Abstracts of talks - Order as in program

Circuits for locomotion

Ole Kiehn

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Movement takes many forms and there is little animal or human existence that can be expressed without motor actions. The capacity for movement is at the center of most behaviors. Among movements, locomotion is one of the most fundamental and expressed throughout animal kingdom. Locomotion requires complex coordination, temporal alteration and dynamic control. In this lecture, I will discuss recent work that has revealed the functional organization of locomotor circuits in the spinal cord and brainstem. I will show that spinal locomotor networks are composed of diversified molecularly defined circuit modules that coordinate limbed movement and set the tempo of locomotion. I will also address the role of designated brainstem circuits that are essential for stop, start and speed control of locomotion or context-dependent selection of the motor behaviour.
https://in.ku.dk/research/ole-kiehn/

Using population isolates to unravel the genetics of severe mental disorders

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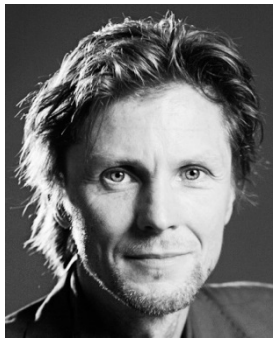
Nordic countries have collected standardized health service data for decades from all residents. These registers provide follow-up data over decades. Finland is also the largest population isolate in Europe. The small founder population, long isolation and rapid population growth have boosted a set of low frequency alleles to frequencies that make their statistical analysis meaningful. The longitudinal health data, the population structure and a favourable, well-educated population, combined with genome data provide possibilities for unique study designs. In the SUPER-study, which is a part of the Stanley Center of Psychiatric Research's Global genetics initiative, we are collecting 10 000 psychosis cases. We will analyze their genetic (GWAS and exome sequence data) and phenotype data and meta-analyze with other international cohorts. The FinnGen study, a large public private partnership aims to collect 500 000 Finns, representing 10% of the population and combine health register data with their genome (GWAS) variant data to improve our understanding of the genetic background of diseases.
https://www.finngen.fi/en
https://www.superfinland.fi/english
https://www.fimm.fi/en/research/groups/palotie

Identification of risk genes in psychiatric disorders using a nationwide Danish population cohort



Anders Børglum

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Psychiatric disorders are among the most heritable common disorders with heritability estimates as high as 70-80 % for, e.g., schizophrenia, autism and ADHD. Genome-wide association studies (GWAS) have during the last decade begun to uncover the risk genes underlying these disorders, most prominently in schizophrenia. Recently, GWAS of major depression, ADHD and autism spectrum disorder have also succeeded in identifying robustly associated common risk variants by substantially increasing the sample sizes. This has been accomplished through widespread international collaboration, including exploiting a nationwide Danish resource of neonatal blood spots in combination with national register information provided by the iPSYCH project. The identified risk loci will be presented as well as significant genetic correlations with other disorders and traits. Fine mapping and integration with orthogonal functional genomics data identify the most likely risk genes/variants, informing on the biological underpinnings.
http://ipsych.au.dk/about-ipsych/research-groups/anders-boerglum-group/

Nansen Neuroscience Network: From neuroscience research to innovation

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Nansen Neuroscience Network works to promote research, innovation and business development based on knowledge about the brain and the central nervous system.

Our members are research institutions, start-up companies, established industry and technology transfer offices. Our goal is for research and development to result in products which patients, their relatives and the society can benefit from, and for neuroscience research and development to contribute to establish a viable health industry in Norway.

We aim to increase the innovation culture in neuroscientific communities, stimulate to collaborations between industry and academia, and create greater visibility of the value and potential in neuroscience.
http://nansenneuro.net/

A critical period for antidepressant-induced acceleration of neuronal maturation in adult dentate gyrus

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New neurons generated throughout life in the dentate gyrus have been shown to be involved in the therapeutic actions of antidepressants. We labeled new neurons in mice by using GFP-expressing viral vectors, and investigated the effect of antidepressants on these neurons at different time points after neuronal birth. We found that antidepressant treatment accelerates neuronal maturation, but only when it was administered during the second week of neuronal birth, suggesting the existence of a critical period for the antidepressant-induced maturation. We propose that the modified integration of new neurons in the critical period may underlie the therapeutic action of antidepressants. Physical exercise is also known to be therapeutic for people suffering from depression and anxiety, and it is known that lactate produced by exercising muscles can activate a receptor in the brain. We wish to find out whether activation of this receptor can lead to similar effects as antidepressant treatment.
https://www.odont.uio.no/iob/?vrtx=person-view&uid=ingraame

Neuromodulators, neuropsychiatric disorders, and metabolic dysregulation

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Numerous chemical substances molecules are involved in brain signaling through various mechanisms. Many of these molecules are also involved in general metabolic regulation. In addition to the classical/nonclassical neurotransmitters and neuromodulators, many signaling molecules mechanisms are yet to be discovered. I will present recent findings on regulatory mechanisms and pharmacological modification of key enzymes involved in monoamine signaling. I will also describe the discovery of an enzyme apparently dedicated to the synthesis of the putative neuromodulatory/ neuroprotective non-classical amino acids and peptides beta-alanine and carnosine in the olfactory bulb. Finally, the involvement of these substances in human neuropsychiatric and metabolic illnesses will be discussed.
https://www.uib.no/en/persons/Jan.Haavik
http://www.uib.no/kgj-npd
https://mind-the-gap.live/

Neuromodulation of cognition: basic research and clinical applications

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Several non-invasive neuroscientific applications are capable of modulating brain systems, and thereby cognitive capabilities. One of the more established approaches that has already been shown to augment cognitive processes is neurofeedback (NF) based on electroencephalography (EEG).

EEG-NF relies on a brain-computer interface that processes brain signals such that an index of ongoing neural activity can be presented to the participant in real-time. Participants learn through operant conditioning to control their brain activity, even though the cognitive processes involved may remain elusive to them.

Here, we will shortly review the current state of EEG-NF as an application for the modulation of cognition in healthy subjects and clinical samples. A specific focus will be on the up-regulation of executive functions, i.e., high-level cognitive processes that predict social functioning and treatment outcome.
www.rjhuster.com

A precision neuroscience approach to auditory hallucinations in schizophrenia

Kenneth Hugdahl

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In my presentation I will give an overview of our research on auditory hallucinations in schizophrenia, with a focus on hallucinations as perceptual phenomena driven by temporal lobe hyper- excitation, not inhibited due to frontal lobe hypo-excitation. Auditory hallucinations are therefore seen as having a neuronal origin in the language areas in the temporal lobes, self-maintained through failure of cognitive inhibition due to dysfunctions of the the frontal lobes. In these studies we are using behavioral, as well as structural and functional MRI, to reveal the underlying neuronal structure of auditory hallucinations, and MR spectroscopy to reveal the underlying neurochemistry of the remarkable phenomenon of “hearing voices that do not exist”. In recent years we have in addition begun using smartphone devices and app technology for cognitive training and in-vivo sampling of symptom data.
http://fmri.uib.no/

Inflammation and genetics in major psychiatric disorders and cognitive impairment

Nils Eiel Steen

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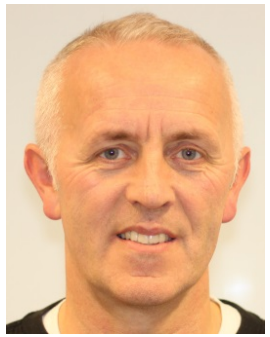
The last few years have seen major breakthroughs in research informing pathophysiological pathways and the polygene nature of severe mental disorders. Among the most striking genetic findings is the involvement of the immune system. In addition to specific genes and epigenetics, inflammatory mechanisms are indicated by analyses of central and peripheral immune markers and pleiotropic effects. A core feature in common of severe mental disorders is cognitive impairment. By detailed neuropsychological and immunological characterization of patients and controls of our sample, we will leverage GWAS data for analyses of cognitive and inflammatory mechanisms in mental disorders using polygenic risk. Moreover, by applying conditional false discovery rate statistics, a novel tool for enhanced discoveries in genetic studies, we have been able to reveal more of the common variants shared between mental disorders, cognitive abilities and structural brain patterns. Examples include shared genetic effects of Alzheimer's disease and the immune-mediated diseases psoriasis and Crohn's disease.
https://www.med.uio.no/klinmed/personer/vit/nilseste/index.html

