibition Prevents the Adult Excitatory-Inhibitory Imbalance Induced by the Reciprocal Interaction Between Neuroinflammation and Oxidative Stress During Development. Schizophrenia Bulletin 2017; 43(Suppl 1):S32. doi:10.1093/schbul/sbx021.084.

ORCID number: 0000-0003-4619-9660

UNIL

www.unil.ch/lcmn/home/menuinst/research-groups/gene-transfer-for-parkinsons.html

Unisciences

www.unil.ch/unisciences/lilianetenenbaum

Laboratory for the Exploration of Memory in Neurosciences LEMENS

Professor Jean-François Démonet
Head of Service, Leenaards Memory Center
Head of the Laboratory for the Exploration of Memory in Neurosciences - LEMENS
Laboratoire d'études mémoire et neurosciences - LEMENS
jean-francois.demonet@chuv.ch

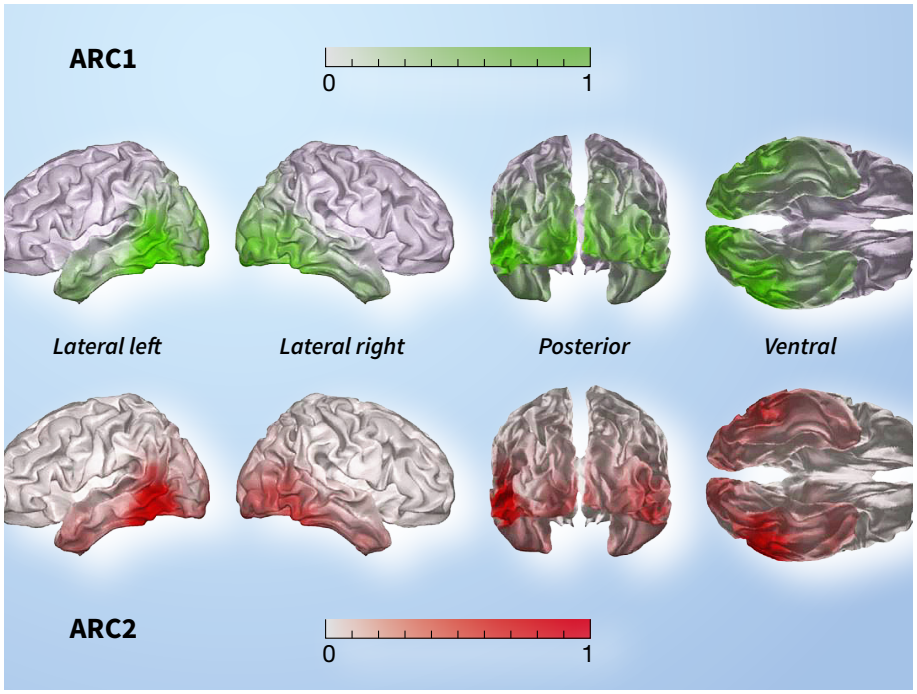
Affiliations
Service of Neurology (NLG)
Leenaards Memory Center CHUV

Keywords
Memory
Language
Cognition
Brain imaging
Biomarkers
Neuro-degenerative diseases
Alzheimer's disease
Amnesia
Diagnosis
Treatment

Laboratory's activity
Laboratory for the Exploration of MEmory in Neuro-Sciences (LEMENS) represents the translational research facet of the Leenaards Memory Centre (www.centrememoire.ch), a Centre devoted to the diagnosis and the 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).

Research interests
I am a Neurologist involved in the neurophysiology of language and memory studied with the combination of cognitive testing and a variety of brain imaging and function mapping in the broadest sense, from EEG to MRI and direct cortical stimulation; as a Physician, I try my best to treat patients and support families facing devastating brain diseases affecting cognition and especially neurodegenerative associated with ageing. My academic career involved a position of Directeur de Recherche at INSERM (France from 1995-2011); currently I am holding a position of full professor at CHUV-UNIL and head of the Leenaards memory centre, one of the «Services» of the Clinical Neurosciences Dept.

Scientific contributions in 2017-2018
> Brain correlates of written language production.
> Recommendation review paper on memory testing in Alzheimer's disease.
> Recommendation review paper on cogntive testing in Alzheimer's disease from JPND working group.
> Sudden amnestic deficits caused by strokes.
> Position paper on the strategy for defining biomarkers in Alzheimer's disease.
> A new antigen responsible for acute auto-immune encephalitis.
> Ageing signatures in detailed spectral analysis of the alpha EEG rhythm.
> Recommendation consensus paper on the diagnosis of dementia from the Swiss Memory Clinics consortium.
> The lifespan effects of adverse circumstances in childhood.



Aging of human alpha rhythm in the EEG signal.

Main publications in 2017-2018

Henchoz Y, Seematter-Bagnoud L, Nanchen D, Büla C, von Gunten A, **Démonet JF**, Santos-Eggimann B. Childhood adversity: A gateway to multimorbidity in older age? Arch Gerontol Geriatr. 2018 Oct 9; 80:31-37.

Knyazeva MG, Barzegaran E, Vildavski VY, **Demonet JF**. Aging of human alpha rhythm. Neurobiol Aging 2018 Sep; 69:261-273.

Michel P, Beaud V, Eskandari A, Maeder P, **Demonet JF**, Eskioglou E. Ischemic Amnesia: Causes and Outcome. Stroke 2017 Aug; 48(8):2270-2273.

Frisoni GB, Boccardi M, Barkhof F, Blennow K, Cappa S, Chiotis K, **Démonet JF**, Garibotto V, *et al*. Strategic roadmap for an early diagnosis of Alzheimer's disease based on biomarkers. Lancet Neurol. 2017 Aug; 16(8):661-676.

van Coevorden-Hameete MH, van Beuningen SFB, Perrenoud M, Will LM, Hulsenboom E, **Demonet JF**, Sabater L, Kros JM, *et al*. Antibodies to TRIM46 are associated with paraneoplastic neurological syndromes. Ann Clin Transl Neurol. 2017 Jul 28; 4(9):680-686.

Cerami C, Dubois B, Boccardi M, Monsch AU, **Demonet JF,** Cappa SF; Geneva Task Force for the Roadmap of Alzheimer's Biomarkers. Clinical validity of delayed recall tests as a gateway biomarker for Alzheimer's disease in the context of a structured 5-phase development framework. Neurobiol Aging 2017 Apr; 52:153-166.

Costa A, Bak T, Caffarra P, Caltagirone C, Ceccaldi M, Collette F, Crutch S, Della Sala S, **Démonet JF**, *et al*. The need for harmonisation and innovation of neuropsychological assessment in neurodegenerative dementias in Europe: consensus document of the Joint Program for Neurodegenerative Diseases Working Group. Alzheimers Res Ther. 2017 Apr 17; 9(1):27.

Planton S, Longcamp M, Péran P, **Démonet JF,** Jucla M. How specialized are writing-specific brain regions? An fMRI study of writing, drawing and oral spelling. Cortex 2017 Mar; 88:66-80.

ORCID number: 0000-0003-0100-6175

CHUV
www.chuv.ch/crn-lemens

www.centrememoire.ch

Unisciences
www.unil.ch/unisciences/jeanfrancoisdemonet

Laboratory of Acute Neurorehabilitation - LNRA

Senior Lecturer, adjunct Professor Karin Diserens
Senior staff member
Head of the Laboratory of Acute Neurorehabilitation - LNRA
Laboratoire de recherche en neurorééducation aiguë
karin.diserens@chuv.ch

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

Laboratory's activity

> To bring accurate identification of Cognitive Motor Dissociation (CMD) among Disorders of Consciousness (DOC) in the acute phase by means of the validation of a new clinical tool; the Motor Behavior Tool-revised (MBTr).
We showed that the MBTr has the ability to identify a subgroup of patients showing residual cognition and subsequent recovery of consciousness, underestimated by the validated clinical scales.
> To demonstrate that a neurosensory-stimulation approach enhanced outdoor is especially meaningful for patients with cognitive motor dissociation.
> To investigate functional/cognitive recovery in patients with CMD.
> 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 test and install very early mobilisation and verticalization for acute care patients.
We showed the benefit of verticalization using a newly designed verticalization robot VEMO (personal contribution to the invention of the VEMO verticalization robot), associated with stepping movements.
> To investigate transition between young adults and adults with neuro-disabilities to provide a follow-up along a continual pathway for these individuals.

Research interests

Overall our research aims to increase detection accuracy of covert awareness/Cognitive Motor Dissociation (CMD) 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 2017-2018

> Validation of the Motor Behavior Tool-revised (MBTr) as clinical means for identification of residual cognition in the acute stage.
> Investigation whether a motor attempt EEG-paradigm coupled with functional electrical stimulation could detect command following.
> Demonstration of the effect of a neurosensory stimulation outdoors on cognition recovery in cognitive motor dissociation.
> Integration of families into a neurosensorial approach to respond to the need of patients with acquired brain injury.
> Finalisation of the production of a new robotic device to verticalize severe instable patients already in the intensive care (project validated by diploma of MicroMBA CHUV).

Main publications in 2017-2018

Attwell C, Jöhr J, Pincherle A, Pignat JM, Kaufmann N, Knebel JF, Berneya L, Ryvlin P, **Diserens K**. Neuro-sensory stimulation outdoors enhances cognition recovery in cognitive motor dissociation: a prospective crossover study. NeuroRehabilitation (in press).

Schneider C, Perdikis S, Silva M, Jöhr J, Pincherle A, Millan JDR, **Diserens K**. Motor Attempt EEG Paradigm as a Diagnostic Tool for Disorders of Consciousness. Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) 18-21 July 2018; 4681-4684. doi:10.1109/EMBC.2018.8513217.

de Goumoëns V, Didier A, Mabire C, Shaha M, **Diserens K**. Families' Needs of Patients with Acquired Brain Injury: Acute Phase and Rehabilitation. Rehabilitation Nursing 2018; 00 (0), 00-00. doi:10.1097/rnj.0000000000000122.

ORCID number: 0000-0002-3000-7794

CHUV

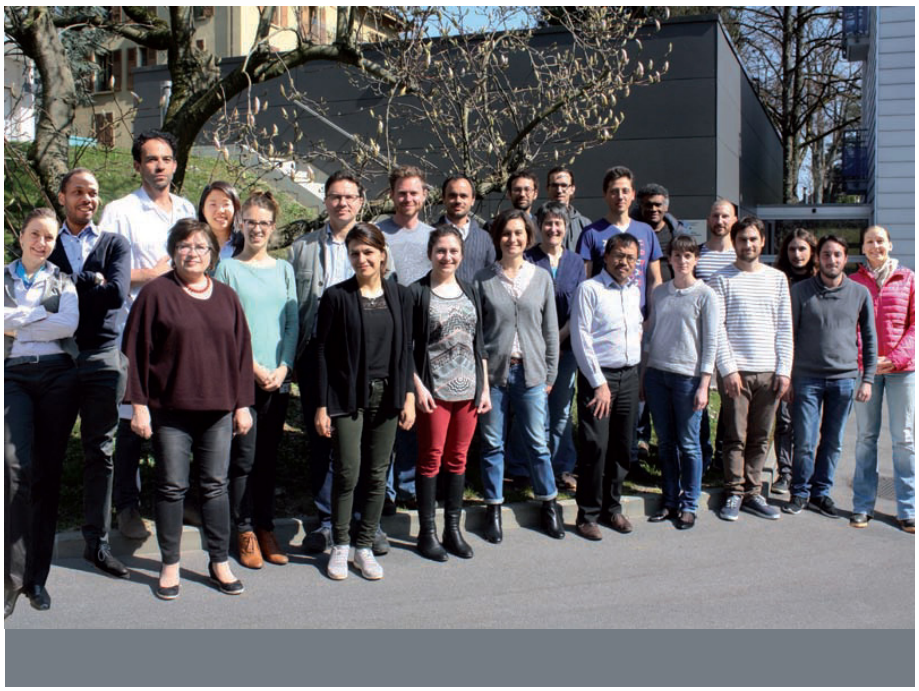
www.chuv.ch/crn-lnra

Unisciences

www.unil.ch/unisciences/karindiserens

Laboratory for Research in Neuroimaging - LREN

Assoc. Professor Bogdan Draganski, Head of laboratory
Senior Lecturer Ferath Kherif, PhD
Senior Lecturer, adjunct Professor Marzia De Lucia
Assist. Professor Antoine Lutti



Laboratory's activity
LREN is a neuroimaging laboratory where clinical and basic neuroscientists study human brain structure and function relevant to neurological disorders and normal cognition. We develop and apply non-invasive neuroimaging methods - magnetic resonance imaging and electro-encephalography to investigate topics including use-dependent brain plasticity, rehabilitation of lost function and neurodegeneration.

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.

LREN's main goal is to translate basic research findings into clinical applications for early diagnosis of disease and for prediction of clinical outcome.

Laboratory for Research in Neuroimaging - LREN

Assoc. Professor Bogdan Draganski, MD
Consultant/attending physician

Head of the Laboratory for Research in Neuroimaging - LREN
Laboratoire de recherche en neuro-imagerie - LREN
bogdan.draganski@chuv.ch

Affiliations
Service of neurology (NLG)
Max-Planck-Institute for Human Cognitive and Brain Sciences, Leipzig Germany

Keywords
Imaging neuroscience
In vivo histology

Research interests
> Brain plasticity
> Preclinical neuroscience
> Healthy ageing
> Neurodegeneration
> Dementia.

Scientific contributions in 2017-2018
> BD is founding member of the Global ECT-MRI Research Collaboration (GEMRIC).
> BD is founder of the Clinical Neuroscience educational programme of the Lemanic Neuroscience Doctoral School.
> BD is the Principal Investigator of the MRI data acquisition project CoLaus-PsyCoLaus (http://www.colaus.ch)- a longitudinal cohort study supported by the Swiss National Science Foundation that collected high-quality MRI data in >1500 CoLaus/PsyColaus participants.
> BD is one of the co-authors of SPMs VBQ toolbox for processing of MRI parametric maps, which is currently distributed under the name hMRI toolbox – www.hmri.info.
> BD is the senior author of a publication validating enhanced tissue priors for subcortical structures of the human brain, which are freely available to all researcher - http://unil.ch/lren/home/menuinst/teaching--utilities/data--utilities.html.

Main publications in 2017-2018
Adaszewski S, Slater D, Melie-Garcia L, **Draganski B**, Bogorodzki P. Simultaneous estimation of population receptive field and hemodynamic parameters from single point BOLD responses using Metropolis-Hastings sampling. Neuroimage 2018 Jan 30; 172:175-193.

