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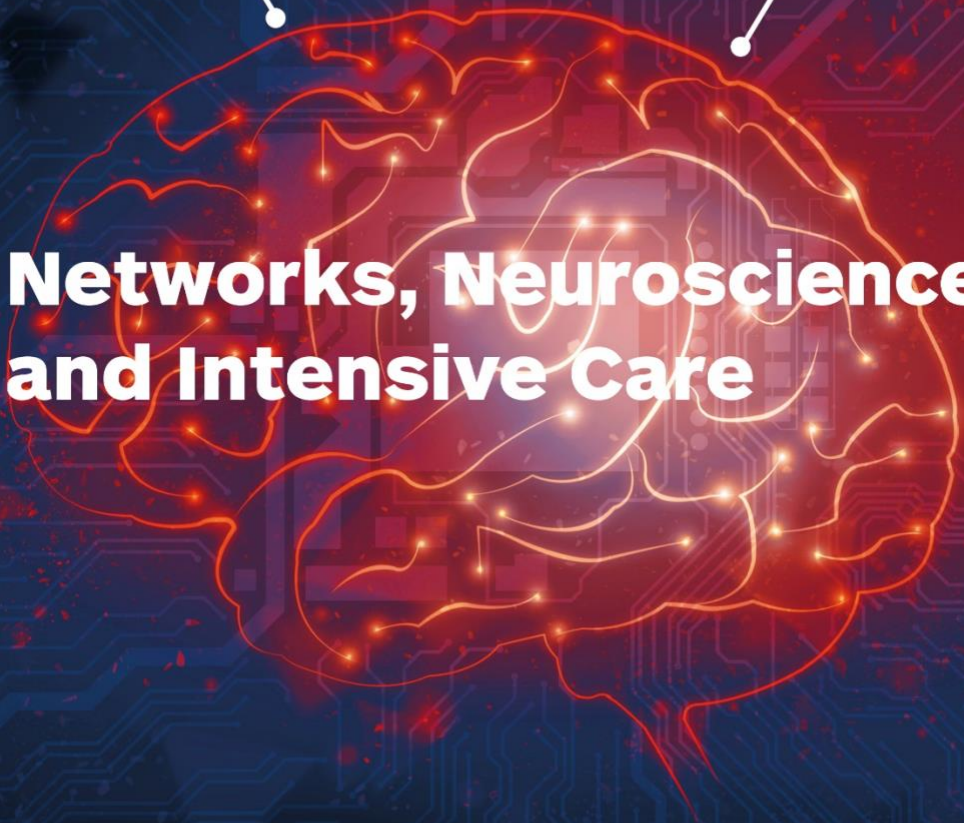

Networks, Neuroscience, and Intensive Care

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THURSDAY 30 JUNE I DAY ONE

8:50AM > 9AM	**CONGRESS OPENING**
9AM > 10:15AM	**INTRODUCTION AND CONTEXT**
9am > 9:20am	Consciousness and Cortical Networks *C. Koch, USA*
9:20am > 9:40am	Network Medicine: From Cellular Networks to the Human Diseasome *A. Barabasi, Boston, USA*
9:40am > 10:00am	Network paradigms in disorders of consciousness *A. Demertzi, Liège, Belgium*
10:00am > 10:15am	Question/Answers live
10:15AM > 11AM	**COFFEE BREAK**
11AM > 12:30PM	**LARGE SCALE CEREBRAL NETWORKS: MODELS**
11am > 11:20am	Lesion, stimulation and neuroimaging studies of cortical networks supporting human consciousness *M. Boly, Madison, USA*
11:20am > 11:40am	Network-based neurodegeneration *W. Seeley, San Francisco, USA*
11:40am > 12:00pm	Anesthesia-Induced Unconsciousness: Mechanisms and Control *E. Brown, Philadelphia, USA*
12:00pm > 12:30pm	Question/Answers live
12:30PM > 1:20PM	**LUNCH BREAK**
1:20PM > 2:30PM	**LARGE SCALE CEREBRAL NETWORKS: ACTIVE AND STIMULATION PARADIGMS**
1:20pm > 1:40pm	Decomposing language processing in the healthy brains with deep learning algorithms *J.R. King, Paris, France*
1:40pm > 2:00pm	Towards a computational neurophysiology of covert auditory processing in comatose patients *J.J. Aucouturier, Besançon, France*
2:00pm > 2:30pm	Question/Answers live
2:30PM > 3:30PM	**CELLULAR AND MOLECULAR NETWORKS**
2:30pm > 2:50pm	Molecular mechanisms underlying neural circuit assembly in the mammalian visual system *A. Kolodkin, Baltimore, USA*
2:50pm > 3:10pm	Astrocyte modulation of synaptic function *M. Cohen-Salmon, Paris, France*
3:10pm > 3:40pm	Question/Answers live
3:40pm > 4pm	**COFFEE BREAK**
4PM > 5:15PM	**CELLULAR AND MOLECULAR NETWORKS (FOLLOWED)**
4pm > 4:20pm	Cerebral organoids for neurologic disease modeling *L. Le Guennec, Paris, France*
4:20pm > 4:40pm	Mapping networks in the awake mouse brain by functional ultrasound imaging *Z. Lenkei, Paris, France*
4:40pm > 5:00pm	Modeling of stroke recovery with advanced brain connectivity imaging *F. Hummel, Lausanne, Switzerland*
5:00pm > 5:15pm	Question/Answers live