Modulation of cognitive function and behaviour by oxidative DNA base lesion repair



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Base excision repair (BER) initiated by DNA glycosylases is traditionally known to preserve genomic integrity by removing damaged bases. We have generated DNA glycosylase deficient mice that display cognitive and behavior abnormalities, or altered recovery after ischemic stroke. Recently, several DNA glycosylases were identified as potential readers of epigenetic modifications and proteins involved in BER have been implicated in active DNA demethylation. However, the impact of DNA glycosylases on the epigenetic landscape in brain remains unknown. Here we report that DNA glycosylases alter epigenetic modifications selectively at gene regulatory regions in the adult hippocampus. Similar DNA methylation changes are induced at gene promoters in young DNA glycosylase deficient mice in an *in vivo* model of cerebral hypoxia-ischemia. Our results suggest that DNA glycosylases modulate the neuronal epigenome with age and in response to acute brain injury, thus uncovering processing of oxidative DNA base lesion as a novel epigenetic layer.
https://www.ntnu.edu/employees/magnar.bjoras
https://www.ous-research.no/bjoras/

Abnormal mitochondrial DNA maintenance in Parkinson's disease

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Parkinson's disease (PD) is a major societal challenge and a leading cause of death and disability. Mitochondrial dysfunction is strongly associated with PD, but the underlying mechanisms have been largely unknown. We show that neuronal mitochondrial DNA (mtDNA) copy number increases with age, compensating against accumulating somatic mutations. This protective response is blunted in individuals with PD, partly due to polygenic enrichment of rare, inherited deleterious mutations in nuclear genes controlling mtDNA maintenance. This impaired regulation of mtDNA provides a potential explanation for the loss of dopaminergic neurons in PD. Intriguingly, long-term use of glitazone antidiabetics, which increase mitochondrial biogenesis via PPAR-γ activation, is associated with approximately 30% reduction of the incidence of PD in our population. Therefore, mitochondrial dysfunction provides a plausible pathogenic model for PD as well as a target for therapy.
https://www.uib.no/personer/Charalampos.(Haris).Charalampos

Mitophagy in neurodegeneration and ageing

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Accumulation of damaged mitochondria is a hallmark of human aging and age-related neurodegeneration, including Alzheimer's disease (AD). However, the molecular mechanisms of the impaired mitochondrial homeostasis and their relationship to AD are still elusive. Mitophagy, a cellular self-clearing process of damaged and superfluous mitochondria, thereby plays a fundamental role in maintaining neuronal function and survival. We hypothesize that defective mitophagy causes accumulation of damaged mitochondria, which further, in combination with the two main AD hallmark factors, Aβ plaques and tau tangles, exacerbates AD progression. Restoration of mitophagy through upregulation of cellular NAD^+, a primary cofactor in human health and life, forestalls pathology and cognitive decline in *C. elegans* and mouse models of AD. In view of the physiological role of NAD^+ in human, our study suggests immediate therapeutic potential.
https://sites.google.com/site/evandrofeifanguiono/
https://www.med.uio.no/klinmed/personer/vit/evandrof/index.html

Neural coding of space and time

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The ability to map space is critical to survival. In mammals, space is mapped by neural networks in the hippocampus and the medial entorhinal cortex. These brain areas contain specialized position-coding cell types, including grid cells, which are active only when animals are at locations that tile environments in a periodic hexagonal pattern. The focus of my talk will be on the representation of time, which is less well understood. I will show how episodic temporal information is encoded across scales from seconds to hours within the overall population state of the lateral part of entorhinal cortex. I will also demonstrate that the representation of time in this region depends on the structure of experience and so may diverge from clock time. In the hippocampus, the task-dependent representation of time in lateral entorhinal cortex may be integrated with spatial inputs from medial entorhinal cortex, allowing the hippocampus to store a unified representation of experience.
https://www.ntnu.no/ansatte/edvard.moser

Replication stress induces age-related disorders via impaired mitochondrial homeostasis

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Aging is defined as the gradual decline of cellular, tissue and organismal homeostasis resulting in cellular senescence, organismal dysfunction and, ultimately, death. Mitochondrial function plays an important role in aging as well as onset of multiple human age-related diseases such as cognitive decline, neurological abnormalities, and cancer. Using various model systems, we have shown that mitochondrial dysfunction results in complex genomic instability, which involves nucleotide metabolism as well as multiple major DNA repair and DNA lesion synthesis/bypass pathways. DNA lesions that escape repair will arrest the replication fork, which can lead to replication stress, DNA breaks, and genome instability. To ensure the continuation of replication at damaged DNA templates, translesion synthesis (TLS) polymerases can transiently displace the replicative polymerases and replicate across the lesion. Since TLS polymerases frequently introduce the incorrect nucleotide opposite the lesion, TLS is a mutagenic process. Rev1 is a TLS polymerase that coordinates the recruitment of other TLS polymerases at the damage site and regulates the TLS. Rev1-deficient mice display mild progeroid symptoms suggesting a role for TLS in preventing premature aging. We investigated the molecular mechanisms underlying progeria in these mice and found that the absence of a functional Rev1 protein causes multifactorial mitochondrial dysfunction including abnormal mitochondrial morphology. This phenotype is particularly evident during cellular stress. The mitochondrial abnormalities appear to be caused by NAD^+ depletion triggered by activation of the DNA damage sensor PARP-1.
https://healthyaging.ku.dk
https://icmm.ku.dk/english/research-groups/juel-rasmussen-group/

The discovery of a new neurodegenerative premature aging disease

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One of the greatest challenges facing the world today is the growing proportion of elderly people in our societies. It is therefore of high importance to expand our knowledge and understanding of the underlying mechanisms of prevalent age-related diseases. Rare premature aging disorders may be useful models to study the aging processes. We now present mechanistic data on a newly discovered premature aging disorders characterized by neurodegeneration and metabolic dysfunction. The disease was discovered through the use of machine learning algorithms such as deep neural networks on clinical and morphometric data. Utilizing in silico, in vitro and in vivo methodologies we have discovered alterations in DNA metabolism as a possible underlying cause of this disease. These findings underscore the idea that maintaining our genome may be a central tenant in our endeavor to provide healthy aging to everyone.
http://scheibye-knudsen.com/
https://icmm.ku.dk/english/research-groups/scheibye-knudsen-group/

Developing targeted therapy for mitochondrial disorders

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Mutations in the mitochondrial or nuclear genomes that alter mitochondrial function manifest with wide-range of clinical symptoms and tissue specificity. Even though conventional wisdom tells us that the primary role of mitochondria is to generate ATP, these essential organelles also have many key functions such as control of intermediate metabolism, calcium storage and ROS signaling. Here, I will present how we use mouse models that mimic human mitochondrial disease mutations and iPSCs derived from mitochondrial disease patients to understand the cell-type specific consequences of mitochondrial dysfunction. We find that different tissue types have unique requirements provided by mitochondria, that cannot be explained simply by ATP deficiency, and unique stress pathways activated in response to mitochondrial impairment. Further, I will discuss how we use this information to develop targeted therapies to interfere with activated toxic stress pathways or altered levels of critical metabolites, which are proving beneficial effects in mice and humans.
https://www.helsinki.fi/en/researchgroups/mitochondrial-medicine