Martin-Brevet S, Rodríguez-Herreros B, Nielsen JA, Moreau C, Modenato C, Maillard AM, Pain A, **Draganski B***, *et al*. Quantifying the effects of 16p11.2 copy number variants on brain structure: A multi-site 'genetic-first' study. Biological Psychiatry in press, *shared last authorship

Melie-Garcia L, Slater D, Ruef A, Sanabria-Diaz G, Preisig M, Kherif F, **Draganski B***, Antoine Lutti*. Networks of myelin covariance. Human Brain Mapping 12/2017; doi:10.1002/hbm.23929. *shared last authorship.

Marquis R, Jastrzębowska M, **Draganski B**: Novel imaging techniques to study the functional organization of the human brain. Clinical and Translational Neuroscience 06/2017; 1(1). doi:10.1177/2514183X177141.04.

Gee M, Dukart J, **Draganski B**, Wayne Martin WR, Emery D, Camicioli R. Regional volumetric change in Parkinson's disease with cognitive decline. J Neurol Sci. 2017; 373:88-94.

Zufferey V, Donati A, Popp J, Meuli R, Rossier J, Frackowiak R, **Draganski B**, von Gunten A, Kherif F. Neuroticism, depression, and anxiety traits exacerbate the state of cognitive impairment and hippocampal vulnerability to Alzheimer's disease. Alzheimer's Dement Diagn Assess Dis Monit. 2017; 7:107-114.

ORCID number: 0000-0002-5159-5919

CHUV
www.chuv.ch/crn-lren

UNIL
www.unil.ch/lren

Unisciences
www.unil.ch/unisciences/bogdandraganski

Laboratory for Research in Neuroimaging - LREN

Senior Lecturer Ferath Kherif, PhD
Group leader

Laboratory for Research in Neuroimaging - LREN
Laboratoire de recherche en neuro-imagerie - LREN
ferath.kherif@chuv.ch

Affiliation
Human Brain Project (HBP)

Keywords
Neuroscience
Neuroimaging
Cognitive sciences
Mathematical computational cognitive anatomy

Research interests
> Neuroscience
> Neuroimaging
> Psychology experimental
> Speech language pathology
> Psychiatry
> Psychology biological behavorial research methods
> Computer science artificial intelligence
> Computer science information systems
> Geriatrics gerontology
> Linguistics
> Mathematical computational biology.

Scientific contributions in 2017-2018
Teaching
The teaching include training to basic statics, advanced multivariate approach, Bayesian models and machine learning.
Fundamental research in clinical neurosciences through neuroimaging
> Study of inter-individual differences tools for a more accurate and comprehensive investigation of neural processes in both normal and clinical populations.
> Brain networks of cognition and personality in Alzheimer's disease (AD) to explain variability in clinical and anatomical patterns and the effects of individual differences in pre-clinical stages of AD in order to develop a more inclusive anatomo-functional model of AD.
> Big data and biological signature of Alzheimer's disease to identify homogeneous groups of patients, characterised by a set of parameterised latent causes called «disease signatures».
Applied research through bioinformatics, medical informatics and statistical sciences
> Medical informatics Platform. I was leading this part of the human brain project. The work focus on building a platform for federating data across many hospitals.
> Methodological platform and redcap to provide methodological tools for the research community not only for the lab but also beyond.
> Construction of a state-of-the-art neuroimaging computing platform next to the MRI scanner and data acquisition platform of LREN. We have already built processing pipeline for big data and state-of-the-art toolbox. In particular, we created first tools for automated MRI multivariate and machine learning analyses.

Main publications in 2017-2018
Martin-Brevet S, Rodríguez-Herreros B, Nielsen JA, Moreau C, Modenato C, Maillard AM, Pain A, **Kherif F**, *et al*. Quantifying the Effects of 16p11.2 Copy Number Variants on Brain Structure: A Multisite Genetic-First Study. Biol Psychiatry 2018 Aug 15; 84(4):253-264. doi:10.1016/j.biopsych.2018.02.1176. ePub 2018 Mar 27. PMID: 29778275.

Melie-Garcia L, Slater D, Ruef A, Sanabria-Diaz G, Preisig M, **Kherif F**, Draganski B, Lutti A. Networks of myelin covariance. Hum Brain Mapp. 2018 Apr; 39(4):1532-1554. doi:10.1002/hbm.23929. ePub 2017 Dec 21.

Melie-Garcia L, Draganski B, Ashburner J, **Kherif F**. Multiple Linear Regression: Bayesian Inference for Distributed and Big Data in the Medical Informatics Platform of the Human Brain Project. bioRxiv 242883; doi:https://doi.org/10.1101/242883.

Slater D, Melie-Garcia L, Adaszewski S, Kay K, Lutti A, Draganski B, **Kherif F**. Convex Optimized Population Receptive Field (CO-pRF) Mapping. bioRxiv 172189; doi:https://doi.org/10.1101/172189.

ORCID number: 0000-0001-5698-0413

UNIL
www.unil.ch/lren

Unisciences
www.unil.ch/unisciences/ferathkherif

Laboratory for Research in Neuroimaging - LREN

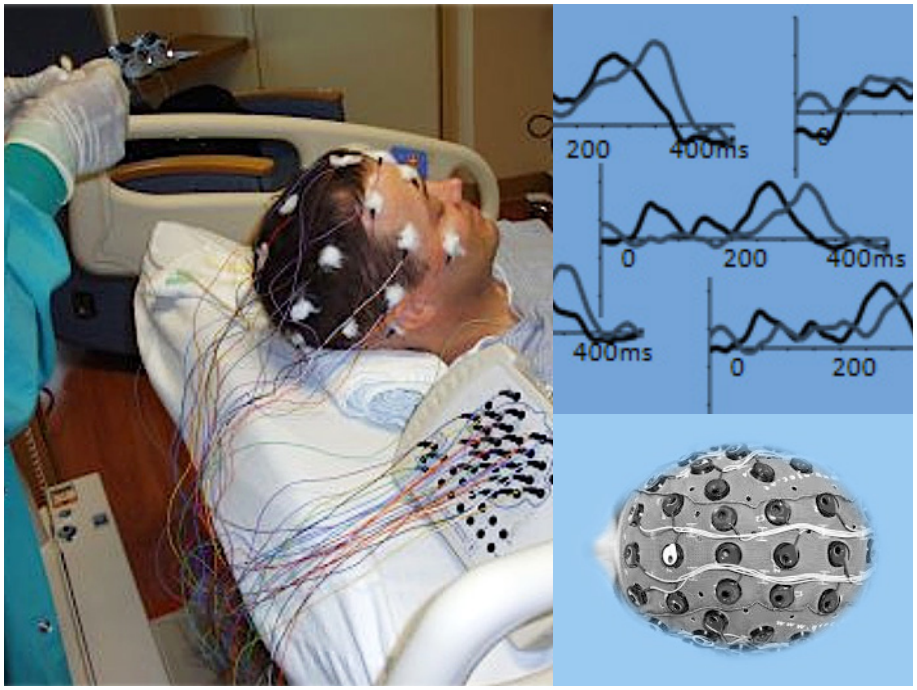
Senior Lecturer, adjunct Professor Marzia De Lucia
Fellow/Postdoctoral researcher
Laboratory for Research in Neuroimaging - LREN
Laboratoire de recherche en neuro-imagerie - LREN
marzia.de-lucia@chuv.ch

Keyword
Electrophysiology
Consciousness

Laboratory's activity
We investigate the extent of preserved neural functions during coma and altered states of consciousness. The interest in these research questions is twofold; on one side understanding brain function in coma can help the development of quantitative markers for predicting a given patient's prognosis; on the other side, in basic neurosciences, comatose patients offers a virtual setting for the investigation of brain functions in altered states of consciousness.
In our studies, we combine electrophysiology with methods of machine learning and computational modeling.

Research interests
> Coma
> Disorders of consciousness
> Statistical regularities
> Interoception

Scientific contributions in 2017-2018
> Validation of an EEG based predictive markers for comatose patients' outcome across four hospital sites and targeted temperature managements.
> Conception, installation and training for the clinical use of test of comatose patients' outcome prediction.
> Development of new experimental protocols for testing the neural sensitivity to regularities based on synchronizing heartbeat to sensory signals.
> Developement of new predictive markers based on EEG functional connectivity of comatose patients.
> Ideation and coordination of a new platform in electrophysiology for human research at the Department of Clinical Neuroscience of Lausanne University Hospital.
> MDL is the academic partner in the EUROSTARS research project, ComAlert in collaboration with g.tec, Austria.



Sensory processing during loss of consciousness.

Main publications in 2017-2018

Pfeiffer C, Nguissi NAN, Chytiris M, Bidlingmeyer P, Haenggi M, Kurmann R, Zubler F, Accolla E, Viceic D, Rusca M, Oddo M, Rossetti AO, **De Lucia M**. Somatosensory and auditory deviance detection for outcome prediction during postanoxic coma. Ann Clin Transl Neurol. 2018; 5(9):1016-1024.

Lasaponara S, D'Onofrio M, Pinto M, Dragone A, Menicagli D, Bueti D, **De Lucia M**, Tomaiuolo F, Doricchi F. EEG Correlates of Preparatory Orienting, Contextual Updating, and Inhibition of Sensory Processing in Left Spatial Neglect. J Neurosci. 2018; 38(15):3792-3808.

Juan E, **De Lucia M**, Beaud V, Oddo M, Rusca M, Viceic D, Clarke S, Rossetti AO. How Do You Feel? Subjective Perception of Recovery as a Reliable Surrogate of Cognitive and Functional Outcome in Cardiac Arrest Survivors. Crit Care Med. 2018; 46(4):e286-e293.

Pfeiffer C, **De Lucia M**. Cardio-audio synchronization drives neural surprise response. Scientific reports 2018; 7 (1):14842.

Pfeiffer C, Nguissi NAN, Chytiris M, Bidlingmeyer P, Haenggi M, Kurmann R, Zubler F, Oddo M, Rossetti AO, **De Lucia M**. Auditory discrimination improvement predicts awakening of postanoxic comatose patients treated with targeted temperature management at 36°C. Resuscitation 2017; 118:89-95.

Guger C, Coyle D, Mattia D, **De Lucia M**, Hochberg L, Edlow BL, Peters B, Eddy B, Nam CS, Noirhomme Q, Allison BZ, Annen J. Trends in BCI research I: Brain-computer interfaces for assessment of patients with locked-in syndrome or disorders of consciousness. Brain-Computer Interface Research: A State-of-the-Art Summary 6. pp105-125. 2017. Publisher Springer, Cham.

ORCID number: 0000-0001-8792-7885

UNIL
www.unil.ch/lren

Unisciences
www.unil.ch/unisciences/marziadelucia

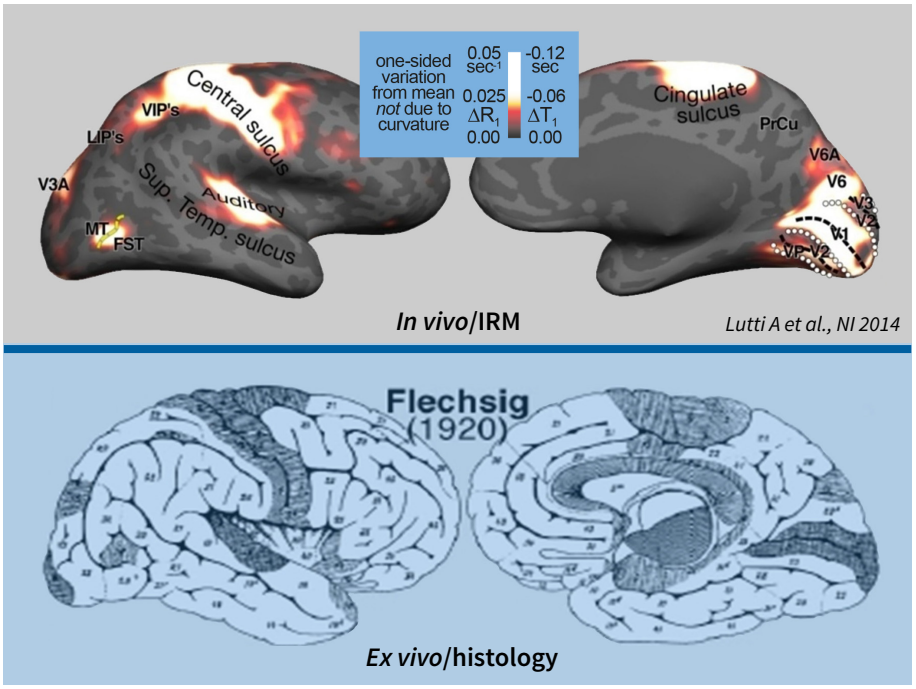
Laboratory for Research in Neuroimaging - LREN

Assist. Professor Antoine Lutti
Group leader
Laboratory for Research in Neuroimaging - LREN
Laboratoire de recherche en neuro-imagerie - LREN
antoine.lutti@chuv.ch

Keywords
MRI data for clinical neuroscience
MRI data quality
Quantitative MRI
In vivo histology

Research interests
> MRI data for clinical neuroscience
> MRI data quality
> Quantitative MRI
> *In vivo* histology

Scientific contributions in 2017-2018
> Establishment of normative myelination trajectories throughout the lifespan.
> Technological development for optimal MRI data quality in non compliant patients.
> Development of a framework for the assessment of MRI data quality.
> Group leader in an international consortium of developers of a software solution for the processing and analysis of quantitative MRI data (www.hmri.info).
> Optimization of a pipeline for the automated processing of MRI data.



My work aims at the development of MRI markers of the brain microstructure allowing in vivo histological analysis of brain tissue ("in vivo histology").

Main publications in 2017-2018

Carey D, Caprini F, Allen M, **Lutti A**, Weiskopf N, Rees G, Callaghan MF, Dick F. Quantitative MRI provides markers of intra-, inter-regional, and age-related differences in young adult cortical microstructure. Neuroimage 2018 Nov 15; 182:429-440. doi:10.1016/j.neuroimage.2017.11.066.

Lee Y, Callaghan MF, Acosta-Cabronero J, **Lutti A**, Nagy Z. Establishing intra- and inter-vendor reproducibility of T1 relaxation time measurements with 3T MRI. Magn Reson Med. 2018 Aug 29. doi:10.1002/mrm.27421.

Castella R, Arn L, Dupuis E, Callaghan MF, Draganski B, **Lutti A**. Controlling motion artefact levels in MR images by suspending data acquisition during periods of head motion. Magn Reson Med. 2018 Apr 24. doi:10.1002/mrm.27214.

Melie-Garcia L, Slater D, Ruef A, Sanabria-Diaz G, Preisig M, Kherif F, Draganski B, **Lutti A**. Networks of myelin covariance. Hum Brain Mapp. 2018 Apr; 39(4):1532-1554. doi:10.1002/hbm.23929. ePub 2017 Dec 21.