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FRIDAY 1 JULY I DAY TWO

8:30AM > 10:45AM	**LARGE-SCALE NETWORK ANALYSIS IN INTENSIVE CARE**
8:30am > 8:50am	Connectome signatures for brain injury prediction and classification *R. Stevens, Baltimore, USA*
8:50am > 9:10am	Task-based EEG analysis in the ICU *J. Claassen, New-York, USA*
9:10am > 9:30am	Resting-state EEG analysis in the ICU *B. Rohaut, Paris, France*
9:30am > 9:50am	Importance, limits and caveats of the use of Disorders of Consciousness to theorize consciousness *L. Naccache, Paris, France*
9:50am > 10:10am	Network adaptations during recovery from severe neurological injury *V. Newcombe, Cambridge, UK*
10:10am > 10:45am	Question/Answers live
10:45AM > 11:15AM	**COFFEE BREAK**
11:15AM > 1:00PM	**NEURO-IMMUNE NETWORK CROSSTALK IN CRITICAL ILLNESS**
11:15am > 11:35am	Cerebral network dysfunction associated with systemic inflammatory signaling *M. Heneka, Bonn, Germany*
11:35am > 11:55am	Epigenetic regulation of microglial cells *A. Jacquens, Lausanne, Switzerland*
11:55am > 12:15pm	The microbiome and immune modulation of cerebral function *M. Rodriguez Aburto, Cork, Irlande*
12:15pm > 12:35pm	Neuromodulation of the immune response in critically ill patients *D. Annane, Paris, France*
12:35pm > 1pm	Question/Answers live
1PM > 2PM	**LUNCH BREAK**
2PM > 3:30PM	**NEURO-IMMUNE NETWORK CROSSTALK IN CRITICAL ILLNESS (FOLLOWED)**
2:pm > 2:20pm	Systemic immune adaptation to brain-injury *A. Roquilly, Nantes, France*
2:20pm > 2:40pm	BLA circuits supporting negative hedonic bias in depression *C. Henry, Paris, France*
2:40pm > 3:00pm	Neuroimmunology of post-sepsis PTSD *A. Mazeraud, Paris, France*
3:00pm > 3:30pm	Question/Answers live
3:30PM > 4PM	**COFFEE BREAK**
4PM > 5:15PM	**BRAIN-CARDIAC NETWORKS IN CRITICAL ILLNESS**
4pm > 4:20pm	Anatomy and physiology of the brain/cardiac axis *J. Sitt, Paris, France*
4:20pm > 4:40pm	Neurological outcomes of ECMO *R. Sonneville, Paris, France*
4:40pm > 5pm	Decoding cardiac signals in acute brain injury *S. Park, USA*
5pm > 5:15pm	Question/Answers live
5:15PM > 6:30PM	**BRAIN-RESPIRATORY NETWORKS IN CRITICAL ILLNESS**
5:15pm > 5:35pm	Brain-lung crosstalk after acute brain injury *K. Asehnoune, Nantes, France*
5:35pm > 5:55pm	Approaches to ventilator-patient dyssynchrony *L. Brochard, Toronto, Canada*
5:55pm > 6:15pm	Brainstem dysfunction in COVID-19 patients *B. Hermann, Paris, France*
6:15pm > 6:30pm	Question/Answers live

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INTRODUCTION AND CONTEXT

Christoph KOCH, PhD
ALLEN INSTITUTE FOR BRAIN SCIENCE
TINY BLUE DOT FOUNDATION
USA

Biosketch

Dr. Christof Koch is a neuroscientist best known for his studies and writings exploring the basis of consciousness, starting with the molecular biologist Francis Crick more than a quarter of a century ago. Trained as a physicist, Dr. Koh was for 27 years a professor of biology and engineering at the California Institute of Technology. In 2015, he became the President of the Allen Institute for Brain Science in Seattle. He is now the Chief Scientist of the MindScope Program at the Allen Institute, and the Chief Scientist of the *Tiny Blue Dot Foundation* in Santa Monica.

CONSCIOUSNESS AND CORTICAL NETWORKS

Human and animals not only act in the world but subjectively experience it, such as the unmistakable taste of *Châteauneuf du Pape* or the sharp sting of an infected tooth. I will discuss progress achieved in locating the footprints of such conscious experiences to the cerebral cortex, the outermost layer of the brain, and closely associated systems, such as the thalamus and the claustrum. I will discuss primarily clinical data that points to posterior, post-rolandic regions of cortex in occipital, parietal and temporal regions as being the physical substrate of experiences. Prefrontal cortex appears to be associated with response execution and planning, reasoning, and intelligence, rather than consciousness *per se*.

Notes

INTRODUCTION AND CONTEXT

Albert-László BARABASI

NORTHEASTERN UNIVERSITY
HARVARD UNIVERSITY
CENTREAL EUROPEAN
UNIVERSITY

Biosketch

Albert-László Barabási is both the Robert Gray Dodge Professor of Network Science and a Distinguished University Professor at Northeastern University, where he directs the Center for Complex Network Research, and holds appointments in the Departments of Physics and Computer Science, as well as in the Department of Medicine, Harvard Medical School and Brigham and Women Hospital, and is a member of the Center for Cancer Systems Biology at Dana Farber Cancer Institute. A Hungarian born native of Transylvania, Romania, he received his Masters in Theoretical Physics at the Eotvos University in Budapest, Hungary and was awarded a Ph.D. three years later at Boston University. Barabási is the author of the forthcoming book “The Formula: The Science of Success,” and his last book was "Bursts: The Hidden Pattern Behind Everything We Do" (Dutton, 2010) available in five languages. He has also authored "Linked: The New Science of Networks" (Perseus, 2002), currently available in eleven languages, and is the co-editor of "The Structure and Dynamics of Networks" (Princeton, 2005).

His work lead to the discovery of scale-free networks in 1999, and proposed the Barabási-Albert model to explain their widespread emergence in natural, techno-logical and social systems, from the cellular telephone to the WWW or online communities.

Barabási is a Fellow of the American Physical Society. In 2005 he was awarded the FEBS Anniversary Prize for Systems Biology and in 2006 the John von Neumann Medal by the John von Neumann Computer Society from Hungary, for outstanding achievements in computer-related science and technology. In 2004 he was elected into the Hungarian Academy of Sciences and in 2007 into the Academia Europaea. He received the C&C Prize from the NEC C&C Foundation in 2008. In 2009, APS chose him Outstanding Referee and the US National Academies of Sciences awarded him the 2009 Cozzarelli Prize. In 2011 Barabási was awarded the Lagrange Prize-CRT Foundation for his contributions to complex systems, awarded Doctor Honoris Causa from Universidad Politécnica de Madrid, became an elected Fellow in AAAS (Physics) and is a 2013 Fellow of the Massachusetts Academy of Sciences.

NETWORK MEDICINE: FROM CELLULAR NETWORKS TO THE HUMAN DISEASOME

Given the functional interdependencies between the molecular components in a human cell, a disease is rarely a consequence of an abnormality in a single gene, but reflects the perturbations of the complex intracellular network. The emerging tools of network medicine offer a platform to explore systematically not only the molecular complexity of a particular disease, leading to the identification of disease modules and pathways, but also the molecular relationships between apparently distinct (patho) phenotypes. Advances in this direction are essential to identify new disease genes, to uncover the biological significance of disease-associated mutations identified by genome-wide association studies and full genome sequencing, and to identify drug targets and biomarkers for complex diseases.