DNA damage signaling to mitochondrial dysfunction in neurodegeneration and aging

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We find that some DNA repair defective diseases with severe neurodegenerarion have mitochondrial dysfunction. Our studies involve cell lines, the worm (C. elegans), and mouse models and include the premature aging syndromes Xeroderma pigmentosum group A, Cockaynes syndrome, Ataxia telangiectasia and Werner syndrome. We find a pattern of hyperparylation, deficiency in the NAD^+ and Sirtuin signaling, and mitochondrial stress. We are pursuing mechanistic studies of this signaling and interventions at different steps to improve mitochondrial health and the neurodegeneration. I will discuss intervention studies in these disease models, including a new Alzheimer mouse model using NAD supplementation. NAD supplementation stimulates mitochondrial functions including mitophagy and stimulates DNA repair pathways. This also happens in an Alzheimer's mouse deficient in DNA polymerase ß, and this will be discussed. DNA Polß affects mitochondrial functions via its nuclear role, and via a newly identified role in mitochondrial DNA repair. The role of mitophagy and targeting it for intervention will be discussed.
https://irp.nih.gov/pi/vilhelm-bohr

Cellular interactions and heterogeneity in the blood microvasculature

Christer Betsholtz

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While all blood microvessels in our bodies are made from the same principal cell types – endothelial and mural cells – they differ fundamentally in their functions between organs. A chief example of microvascular organotypicity is the blood-brain barrier (BBB), which is conceived as central nervous system-specific endothelial specialization. Dysfunction of the BBB may contribute to the pathogenesis of brain diseases, including both common (stroke, Alzheimer's), and rare (e.g. CADASIL, cerebral cavernous malformation, primary familial brain calcification and others) diseases through leakage of neurotoxic substances from the blood to the brain. Conversely, intact BBB functions contribute to the resistance of brain tumors to pharmacological therapy. Cancer drugs are generally blocked from entering the brain through the presence of efflux transporters in the brain endothelium; these recognize xenobiotic compounds, including most low molecular weight drugs. However, the molecular and cellular nature of the BBB is still incompletely understood. For example, it remains unclear if the brain endothelial junctions have unique molecular composition, and to what extent cells other than endothelial cells, including pericytes and other perivascular cell types, contribute to the BBB. To shed light on these and other questions, we have begun constructing a molecular atlas of the BBB and other organotypic vasculatures using single cell RNA sequencing (scRNASeq) and proteomic analysis. I will discuss how this data provides fundamental and specific information about microvascular organotypicity. I will also exemplify how scRNASeq information provides insights into arterio-venous specialization and identifies hitherto unrecognized vascular cell types and subtypes.
http://igp.uu.se/research/vascular-biology/christer-betsholtz/?languageId=1

Control of brain blood flow by pericytes in health and disease

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Brain blood flow is regulated to ensure adequate power for neuronal computation. Blood flow is increased to areas where neurons are active, and this increase underlies non-invasive brain imaging using BOLD fMRI. Blood flow is controlled at the arteriole level by smooth muscle, but there is controversy over whether it is also regulated by pericytes at the capillary level. I will demonstrate that neuronal activity mainly increases cerebral blood flow by dilating capillaries via pericytes, that this involves signalling via astrocytes, and that dilation of capillaries and dilation of arterioles are mediated by different messengers. Ischaemia leads to pericytes constricting and dying, thus producing a long-lasting decrease of blood flow, making pericytes a therapeutic target in stroke. I will show that similar events occur in Alzheimer's disease.
https://www.ucl.ac.uk/biosciences/departments/npp/people/da

Exercise benefits the brain through the lactate receptor HCAR1

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We showed that stimulation of the lactate receptor HCAR1, either by lactate injections or intense physical exercise, leads to increased levels of vascular endothelial growth factor (VEGF), which is required for normal functioning of neurons as well as vasculature, and to the formation of new cerebral blood vessels (angiogenesis). The changes did not occur in knockout mice lacking HCAR1. This is the first time a substance that is produced in exercising skeletal muscle, is shown to benefit the brain through an identified receptor. These findings open a new field of research, which could link lactate receptor action to the known beneficial effects of physical exercise against a multitude of conditions inflicting the brain, ranging from depression to ischemic stroke and dementia. They indicate HCAR1 as a potential target of intervention in brain disorders.
https://healthyaging.ku.dk/research/energylevelsinhuman/lindabergersensgruppe/
https://www.odont.uio.no/iob/english/people/aca/lindabe/index.html

Web-based testing of cognitive function combined with MRI and health data in population cohorts

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Dr Håberg has worked with animal models of neurological disease, in healthy volunteers and patient groups (traumatic brain injury, preterm birth and stroke) using functional and structural MR imaging and spectroscopy. The neuronal basis of memory and attention, and how best to maintain these abilities are of particular interest and has led to the development of web-based methodology for large-scaled epidemiological studies of cognition in general populations such as HUNT (Nord-Trøndelag health study). The talk covers the development of Memoro, our web-based cognitive assessment tool which builds on a combination of traditional neuropsychological and fMRI based tests, and particularities related to web-based cognitive testing. Examples of deployment of Memoro in the HUNT study and results from combining the cognitive data with brain MRI and prospectively collected demographic, lifestyle, somatic and psychiatric health data and clinical measures going back to the mid-1980s will be presented.
https://www.ntnu.edu/employees/asta.haberg
http://www.funksjonellmr.no/
https://www.ntnu.edu/cius

Advanced analysis of brain activity-behavior relations

Stephen LaConte

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Over the last several years we have developed a real-time fMRI system using supervised learning to model the relationship between brain images and their corresponding sensory/behavioral/cognitive states. In our implementation, this intensive computational modeling can be done during and immediately after a training run. Once a model is trained, it can be used to decode new images in a computationally efficient manner. Although direct, real-time access to the default mode network (DMN) and other resting state networks for scientific investigation has been previously impossible, our latest technological development in this area has been the ability to track resting state networks in both offline and real-time fMRI settings. We are actively pursuing this capability as a tool for neurofeedback to study the mechanism of DMN regulation and its role in psychiatric and neurological disorders. This talk will present our methodology and latest results from ongoing neurofeedback experiments.
http://lacontelab.org/

Reception and Buffet at the Oslo City Hall (venue of the Nobel Peace Prize ceremony), hosted by the Mayor of Oslo

Current trends in neurology

Espen Dietrichs

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Diagnostic and therapeutic advances over the last twenty years have changed neurology into a very active clinical specialty with plenty of options, and recent and ongoing research are pushing the limits even further. Recently introduced drugs may modify disease mechanisms in entirely new ways, cell therapies are tested, and better device-aided therapies are introduced. Not only symptomatic, but also disease modifying therapies have come into use. Examples from management of disorders like stroke, multiple sclerosis, Parkinson's disease and other movement disorders will be given.
https://www.ous-research.no/dietrichs/