ORCID number: 0000-0003-3281-5477

UNIL
www.unil.ch/lren

Unisciences
www.unil.ch/unisciences/antoinelutti

Laboratories of Neuroimmunology

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

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

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 (iPCS).

Laboratory of Neuroimmunology/Multiple Sclerosis LNIS

Professor Renaud Du Pasquier
Head of the Neurology Service

Head of the Laboratory of Neuroimmunology/Multiple Sclerosis - LNIS
Laboratoire de Neuroimmunologie/Sclérose en plaques
renaud.du-pasquier@chuv.ch

Affiliations
Service of neurology (NLG)
Service of immunology and allergy (LIA)

Keywords
Neuroimmunology
Multiple sclerosis
$CD8^+$ T cells
Induced pluripotent stem cells (iPSC)
Epstein-Barr virus
HIV

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. Recently, we have established a program of induced pluripotent stem cells (iPSC). Thanks to this tool, several new opportunities open to us, as we are now able to observe central nervous system (CNS) cells of MS patients, which so far were out of reach. We have now the possibility to put auto-reactive peripheral immune cells in contact with autologous CNS cells and be in a position to determine if, indeed, there is recognition of autoantigens in the brain.

The Lab team is also actively involved in the monitoring of the long-term effects of DMTs used in MS on immune responses. Especially, we are trying to understand the interaction between these treatments and the biology of JC virus, the agent of progressive multifocal leukoencephalopathy (PML) to better handle the risk of developing PML.

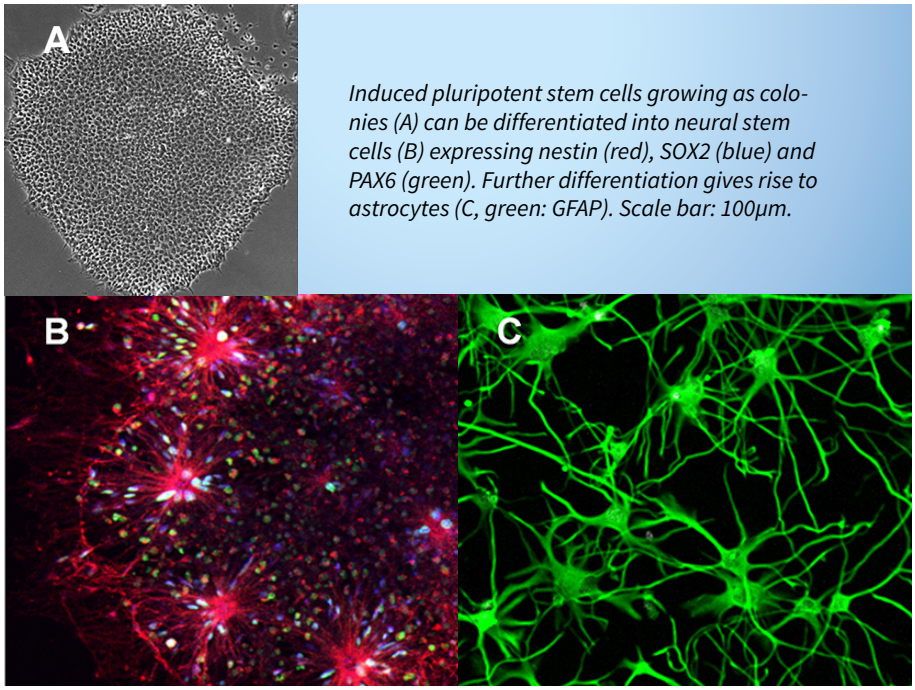
Finally, together with clinicians, the Laboratory holds a research program dealing with the neurocognitive disorders in HIV^+ patients.

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 2017-2018

> Perriot S, Mathias A, Perriard G, [...] Déglon N, Du Pasquier R. Human Induced Pluripotent Stem Cell-Derived Astrocytes Are Differentially Activated by Multiple Sclerosis-Associated Cytokines. ESGCT Lausanne 2018.
> Perriot S, Du Pasquier R. Establishment of iPSC-derived oligodendrocytes to screen for putative autoreactive T cells in MS patients YIM, Tschiertschen 2018.
> Mathias A, Perriot S, Canales M, [...] Engelhardt B, Du Pasquier R. Fatal PML associated with FTY therapy: a four-year retrospective longitudinal study of T cell profile of migration to the CNS and JCV-specific responses State of the Art Swiss MS society Lucern 2018.
> Du Pasquier R. Multiple sclerosis: a novel approach to get a glimpse of the black box. Joint Annual Meeting SSAI and SSR, Interlaken, August 31, 2018.
> Perriot S, Du Pasquier R. Studying T cell pathogenicity in Multiple Sclerosis using an iPSC-derived CNS model YIM, Bern 2017.
> Perriot S, Perriard G, Mathias A, Canales M, Déglon N, Du Pasquier R. Distinct activation profiles of iPSC-derived astrocytes are triggered by different MS-linked inflammatory cytokines. ARSEP, Paris 2017.



Induced pluripotent stem cells growing as colonies (A) can be differentiated into neural stem cells (B) expressing nestin (red), SOX2 (blue) and PAX6 (green). Further differentiation gives rise to astrocytes (C, green: GFAP). Scale bar: 100µm.

Main publications in 2017-2018

Perriot S, Mathias A, Perriard G, Canales M, Jonkmans N, Merienne N, Meunier C, El Kassar L, Perrier AL, Laplaud DA, Schluep M, Déglon N, **Du Pasquier R**. Human Induced Pluripotent Stem Cell-Derived Astrocytes Are Differentially Activated by Multiple Sclerosis-Associated Cytokines. Stem Cell Reports 2018 Oct 12. ePub.

Mathias A, Perriot S, Canales M, Blatti C, Gaubicher C, Schluep M, Engelhardt B, **Du Pasquier R**. Impaired T-cell migration to the CNS under fingolimod and dimethyl fumarate. Neurol Neuroimmunol Neuroinflamm. 2017; 4(6):e401.

Merienne N, Vachey G, de Longprez L, Meunier C, Zimmer V, Perriard G, Canales M, Mathias A, [...] Perrier A, **Du Pasquier R**, Déglon N. The Self-inactivating KamiCas9 System for the Editing of CNS Disease Genes. Cell Rep. 2017; 20(12):2980-2991.

Perrotta G, Bonnier G, […] **Du Pasquier R**, Granziera C. Rivastigmine decreases brain damage in HIV patients with mild cognitive deficits. Ann Clin Transl Neurol. 2017; 4(12):915-920.

Clottu AS, Mathias A, Sailer AW, Schluep M, Seebach JD, **Du Pasquier R**, Pot C. EBI2 Expression and Function: Robust in Memory Lymphocytes and Increased by Natalizumab in Multiple Sclerosis. Cell Rep. 2017; 18(1):213-224.

Mathias A, Perriard G, Canales M, Soneson C, Delorenzi M, Schluep M, **Du Pasquier R**. Increased *ex vivo* antigen presentation profile of B cells in multiple sclerosis. Mult Scler. 2017; 23(6):802-809.

ORCID number: 0000-0002-2786-3434

CHUV
www.chuv.ch/crn-neuroimmunologie

Unisciences
www.unil.ch/unisciences/renauddupasquier

Laboratory of Experimental Neuroimmunology - LNIE

Assist. Professor Caroline Pot, MD
Group leader, consultant neurology

Head of the Laboratory of Experimental Neuroimmunology - LNIE
Laboratoire de neuroimmunologie expérimentale - LNIE
caroline.pot-kreis@chuv.ch

Affiliation
Service of immunology and allergy (LIA)

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

Laboratory's activity

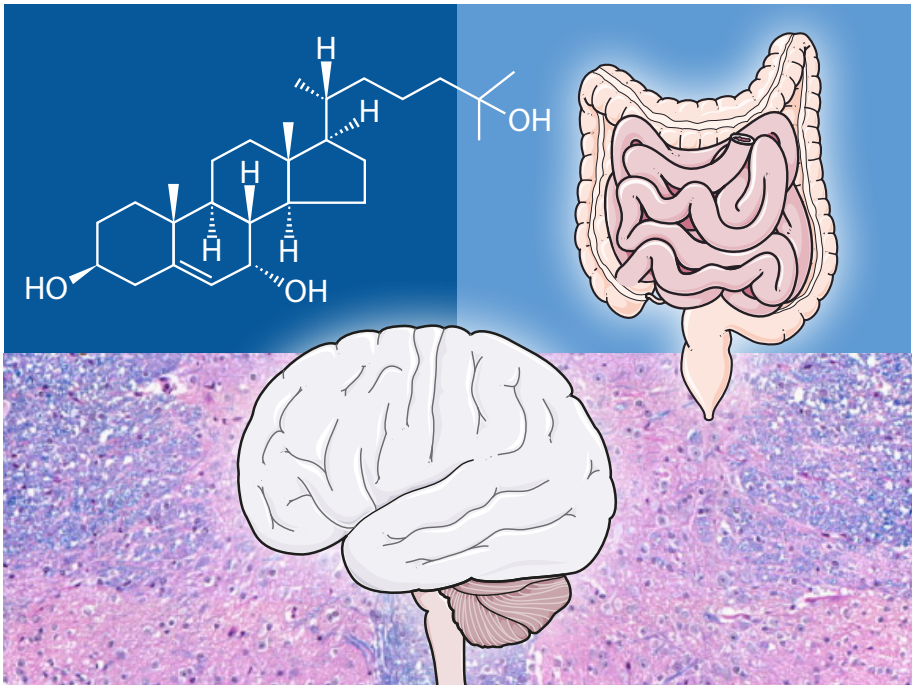
Multiple sclerosis (MS) is a common autoimmune disorder affecting young patients. MS and its animal model, the experimental autoimmune encephalomyelitis (EAE), are characterized by inflammatory cell infiltrates and demyelination of the central nervous system (CNS). The development of this disease is under the control of both genetic and environmental factors. While risk factors such as viral infections or smoking are well established, the role of cholesterol metabolism, intestinal immune responses and gut microbiota remains unclear.
In our laboratory, we are interested in understanding the role of lipid metabolism and of the gut-brain axis during neuroinflammation using the EAE model. Interest in the field of immunometabolism has been accelerated by the actual obesity epidemic and by the observation that obesity promotes inflammation that drives chronic diseases. Our ongoing work focuses on understanding the role of oxysterols, oxidized forms of cholesterol, during autoimmunity. We further examine the impact of oxysterols on gut homeostasis and gut flora during CNS inflammation using dietary approaches and mouse deficient for oxysterols.

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 2017-2018

> January 6-7th 2017_"Rencontres Lucien Rumbach". Location: Annecy, France. Invited speaker.
> June 9 2017_Swiss and French MS Societies meeting. Location: Paris, France. Invited speaker.
> September 21-22 2017_7th European Network on Oxysterol Research (ENOR) meeting. Location: Brussels, Belgium. Poster presentation.
> October 25-28, 2017_7th Joint European-Committee-for-Treatment-and-Research-in-Multiple-Sclerosis (ECTRIMS)-Americas-Committee-for-Treatment-and-Research-in-Multiple-Sclerosis (ACTRIMS) Meeting. Location: Paris, France; Poster presentation; Meeting Abstract: P477, MSJ , Volume 23, Sup: 3, Pages: 202-203; Published: Oct 2017.
> August 30-31 2018_Swiss Society for Allergology and Immunology/rheumatology (SSAI/SSR) Joint annual meeting. Location: Interlaken, Switzerland. Co-organizer and chairman for the session Neuroimmunology.
> October 10-12 2018 34th_European-Committee-for-Treatment-and-Research-in-Multiple-Sclerosis (ECTRIMS). Location: Berlin, Germany; Poster presentation; Meeting Abstract: P335, P739, P815.



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 2017-2018

Steinemann N, Kuhle J, Calabrese P, Kesselring J, Disanto G, Merkler D, **Pot C**, Ajdacic-Gross V, Rodgers S, Puhan MA, von Wyl V. The Swiss Multiple Sclerosis Registry (SMSR): study protocol of a participatory, nationwide registry to promote epidemiological and patient-centered MS research. BMC Neurol. 2018 Aug 13; 18(1):111.

Barin L, Salmen A, Disanto G, Babačića H, Calabrese P, Chan A, Kamm CP, Kesselring J, Kuhle J, Gobbi C, **Pot C**, Puhana MA, Von Wyl V. The disease burden of Multiple Sclerosis from the individual and population perspective: which symptoms matter most? Mult Scler Relat Disord. 2018 Jul 21; 25:112-121.

Vigne S, Chalmin F, Duc D, Clottu A, Apetoh L, Lobaccaro JMA, Christen I, Zhang J and **Pot C**. IL-27-induced type 1 regulatory T-cells produce oxysterols that constrain IL-10 production. Front Immunol. 2017 Sep 25; 8:1184.

Lalive PH, Kreutzfeldt M, Devergne O, Metz I, Bruck W, Merkler D, **Pot C**. Increased interleukin-27 cytokine expression in the central nervous system of multiple sclerosis patients. J Neuroinflammation 2017 Jul 24; 14(1):144.

Clottu A, Mathias A, Sailer AW, Schluep M, Seebach JD, Du Pasquier R, **Pot C**. EBI2 expression and function: robust in memory lymphocytes and increased by natalizumab in multiple sclerosis. Cell Rep. 2017 Jan 3; 18(1):213-224.