Notes

INTRODUCTION AND CONTEXT

Athena DEMERTZI, PhD
UNIVERSITY OF LIEGE
BELGIUM

Biosketch

Dr Demertzi is a tenured FNRS Research Associate at the ULiège GIGA Institute, in Belgium. She graduated as a psychologist from the Aristotle University of Thessaloniki, with a subsequent MSc specialization in Cognitive Neuroscience and Neuropsychology at Maastricht University. She holds a PhD in Medical Sciences from ULiège. Dr. Demertzi currently directs the Physiology of Cognition Lab. With her team, they investigate brain-body interactions as a proxy to human sentience in health and disease by means of high- and low-tech methodologies. In the past, she has conducted behavioral and neuroimaging studies in physiological (hypnosis), pathological (brain injury) and pharmacological (anesthesia) conditions. Using artificial intelligence, she has determined neuromarkers of conscious states, and contributing to individualized patient care. As this type of research touches upon philosophical and ethical issues, the entailing socio-ethical implications interest her deeply. In 2020 she was awarded by the AstraZeneca Foundation with the Scientific Award in "Patient Care in the AI Era 2020" for her contribution to individualized patient care by means of machine learning applications. In the past, she was FNRS Postdoctoral Researcher, and an INSERM fellow at the Institut du Cerveau et de la Moelle épinière (ICM) of the Hospital Pitié-Salpêtrière in Paris.

NETWORK PARADIGMS IN DISORDERS OF CONSCIOUSNESS

Individuals in disorders of consciousness are unable to communicate intentionally with the environment. Consequently, their mental state needs to be inferred by means of meaningful proxies. The fMRI resting paradigm has been a great asset to that matter, as it quantifies brain function by surpassing the need for communication of experience or behavioral output. Overall, studies in disorders of consciousness point to lesser functional connectivity between regions that are within the same network but also across different systems. In my talk, I will show how the brain's intrinsic network architecture configures differentially in different states of consciousness, what are the potential biological substrates of these configurations, and how network-wise organization can be used for clinical purposes.

Notes

LARGE SCALE CEREBRAL NETWORKS: MODELS

Melanie BOLY
UNIVERSITY OF WISCONSIN
MADISON
USA

Biosketch

Melanie Boly is a neurologist and neuroscientist who has worked for twenty years in the field of altered states of consciousness such as vegetative state, sleep and anesthesia, under the mentorship of Pr. Steven Laureys, Pierre Maquet, Adrian Owen, Marcello Massimini and Karl Friston. Her research aims at combining neuroimaging techniques such as PET, functional MRI, TMS-EEG, high-density EEG and intracranial recordings to a theoretical framework, the Integrated Information Theory of Consciousness, hoping to uncover the neural mechanisms of the level and contents of consciousness in healthy subjects and neurological patients in order to improve both diagnosis and therapies. She is board certified in neurology in both Europe and the US. Her work has led to date to numerous publications in international peer-reviewed journals (>150 Pubmed-indexed articles, current Google Scholar H-index 80) and invited talks at international conferences. She is also Associate Editor of the journals Neuroimage, Frontiers in Consciousness Research, Frontiers in Brain Imaging Methods and Neuroscience of Consciousness.

LESION, STIMULATION AND NEUROIMAGING STUDIES OF CORTICAL NETWORKS SUPPORTING HUMAN CONSCIOUSNESS

I will review evidence for cortical networks supporting human consciousness coming from human lesion studies, direct electrical stimulation studies in epileptic patients, and recent neuroImaging studies distilling consciousness from its cognitive consequences. Coherent findings from these three lines of evidence suggest that many contents of consciousness are specified by posterior cortical networks, and that the integrity of these cortical networks also best predicts recovery from traumatic or anoxic brain injury. I will finish by suggesting some promising directions for future research.

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LARGE SCALE CEREBRAL NETWORKS: MODELS

William W. SEELEY, MD

UNIVERSITY OF CALIFORNIA
SAN FRANCISCO
USA

Biosketch

Dr. Seeley's clinical practice focuses on patients with neurodegenerative disease, especially those suffering from dementia. His research has two primary goals. The first goal is to clarify mechanisms of selective vulnerability by blending anatomy, neuroimaging, and pathology with molecular-genetic analyses. The second goal is to accelerate drug discovery by developing network-based neuroimaging biomarkers for monitoring disease progression. In 2011, Dr. Seeley was awarded a MacArthur Foundation Fellowship in recognition of his work. He directs the UCSF Neurodegenerative Disease Brain Bank, and he holds the Zander Family Endowed Professorship in Neurology, with a secondary appointment in Pathology, at UCSF.

NETWORK-BASED NEURODEGENERATION

Large-scale neural networks organize diverse forms of thought, feeling, and action. Clinical and neuropathological studies have long suggested that each neurodegenerative disease targets a specific neural network. In recent years, methodological advances have enabled researchers to build support for this hypothesis and to explore "network-based neurodegeneration" mechanisms in cells, model organisms, and patients. This lecture will provide an overview of this field, with a focus on neuroimaging observations made in patients. Findings to date support a conceptual framework with the potential to clarify important and mysterious aspects of neurodegenerative disease, improve early detection, and facilitate therapeutic discovery.

Notes

LARGE SCALE CEREBRAL NETWORKS: MODELS

Emery N. BROWN

HARVARD MEDICAL SCHOOL
MASSACHUSSETS GENERAL HOSPITAL
USA

Biosketch

Emery N. Brown, M.D., Ph.D. is the Edward Hood Taplin Professor of Medical Engineering and Computational Neuroscience at MIT; the Warren M. Zapol Professor of Anaesthesia at Harvard Medical School; and an anesthesiologist at Massachusetts General Hospital (MGH). He received his B.A. in Applied Mathematics (*magna cum laude*) from Harvard College, his M.A. and Ph.D. in statistics from Harvard University and his M.D. (*magna cum laude*) from Harvard Medical School.

Dr. Brown completed his internship in internal medicine at the Brigham and Women's Hospital and his anesthesiology residency at MGH.

He is an anesthesiologist-statistician whose research has established that a primary mechanism of anesthetic action is the induction and maintenance of oscillation in local field potentials that disrupt normal intracerebral communication. He also develops statistical methods for neuroscience data analysis.

Dr. Brown is a fellow of the American Academy of Arts Sciences and the U. S. National Academy of Inventors. He is a member of the U.S. National Academy of Medicine, U.S. National Academy of Sciences, and the U.S. National Academy of Engineering.

Dr. Brown has received a U.S. National Institutes of Health Director's Pioneer Award, a Guggenheim Fellowship in Applied Mathematics, the American Society of Anesthesiologists Excellence in Research Award, the Dickson Prize in Science, the Swartz Prize for Theoretical and Computational Neuroscience, and a Doctor of Science *Honoris Causa* from the University of Southern California.

ANESTHETIA - INDUCED UNCONSCIOUSNESS: MECHANISMS AND CONTROL

General anesthesia is a drug-induced, reversible condition comprised of five behavioral states: unconsciousness, amnesia (loss of memory), antinociception (loss of pain sensation), akinesia (immobility), and physiological stability. Our work shows that a primary mechanism through which anesthetics create these altered states of arousal is by initiating and maintaining highly structured oscillations in local field potentials.