NorClinBrain: A Norwegian Centre for Clinical Treatment and Research

Hanne Flinstad Harbo on behalf of the NorClinBrain study group chaired by John-Anker Zwart
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Neurological disorders was ranked as the leading cause of disability-adjusted life-years (DALYs) in 2015, comprising 10.2% of global DALYs and the second-leading cause group of deaths, comprising 16.8% of global deaths. Neurological disorders are an important cause of disability and death worldwide, and the burden of neurological disorders has increased substantially over the past 25 years because of expanding population numbers and ageing, and will continue to increase. In acknowledgement of the enormous burden of neurological disorders, the Health Authorities in Norway endorsed the National Brain Health Strategy December 2017 that was press released at Oslo University Hospital. To target the substantial challenges, the NorClinBrain study group will bring together skilled clinicians and researchers who are international opinion leaders within their respective fields with extensive collaboration networks and experience in leading large clinical trials, international consortia and EU projects. The network of participating centres from all parts of Norway will ensure and facilitate recruitment of patients in clinical trials from all regions. NorClinBrain will exploit the advantages of the unique health care system in Norway and the extensive data rich registries and biobanks with the key goal to establish a leading research environment and collaborative platform for clinical research and basic sciences to facilitate translation and develop novel approaches for performing clinical studies. The Centre will embrace leading researchers from leading Universities and institutions across Norway, including renowned neuroscience researchers and Nobel Prize laureates at the Kavli Institute. Brought together in NorClinBrain we will exploit key aspects of the Norwegian health care system including its specific emphasis on user involvement as an arena for the implementation of novel randomized controlled trials (RCTs), supported with eHealth approaches to improve the treatment of patients with serious neurological diseases and to establish NorClinBrain as a leading international research and training environment.
https://www.ous-research.no/harbo/
https://www.med.uio.no/klinmed/personer/vit/harbo/index.html

Brain health promotion – opportunities and priorities

Anne Hege Aamodt
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Board member of the Norwegian Brain Council
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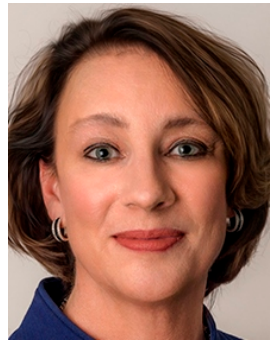
Along with the scientific progress and the development of new treatment options for brain diseases significant efforts have been made to put brain health on the political agenda. The annual Brain Awareness Week, The Year of the Brain in 1995 and 2015[1] and countless numbers of popular science books, lectures and presentations in media have been important contributions to increase awareness of brain health. At the end of the Norwegian Year of the Brain in 2015 the national health authorities decided to make a national status report of brain health.[2] As a result of this report a national brain strategy plan was published by the Ministry of Health in December 2017[3,4]. The follow-up process is now led by the Norwegian Directorate of Health who have invited relevant representatives including user and professional organizations and the Norwegian Brain Council in a partnership. The main elements in the Norwegian brain strategy plan will be presented along with the political process forward to an action plan for brain health. International initiatives, such as the European Brain Council Research Project - The Value Of Treatment for brain disorders[5] and international disease specific action plans will be highlighted.

An important basis for the promotion for of brain health is documentation of the burden of brain diseases. Data from the Global Burden of Disease[6] project with comparing brain diseases to other large disease groups will be presented on the congress. https://www.ous-research.no/aamodt/

1. http://legeforeningen.no/Fagmed/Norsk-nevrologisk-forening/Hjernearet-2015/
2. https://helsedirektoratet.no/Lists/Publikasjoner/Attachments/1280/Statusrapport%20hjernehelse%20endelig.pdf
3. https://www.regjeringen.no/contentassets/8eba3248e9e843f6b09e97a84a97a153/hjernehelsestrategi_2018-24_121217.pdf
4. English version of the Norwegian Brain Strategy – translated by the Norwegian Brain Council: http://www.hjerneradet.no/wp-content/uploads/2017/11/171222-Hjernehelsestrategien-engelsk-og-norsk-utgave-samlet.pdf
5. http://www.braincouncil.eu/activities/projects/the-value-of-treatment
6. http://www.healthdata.org/gbd

Prospects of innovation for global brain health: Challenges, opportunities and cause for optimism



Sharon Hemond Hrynkow
Sen VP, CTD Holdings; former executive at NIH, US State Dept, and President, Global Virus Network
sharonhrynkow@gmail.com

In introducing the panel, anecdotes will be provided to create a framework on challenges and opportunities to move the field of global brain health forward. We will look through the lens of new funding paradigms that are working to spur knowledge in the field, will recognize the complex genetic and social underpinnings of brain health and disease, and will comment new technological tools, such as artificial intelligence, that are changing treatment paradigms for complex and acute brain challenges, including stroke.
www.ctd-holdings.com

Beyond symptom suppression: The emerging transformation of psychiatry

Robert L. Trestman
Chair, Psychiatry and Behavioral Medicine, Virginia Tech Carilion School of Medicine and Carilion Clinic
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Over the past 50 years, Psychiatry evolved from psychoanalysis to psychopharmacology and evidence based psychotherapies. We are now poised to go beyond symptom suppression to genuine illness modulation. By integrating epigenetic markers, functional neuroimaging, computational psychiatry insights, and traditional phenomenology, we are poised to redefine the pathophysiology underlying psychiatric illness. We now have the basic tools to distinguish the mediators and moderators of treatment response, enhancing individual-specific differential therapeutic selection. AI, deep learning, and machine learning approaches are rapidly redefining how we utilize technology in hypothesis development and diagnosis. Individualized behavioral technologies may soon make use of the neuroplasticity induced by interventional approaches (e.g., DBS, ECT, TMS, NMDA receptor antagonists) to support enduring therapeutic benefit.
https://www.carilionclinic.org/cdp/psychiatry-behavioral-medicine#about

"Prospects of innovation for global brain health" Panel discussion:
Aamodt, Dietrichs, Harbo, Hrynkow, Trestman, Haugstad
Moderator, summing up: **Tor Haugstad**
Neuroscience Chair, Sunnaas Rehabilitation Hospital, Norway
tor.haugstad@sunnaas.no ; tor@haugstad.org
https://www.sunnaas.no/sunnaas-rehabilitation-hospital
Video (from 27') at https://www.youtube.com/watch?v=OM6EP47P9_Q

Arc protein: a specialized master organizer of synaptic plasticity and cognition

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The extraordinary plasticity of the brain shapes individual human personality, knowledge, and cognition - the ability to negotiate everyday life. The protein encoded by the immediate early gene Arc is recognized as a critical regulator of long-term synaptic plasticity, memory formation and cognitive flexibility. However, the molecular basis of Arc as a master regulator remains a puzzle. Recent work implicates Arc as a protein interaction hub. In this scenario, Arc is a dynamic and versatile and regulator of intracellular signaling. By binding to various effector proteins, Arc mediates different forms of synaptic plasticity. In remarkable contrast, Arc can also self-assemble into retrovirus-like capsids that are released inextracellular vesicles d capable of intercellular transfer of RNA. Thus, Arc appears to have radically divergent functional states – potentially coupling synaptic plasticity to intercellular RNA transfer in neural networks. https://www.uib.no/en/rg/bramham

Modulation of sensory evoked potentials as a non-invasive method to study LTP-like neural plasticity

Stein Andersson
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When identical visual or auditory stimuli are presented as tetanic high frequency stimulation (HFS), the amplitudes of the visual evoked potential (VEP) or auditory evoked potential (AEP) increase compared to pre-HFS level, reflecting change in post-synaptic strength. Animal studies have shown that such non-invasive stimulus-specific response potentiation (SRP) resembles electrically induced long-term potentiation (LTP), sharing basic neurobiological mechanisms. From our studies using visual SRP paradigms indexing LPT-like neural plasticity we replicate SRP effects in normal subjects, its temporal stability, its relation to higher order learning and memory function, and how SRP is reduced in patients with neuropsychiatric disorders. Although preliminary, we regard modulation of SRP to be promising as a reliable non-invasive index of LTP-like synaptic plasticity in humans, potentially bringing new insights on basic mechanisms underlying cognitive decline in neuropsychiatric disorders.
https://www.sv.uio.no/psi/personer/vit/stean/index.html

Influence of vasopressin on hippocampal network events during birth and birth asphyxia