ORCID number: 0000-0002-1146-3129

Unisciences

www.unil.ch/unisciences/carolinepot

Laboratory of Brain Tumour Biology and Genetics LBGT

Professor Monika E. Hegi, Head of laboratory

Senior Lecturer, adjunct Professor 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. Over the last years, we have analyzed multidimensional OMICs datasets derived from gliomas of patients treated in our clinical trials and retrieved from public databases that yielded predictive factors and potential new targets that we are further investigating in the laboratory. We aim at bridging this knowledge with the developing Brain Tumor Center headed by PD Dr 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, PhD
Head research laboratory

Head of the Laboratory of Brain Tumour Biology and Genetics - LBGT
Laboratoire de biologie et génétique des tumeurs cérébrales - LBGT
monika.hegi@chuv.ch

Affiliations
Service of neurosurgery (NCH)
Swiss Cancer Center Léman (SCCL)

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

Laboratory's activity

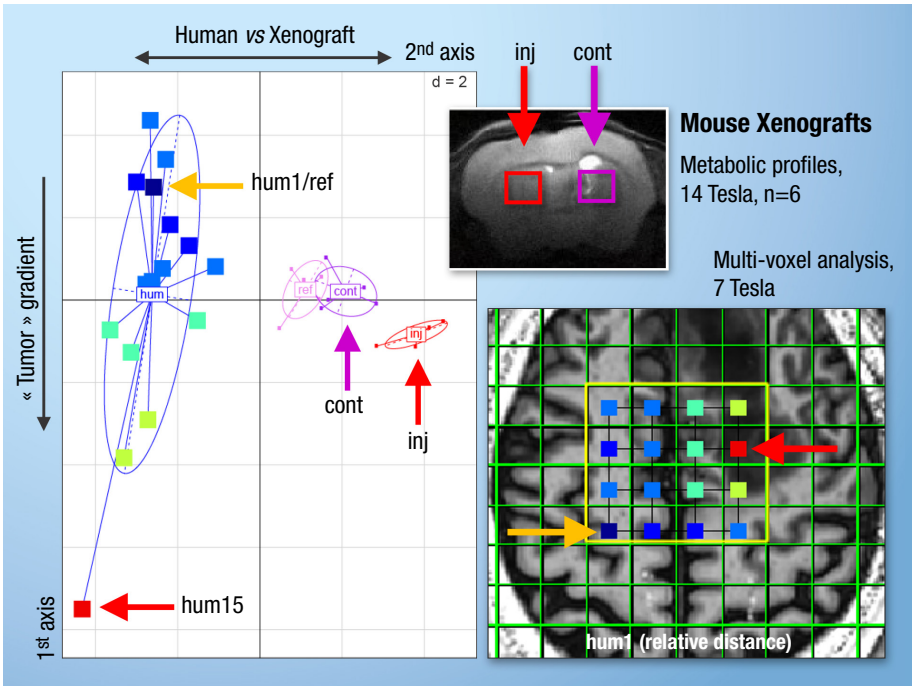
We work at the interphase of clinical and basic cancer research, analyzing multidimensional molecular profiles of glioma from patients treated in clinical trials. We aim at identifying predictive factors for response to therapy and new druggable targets, with a particular focus on tumour epigenetics. We have completed the methylome from over 500 glioma of patients treated in 3 clinical trials for low and high grade glioma. Epigenetic changes contribute substantially to the malignant behaviour of tumours, but may constitute a druggable "Achilles-heel" as we have shown for the repair gene MGMT that when epigenetically silenced renders glioblastoma sensitive to alkylating chemotherapy. Along these lines, we use a systems medicine approach with the aim of overcoming resistance by developing rational combinations with epigenetic drugs. In an interdisciplinary project with PD Dr Hottinger from NRG/ONC, the SIB and CIBM-EPFL we analyze patient derived glioblastoma xenografts in the mouse and their human counterparts using high resolution magnetic resonance spectroscopy and molecular profiling to identify metabolic patterns for the design of translational clinical trials.

Research interests

> (Epi)genomics of glioma, their relevance for tumor biology, classification, and therapeutic strategies.
> Molecular mechanisms and biomarkers of resistance.
> Translational research.

Scientific contributions in 2017-2018

> We determined a clinical cutoff with a safety margin for MGMT methylation in glioblastoma that allows patient selection for therapy without temozolomide, avoiding undue toxicity in patients with a truly unmethylated MGMT promoter who do not profit from this treatment, while not withholding it from others.
> In IDH mutant low-grade glioma we identified methylation based inactivation of DNA damage repair (DDR) genes. Notably, high MGMT promoter methylation was predictive for benefit from temozolomide as opposed to radiotherapy, and may support clinical decision on deferring radiotherapy for long-term preservation of cognitive function.
> We discovered methylation of the PD-L1 gene promoter associated with IDH mutations in low and high gliomas, attenuating expression. This is of clinical relevance, as PD-L1 is an important target for treatment with immune checkpoint.
> We provided first *in vivo* evidence for significant glucose oxidation in glioma cells based on 13C Magnetic Resonance Spectroscopy (MRS) upon infusion of [1,6-13C] glucose and 18FDG positron emission tomography (PET) of highly invasive patient derived xenografts, questioning the glycolytic switch, and suggesting environmental triggers to induce metabolic reprograming of tumor cells.



Metabolic Profiles of Glioblastoma & Corresponding Xenografts (PCA). ^{1}H Magnetic Resonance Spectroscopy.

Principal Component Analysis (PCA) for absolute metabolite concentrations for human glioblastoma and corresponding xenograft datasets. The color gradient for human dataset corresponds to the image on the lower right. The mouse dataset is represented as ref (1st scans on contralateral side); inj, last scans on the injected side; cont, last scans on contralateral side. The color gradient of the human dataset is mostly aligned along the 1st axis of the PCA, indicative of «metabolic» distance from the tumor «core». The 2nd axis determines difference between human and mouse/Xenograft. The mouse gradient passes from «ref», to «cont» and «inj». The 1st axis of the mouse Xengrafts corresponds to the infiltration zone of the human dataset.

Main publications in 2017-2018

Hegi ME, Genbrugge E, Gorlia T, *et al*. MGMT Promoter methylation cutoff with safety margin for selecting glioblastoma patients into trials omitting temozolomide. A pooled analysis of four clinical trials. Clin Cancer Res. 2018. PMID 30514777.

Lai M, Vassallo I, Lanz B, Poitry-Yamate C, Hamou MF, Cudalbu C, Gruetter R, **Hegi ME**. *In vivo* characterization of brain metabolism by (1) H MRS, (13) C MRS and (18) FDG PET reveals significant glucose oxidation of invasively growing glioma cells. Int J Cancer 2018; 143(1):127-138. PMID: 29417580.

Bady P, Kurscheid S, Delorenzi M, **Hegi ME**, *et al*. The DNA methylome of DDR genes and benefit from RT or TMZ in IDH mutant low-grade glioma treated in EORTC 22033. Acta Neuropathol. 2018; 135(4):601-615. PMID 29368212.

Gusyatiner O, **Hegi ME**. Glioma epigenetics: From subclassification to novel treatment options. Semin Cancer Biol. 2018; 51:50-58. PMID: 29170066.

Stupp R, Taillibert S, Kanner A, **Hegi ME**, *et al*. Effect of Tumor-Treating Fields plus maintenance temozolomide *vs* maintenance temozolomide alone on survival in patients with glioblastoma: A randomized clinical trial. JAMA 2017; 318(23):2306-2316. PMID 29260225.

Oikonomaki M, Bady P, **Hegi ME**. Ubiquitin Specific Peptidase 15 (USP15) suppresses glioblastoma cell growth *via* stabilization of HECTD1 E3 ligase attenuating WNT pathway activity. Oncotarget 2017; 8(66):110490-110502. PMID 29299163.

ORCID number: 0000-0003-0855-6495

CHUV
www.chuv.ch/crn-lbgt

Unisciences
www.unil.ch/unisciences/monikahegi

Laboratory of Brain Tumour Biology and Genetics - LBGT

Senior Lecturer, adjunct Professor Andreas F. Hottinger, MD
Head of the Neurooncology Unit
Laboratory of Brain Tumour Biology and Genetics - LBGT
Laboratoire de biologie et génétique des tumeurs cérébrales - LBGT
andreas.hottinger@chuv.ch

Affiliations
Service of neurology (NLG)
Service of oncology

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.

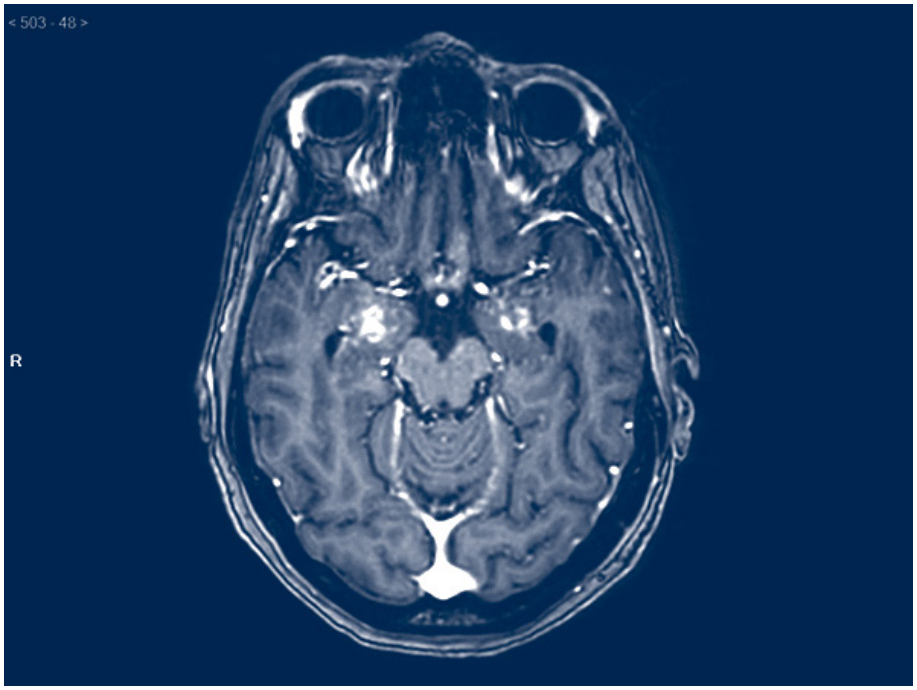
Translational research
A first area of focus is the development and evaluation of xenograft models of glioblastoma (collaboration work with the laboratory of brain tumor biology and genetics (LBGT) and the Center of Biomedical Imaging (CIBM, CHUV).
In a collaboration with the Laboratory for Research 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 Brain Tumor Group of the SAKK and the European Organization for Research and Treatment of Cancer (EORTC) as well as a number of pharmacological companies.

Scientific contributions in 2017-2018

> Over 70 patients screened and over 40 patients with primary brain tumors included in clinical trials.
> Participation in the development and validation of alternating electric field therapy in the management of patients with newly diagnosed glioblastoma.
> Development of a novel treatment strategy for patients developing autoimmune encephalitis following treatment with immune checkpoint inhibitors.
> First description of a novel treatment strategy for patients with leptomeningeal dissemination of BRAF mutated primary brain tumors.



Patient with small cell lung cancer treated with the immune checkpoint inhibitors ipilimumab and nivolumab for tumor recurrence developed severe disorientation and short term memory deficits. An MRI of the brain shows bilateral contrast enhancing lesions.

Main publications in 2017-2018

Wirsching HG, Tabatabai G, Roelcke U, **Hottinger AF,** Jörger F, Schmid A, Plasswilm L, Schrimpf D, Mancao C, Capper D, Conen K, Hundsberger T, Caparrotti F, von Moos R, Riklin C, Felsberg J, Roth P, Jones DTW, Pfister S, Rushing EJ, Abrey L, Reifenberger G, Held L, von Deimling A, Ochsenbein A, Weller M. Bevacizumab plus hypofractionated radiotherapy *versus* radiotherapy alone in elderly patients with glioblastoma: the randomized, open-label, phase II ARTE trial. Ann Oncol. 2018 Apr 10. doi:10.1093/annonc/mdy120.

Astaras C, de Micheli R, Moura B, Hundsberger T, **Hottinger AF**. Neurological Adverse Events Associated with Immune Checkpoint Inhibitors: Diagnosis and Management. Curr Neurol Neurosci Rep. 2018 Feb 1; 18(1):3.

Hottinger AF, de Micheli R, Guido V, Karampera A, Hagmann P, Du Pasquier R. Natalizumab may control immune checkpoint inhibitor-induced limbic encephalitis. Neurol Neuroimmunol Neuroinflamm. 2018 Jan 11; 5(2):e439.

Taphoorn MJB, Dirven L, Kanner AA, Lavy-Shahaf G, Weinberg U, Taillibert S, Toms SA, Honnorat J, Chen TC, Sroubek J, David C, Idbaih A, Easaw JC, Kim CY, Bruna J, **Hottinger AF**, Kew Y, Roth P, Desai R, Villano JL, Kirson ED, Ram Z, Stupp R. Influence of Treatment With Tumor-Treating Fields on Health-Related Quality of Life of Patients With Newly Diagnosed Glioblastoma: A Secondary Analysis of a Randomized Clinical Trial. JAMA Oncol. 2018; 4(4):495-504.

Brouland JP, **Hottinger AF**. Revised classification 2016 of gliomas: what's new, Rev Med Suisse 2017; 13(579): 18051808.

Stupp R, Taillibert S, Kanner A, Read W, Steinberg D, Lhermitte B, Toms S, Idbaih A, Ahluwalia MS, Fink K, Di Meco F, Lieberman F, Zhu JJ, Stragliotto G, Tran D, Brem S, **Hottinger AF**, Kirson ED, Lavy-Shahaf G, Weinberg U, Kim CY, Paek SH, Nicholas G, Bruna J, Hirte H, Weller M, Palti Y, Hegi ME, Ram Z. Effect of Tumor-Treating Fields Plus Maintenance Temozolomide *vs* Maintenance Temozolomide Alone on Survival in Patients With Glioblastoma: A Randomized Clinical Trial. JAMA 2017 Dec 19; 318(23):2306-2316.

Weller M, Butowski N, Tran DD, **Hottinger AF**, *et al.* Rindopepimut with temozolomide for patients with newly diagnosed, EGFRvIII-expressing glioblastoma (ACT IV): a randomised, double-blind, international phase 3 trial. Lancet Oncol. 2017; 18(10):1373-1385.

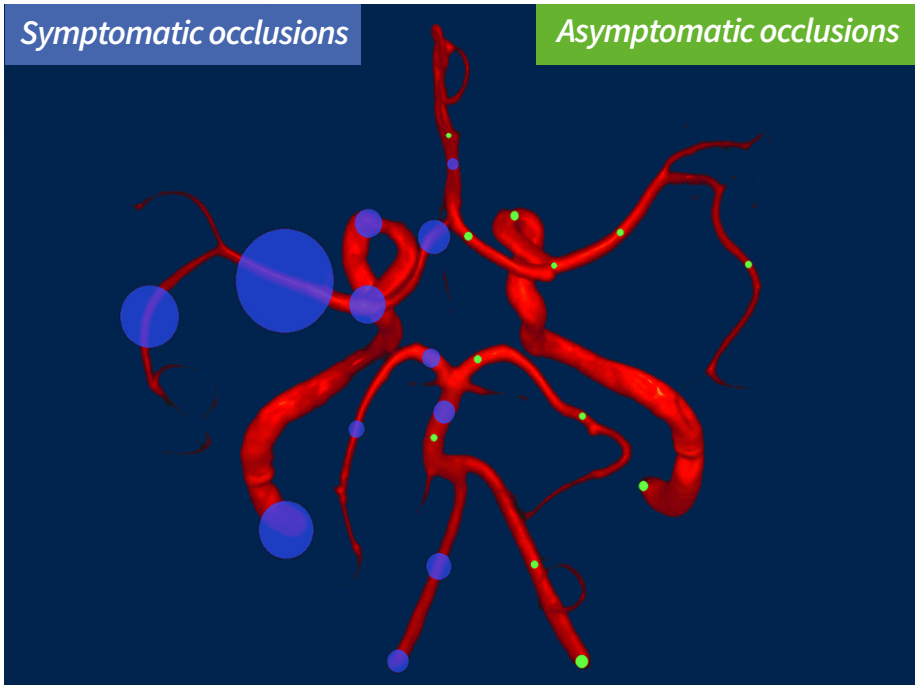
ORCID number: en cours de demande

Unisciences
www.unil.ch/unisciences/andreashottinger

Laboratories of Stroke Research - LMCV

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

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



Site and frequency of arterial occlusions in 2'209 consecutive patients with CT-angiography in the STroke Registry and Analysis of Lausanne (Ref: Rotzinger D et al, Am J Neurorad 2017; 38:868-874).