These oscillations impair communication among brain regions. We illustrate this effect by presenting findings from our human and non-human primate studies using high-density EEG recordings and intracranial recordings. These studies have allowed us to give a detailed characterization of the neurophysiology of loss and recovery of consciousness due to propofol, and more recently ketamine. We demonstrate that the state of general anesthesia can be controlled using closed loop feedback anesthesia delivery systems. The success of our research has depended critically on tight coupling of experiments, signal processing research and mathematical modeling.

Notes

LARGE SCALE CEREBRAL NETWORKS: ACTIVE AND STIMULATION PARADIGMS

Jean-Rémi KING

CNRS
PARIS
FRANCE

DECOMPOSING LANGUAGE PROCESSING IN THE HEALTHY BRAINS WITH DEEP LEARNING ALGORITHMS

The Deep learning has recently made remarkable progress in natural language processing. Yet, the resulting algorithms fall short of the language abilities of the human brain. To bridge this gap, we here explore the similarities and differences between these two systems using large-scale datasets of magneto/electro-encephalography (M/EEG, n=1,946 subjects), functional Magnetic Resonance Imaging (fMRI, n=589), and intracranial recordings (n=176 patients, 20K electrodes). After investigating where and when deep language algorithms map onto the brain, we show that enhancing these algorithms with long-range forecasts makes them more similar to the brain. Our results further reveal that, unlike current deep language models, the human brain is tuned to generate a hierarchy of long-range predictions, whereby the fronto-parietal cortices forecast more abstract and more distant representations than the temporal cortices. Overall, our studies show how the interface between AI and neuroscience clarifies the computational bases of natural language processing.

Notes

LARGE SCALE CEREBRAL NETWORKS: ACTIVE AND STIMULATION PARADIGMS

Jean-Julien AUCOUTURIER

FEMTO-ST Institute (CNRS / UNIVERSITY OF BOURGOGNE Franche-Comté)
BESANCON
FRANCE

Biosketch

Jean-Julien Aucouturier was trained at SONY Computer Science Laboratories with François Pachet and holds a PhD in Computer Science from Université Pierre et Marie Curie (2006). JJ has then held several postdoctoral positions in cognitive neuroscience at the University of Tokyo with Takashi Ikegami and at the RIKEN Brain Science Institute with Kazuo Okanoya. After a decade at IRCAM in Paris where he directed the ERC-funded CREAM music neuroscience team, he is now a CNRS Research Director (equiv. to Full Professor) at the FEMTO-ST Institute (CNRS/Université de Bourgogne Franche-Comté) in Besançon, France. His research program in FEMTO-ST is based on data-driven, system-science approaches to clinical neurophysiology, with a focus on the auditory/speech modality, and health technology applications in neurology and psychiatry. Lab website: https://neuro-team-femto.github.io

TOWARDS A COMPUTATIONAL NEUROPHYSIOLOGY OF COVERT AUDITORY PROCESSING IN COMATOSE PATIENTS

The past 10 years have seen the emergence in the cognitive neuroscience community of a novel class of 'data-driven' methods inspired by psychophysical reverse-correlation, which allow researchers to model a participant's neurophysiological responses to arbitrarily generated visual or auditory stimuli (Adolphs et al. 2016). Taking the example of some of our recent results on the perception of speech prosody (Ponsot et al., PNAS 2018; Goupil et al. Nature Communications 2021), I will show how to use these new methodologies to identify the sensory mechanisms that underly covert auditory processing in neurological patients in stroke and coma.

Notes

CELLULAR AND MOLECULAR NETWORKS

Martine COHEN-SALMON

CNRS
PARIS
FRANCE

Biosketch

Martine Cohen-Salmon (DR2 CNRS) is a molecular neurobiologist with a specific expertise in the field of astrocytes. She heads a research group "Physiology and physiopathology of the gliovascular unit" at the CIRB (INSERM U1050/CNRS UMR 7241, Collège de France). She developed innovative approaches to characterize the role of astrocytes at the vascular and neuronal interfaces. She recently discovered that astrocytes organize local translation, which allowed her to propose a totally new angle of research to understand how astrocytes regulate their polarity and functions at the vascular and synaptic interfaces.

ASTROCYTE MODULATION OF SYNAPTIC FUNCTION

Astrocytes constitute the most abundant population of glial cells in the mammalian brain. They are morphologically complex cells, with many ramifications extending towards both blood vessels and neurons. Specific domains called endfeet contact the blood vessels and enable astrocytes to modulate important vascular functions, such as blood-brain barrier integrity, immunity and cerebral blood flow. The perisynaptic astrocytic processes (PAP) interact with both synapses and dendrites, and regulate synaptic transmission. Understanding how this astrocytic functional polarity is set is crucial because aberrant communication between neurons, brain vessels and astrocytes contributes to several brain diseases.

Mechanisms involved in astrocytic polarity are complex. We recently showed that local synthesis of proteins (translation) occurs in astrocyte perivascular and perisynaptic interfaces. We characterized local translation in PAPs in the dorsal hippocampus, a region of the brain involved in memory and learning. We showed that PAPs contain the machinery for translation. We characterized the repertoire of translating mRNAs in PAPs and compared it to the one expressed in the whole astrocyte. We found that a specific pool of mRNAs was highly polarized at the synaptic interface. These transcripts composed an unexpected molecular repertoire encoding proteins involved in iron homeostasis, translation, cell cycle and cytoskeleton.

Remarkably, we observed alterations in RNA distribution and ribosome-bound status of some PAP-enriched transcripts after fear conditioning, indicating the role of astrocytic local translation in memory and learning.

Altogether our work suggests that astrocyte perisynaptic polarity is be sustained by local translation. Our findings also constitute the first evidence of a correlation between fear conditioning and translational changes in PAPs – changes that might be linked to the regulation of synaptic and circuit functions underlying complex behaviors.

Mazare, N., M. Oudart, and M. Cohen-Salmon. 2021. Local translation in perisynaptic and perivascular astrocytic processes - a means to ensure astrocyte molecular and functional polarity? J Cell Sci. 134.

Mazare, N., M. Oudart, J. Moulard, G. Cheung, R. Tortuyaux, P. Mailly, D. Mazaud, A.P. Bemelmans, A.C. Boulay, C. Blugeon, L. Jourdren, S. Le Crom, N. Rouach, and M. Cohen-Salmon. 2020b. Local Translation in Perisynaptic Astrocytic Processes Is Specific and Changes after Fear Conditioning. Cell Rep. 32:108076.

Oudart, M., R. Tortuyaux, P. Mailly, N. Mazare, A.C. Boulay, and M. Cohen-Salmon. 2020. AstroDot - a new method for studying the spatial distribution of mRNA in astrocytes. J Cell Sci. 133.