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kai.kaila@helsinki.fi

A prominent activation of the fetal hypothalamic-pituitary-adrenal (HPA) axis is associated with mammalian birth, leading to massive secretion of stress hormones, including arginine vasopressin (AVP) into the fetal circulation. These stress hormones are known to activate endogenous protective mechanisms by pre-adjusting cardiorespiratory, metabolic and thermoregulatory functions so as to assure the neonate's survival during and after birth. AVP is released in response to hypoxia and, accordingly, birth complications such as prolonged labor and perinatal asphyxia will further potentiate the peripheral secretion of AVP. However, whether *central actions of vasopressinergic signaling* might exert protective effects on the fetal/neonatal brain during and immediately after birth has not been examined. In my talk, I will present data suggesting that fetal, centrally-released AVP has a powerful suppressing action on spontaneous network events (Giant Depolarizing Potentials, GDPs; and Sharp Waves, SPWS) in the perinatal hippocampus in both rats and guinea pigs, pointing to an evolutionarily conserved phenomenon. The suppression of network events is caused by V1aR-mediated activation of CA3 stratum lucidum-radiatum interneurons, leading to a decrease in the phasic, synchronous GABAergic drive that is needed for the generation of both GDPs and SPWs. This effect of AVP does not depend on the general level of brain maturation at birth or on the level of E_{GABA} in the perinatal pyramidal neurons, as is evident from its presence in both the rat (an altricial species where GABA is depolarizing at birth) and guinea pig (a precocial species where GABA is hyperpolarizing). The protective actions of AVP at birth might include at least the following: First, the suppression of correlated principal-neuron activity is likely to prevent the formation of maladaptive connectivity in response to the intense and coincident multimodal sensory stimuli that are activated during parturition, and that have no relevant counterpart later in life. Secondly, a neuroprotective effect might be caused by a reduction in the energy consumption needed for sustaining correlated network events, which are based on energetically expensive co-activation of GABAergic and glutamatergic transmission (see Buzsaki, Kaila, Raichle 2007 Neuron). The present findings suggest central perinatal vasopressinergic signaling as a possible therapeutic basis for the design of new therapeutic strategies during birth asphyxia and related conditions. http://www.helsinki.fi/neurobiology/

Flash-Presentations of Posters

Moderator: **Ingrid Åmellem**

Of the 16 poster presenters, 14 delivered Flash Presentations

Link to Poster Abstracts:
http://www.vnpn.science/VNPN2_Posters.pdf

Mitophagy induction inhibits Tau phosphorylation in human cells and improves memory in a Tau *C. elegans* model of Alzheimer's disease

Yahyah Aman
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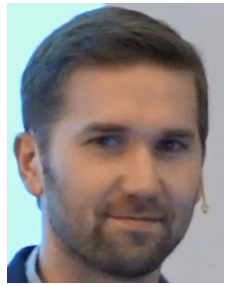
Correlation between immunohistochemistry and DNA sequencing for determining TP53 mutation status: A comparative study of 41 glioblastoma patients



Christopher M. Busch
Division of Neurosurgery, Carilion Clinic, Roanoke, and Virginia Tech, Blacksburg, Virginia, USA
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Microglial involvement in inhibitory axosomatic synaptic loss in chronic *Toxoplasma gondii* infection

Gabriela Carrillo
Graduate program in Translational Biology, Medicine, and Health, Virginia Tech, Blacksburg, and Virginia Tech Carilion Research Institute, Roanoke, Virginia, USA
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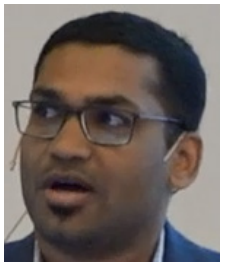
Mitochondrial function is a potential link between statin usage and risk of diabetes type II and myalgia

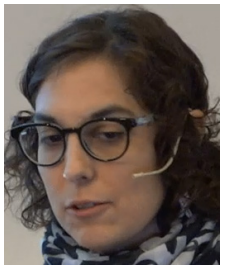
Claus Desler
Center for Healthy Aging, Department of Cellular and Molecular Medicine, University of Copenhagen, Copenhagen, Denmark
cdesler@gmail.com

Real-time fMRI neurofeedback for episodic future thinking reduces impulsivity in alcohol users



Harshawardhan U. Deshpande
Virginia Tech Carilion Research Institute, Roanoke, and School of Biomedical Engineering and Sciences, Virginia Tech, Blacksburg, Virginia, USA
harsh87@vt.edu

GABA promotes neuronal survival and axonal regeneration after spinal cord injury in lampreys



Blanca Fernández-López
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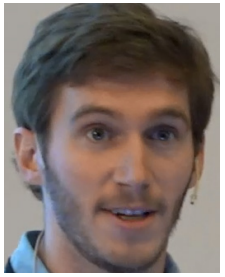
Early life exposure to SSRI antidepressants induces depression-like behavior in adult offspring through changes in perinatal hippocampal DNA methylation



Matthew E. Glover
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Insula, but not dACC, is necessary for risky decision-making under social influence: a lesion study

Mark A. Orloff
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PIK3CB/p110β is a selective survival factor for glioblastoma

Cara M. Rogers
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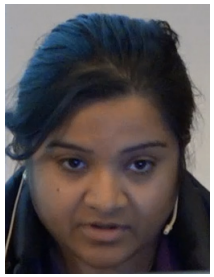
Identification of mechanisms that protect dopaminergic neuron health



Tanima SenGupta
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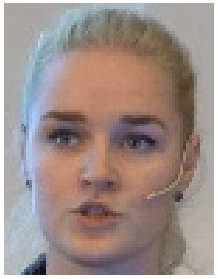
CDNF is neuroprotective in a toxin model of Huntington's disease



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Temporal changes in cardiorespiratory fitness and incident dementia and dementia mortality

Atefe R. Tari
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Potential role of N-benzylcinnamide in inducing neuronal differentiation from human amniotic fluid mesenchymal stem cells

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Lynxl modulates the activity of nAChRs to maintain and repair adult synapses

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Link to 'Best Poster Award':
http://www.vnpn.science/VNPN2_BestPosterAward.pdf

Modulation of cognitive networks

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Network-based neurological diseases, such as epilepsy, Parkinson's disease, Alzheimer's disease and traumatic brain injury affect millions of the world population. These chronic diseases have in common a large portion of medically refractory cases associated with cognitive impairment, mortality, psychosocial dysfunction, and significantly degraded quality of life. They also have in common the possibility of lessening their impacts through modulation of network function.

Of the emerging therapeutic modalities for treatment, one of the most intriguing is the field of neuromodulation. Neuromodulatory treatment, which consists of administering electrical pulses to modulate brain activity, can be an option for these patients. Modulation may well occur through the tripartite neuro-astroglial network. Current modalities consist of both open and closed loop stimulation. Improved technology offers the hope of better, more precise regulation of network functions.
https://www.carilionclinic.org/providers/mark-r-witcher-md-phd

Perineuronal nets as drug target for tumor associated epilepsy

Bhanu P. Tewari[1], Lata Chaunsali[1], Susan L. Campbell[1], Dipan C. Patel[1], Adam E. Goode[2], and **Harald Sontheimer**[1,3]
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[2]Virginia Tech Carilion School of Medicine and Research Institute
[3]School of Neuroscience, College of Science, Virginia Tech, USA
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Brain tumor patients often present with epileptic seizures. These are due to excitation inhibition imbalance imparted in parts by the assiduous release of glutamate from the tumor. We now show that tumor-associated seizures additionally involve impaired GABAergic inhibition due to an overall loss of peritumoral fast spiking interneurons (FSNs) concomitant with a significantly reduced firing rate of those that remain. FSNs in proximity of the tumor show degraded perineuronal nets (PNNs) that surround FSNs. We show that FSNs with PNNs fire at a much higher rate than those without. Tumor-released proteolytic enzymes particularly MMPs degrade PNNs, resulting in reduced firing, and hence decreased GABA release. Proteolysis of PNN in normal brain is sufficient to induce epileptiform activity, and inhibition of MMPs in tumor brain suppresses hyperexcitability. These studies suggest that PNNs tune the firing rate of interneurons and their degradation contributes to tumor-associated seizures. Disruption of PNNs may similarly account for excitation-inhibition imbalances in other forms of epilepsy and PNN protection through proteolytic inhibition may provide therapeutic benefits.
http://research.vtc.vt.edu/people/harald-sontheimer/