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.

Laboratory of Stroke Research

Assoc. Professor Lorenz Hirt
Consultant/senior staff member
Head of the Laboratory of Stroke Research
Laboratoire des maladies cérébrovasculaires
lorenz.hirt@chuv.ch

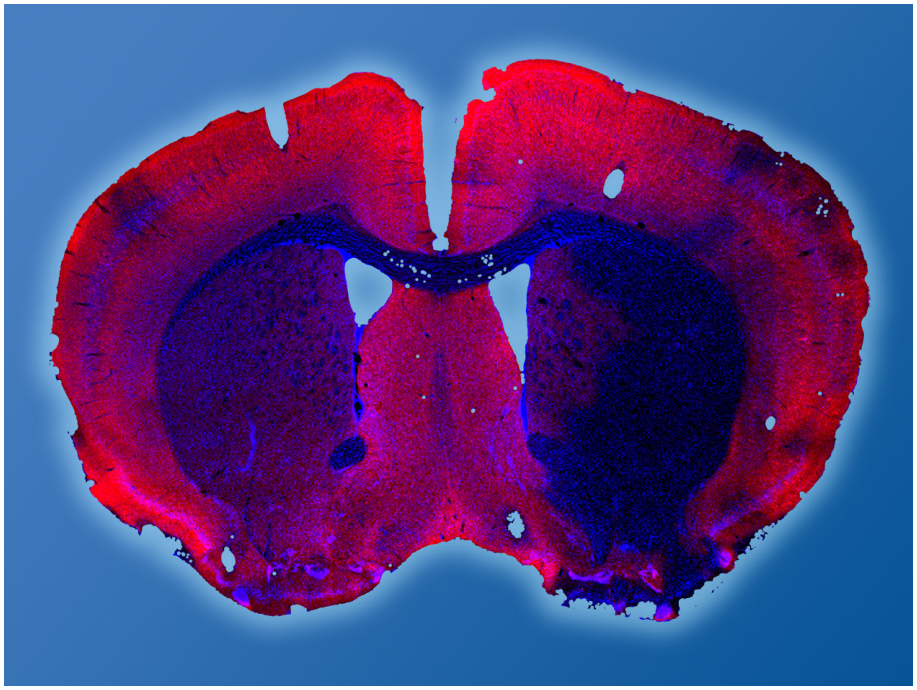
Affiliation
Service of neurology (NLG)

Keywords
Stroke
Cerebral ischemia
Experimental
Neuroprotection
Lactate

Laboratory's activity
The stroke laboratory is studying mechanisms of cell death after cerebral ischemia using experimental models both *in vivo* (mouse middle cerebral artery occlusion) and *in vitro* (oxygen and glucose deprivation in organotypic hippocampal slice cultures). We are studying lactate as a neuroprotective agent as well as neuroprotective mechanisms involving its receptor and transporters. We have shown that lactate's mode of action is dual, both metabolic and as a signalling molecule. Lactate is known to be involved in angiogenesis and we are currently investigating the effect of lactate on pericytes, endothelial cells as well as the blood brain barrier after stroke. We are characterizing neuroinflammatory changes in the brain parenchyma after ischemia and in a collaborative project. In an SNF project we are studying caveolin-1 in cerebral ischemia and have shown its involvement in astrogliosis and neovascularization. In another collaborative SNF project we are using hyperpolarized substrates to characterize brain metabolism and brain perfusion and neuroprotection after stroke in the mouse. Lab members are Lara Buscemi PhD; Melanie Price, PhD; Camille Blochet, 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. In clinical research, we are exploring our newly established large retrospective Doppler US database.

Scientific contributions in 2017-2018
> Endogenous caveolin-1 is involved in astrogliosis and vasculogenesis after ischemic stroke.
> AQP9 is involved in astroglia reaction to ischemia and cell process protusion.
> The absence of endogenous AQP4 improves the long term outcome after MCAO in mice.



A transient 30-minute occlusion of the left middle cerebral artery in the mouse induces an ischemic stroke shown here after 48h. The loss of red labelling (MAP2) illustrates the neuronal damage.
(Courtesy of L. Buscemi)

Main publications in 2017-2018

Hirt L, Price M, Mastour N, Brunet JF, Barriere G, Friscourt F, Badaut J. Increase of aquaporin 9 expression in astrocytes participates in astrogliosis. J Neurosci Res. 2018; 96:194-206.

Hirt L, Price M, Benakis C, Badaut J. Aquaporins in neurological disorders. Clinical and Translational Neuroscience 2018; 2:1-7.

Blochet C, Buscemi L, Clement T, Gehri S, Badaut J, **Hirt L**. Involvement of caveolin-1 in neurovascular unit remodeling after stroke: Effects on neovascularization and astrogliosis. J Cereb Blood Flow Metab. 2018; 271678X18806893.

Carteron L, Solari D, Patet C, Quintard H, Miroz JP, Bloch J, Daniel RT, **Hirt L**, Eckert P, Magistretti PJ, Oddo M. Hypertonic lactate to improve cerebral perfusion and glucose availability after acute brain injury. Crit Care Med. 2018; 46:1649-1655.

Hirt L, Fukuda AM, Ambadipudi K, Rashid F, Binder D, Verkman A, Ashwal S, Obenaus A, Badaut J. Improved long-term outcome after transient cerebral ischemia in aquaporin-4 knockout mice. J Cereb Blood Flow Metab. 2017; 37:277-290.

Hirt L, Carrera E. Antiplatelet therapy in secondary stroke prevention. Revue medicale suisse 2017; 13:907-910.

ORCID number: 0000-0002-2921-5000

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

UNIL
wwwfbm.unil.ch/dnf/group/lorenz-hirt/member/hirt-lorenz-hirt

Unisciences
www.unil.ch/unisciences/lorenzhirt

Laboratory of Clinical Stroke Research Unit

Assoc. Professor Patrik Michel
Head of Unit
Head of the Laboratory of Clinical Stroke Research Unit
Laboratoire de l'unité de recherche cérébrovasculaire clinique
patrik.michel@chuv.ch

Affiliation
Service of neurology (NLG)

Keywords
Stroke
Thrombolysis
Thrombectomy
CT angiography
CT perfusion

Laboratory's activity

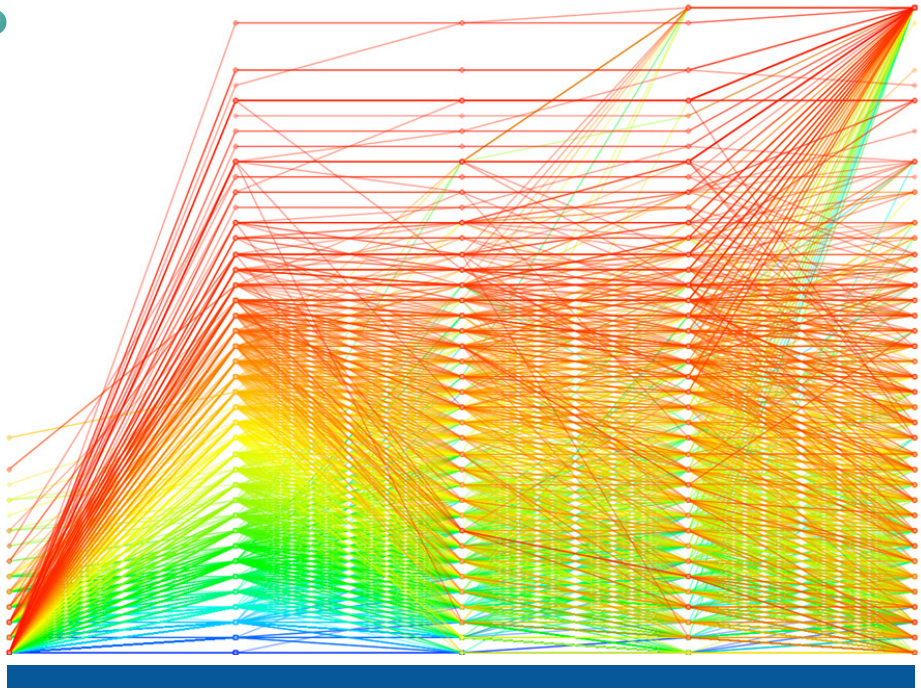
The Clinical Stroke Research team maintains since 2003 the ASTRAL registry (Acute STroke Registry and Analysis of Lausanne). It contains >5'000 acute stroke patients, each with >300 variables including demographic, clinical, comorbidity, multimodal imaging, etiological, metabolic and outcome data. CT 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

Patrik Michel's research interests concern clinical stroke syndromes, acute stroke management, acute stroke perfusion and arterial imaging, and stroke prognosis. He and his collaborators have derived the ASTRAL-prognostic, the ASTRAL-occlusion, the ASTRAL-recanalisation and the ASTRAL recurrence scores. Publications on stroke syndromes concern rare stroke causes (air embolism, Doppler-related stroke, hair-dresser strokes, NIHSS zero strokes, amnesic strokes), stroke mimics and chameleons, stroke severity, and early worsening. Regarding prognosis, he has investigated the influence of specific patient features (cardiac failure, haematological values, PFO, insurance type), acute metabolic values (early blood pressure dynamics, hyperglycemia), and of early neuroimaging. In the area of acute stroke treatment, research is performed on the response to thrombolysis and thrombectomy in different populations (stroke severity, renal failure, body weight, arterial occlusion status). Further research interest include acute arterial occlusion patterns, predictors of recanalisation with and without treatment, impact of collaterals and of brain perfusion imaging. He collaborates with several international teams on the methods and clinical value acute perfusion-CT imaging, thrombolysis, thrombectomy, PFO-related stroke and basilar artery occlusion.

Scientific contributions in 2017-2018

> 32 peer-reviewed articles in leading cerebrovascular journals, including co-authorship in the NEJM.
3 editorials.
2 book chapters.
> 1 Swiss National Science Foundation grant as PI; 2 others as co-applicant.
1 Swiss Cardiology Foundation grant.
Partner in a EU Horizon 2020 project.
> 1 MD thesis UNIL completed.
2 European Master in Stroke Medicine thesis completed, Danube University, Krems/Austria.
2 PhD thesis under way (one with Larissa, Greece).
> Multiple invitations for national and international conferences and teaching courses.
> Active in the Swiss Stroke Society, European Stroke Organisation, World Stroke Organisation, and World Health Organisation.



Severity of neurological deficits in 3'443 consecutive ischemic stroke patients from the ASTRAL registry (Acute STroke Registry and Analysis of Lausanne) at 5 time points (from left to right): before the stroke, on arrival at the CHUV, at 6 hours, 24 hours and 7 days later.

Main publications in 2017-2018

Eskioglou E, Huchmandzadeh Millotte M, Amiguet M, **Michel P**. NIHSS zero strokes: immeasurable but not innocent. Stroke 2018; 49:3057-3059.

Ntaios K, Papavasileiou V, Sagris D, Makaritsis K, Vemmos K, Steiner T, **Michel P**. PFO closure *vs* medical therapy in patients with cryptogenic stroke or transient ischemic attack: updated systematic review and meta-analysis. Stroke 2018; 49:412-418.

Pallesen LP, Lambrou D, Eskandari A, Barlinn J, Barlinn K, Reichmann H, Dunet V, Maeder Ph, Puetz V, **Michel P**. Perfusion CT in Posterior Circulation Stroke: Predictors and Prognostic Implications of Focal Hypoperfusion. Eur J Neurol. 2018; 25:725–731.

Bill O, Faouzi M, Meuli R, Maeder Ph, Wintermark M, **Michel P**. Added value of multimodal CT imaging: analysis of 1'994 acute ischemic strokes. Eur J Neurol. 2017; 24:167-174.

Eskioglou E, Beaud V, Maeder Ph, Demonet JF, **Michel P**. Ischemic amnesia: causes and outcome. Stroke 2017; 48:2270-2273.

Mas JL, Derumeaux G, Guillon B, [...] **Michel P**, [...] , Chatellier G; CLOSE Investigators. Patent Foramen Ovale Closure or Anticoagulation *vs* Antiplatelets after Stroke. N Engl J Med. 2017; 377:1011-21.

ORCID number: 0000-0003-4954-7579

CHUV

www.chuv.ch/centre-cerebrovasculaire

Unisciences

www.unil.ch/unisciences/patrikmichel

Laboratory of Nerve-Muscle Unit - NMUL

Adjunct Professor Thierry Kuntzer
Consultant/attending physician
Head of the Laboratory of Nerve-Muscle Unit - NMUL
Laboratoire de l'unité nerf-muscle - LUNM
thierry.kuntzer@chuv.ch

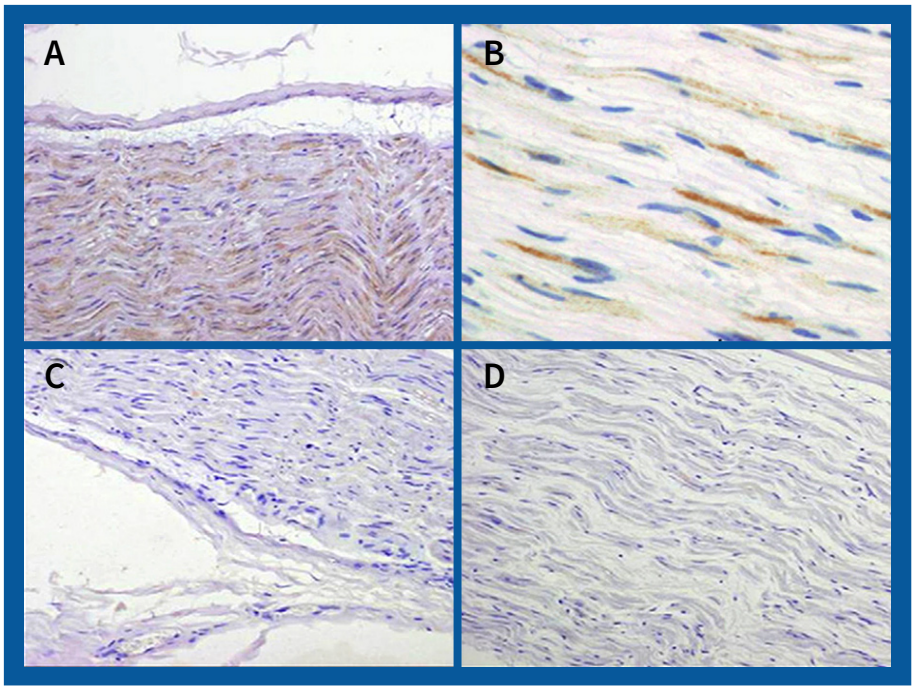
Affiliation
Service of neurology (NLG)

Keywords
Muscle diseases
Peripheral nerve disorders
Gene expression in skin punch biopsies
Electrophysiology in animal models
Clinical Neurophysiology

Laboratory's activity
The Lab is specialized in studying gene expression from skin in inflammatory nerve or degenerative disorders, in quantifying skin denervation by histology and studying axon reflex reaction. The other activities include assessement of nerve-muscle disorders by clinical neurophysiology (large and small nerve fibers), muscle whole body MRI studies, and clinometric measures of muscle function.