Notes

LARGE-SCALE NETWORK ANALYSIS IN INTENSIVE CARE

Robert D. STEVENS, MD, FCCM

JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE
BALTIMORE
USA

Biosketch

Dr. Stevens is Director of the Division of Informatics, Integration and Innovation and of Precision Medicine, and he co-directs the Johns Hopkins Precision Medicine Center of Excellence in Neurocritical Care at Johns Hopkins University School of Medicine. Dr. Stevens is a practicing intensive care specialist and funded investigator who is deeply invested in clinical and translational science, program building, and education He is actively engaged in collaborations with investigators in the Johns Hopkins Schools of Medicine, Engineering and Public Health. He is an enthusiastic educator and mentor, teaching courses at Johns Hopkins and internationally, participating in the training of intensive care residents and fellows, and supporting graduate and undergraduate students in independent and degree-oriented academic projects.

Dr Stevens' research focuses on computational approaches in the evaluation and treatment of patients with critical illness and injury. He founded the Laboratory for Computational Intensive Care Medicine (https://lcicm.jhmi.edu/) with the goal to enhance the precision of decision-making in intensive care. This groups uses algorithmic methods to decode patterns in high-dimensional data from sources such as electronic health records, wearable biosensors, high-frequency physiological recordings, and medical imaging. The overarching vision is to advance biomedical science by catalyzing the convergent power of clinical excellence, artificial intelligence and engineering.

CONNECTOME SIGNATURES FOR BRAIN INJURY PREDICTION AND CLASSIFICATION

Processing in the brain relies on dynamic integration within and between regions mediated through large-scale networks. Networks are identified and characterized using advanced structural and functional imaging as well as EEG, MEG, and combined studies such as TMS/EEG. Network disruptions are observed in critical neurological conditions such as stroke, trauma, or cardiac arrest and represent putative substrates for endotype classification, outcome prediction, as well as treatment selection.

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LARGE-SCALE NETWORK ANALYSIS IN INTENSIVE CARE

Jan CLAASSEN, MD

COLUMBIA UNIVERSITY
NEW YORK PRESBYTERIAN HOSPITAL
USA

Biosketch

Dr. Jan Claassen is an Associate Professor in the Department of Neurology and the Chief of the Division of Critical Care & Hospitalist Neurology and Head of Neurocritical Care at Columbia University College of Physicians and Surgeons. He studied medicine at the University of Hamburg, Germany, and underwent post-doctoral research training and clinical training in neurology, electrophysiology, and neurocritical care at Columbia University, NY. His research characterizes physiologic underpinnings of acute disorders of consciousness focusing on understanding underlying mechanisms, prognosis and treatment of unconscious patients early after brain injury. Dr Claassen's group has focused on the use of innovative brain monitoring techniques and linked covert consciousness diagnosed within days of coma to long term functional outcomes.

Dr Claassen has been intimately involved with national and international guideline development for patients with acute brain injury. He has authored over 300 peer-reviewed articles and is the editor of several books including the most recent edition of Plum and Posner's "Diagnosis and Treatment of Stupor and Coma". He is supported by federal and foundation funding.

TASK-BASED EEG ANALYSIS IN THE ICU

Dr Claassen will discuss novel approaches of task-based EEG paradigms and analysis applied shortly after onset of coma in the ICU context. He will discuss the potential of these techniques for diagnosis, prognostication and treatment of unconscious patients. He will focus in particular on the significance of covert consciousness and our current understanding of the underlying mechanisms of this phenomenon.

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LARGE - SCALE NETWORK ANALYSIS IN INTENSIVE CARE

Lionel NACCACHE

SORBONNE UNIVERSITY
PITIE SALPETRIERE HOSPITAL
PARIS
FRANCE

IMPORTANCE, LIMITS, AND CAVEATS OF THE USE OF DISORDERS OF CONSCIOUSNESS TO THEORIZE CONSCIOUSNESS

The clinical and fundamental exploration of patients suffering from disorders of consciousness (DoC) is commonly used by researchers both to test some of their key theoretical predictions and to serve as a unique source of empirical knowledge about possible dissociations between consciousness and cognitive and/or neural processes. For instance, the existence of states of vigilance free of any self-reportable subjective experience [e.g. “vegetative state (VS)” and “complex partial epileptic seizure”] originated from DoC and acted as a cornerstone for all theories by dissociating two concepts that were commonly equated and confused: vigilance and conscious state. In the present article, we first expose briefly the major achievements in the exploration and understanding of DoC. We then propose a synthetic taxonomy of DoC, and we finally highlight some current limits, caveats and questions that have to be addressed when using DoC to theorize consciousness. In particular, we show (i) that a purely behavioral approach of DoC is insufficient to characterize the conscious state of patients; (ii) that the comparison between patients in a minimally conscious state (MCS) and patients in a VS [also coined as unresponsive wakefulness syndrome (UWS)] does not correspond to a pure and minimal contrast between unconscious and conscious states and (iii) we emphasize, in the light of original resting-state positron emission tomography data, that behavioral MCS captures an important but misnamed clinical condition that rather corresponds to a cortically mediated state and that MCS does not necessarily imply the preservation of a conscious state.

Notes

LARGE - SCALE NETWORK ANALYSIS IN INTENSIVE CARE

Virginia NEWCOMBE

UNIVERSITY OF CAMBRIDGE
UNITED KINGDOM

Biosketch

Dr. Virginia Newcombe is a consultant in Neurosciences and Trauma Critical Care Medicine, and Emergency Medicine at Addenbrooke's Hospital, Cambridge. Originally from Australia she came to Cambridge to complete a MPhil in Epidemiology and stayed to undertake a PhD and clinical training. She is a Royal College of Emergency Medicine Associate Professor and holds an Academy of Medical Sciences and Health Foundation Clinician Scientist Fellowship.

NETWORK ADAPTATIONS DURING RECOVERY FROM SEVERE NEUROLOGICAL INJURY

Her main research interests focus on prognostication, neuroimaging and the use of biomarkers after traumatic brain injury as well as long-term outcomes after critical illness. Her work has been recognised with awards from European Society of Intensive Care Medicine, the International Society for Cerebral Blood Flow and Metabolism, the International Society for Magnetic Resonance Medicine, National Neurotrauma Society (USA) and a Churchill Fellowship.

Notes

NEURO-IMMUNE NETWORK CROSSTALK IN CRITICAL ILLNESS

Alice JACQUENS

PITIE - SALPETRIERE UNIVERSITY HOSPITAL
PARIS
FRANCE

Biosketch

Dr Alice Jacquens is a French doctor specializing in anaesthesia and intensive care at the neurosurgical intensive care unit of the Pitié-Salpêtrière Hospital. She completed a thesis in the laboratory of Pr. Pierre Gressens (Inserm U1141, Hopital Robert Debré, Paris) on the inflammatory mechanisms involved in the genesis of late post-cranial trauma lesions. She has been working for several years with Pr. Vincent Degos on the interest of diffusion tensor MRI in the diagnosis, follow-up and prognosis of head trauma patients.
She is currently a post-doctoral fellow in the laboratory of Professor Olivier Baud (Development and Growth Laboratory, UNIGE, Geneva) and is developing a project that focuses on modulating the activation of oxytocinergic neurons in a model of head trauma by DREADDs.