Perineuronal nets and brain plasticity

Torkel Hafting Fyhn

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In the adult brain, the extracellular matrix influences neuronal plasticity and impacts recovery after brain injury, learning and memory processes. Recently, it was proposed that the specialized extracellular matrix structures called perineuronal nets (PNNs) may be a physical framework for long-term memory storage. Perineuronal nets condense around the soma and proximal dendrites of subpopulations of neurons and stabilize synaptic connections. We tested if remote visual fear memories depend on intact PNNs in the lateral secondary visual cortex (V2L) in rats. In order to investigate the contribution of PNNs for memory stability, we induced a remote visual fear memory in adult Sprague Dawley rats using Pavlovian fear conditioning and experimentally degraded the PNNs by local injections of the enzyme chondroitinase ABC (chABC) into V2L. We found that degrading the PNNs in V2L prior to the remote memory retrieval test selectively disrupted the visual fear memory (Thompson et al., 2018). Degrading the PNNs in the primary visual cortex had no effect on the memory test. Supporting our behavioral findings, increased synchronized theta oscillations between V2L and basolateral amygdala, a physiological correlate of successful recall, was absent in rats with degraded PNNs in V2L. Together, our findings show that intact PNNs in V2L are required for recall of remote fear memory, without influencing memory processing at early time points.
https://www.mn.uio.no/ibv/english/research/sections/fyscell/cinpla/
https://www.med.uio.no/imb/english/people/aca/torkelh/index.html

Early diagnosis of Alzheimer's disease

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Alzheimer's disease is by far the most common cause of dementia, causing 60% or more of the cases. After a dementia diagnosis, loss of self-sustainability and a relentless clinical progression including loss of ambulation, incontinence, dysphagia etc., death follows typically after 8-12 years. Alzheimer's disease dementia is the end stage of a disease continuum, stretching over 2-3 decades prior to dementia. I will present clinical, biomarker and imaging research data from pre-dementia disease cohorts and discuss central pathological features including synaptic pathology and innate immunity.
Key questions to be discussed are:
What is early diagnosis?
How can early diagnostics help us in the drive towards intervention therapy for Alzheimer's disease?
https://www.med.uio.no/klinmed/english/people/aca/tormodfl/index.html

Hippocampal circuitry and early tau pathology

A. Rory McQuiston

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The microtubule associated protein tau normally binds to and stabilizes axon microtubules, but in Alzheimer's disease (AD) tau becomes hyperphosphorylated, dissociates from microtubules, and becomes part of neurofibrillary tangles as well as soluble pathogenic oligomers. These soluble tau oligomers can now migrate into the soma and dendrites of neurons where they can affect excitability and postsynaptic function. Soluble tau oligomers have also been shown to trans-synaptically spread between connected brain regions in human AD patients and animal models. However, the vulnerability of specific subtypes of neurons to trans-synaptic spread of tau is unclear. In this seminar, I will discuss recent studies from our lab that have investigated trans-synaptic spread of pathogenic tau (P301L) from the mouse medial entorhinal cortex into different subsets of hippocampal neurons. Furthermore, I will present data on the effect of pathogenic tau on the excitability of hippocampal neurons.

https://medschool.vcu.edu/expertise/detail.html?id=amcquiston http://www.people.vcu.edu/~amcquiston/
http://www.people.vcu.edu/~amcquiston/

Alzheimer's disease as an mTORopathy

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gsb4g@virginia.edu

Alzheimer's disease (AD) is characterized by memory and cognitive loss, and the accumulation in brain of two types of abnormal structures, plaques and tangles, that comprise poorly soluble filaments polymerized respectively from amyloid-β (Aβ) peptides and the neuron-specific microtubule-associated protein, tau. We have found that extracellular Aβ oligomers (AβOs) and cytoplasmic tau, which are highly soluble building blocks of plaques and tangles, work together to cause neuronal cell cycle re-entry, a prelude to neuron death in AD, and to inhibit Nutrient-induced Mitochondrial Activity (NiMA) by dysregulating mTOR, a protein kinase that regulates myriad aspects of cellular behavior in response to extracellular nutrients and trophic factors. In light of how AβOs and tau compromise mTOR function during seminal stages of AD pathogenesis, we propose that AD should be classified as an mTORopathy.

http://bio.as.virginia.edu/people/gsb4g

Oral infection and late-onset Alzheimer's disease

Ingar Olsen

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ingar.olsen@odont.uio.no

Alzheimer's disease (AD) is a scourge of longevity that will drain enormous resources from public health budgets in the future. AD can be of early familial-onset or sporadic with a late-onset. Apart from the two main hallmarks, amyloid-beta and neurofibrillary tangles, inflammation is a characteristic feature of AD neuropathology. Inflammation may be caused by a local central nervous system insult and/or by peripheral infections. Numerous microorganisms are suspected in AD including bacteria, viruses and yeasts. Periodontitis can provide the brain with these microorganisms and inflammatory mediators through daily, transient bacteremias. Chronic periodontitis is a twofold risk factor for development of AD and a timeline of ten years for this risk factor to develop has been found. Oral infections with *Porphyromonas gingivalis*, the keystone pathogen of periodontal disease, or introduction of its LPS in mouse models have caused development of key features of AD neuropathology. Reports of inflammation, amyloid-beta together with the clinical phenotype showing impaired learning and spatial memory have been presented. As periodontitis is modifiable, preventing it with regular surveillance and good oral hygiene throughout life is likely to reduce the incidence of AD.

https://www.odont.uio.no/iob/english/people/aca/ingaro/index.html

Brain inflammation and Parkinson's disease

Vidar Gundersen

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Brain inflammation is increasingly recognised as a key mechanism underlying the progressive loss of dopamine neurons in Parkinson's disease (PD). Activation of microglia and secretion of pro-inflammatory cytokines, such as tumor necrosis factor alpha (TNF-alpha), is pivotal for the inflammatory cascades leading to death of dopamine neurons. In this presentation I will discuss changes in microglia morphology and microglia-neuron contacts in lipopolysaccharide (LPS) induced brain inflammation and in the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) model of PD. I will also discuss how alpha-synuclein fibrils trigger changes in TNF-alpha receptors in monoaminergic cells. These cellular events may provide new understanding of the pathophysiology of Parkinson's disease.

https://www.ous-research.no/home/dietrichs/Staff/7077

Developing new disease modifying treatment for Parkinson's disease

Mart Saarma

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In Parkinson's disease (PD) dopamine (DA) neurons located in the substantia nigra (SN) degenerate and die. Since all current therapies are symptomatic our attempt is to develop novel disease modifying therapies for PD. We have discovered a new endoplasmic reticulum (ER) located neurotrophic factor (NTF) - cerebral dopamine neurotrophic factor (CDNF) and found that it completely differs from other known NTFs. We have demonstrated that CDNF can protect and repair midbrain DA neurons in rodent 6-OHDA and primate MPTP models of PD more efficiently than other NTFs. Differently from other NTFs, CDNF is mainly located in the ER, where it regulates ER stress and unfolded protein response (UPR) pathways. To understand the role of CDNF in mammals we created CDNF knockout mice that surprisingly develop an age-dependent loss of enteric neurons and constipation, similar to PD patients. Although the number of nigrostriatal dopamine neurons in CDNF knockout mice is normal there is also an age-dependent amphetamine-induced hyperactivity in *Cdnf*$^{-/-}$ mice that most probably is the result of aberrant dopamine transporter function. CDNF is currently tested in phase I-II clinical study on PD patients.
https://www.helsinki.fi/en/researchgroups/neurotrophic-factors-and-regeneration