Research interests
> Gene expression from skin in inflammatory nerves (CIDP and Guillain-Barré syndrome).
> Quantitative skin denervation by histology.
> Clinical neurophysiology.
> New tools to assess muscle function.

Scientific contributions in 2017-2018
> Developed quantification of axon-reflex in small-fiber neuropathies.
> President elect of the francophone peripheral nerve society.



MSRV-Env is expressed in peripheral nerves biopsies from CIDP patients. Representative immunohistological analysis showing that MSRV-Env immunoreactivity (brown) is found in the cytoplasm of Schwann cells (low magnification: A; high magnification: B). No staining is observed in the corresponding serial section of the same biopsy incubated with a non-relevant isotype antibody (C) or in a biopsy from a control neuropathy (D). Scale bar: 0.5 μm. *(In: EBioMedecine. 2016 Apr;6:190-8. doi: 10.1016/j. ebiom.2016.03.001. Human Endogenous Retrovirus and Neuroinflammation in Chronic Inflammatory Demyelinating Polyradiculoneuropathy)*

Main publications in 2017-2018

Faucard R, Calero-Romero I, Suter MR, Waeber B, Feihl F, **Kuntzer T**. Axon reflex-mediated vasodilation is reduced in proportion to disease severity in TTR-FAP. Neurol Genet. 2018.

Svahn J, Petiot P, Antoine JC, Vial C, Delmont E, Viala K, Steck AJ, Magot A, Cauquil C, Zarea A, Echaniz-Laguna A, Iancu Ferfoglia R, Gueguen A, Magy L, Léger JM, **Kuntzer T**, Ferraud K, Lacour A, Camdessanché JP. Francophone anti-MAG cohort Group. Anti-MAG antibodies in 202 patients: clinicopathological and therapeutic features. J Neurol Neurosurg Psychiatry 2018.

van Eijk JJJ, Dalton HR, Ripellino P, Madden RG, Jones C, Fritz M, Gobbi C, Melli G, Pasi E, Herrod J, Lissmann RF, Ashraf HH, Abdelrahim M, Masri OABAL, Fraga M, Benninger D, **Kuntzer T,** Aubert V, Sahli R, Moradpour D, Blasco-Perrin H, Attarian S, Gérolami R, Colson P, Giordani MT, Hartl J, Pischke S, Lin NX, Mclean BN, Bendall RP, Panning M, Peron JM, Kamar N, Izopet J, Jacobs BC, van Alfen N, van Engelen BGM. Clinical phenotype and outcome of hepatitis E virus-associated neuralgic amyotrophy. Neurology 2017.

Stebler K, Martin R, Kirkham KR, **Küntzer T**, Bathory I, Albrecht E. Electrophysiological Study of Femoral Nerve Function After a Continuous Femoral Nerve Block for Anterior Cruciate Ligament Reconstruction: A Randomized, Controlled Single-Blind Trial. Am J Sports Med. 2017.

ORCID number: 0000-0002-7788-1673

CHUV

www.chuv.ch/crn-maladies-neuromusculaires

Unisciences

www.unil.ch/unisciences/thierrykuntzer

Laboratory of Cortical Excitability and Arousal Disorders - LE²C

Professor Philippe Ryvlin, Head of laboratory
Assoc. Professor Andrea Rossetti
Senior Lecturer, adjunct Professor Jan Novy
Carolina Ciumas, MD, PhD

Laboratory's activity

Our laboratory's activities are focusing on clinical research in patients with epilepsy or disorders of consciousness of various origin, including status-epilepticus and post-anoxic coma.
In epilepsy, six main research objectives are being developed:

> Pathophysiology and prevention of Sudden Unexpected Death in Epilepsy Patients (SUDEP).
> Seizure detection in ambulatory patients using mobile health technology.
> Optimisation of pre-surgical evaluation and epilepsy surgery.
> Point-of-care testing of antiepileptic drugs plasma dosage.
> Pharmacogenomic/biomarkers of the disease.
> 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.
The methods used in our laboratory include clinical neurophysiology (scalp-EEG, intra-cerebral EEG, evoked potentials), neuroimaging (MRI, functional MRI, PET), biology (dosage of AEDs, genomic), epidemiology and randomized controled trials.

Research interests

Our primary research interests are the pathophysiology and prevention of sudden unexpected death in epilepsy (SUDEP), seizure detection in ambulatory settings, and optimisation of epilepsy surgery. All three topics are driven by the development of novel technologies and mobile health.

Laboratory of Cortical Excitability and Arousal Disorders - LE²C

Professor Philippe Ryvlin
Head of the Department of Clinical Neurosciences
Head of the Laboratory of Cortical Excitability and Arousal Disorders - LE²C
Laboratoire des troubles de l'excitabilité et de l'éveil cortical
philippe.ryvlin@chuv.ch

Affiliation
Service of neurology (NLG)

Keywords
Epilepsy
Sudden unexpected death in epilepsy
Neuroimaging
Intracerebral EEG
Seizure detection
Neurotechnologies

Scientific contributions in 2017-2018

> In this French national multicentric prospective study, we investigated 107 generalized tonic-clonic seizures (GTCS) in 73 patients undergoing video-EEG monitoring with concurrent pulse oxymetry. A transient hypoxemia (SPO2 <90%) was observed in 86% of GTCS. Postictal hypoxemia was significantly lower and recovered more rapidly when oxygen was administered early ($p = 0.046$). Furthermore, temporal lobe seizures were associated with greater risk of ictal hypoxemia before GTCS and longer postictal hypoxemia.

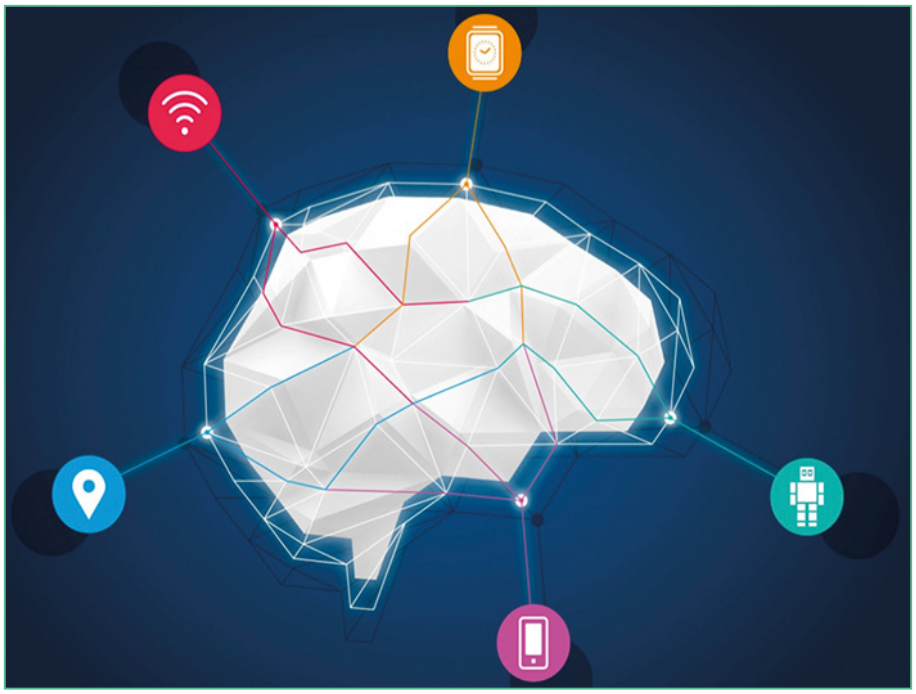
> In this study of more than 40'000 North-American patients treated with vagus nerve stimulation (VNS) and followed for an average duration of 7 years, we observed a steady reduction of the incidence of sudden unexpected death in epilepsy (SUDEP) during follow-up. This finding suggests that the risk of SUDEP might decrease over time for reasons that remain to be determined and are not necessarily related to VNS treatment proper.

> In this study, we investigated 13 children with benign childhood epilepsy with centre-temporal spikes (BCECTS) and 11 age-matched controls using functional magnetic resonance imaging during an emotional discrimination task. Children with BCECTS showed significantly reduced bilateral activation in the insular cortex, caudate, and lentiform nuclei when performing a fearful faces detection task but not for the detection for happy faces. Correlation with age and time since last seizure suggest that these selective abnormalities reflect a maturational defect in the brain network involved in both BCECTS and social cognition.

> We participated as last senior author to the systematic review and edition of the first practice guidelines of the American Academy of Neurology on the incidence and risk factors of SUDEP. The latter estimated that the average incidence of SUDEP in adult patients with epilepsy is 1.1/1000 patient-years, and that the main risk factor remains the presence and frequency of GTCS.

> In this article, we have proposed new standard for relevant clinical evaluation of non-EEG based methods for seizure detection. These standards are based on four key features (subjects, recordings, data analysis and alarms, and reference standa) and delineate five classes of trials (0-4) reminiscient of those used for classic pharmacological studies.

> In this unique study where we performed simultaneous recording of intracerebral EEG and functional MRI (fMRI) BOLD signals in epilepsy patients undergoing invasive EEG monitoring, we demonstrated the possibility to record reliable gamma-band activity from intracerebral electrodes while performing a cognitive task during fMRI. This feasibility study opens the way to directly compare task-induced gamma-band activity and BOLD signal in the Human brain.



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 2017-2018

Rheims S, Alvarez BM, Alexandre V, Curot J, Maillard L, Bartolomei F, Derambure P, Hirsch E, Michel V, Chassoux F, Tourniaire D, Crespel A, Biraben A, Navarro V, Kahane P, De Toffol B, Thomas P, Rosenberg S, Valton L, Bezin L, **Ryvlin P**. REPO2MSE study group. Neurology 2018 Dec 19. pii:10.1212/WNL.0000000000006777. doi:10.1212/WNL.0000000000006777. [ePub ahead of print]

Beniczky S, **Ryvlin P**. Standards for testing and clinical validation of seizure detection devices. Epilepsia 2018 Jun; 59 Suppl 1:9-13.

Ryvlin P, So EL, Gordon CM, Hesdorffer DC, Sperling MR, Devinsky O, Bunker MT, Olin B, Friedman D. Long-term surveillance of SUDEP in drug-resistant epilepsy patients treated with VNS therapy. Epilepsia 2018 Mar; 59(3):562-572.

Ciumas C, Laurent A, Saignavongs M, Ilski F, de Bellescize J, Panagiotakaki E, Ostrowsky-Coste K, Arzimanoglou A, Herbillon V, Ibarrola D, **Ryvlin P.** Behavioral and fMRI responses to fearful faces are altered in benign childhood epilepsy with centrotemporal spikes (BCECTS). Epilepsia 2017 Oct; 58(10):1716-1727.

Harden C, Tomson T, Gloss D, Buchhalter J, Cross JH, Donner E, French JA, Gil-Nagel A, Hesdorffer DC, Smithson WH, Spitz MC, Walczak TS, Sander JW, **Ryvlin P**. Practice guideline summary: Sudden unexpected death in epilepsy incidence rates and risk factors: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology 2017 Apr 25; 88(17): 1674-1680.

Saignavongs M, Ciumas C, Petton M, Bouet R, Boulogne S, Rheims S, Carmichael DW, Lachaux JP, **Ryvlin P**. Neural Activity Elicited by a Cognitive Task can be detected in Single-Trials with Simultaneous Intracerebral EEG-fMRI Recordings. Int J Neural Syst. 2017 Feb; 27(1):1750001.

ORCID number: 0000-0001-7775-6576

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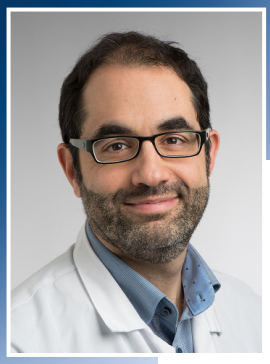
www.unil.ch/unisciences/philipperyvlin



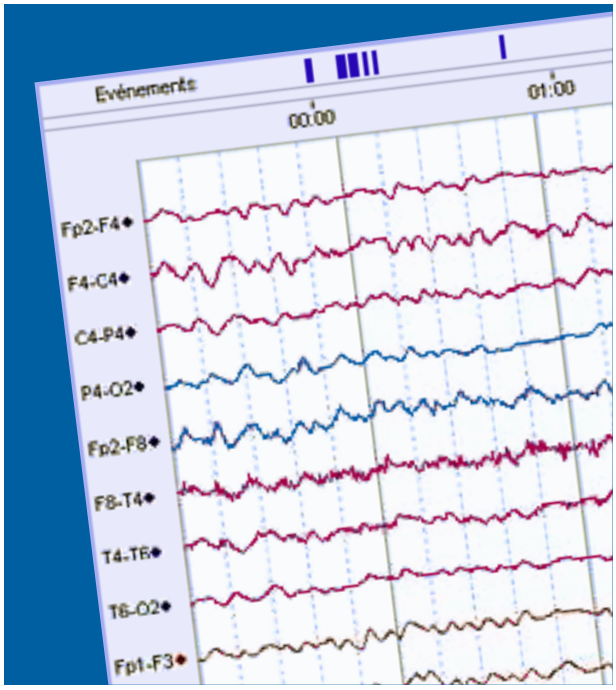
Laboratory of Cortical Excitability and Arousal Disorders - LE²C

Assoc. Professor Andrea Rossetti
Consultant/attending physician

Laboratory of Cortical Excitability and Arousal Disorders - LE²C
Laboratoire des troubles de l'excitabilité et de l'éveil cortical
andrea.rossetti@chuv.ch

Affiliation
Service of neurology (NLG)

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
Nosology and treatment of status epilepticus prognostication of acuta coma; EEG monitoring in intensive care unit.