EPIGENETIC REGULATION OF MICROGLIAL CELLS

Microglia is the main immune cell of the brain and the first cell to react to any small change in brain homeostasis. It plays a central role in the defense against cerebral aggressions of vascular, traumatic or infectious origin. Its activation is rapid and, as we know today, it can take on several phenotypes and communicate rapidly with other cerebral cell types such as astrocytes, oligodendrocytes and neurons. It thus plays a key and central role in neuroinflammation. More interestingly, it can also memorize cerebral aggressions and thus remain activated several weeks, months and years later. This memorization is expressed in particular by a greater response to a second stimulus. This memorization is probably underpinned by epigenetic mechanisms involving microRNA or histone modifications that can lead to modifications of the chromatin status and transcriptomic and phenotypic modifications. These epigenetic modifications could possibly explain the differences in severity and outcome of patients as well as in responses to treatments in the context of brain aggression. These epigenetic signatures are emerging as potential therapeutic targets.

Notes

NEURO-IMMUNE NETWORK CROSSTALK IN CRITICAL ILLNESS

Djillali ANNANE

PARIS SACLAY UNIVERSITY
RAYMOND POINCARE
HOSPITAL
PARIS
FRANCE

Biosketch

Djillali Annane, MD,PhD, is a professor in medicine at University Paris Saclay-UVSQ. He is director of General ICU at Raymond Poincaré Hospital, director of FHU SEPSIS, and Dean of Medical School Simone Veil. He is ranked among the top 0.1% in the field of sepsis. He has contributed to international and multi-disciplinary guidelines, to about 570 peer–reviewed articles and about 150 book chapters. His H-index is of 105, with 100073 citation (Google scholar). He has mentored young colleagues, who became faculty members in French, Belgium, US or Canadian Universities. He is the founder of the CRICS-TRIGGERSEP network. He has obtained funding from Ministry of Health, Ministry of Higher Education and Research European Commission, non-profit organizations, and private companies. He held or currently holds high-level strategic position in the public sector, including Chief Counsellor of the French Minister of Health from 2012 to 2017, Chair of the Health Ministry Task Force against Sepsis, member of the board of directors of the Curie Institute (current), Vice-President of the board of directors of APHP, member of the WHO Working Groups, President of the French Society of Intensive Care Medicine in 2011-2012, President elect of the national council of deans of medical school 2011-2012.

NEUROMODULATION OF THE IMMUNE RESPONSE IN CRITICALLY ILL PATIENTS

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NEURO-IMMUNE NETWORK CROSSTALK IN CRITICAL ILLNESS

Antoine ROQUILLY

CHU NANTES
FRANCE

Biosketch

Antoine Roquilly is a Professor of the University of Nantes (France) with a dual appointment in the Intensive Care Unit of the University Hospital of Nates and the Department of Microbiology and Immunology at the University of Medicine of Nantes (France). Antoine obtained his Ph. D. from the University of Nantes in 2013. Subsequently, he trained at Melbourne University in Prof. Villadangos Lab (Victoria Australia). He is now leading the Team 6 UMR1064 Center of Research in Transplantation and Translational Immunology where he develops translational research in immunology from mice model to randomized clinical trials in critically ill patients. Antoine has received funding from the European Research Council as coordinator of a Horizon H2020 for the development of immunotherapies for hospital-acquired pneumonia, from French Ministry of Health, for the region Pays de la Loire and is a Chief Investigator in one NHMRC grant.

SYSTEMIC IMMUNE ADAPTATION TO BRAIN-INJURY

The in-hospital mortality of critically ill patients hospitalized in intensive care units has decreased regularly in the last decades, and the number of critical illness survivors has thus drastically increased worldwide. It has recently been described that critically ill patients have prolonged alterations of immune functions a phenomena so-called **trained innate immunity.** Understanding the long-term impact of acute inflammation on immune homeostasis holds great promise to **develop targeted host-directed immunotherapy to prevent and treat infections and cancer**.

Brain injury induces systemic immunosuppression increasing the risk of viral reactivations and altering neurological recovery. By analysing the monocyte programming in brain-injured patients, we defined a specific monocyte signature which is associated with HSV reactivation and predicts poor recovery after brain injury. The alterations of the immune control of Herpesviridae replication are understudied and represent a novel therapeutic target.

Selected Publications

1.Chaumette T, Cinotti R, Mollé A, Solomon P, Castain L, Fourgeux C, McWilliam HEG, Misme-Aucouturier B, Broquet A, Jacqueline C, Vourc'h M, Fradin D, Bossard C, David L, Montassier E, Braudeau C, Josien R, Villadangos JA, Asehnoune K, Bressollette-Bodin C, Poschmann J, **Roquilly A**. Monocyte signature associated with Herpes Simplex Virus reactivation and neurological recovery after brain injury. **Am J Respir Crit Care Med** 2022 In press.

2.**Roquilly A**, Mintern JD, Villadangos JA. Spatiotemporal Adaptations of Macrophage and Dendritic Cell Development and Function. **Annu Rev Immunol**. 2022 Feb 7. doi: 10.1146/annurev-immunol-101320-031931.

3.**Roquilly A**, Moyer JD, Huet O, Lasocki S, Cohen B, Dahyot-Fizelier C, Chalard K, Seguin P, Jeantrelle C, Vermeersch V, Gaillard T, Cinotti R, Demeure Dit Latte D, Mahe PJ, Vourc'h M, Martin FP, Chopin A, Lerebourg C, Flet L, Chiffoleau A, Feuillet F, Asehnoune K; Atlanrea Study Group and the Société Française d'Anesthésie Réanimation (SFAR) Research Network.J Effect of Continuous Infusion of Hypertonic Saline vs Standard Care on 6-Month Neurological Outcomes in Patients With Traumatic Brain Injury: The COBI Randomized Clinical Trial. **JAMA**. 2021 May 25;325(20):2056-2066.

4.Kreutmair S, Unger S, Gonzalo Núñez N, Ingelfinger F, Alberti C, Donatella De Feo, Krishnarajah S, Kauffmann M, Friebel E, Babaei S, Gaborit M, Lutz M, Jurado NP, Malek NP, Goepel S, Rosenberger P, Häberle H, Ayoub I, Al-Hajj S, Nilsson J, Claassen M, Liblau R, Martin-Blondel G, Bitzer M, **Roquilly A**, **Becher** B. Distinct immunological signatures discriminate severe COVID-19 from non-SARS-CoV-2-driven critical pneumonia. **Immunity** 2022 Feb 8;55(2):366-375. doi: 10.1016/j.immuni.2022.01.015.