Genetic risk for Parkinson's disease - implications for personalized treatments

Mathias Toft

Senior consultant and Professor, Department of Neurology, Oslo University Hospital and University of Oslo, Norway
mathias.toft@medisin.uio.no

Brief abstract: Genetic research has a major role to play in the effort to elucidate the pathogenesis of Parkinson's disease (PD) on a molecular level. PD was traditionally seen as a non-genetic disorder, but a range of studies mainly from the last decade has gradually changed this view. With respect to the sporadic, complex form of the disease, a major advance in recent years has been the identification of susceptibility loci through large-scale genome wide association studies (GWAS). In our group we are interested in refining and expanding the understanding of GWAS association signals to identify disease related pathways. Increasing evidence is pointing towards the involvement of autophagy and lysosomal dysfunction on PD pathogenesis. Several drugs with disease-modifying potential targeting this pathway is currently being investigated in clinical trials.
http://www.ous-research.no/toft

VNPN Festive Dinner, at Voksenåsen – Center for Swedish-Norwegian Cooperation

Master of Ceremony: **Linda Hildegard Bergerseen**

Best Poster Award:

The recipient of the Best Poster Award is Sydney Vaughan

Link to 'Best Poster Award':
http://www.vnpn.science/VNPN2_BestPosterAward.pdf

Presented by: **Ingrid Åmellem**
Selected by Conference Executive Staff:
Ingrid Åmellem (Leader), Alena Hadzic, Anna Zajkowska, Hanne Margrethe Weidemann, Imen Belhaj, Lars Henrik Bjørsrud,
based on scientific content, poster display and flash-presentation.

After Dinner Speech:

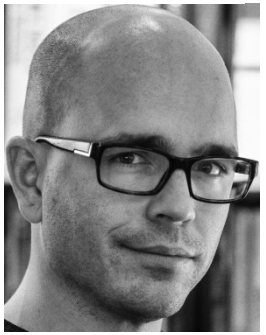
The discovery of LTP

Terje Lømo

Professor emeritus, Institute of Basic Medical Sciences, University of Oslo, Norway
terje.lomo@basalmed.uio.no

The property of long-term potentiation (LTP) at synapses in the brain appears fundamental to our ability for learning and memory; so what is LTP, what does it do, and why is it so important? And how did I, who did not particularly look for LTP, discover it, when others, who did look for it, failed? The discovery was made in Per Andersen's lab in Oslo in 1966 (Acta Physiol Scand 68 (Suppl 277): 128, 1966). Tim Bliss came to Per's lab as a postdoc in 1968 and in 1968-1969 we did the experiments that resulted in a landmark paper on LTP in The Journal of Physiology 4 years later (1973). Why such long incubation period? And why did Tim in his lab and Tony Gardner Medwin and I in my lab subsequently fail to reproduce our earlier results, a failure that led Tim to give up experimental work on LTP for several years and Tony and I for good? Why was the response to our 1973 paper so muted and what happened in the mid 1980s that brought LTP to the forefront in brain science? In this "after dinner speech" I will try to answer these and other questions (see also doi: 10.1111/apha.12921), while telling a few stories that I hope will at least partially fill the need for amusement at this point.

Synthetic viruses for precision therapies in brain disorders and for mapping of synaptic connectivity



Tomas Björklund

Molecular Neuromodulation, Wallenberg Neuroscience Center, Lund University, Sweden
tomas.bjorklund@med.lu.se

While single-cell genomics has revealed a fascinating diversity in neuronal subtypes, a key determinant of unique function remains the connectivity pattern of each neuron. To understand complex brain function we need to start to tackle the question of long distance connectomics on a single cell level. The development of novel therapeutic methodologies will also be greatly facilitated by clinically applicable vehicles which can target gene delivery based on connectivity or other functional properties if a neuronal subset. In this talk I will present the recent advances in AAV capsid engineering, viral vector barcoding, mono-synaptic tracing techniques and spatially resolved sequencing and our efforts to merge these technologies onto a framework for mapping neuronal circuit connectomics at a single cell level. I will also show the first data suggesting that circuit plasticity during brain repair in Parkinson's disease retains the endogenous capacity to distinguish beneficial from detrimental de novo connections.
www.neuromodulation.se

Brain drainage of waste and glial cell activity during sleep

Erlend A. Nagelhus

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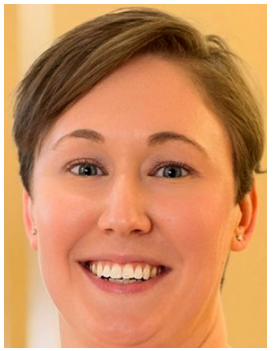
Since the brain lacks lymphatic vessels it has been an enigma how interstitial fluid and waste are removed. Recently it was shown that water channels in glial cells facilitate clearance of brain water and waste along blood vessels. The waste included amyloid, a toxic protein which accumulates in Alzheimer's disease. Mimicking the drainage function of the peripheral lymphatic system, the glia-dependent clearance route was coined the glymphatic pathway. The discovery that glymphatic function and "brain washing" are activated during sleep raises questions about regulatory mechanisms. The lecture will present and discuss essential elements of the glymphatic concept and present novel data on glial cell activity during sleep. A deeper understanding of glial cell function during sleep may pave the way for new treatment strategies of Alzheimer's disease and other neurodegenerative disorders in which removal of toxic waste is impaired.
https://www.med.uio.no/imb/english/people/aca/enagelh/index.html

The role of glia in the development, maintenance and regeneration of the nervous system



Sarah Kucenas

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sk4ub@virginia.edu

Traditionally, the central and peripheral nervous systems (CNS and PNS, respectively) have been thought of as two, distinct halves of one organ system that are only connected by small bundles of motor and sensory axons. However, recently, my lab has demonstrated that the CNS and PNS are not two distinct halves of one organ, but instead, extensions of the same nervous system connected by dynamic populations of glia, which has major implications for human development and disease. Overall, my research group's interests lie in investigating the role of glia in nervous system development and disease, with the goal that the information we learn will lay the groundwork for a more fundamental understanding of the rules that form a functional nervous system and shed light on mechanisms that could be perturbed in disease. Using Danio rerio (zebrafish), my lab combines genetic perturbation, single-cell manipulation, laser ablation/axotomy, small molecule drug screening and in vivo, time-lapse imaging to directly and continuously observe glial cell origins, behaviors and interactions in an intact vertebrate system.
www.kucenaslab.com

Targeting astrocytes in post-traumatic epilepsy

Stefanie Robel

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Assistant Professor School of Neuroscience, Virginia Tech, Blacksburg VA
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Focal traumatic brain injury (TBI) induces glial scar formation, which seals focal injuries off from healthy brain tissue. It is these glial scars that are associated with epilepsy. Yet, the vast majority of human TBIs also presents with diffuse injury caused by acceleration-deceleration forces on the brain tissue. The resulting diffuse tissue damage differs from focal lesions that would trigger glial scar formation. Diffuse TBI was modeled in mice using a closed head weight drop injury paradigm. Despite the absence of focal tissue lesions and classic glial scar formation spontaneous recurrent seizures developed after a latency period reminiscent of post-traumatic epilepsy in patients. However, some astrocytes responded with rapid and sustained loss of key homeostatic proteins in the absence of typical astrogliosis markers. Mimicking this phenotype by astrocyte ablation (genetically or by laser) resulted in hyperexcitability and seizures suggesting that astrocytes might contribute to epileptogenesis after TBI.
http://robellab.wixsite.com/robel-lab-vtcri