Main publications in 2017-2018

Juan E, De Lucia M, Beaud V, Oddo M, Rusca M, Viceic D, Clarke S, **Rossetti AO**. How do you feel? Subjective perception of recovery as a reliable surrogate of cognitive and functional outcome in cardiac arrest survivors. Crit Care Med 2018; 46:e286-e293.

Rossetti AO, Schindler K, Alvarez V, Sutter R, Novy J, Oddo M, Warpelin-Decrausaz L, Rüegg S. Does continuous video-EEG in patients with altered consciousness improve patient outcome? Current evidence and randomized controlled trial design. J Clin Neurophysiol 2018; 35:359-364.

Delaj L, Novy J, Ryvlin P, Marchi NA, **Rossetti AO**. Refractory and super-refractory status epilepticus in adults: a 9-year cohort study. Acta Neurol Scand 2017; 135:92-99.

Solari D, **Rossetti AO**, Carteron L, Miroz JP, Novy J, Eckert P, Oddo M. Early prediction of coma recovery after cardiac arrest with blinded pupillometry. Ann Neurol 2017; 81:804-810.

Beuchat I, Novy J, **Rossetti AO**. Newer antiepileptic drugs in status epilepticus: prescription trends and outcomes in comparison with traditional agents. CNS Drugs 2017; 31:327-334.

Rossetti AO, Tovar Quiroga DF, Juan E, Novy J, White RD, Ben-Hamouda N, Britton J, Oddo M, Rabinstein AA. EEG predicts poor and good outcome after cardiac arrest: a two center study. Crit Care Med 2017; 45: e674-e682.

ORCID number: 0000-0002-7878-172X

Unisciences
www.unil.ch/unisciences/andrearossetti

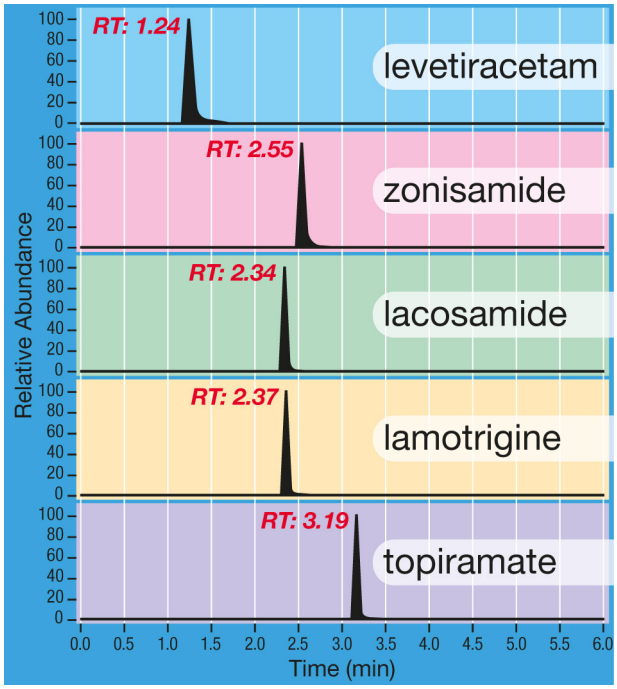
Laboratory of Cortical Excitability and Arousal Disorders - LE²C

Senior Lecturer, adjunct Professor Jan Novy
Consultant/attending physician

Laboratory of Cortical Excitability and Arousal Disorders - LE²C
Laboratoire des troubles de l'excitabilité et de l'éveil cortical
jan.novy@chuv.ch

Affiliation
Service of neurology (NLG)

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



Scientific contributions in 2017-2018

> We explored the caused of mortality in people with epilepsy in general population, and its relationships with the disease.

> We set up the randomised trial assess therapeutic drug monitoring in epilepsy.

> We set up several studies (including a randomized trial) assessing the relationship between drug levels and clinical response in chronic epilepsy as well as in status epilepticus.

> We explored the phenotype of several rare genetic condition involving cortical excitability.

Main publications in 2017-2018

D'Anto J, Wnuk W, Rossetti AO, Decosterd LA, Buclin T, **Novy J**.Lamotrigine serum levels: Ceiling effect in people with epilepsy in remission? Epilepsy Behav. 2017; 74:41-44.

ORCID number: 0000-0002-6862-7083

Unisciences
www.unil.ch/unisciences/jannovy

Laboratory of Cortical Excitability and Arousal Disorders - LE²C

Carolina Ciumas, MD, PhD
Fellow/Postdoctoral researcher

Laboratory of Cortical Excitability and Arousal Disorders - LE²C
Laboratoire des troubles de l'excitabilité et de l'éveil cortical
carolina.ciumas@chuv.ch

Affiliation
Service of neurology (NLG)

Keywords
fMRI
MRI
Multimodal imaging
Epilepsy
EEG
Intracranial EEG
Simultaneous recordings
SUDEP
Cognitive neuroscience
Connected devices
Neurotechnology
Biosignals detection

Research interests
My main interest is the study of human epilepsy using a multi-methodological approach. I have worked in functional intracranial EEG and MRI projects in epilepsy for several years now. Currently, I am interested in finding a reliable brainstem biomarker for the prevention of sudden unexpected death in epilepsy (SUDEP), a project initiated at CHUV and conducted in parallel in the USA. This study specifically examines brainstem responses to apnea challenges in patients with intractable epilepsy. I am also interested in the presurgical evaluation of patients with intractable epilepsy and optimization of their epilepsy surgery outcome, as well as use of wearable devices in seizure detection.

Scientific contributions in 2017-2018
> Established the collaboration with Case Western Reserve University, USA to run our project in a larger cohort of patinets.
> Our work was recognized by the Innocentive SUDEP Institute Challenge with an award for the development of an imaging biomarker for SUDEP. I supervised and advised on institution of imaging protocols for apnea challenges at Case Western Reserve University. Our joint work was recognized with an award by the 2018 Annual Epilepsy Foundation meeting in San Francisco.
> Obtained two grants for financing our research.
> Found that the behavioral and fMRI responses to fearful faces are altered in benign childhood epilepsy with centrotemporal spikes.

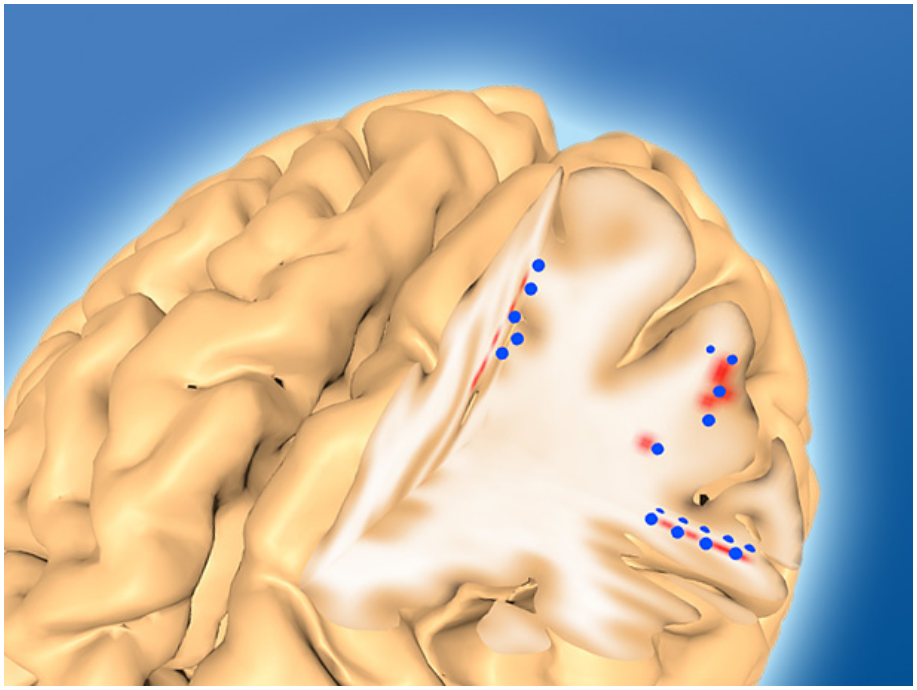


Figure illustrates simultaneous acquisition of intracranial (ic)EEG-fMRI.
In blue: high frequency oscillations (icEEG).
In red: BOLD signal (fMRI).

Main publications in 2017-2018

Ryvlin P, **Ciumas C**, Wisniewski I, Beniczky S. Wearable devices for sudden unexpected death in epilepsy prevention. Epilepsia 2018; 59 Suppl 1, 61-66.

Saignavongs M*, **Ciumas C***, Petton M, Bouet R, Boulogne S, Rheims S, Carmichael DW, Lachaux JP, Ryvlin P. Neural Activity Elicited by a Cognitive Task can be Detected in Single-Trials with Simultaneous Intracerebral EEG-fMRI Recordings. Int J Neural Syst. 2017; 27(1), 1750001. *-co-first authors.

Ciumas C, Ryvlin P. Sudden Unexpected Death in Epilepsy. Epileptologie 2017; 34, 128.

Ciumas C, Laurent A, Saignavongs M, Ilski F, de Bellescize J, Panagiotakaki E, Ostrowsky-Coste K, Arzimanoglou A, Herbillon V, Ibarrola D, Ryvlin P. Behavioral and fMRI responses to fearful faces are altered in benign childhood epilepsy with centro-temporal spikes (BCECTS). Epilepsia 2017; 58(10), 1716-1727.

ORCID number: 0000-0001-9974-2714

Laboratory MySpace

Assist. Professor Andrea Serino
Head of laboratory

Head of the Laboratory MySpace
Laboratoire MySpace
andrea.serino@chuv.ch

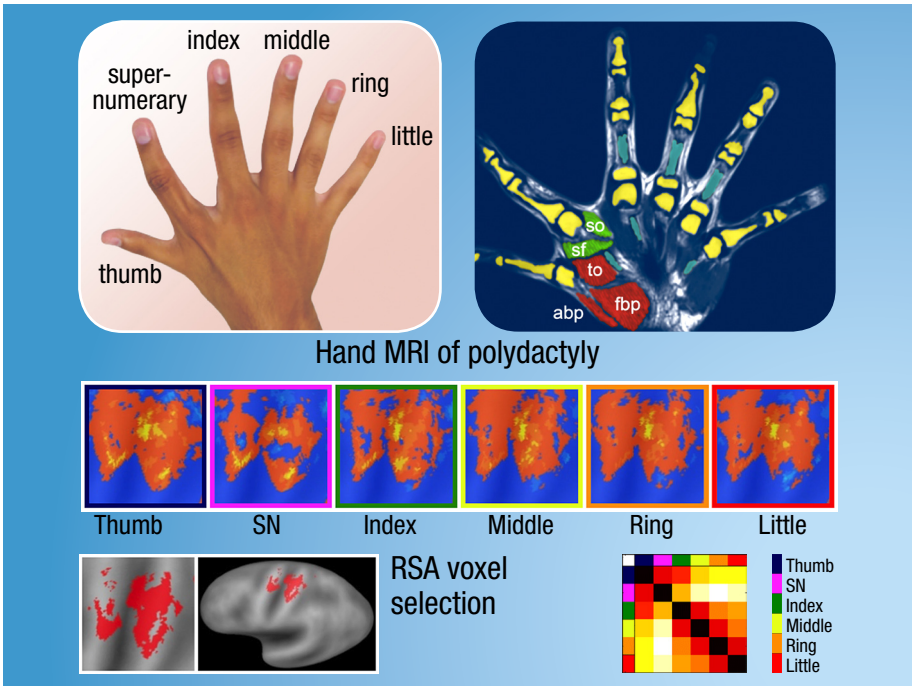
Affiliation
Service of neuropsychology and neurorehabilitation (NPR)

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 cognition. To this aim, we use different techniques from cognitive neuroscience, including psychophysics, virtual reality, fMRI, intracranial and scalp EEG, neuropsychology and neural network modelling to study the multisensory mechanisms underlying the representation of the so-called peripersonal space (PPS).
From such basic knowledge, our aim is to build translational approaches helping to understand and potentially counteract the consequences of brain damages.
The MySpace Lab is mainly funded by an SNSF Professorship grant and sustained by the Leenaards Fundation, the Carigest, the Marie Sklodowska-Curie program and the Faculty of Biology and Medicine of UNIL.

Research interests
With his group, Andrea Serino carries out research to unravel the neural and cognitive basis of body and self experience in space.

Scientific contributions in 2017-2018
> Revealing the neural bases of the multisensory representation of peripersonal space in the human brain *via* intracranial EEG and fMRI.
> Developing a psychophysical tool based on virtual and augmented reality to assess peripersonal space in humans.
> Proposing an updated neural network model of peripersonal space in the human brain.
> Showing how peripersonal space representation affects self-consciousness and social cognition.



Tactile and motor representations of hands with 6 fully developed fingers due to congenital polydactily, as revealed by 7T fMRI and Representational Similarity Analysis (by Dr Michel Akselrod). These results show that the human brain is able to control a functional limb with more sensory and motor abilities than standard bodies.

Main publications in 2017-2018

Bernasconi F, Noel JP, Park HD, Faivre N, Seeck M, Spinelli L, Schaller K, Blanke O, **Serino A**. Audio-Tactile and Peripersonal Space Processing Around the Trunk in Human Parietal and Temporal Cortex: An Intracranial EEG Study. Cereb Cortex 2018 Sep 1; 28(9):3385-3397. doi:10.1093/cercor/bhy156. PubMed PMID:30010843; PubMed Central PMCID: PMC6095214.

Pellencin E, Paladino MP, Herbelin B, **Serino A**. Social perception of others shapes one's own multisensory peripersonal space. Cortex 2018 Jul; 104:163-179. doi: 10.1016/j.cortex 2017.08.033. ePub 2017 Sep 6. PubMed PMID:28965705.

Noel JP, Blanke O, **Serino A**. From multisensory integration in peripersonal space to bodily self-consciousness: from statistical regularities to statistical inference. Ann N Y Acad Sci. 2018 Jun 6. doi:10.1111/nyas.13867. [ePub ahead of print] Review. PubMed PMID:29876922.

Noel JP, Blanke O, Magosso E, **Serino A**. Neural adaptation accounts for the dynamic resizing of peripersonal space: evidence from a psychophysical-computational approach. J Neurophysiol. 2018 Jun 1; 119(6):2307-2333. doi:10.1152/jn.00652.2017. ePub 2018 Mar 14. PubMed PMID:29537917; PubMed Central PMCID: PMC6032111.