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Notes

NEURO-IMMUNE NETWORK CROSSTALK IN CRITICAL ILLNESS

Chantal HENRY

GHU PARIS PSYCHIATRY and NEUROSCIENCES
FRANCE

Biosketch

Chantal Henry, MD, PhD. Professor of Psychiatry at the University of Paris, practices psychiatry at the GHU of Paris (Sainte-Anne site) and is involved in the neurosciences department of the Institut Pasteur (perception and memory unit). She coordinated the European Network of Centers of Excellence on Bipolar Disorders (ENBREC, funded by FP7), established the network of expert centers in France (bipolar, schizophrenia, resistant depression, asperger) and has joined in September the department that started modern psychiatry (discovery of the effects of neuroleptics by Delay and Deniker).

BLA CIRCUITS SUPPORTING NEGATIVE HEDONIC BIAS IN DEPRESSION

Negative emotional bias is an essential hallmark of depression. It is reflected by disrupted hedonic valence of emotional stimuli. We show a negative bias in a corticosterone-induced mouse model for depression. Given the crucial role of amygdala in valence coding, we hypothesized that specific basolateral amygdala (BLA) circuits alterations may support this negative emotional bias. Here, we found that corticosterone administration reduced BLA-to-nucleus accumbens neuronal activity while increasing BLA-to-central amygdala neuronal activity, circuits previously involved respectively in positive and negative valence encoding. What might be the links between these activation imbalances and immunoinflammatory relationships?

Notes

NEURO-IMMUNE NETWORK CROSSTALK IN CRITICAL ILLNESS

Aurélien MAZERAUD

SAINTE ANNE HOSPITAL
PARIS
FRANCE

Biosketch

Aurelien Mazeraud is an anaesthesiologist and an intensivist. He worked at Institut Pasteur as a PhD and worked on fear and traumatic memory in the context of sepsis. His work led to a patent and a randomised controlled trial in septic shock. He has also led a nationwide Trial in Covid-19 and has been working on the emotional and behavioral network in ICU in GHU Paris Psychiatry and Neurosciences.

NEUROIMMUNOLOGY OF POST-SEPSIS PTSD

Notes

BRAIN-CARDIAC NETWORKS IN CRITICAL ILLNESS

Jacobo Diego SITT, MD, PhD, HDR

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Biosketch

Jacobo_Diego_SITT (https://scholar.google.fr/citations?user=01sft6QAAAAJ&hl=en)
Dr Jacabo Sitt is Director of Research at the French National Institute of Health and Medical Research (INSERM). He has applied his background in Physics to the field of Psychiatry, with his research focusing on the Neuroscience of Consciousness. His research aims specifically testing the causal role of neural markers of consciousness using different experimental models, neuro-imaging methods and stimulation techniques. He specialises in neuro-imaging signal analysis, mathematical modelling, nonlinear dynamics, information theory, and machine learning.

ANATOMY AND PHYSIOLOGY OF THE BRAIN / CARDIAC AXIS

Heart rate has natural fluctuations that are typically ascribed to autonomic function. Recent evidence suggests that conscious processing can affect the timing of the heartbeat. In this presentation I will test the hypothesis that heart rate is modulated by conscious processing and therefore dependent on attentional focus. To do so, we leverage the observation that neural processes can be synchronized between subjects by presenting an identical narrative stimulus. As predicted, we find significant inter-subject correlation of the heartbeat (ISC-HR) when subjects are presented with an auditory or audiovisual narrative. Consistent with the conscious processing hypothesis, we find that ISC-HR is reduced when subjects are distracted from the narrative, and that higher heart rate synchronization predicts better recall of the narrative. Finally, I will show that patients with disorders of consciousness who are listening to a story have lower ISC-HR, as compared to healthy individuals. However, patients' individual ISC-HR might predict a patients' prognosis. We conclude that heart rate fluctuations are partially driven by conscious processing, depend on attentional state, and may represent a simple metric to assess conscious state in unresponsive patients.

Notes

BRAIN-CARDIAC NETWORKS IN CRITICAL ILLNESS

Romain SONNEVILLE

BICHAT CLAUDE BERNARD UNIVERSITY HOSPITAL
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Biosketch

Romain Sonneville (1977) is an intensivist in the Bichat Claude Bernard university hospital, Paris, France. He finished his training in neurology and intensive care medicine in 2007. He completed his PhD at the University of Leuven, Belgium. Currently, he is engaged in clinical care and research projects involving patients with acute encephalitis and central nervous system infections and in neurologic complications of critical illness.

NEUROLOGICAL EFFECTS OF ECMO

Notes

BRAIN-CARDIAC NETWORKS IN CRITICAL ILLNESS

Soojin PARK

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Biosketch

Dr. Soojin Park is an Associate Professor of Neurology and Biomedical Informatics at Columbia University, and directs the Program for Hospital and Intensive Care Informatics. She is the Program Director for Fellowship Training in Neurocritical Care at NewYork-Presbyterian Hospital (Columbia and Cornell), an Associate Editor for Neurocritical Care and a Board Trustee of the Neurocritical Care Foundation. Her research is supported by the NINDS and focuses on the development and clinical evaluation of predictive models to improve timeliness and precision of management in neurocritical care, using physiologic monitors and digitized medical record data.

DECODING CARDIAC SIGNALS IN ACUTE BRAIN INJURY

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BRAIN-RESPIRATORY NETWORKS IN CRITICAL ILLNESS

Karim ASEHNOUNE

CHU (UNIVERSITY HOSPITAL OF) NANTES
FRANCE

Biosketch

Karim Asehnoune (France) is a Professor of Anaesthesiology and Critical Care Medicine at the University of Nantes, France. He is the director of a French network of ICUs (www.ATLANREA.org), and was the coordinator of several multicenter trials, 2 trials were published in the JAMA and one in BMJ in 2021. His main area of interest is brain injury and major surgery.

BRAIN-LUNG CROSSTALK AFTER ACUTE BRAIN INJURY

Acute brain injury (ABI) causes damages of extracranial organs and in this setting, lung is probably particularly vulnerable. The pathophysiology of brain to lung interactions is complex and remains a matter of debate. Brain and lungs are connected via complex pathways including brain and systemic inflammation as well as systemic immune suppression, dysfunction of the autonomic system and neuro-degeneration. The catecholamine “storm” that follows BI is responsible for neurologic pulmonary oedemaC. The release of inflammatory mediators creates an inflammatory environment rendering the lung prone to secondary injuries like mechanical ventilation (MV), surgery and infections. Brain and lungs interact from the brain to the lung but also from the lung to the brain. Indeed, MV per see may induce brain damages, and the hippocampus (involved in learning and memory processes) is particularly vulnerable to hypoxia. The impact of different strategies of MV (protective versus non-protective) is therefore important since it was demonstrated, in animal models, that high tidal volumes increases c-fos expression (a marker of neuronal activation) in specific areas of the brain.