Serino A, Akselrod M, Salomon R, Martuzzi R, Blefari ML, Canzoneri E, Rognini G, van der Zwaag W, Iakova M, Luthi F, Amoresano A, Kuiken T, Blanke O. Upper limb cortical maps in amputees with targeted muscle and sensory reinnervation. Brain 2017 Nov 1; 140(11):2993-3011. doi:10.1093/brain/awx242. PubMed PMID:29088353.

Grivaz P, Blanke O, **Serino A**. Common and distinct brain regions processing multisensory bodily signals for peripersonal space and body ownership. Neuroimage 2017 Feb 15; 147:602-618. doi:10.1016/j.neuroimage 2016.12.052. Epub 2016 Dec 23. PubMed PMID: 28017920.

ORCID number: 0000-0001-7475-6095

CHUV
www.chuv.ch/crn-myspace

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

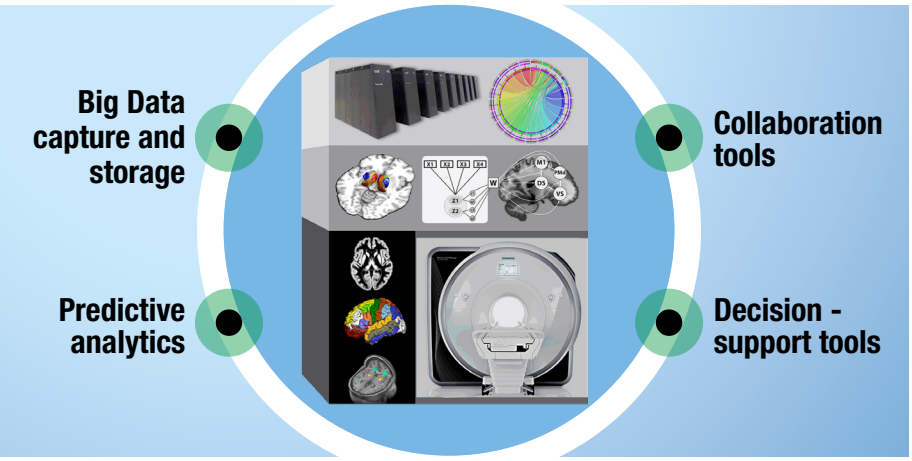
Unisciences
www.unil.ch/unisciences/andreaserino

Neuroscience Research Center

Platforms Presentation

Magnetic Resonance Imaging Platform (MRI)

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



The cornerstone of our strategy for translational neuroscience with direct impact on clinical decision-making and patient care is the MRI platform of the Department of Clinical Neurosciences, CHUV, that was established end 2013 thanks to the generous support from the charitable Foundation Roger De Spoelberg and the Foundation Partridge.
We assist all platform users with the most suitable advanced image acquisition and analysis techniques, but also education and training. The MRI platform is built on two main pillars: high-performance data acquisition and advanced automated data processing.

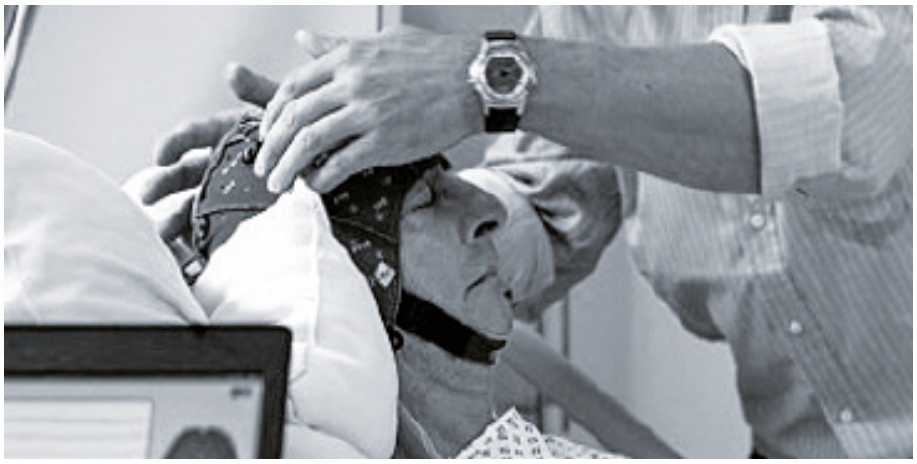
High-performance data acquisition
Scientific instrumentation
> High-end 3T MR system offering optimal signal-to-noise ratio (SNR), speed and stability.
> A complete panel of equipment for real-time assessment of study participants' behaviour during data acquisition.
> Pioneering prospective motion correction system allowing exceptional data quality.

Expertise
> In-house developed brain imaging acquisition sequences for optimal sensitivity in cross-sectional and longitudinal studies.
> Full-range of customized protocols for assessment of brain anatomy and function.

Support team
> MRI engineers for customized solutions to the most challenging demands of neuroimaging research.
> MRI physicists for tailored acquisition protocols and optimal scientific output in all neuroscience studies.
> Close monitoring of scanner performance for sustained optimal data quality.

Electrophysiology Platform (EEG Platform)

Senior Lecturer, adjunct Professor Marzia De Lucia
Head of the EEG Platform



The Electrophysiology Platform of the Clinical Neuroscience Department, Lausanne University Hospital, is a collaborative initiative dedicated to advanced techniques for the analysis of electroencephalography and stereoelectroencephalography recordings in humans.

The platform is coordinated by Dr Marzia De Lucia and aims at:
> sharing a comprehensive set of user-friendly tools for the analysis of electrophysiological recordings
> developing tools that can support the development of common scientific topics
> promoting discussions about future projects in order to optimize available resources and benefiting from the established know-how in the department
> getting updates about ongoing projects.

Since March 2017 and every two months, the platform organizes meetings with the goal of sharing innovative latest progresses in electrophysiology-based projects in the department. Each seminar focuses on a scientific project and on the methods used for data analyses. A repository of meetings abstracts and news about the platform are available at a dedicated website:

https://eegplatformdnc.wordpress.com/

Unisciences
www.unil.ch/unisciences/marziadelucia

Neuroscape Facility

Senior Lecturer, adjunct Professor Arseny Sokolov, MD
Head of the Neuroscape Facility

The Neuroscape Facility has been established since January 2018. It is co-directed by Dr Arseny Sokolov and Prof. Andrea Serino and located in Pavillon 4 at the CHUV. The Facility is a founding member of the Neuroscape Alliance, spear-headed by the Neuroscape Center at the University of California San Francisco.

Equipment & Expertise
The Neuroscape Facility is equipped with an immersive driving simulator, a giant screen, high-end computer graphics, whole-body tracking, head-mounted virtual reality devices, wearable physiological sensors and mobile devices. Research staff and collaborators consist of engineers, neuroscientists, neuropsychologists, physical therapists and neurologists with expertise in cognitive and physical rehabilitation for neurological patients, in both clinical and experimental settings.

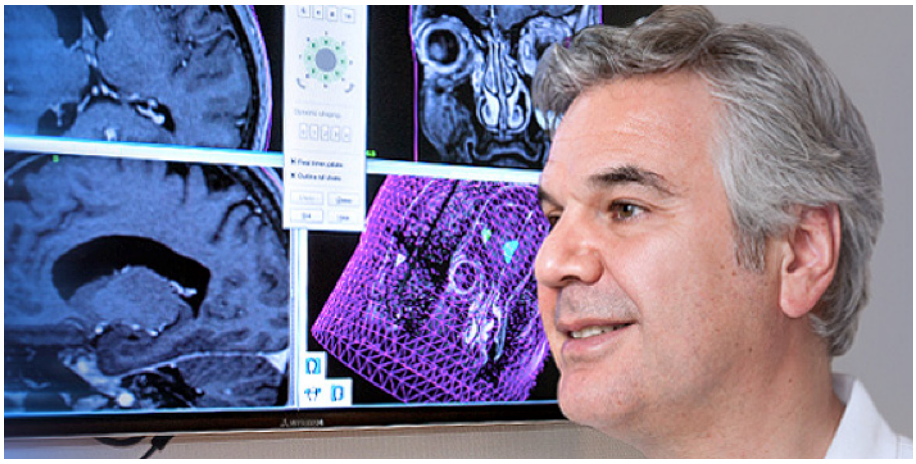
Mission & Services
The mission of the Neuroscape Facility represents designing, testing, validating and implementing novel gamified technological approaches for the assessment and rehabilitation of cognitive function and behavior in neurological patients. To this end, the Facility initiates projects 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.

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

Unisciences
www.unil.ch/unisciences/arsenysokolov

Gamma Knife Center

Professor Marc Levivier, MD, PhD
Head of the Neurosurgery Service
Head of the Gamma Knife Center



The Gamma Knife Center in the CHUV started its clinical activity in July 2010 and treats on regular basis patients with a large spectrum of neurosurgical conditions. The indications are multiple and Gamma Knife radiosurgery can be proposed as an alternative to a classical microsurgical excision, as a complement of the former, or when surgery is not possible. More than 1200 patients have been treated up-to-date. Since June 2016, our Gamma knife Center is equipped with the last model and new functionalities, the Leksell Gamma Knife ICON. The research activity is an integrated part.

Research activity involves two main aspects:
> Clinical (in partnership with the Neurosurgery Service in the CHUV, but also with other university hospitals, including those from Marseille, London, Oxford or Lille)
> Fundamental (mainly in partnership with the Swiss Federal Institute of Technology, EPFL, University of Geneva and the Timone Hospital in Marseille)

Our clinical research focuses on the study of clinical outcomes related to functional neurosurgery (in particular pain, as in trigeminal or glossopharyngeal neuralgia), as well as the optimization of functional results after Gamma Knife treatment in benign tumours, such as vestibular schwannomas (hearing preservation, treatment of the acute effects, combined approaches with microsurgery), meningiomas (multicentric studies, place of hypofractionation) or vascular malformations (study of the predictive factors for obliteration). Collaboration with London and Oxford is currently evaluating the possibility of establishing complex algorithms for dose prescription, allowing increasing the efficacy and diminishing the toxicity of certain radiosurgical procedures.

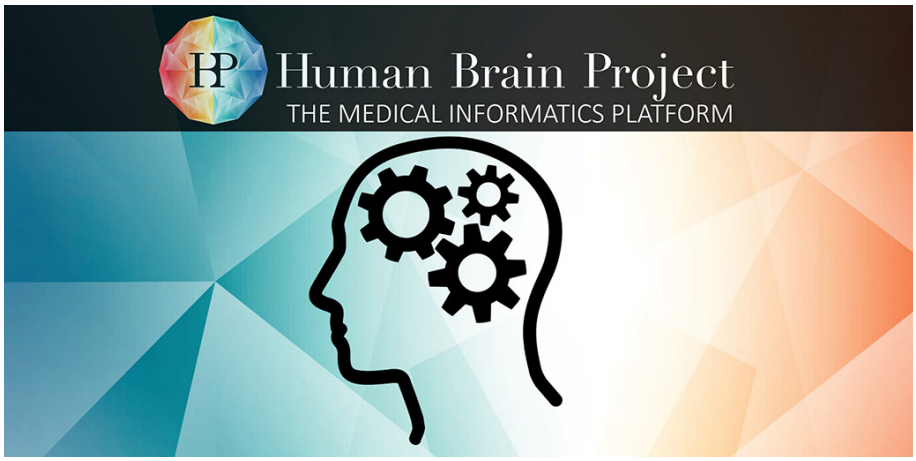
Regarding fundamental research, it focuses on the study of structural and functional brain connectivity, by using 3 Tesla or higher (7 Tesla) MRI. The purpose is to ameliorate the management of patients with essential tremor, grace to multiple aspects, allowing optimizing the targeting and also better understanding the clinical response after Gamma Knife thalamotomy. This is mainly evaluating the therapeutic response in function of different phenotypes of the disease. They are integrated in a research work in the frame of an MD-PHD and PhD program. Radiophysical fundamental research (dosimetric comparaisons) is realized also with the Radiophysical Institute in Lausanne.

CHUV
www.chuv.ch/gamma-knife

Unisciences
www.unil.ch/unisciences/marclevivier

Medical Informatics Platform of HBP (Subproject 8)

Professor Philippe Ryvlin
Head of the Medical Informatics Platform of HBP



For the past few years, the Department for Clinical Neuroscience of CHUV has been coordinating the developments and operation of one of the infrastructure platform of the Human Brain Project: the Medical Informatics Platform (MIP).

165 million Europeans are living with a brain disorder, causing a global cost (direct and indirect) exceeding 800 billion euros for the National Health budgets.
Through Sub-Project 8 (SP8), the Human Brain Project (HBP) specifically addresses one of EU's health priorities to reduce this burden by promoting novel knowledge and understanding of brain diseases towards personalized medicine and treatment.
SP8 develops and operates the Medical Informatics Platform (MIP), a privacy preserving data analytics application for clinicians and researchers, enabling them to run analysis on health-related data distributed across different hospitals and research centers, without moving the data outside their original storage.
MIP helps users investigate and compare harmonized medical data extracted from pre-processed neuroimaging, neurophysiological, -omics and medical records. It features a user-friendly interface to run statistical analysis and predictive models using machine learning on large datasets.
MIP relies on citizens and patients allowing research to use their private medical data. One of SP8's mission is to highlight the potential benefits as well as the risks associated with its activities, by explaining how sharing medical data is crucial to achieve progress in medicine, diagnosis and treatment, and how these data can be thoroughly protected to ensure privacy preservation. HBP and SP8 not only comply with regulation and ethics standards, but are at the forefront of best practices in the area.

The Human Brain Project (HBP) is building a research infrastructure to help advance neuroscience, medicine and computing. It is one of the two largest scientific projects ever funded by the European Union. The 10-year Project began in 2013 and directly employs some 500 scientists at more than 100 universities, teaching hospitals and research centres across Europe
Six ICT research Platforms form the heart of the HBP infrastructure: Neuroinformatics (access to shared brain data), Brain Simulation (replication of brain architecture and activity on computers), High Performance Analytics and Computing (providing the required computing and analytics capabilities), Medical Informatics (access to patient data, identification of disease signatures), Neuromorphic Computing (development of brain-inspired computing) and Neurorobotics (use of robots to test brain simulations).
The HBP also undertakes targeted research and theoretical studies, and explores brain structure and function in humans, rodents and other species. In addition, the Project studies the ethical and societal implications of HBP's work.

https://www.humanbrainproject.eu/en/

Twitter: HBPmedical

Neuroscience Research Center

Centre de recherche en neurosciences, CHUV

Prof. Nicole Déglon, Head of CRN

www.chuv.ch/crn
info.crn@chuv.ch

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