Brain and lungs strongly interact especially after BI, and further studies are warranted to explore pathophysiological processes. Therapeutic strategies should aim to protect both organs, finally a strict monitoring of respiratory and cerebral parameters is needed to optimize the management of patients suffering from BI.

Notes

BRAIN-RESPIRATORY NETWORKS IN CRITICAL ILLNESS

Laurent BROCHARD

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Biosketch

Pr. Laurent Brochard is Director of the Interdepartmental Division of Critical Care Medicine, University of Toronto, Canada since 2014. He holds the Keenan Chair in Critical Care. He is Clinician Scientist, Critical Care, at St. Michael's Hospital, Unity Health Toronto. He leads an international group on respiratory physiology (PLUG) and leads the Centre of Excellence in Mechanical Ventilation in Toronto.
He mentored and directed numerous PhD, many of whom are leaders in Critical Care. He published over > 600 peer-reviewed publications (H-index 112).

APPROACHES TO VENTILATOR-PATIENT DYSSYNCHRONY

Patient-ventilator dyssynchrony is a mismatch between the patient's respiratory demands and the ventilator. Roughly, it could be described as inadequate timing or dose of ventilatory support in relation to patient's neural breathing time. Sedation plays an important role as it modulates the ventilatory demand from the patient. The transient increases in distending pressure and/or the eccentric contraction of the diaphragm seen with some forms of dyssynchronies can be potentially harmful for the lungs and respiratory muscles. Dyssynchrony in general has been associated with poor outcomes in the mechanically ventilated population, from longer duration of mechanical ventilation and ICU stay to higher mortality but there are multiple pathways which could explain this association.
Patient-ventilator interactions often reflects an inadequate respiratory drive (i.e., excessive or insufficient sedation or ventilatory support). One very frequent form of asynchrony exists only in the absence of apparent neural drive to breathe, and is called reverse triggering, often in the forms of a respiratory entrainment by the ventilator. A specific level of brain activation is probably necessary to allow this phenomenon. From a pathophysiological point of view, dyssynchronies can be classified as insufficient assistance usually related to high respiratory drive or over assistance in the context of low respiratory drive. Treating dyssynchrony often makes sense but should be done in the context of understanding the mechanisms.

Notes

BRAIN-RESPIRATORY NETWORKS IN CRITICAL ILLNESS

Bertrand HERMANN

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Biosketch

Bertrand Hermann, MD, PhD is an intensivist trained in neurology working in the neuroICU of the GHU Psychiatrie & Neuroscience, Université de Paris Cité and Brain & Spine Institute in Paris, France.

His clinical and research topics of interest are the clinical and brain-imaging assessment of coma and disorders of consciousness with a special expertise on quantitative electrophysiology.

BRAINSTEM DYSFUNCTION IN COVID-19 PATIENTS

Since the onset of the SARS-COV-2 pandemic, neurological manifestations have been increasingly recognized as a hallmark of severe COVID-19 infections, notably in patients requiring ICU admission. Aside from rare neurologic manifestations such as encephalitis or Guillain-Barré syndrome, the most frequent neurological conditions in patients with severe COVID-19 and predominant respiratory symptoms at admission are acute encephalopathy with coma, delirium and prolonged disorders of consciousness. The extent to which these conditions are related to a direct brain tropism of the virus or to a more systemic vasculopathy and inflammatory response to the infection is still debated. However, regardless of the exact pathophysiological mechanisms, histological, clinical and brain-imaging evidence of brainstem involvement in severe COVID-19 are accumulating. The dysfunction of this key anatomical and functional region supporting arousal and cardio-respiratory autonomic control may explain some features of severe COVID-19 infections and portend poor prognosis significance.

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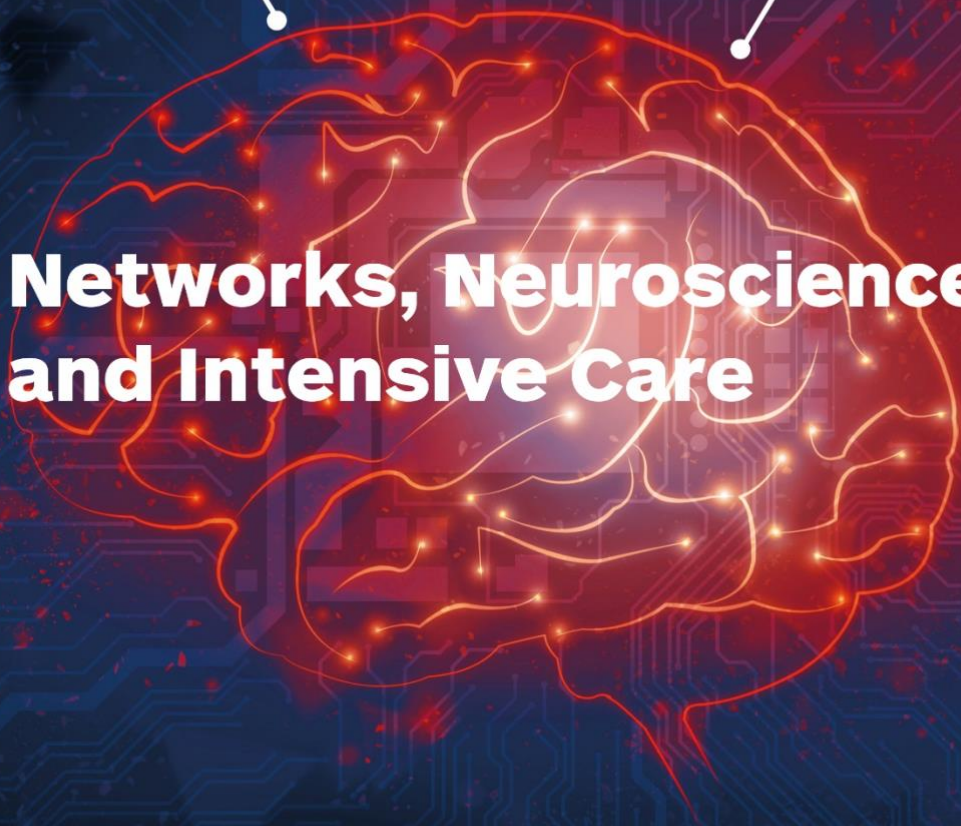

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