Targeted anti-inflammatory treatment for acute stroke

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Acute ischemic stroke (death of brain cells due to lack of oxygenated blood) occurs in the setting of cerebral blood vessel occlusion, which results in irreversible brain damage unless blood flow is restored quickly. Therefore, the major aim of stroke treatment is arterial recanalization to restore blood flow and cerebral blood perfusion. Recent innovations in the treatment of clinical stroke have transformed stroke care achieving high rate of arterial recanalization. However, despite ensuring vessel recanalization these methods are frequently powerless to fully reperfuse the ischemic brain with resulting poor patient outcomes (futile recanalization). The explanation for futile recanalization is multifactorial, in part explained by the presence of an inflammatory penumbra, an area surrounding the necrotic core where tissue is only partially perfused and potentially salvageable with restoration of blood flow and cerebral perfusion. This inflammatory penumbra is a result of the inflammatory cascade activated immediately after vessel occlusion and continuing the first hours after stroke. Recent data from clinical trials have highlighted the role of inflammation in this at risk area, suggesting it as a therapeutic option during the subacute phase of stroke.
https://www.ous-research.no/home/skjelland/Group member list/18562

Precision medicine for pain disorders

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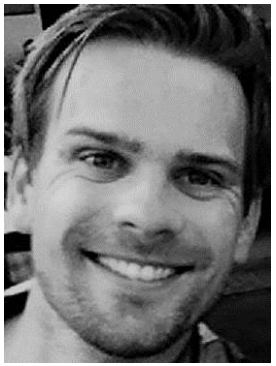
Chronic pain disorders constitute a huge world-wide health problem. Pain disorders may transform from an acute or episodic state to a chronic pain disorder. Our recent efforts are concentrated on understanding the mechanisms for this transition. We have used different approaches to identify risk factor for development of chronic pain disorders, including both human “surrogate” models, questionnaire based profiling and genetic studies. Identification of relevant and reliable risk factors for development of chronic pain may improve the effectiveness and precision of our treatments.
www.oslo-universitetssykehus.no

Microneurography of C-nociceptors in peripheral neuropathic pain



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Peripheral neuropathic pain is a common condition which can be difficult to treat, but it is unclear which underlying mechanisms are most relevant for such pain. Increased nociceptive input due to abnormal discharges from hyperexcitable nociceptors may be of crucial importance, but the presumed most relevant features of these nerve fibers are hard to study. However, the method of microneurography permits recordings of action potentials from peripheral nerve fibers in humans, including single unmyelinated C-nociceptors. Such recordings have provided detailed information about nociceptors in both acute nociceptive pain and pathological pain - including the segregation of C-nociceptors into different functional subclasses; the "polymodal" CM-nociceptors and the "silent" CMi-nociceptors. Findings from microneurography recordings from peripheral nociceptors in patients with painful neuropathic conditions will be presented.
https://www.ous-research.no/home/jorum/Group%20members/7071

Cortical changes associated with smell, taste and pain disturbances in humans

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The insular cortex has been described as the region of the brain that processes olfactory and gustatory information. Changes in the insular cortex have been observed in patients with smell and taste disorders. In patients with conditions like burning mouth syndrome, where patients complain of both burning pains and taste disturbances, changes are found in both the pain matrix and the taste cortex. The primary taste and smell cortex has been clearly defined, but the representation of secondary smell and taste cortex is yet not elucidated. Furthermore, the laterality of taste function is also under debate. An overview of smell and taste disturbances, their evaluation and management will be discussed in this presentation.
https://www.odont.uio.no/iko/english/people/aca/preetb/index.html

A comprehensive translational approach to functional recovery after spinal cord injury

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Spinal cord injury severely affects individuals, their family, and represents an economical burden for society. Intensive research using rodents has produced great advances in the characterization of the injury mechanisms and the identification of factors that prevent the tissue regeneration. Although multiple therapeutic attempts (stem cell-based regeneration therapy, neuroprotection, tissue regeneration, etc.) performed in small animals have shown promising results, past clinical trials based on them have shown varying results without fundamental breakthroughs. Clearly, larger animal models are needed to build a bridge over this gap. In this presentation, I will start with an overview of our recent efforts towards understanding adaptive plasticity after a mouse injury. I will further explain the difficulties we met in working with a large animal model and I will present our solution to replace urinary bladder function that we hope will successfully translate.
https://www.mendeley.com/profiles/jean-luc-boulland/?viewAsOther=true

Dynamic synaptic plasticity states in the neocortex in development and after injury

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Synapses within the neocortex undergo dramatic long term changes in efficiency through both up (LTP) and down (LTD) regulation throughout the lifespan. These forms of plasticity are subject to sliding modification thresholds. We set out to define the locus of these dynamic properties - cell wide vs. synapse specific control and if experience affects this locus. Using patch clamp recording from acute brain slices of visual cortex from normally reared and visually deprived mice, we found that the locus of this plasticity regulation is the synapse and is modulated by early visual experience. In another series of experiments, we evaluated the how the pattern of synaptic conditioning of multiple afferents or individual neurons affects plasticity in controls and after mild traumatic brain injury (mTBI). These patterns had different effects on plasticity outcomes in controls for multiple afferent activation and for single presynaptic cell activation. Moreover, there were differences between controls and mTBI neurons, particularly with irregular patterns of synaptic conditioning where the patterns that trigger LTD in controls, trigger LTP in mTBI.
http://research.vtc.vt.edu/people/michael-j-friedlander/

Set to change? Factors influencing neurocognitive trajectories and plasticity through the lifespan

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Are we set to change neurocognitively in certain ways? In this presentation, I use magnetic resonance imaging, standardized and experimental cognitive data, population registry and twin data to show how individual differences in neurocognitive change and plasticity are influenced by factors through the lifespan. Example influences discussed include prenatal environment, genetics and lifestyle variables. Taking factors present at birth into account may further understanding of the mechanisms at work at also later life stages. Preliminary data on genetic and environmental variance underlying differences in learning are included, to illuminate whether and to what extent we are set to change.

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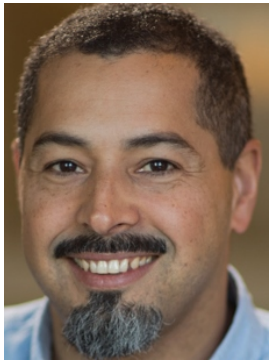
Maintaining healthy synapses



Gregorio Valdez

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Several lines of evidence indicate that dysfunction of the cholinergic system may contribute to aging of skeletal muscles and their synapses, called neuromuscular junctions (NMJs). First, cholinergic transmission is crucial for the function and viability of skeletal muscles. Second, acetylcholine (ACh) acts as an anti-synaptogenic factor in addition to its central function in initiating cholinergic transmission. In this talk, I will show that moderately increasing ACh at the synaptic cleft causes NMJs to prematurely acquire age-associated morphological features. I will also show that a moderate increase in ACh accelerates NMJ degeneration in a mouse model of ALS an age-associated disease in which NMJs invariably degenerate. Finally, I will show data indicating that skeletal muscle fail to adequately utilize a modulator of nicotinic AChRs, Lynx1, during aging.

http://research.vtc.vt.edu/people/gregorio-valdez/

Shedding new light on mechanisms that drive visual circuit development

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It has long been thought that the mammalian visual system is organized into parallel pathways, with incoming visual signals being parsed in the retina based on feature (e.g. color, contrast and motion) and then transmitted to the brain in unmixed, feature-specific channels. To faithfully convey feature-specific information from retina to cortex, thalamic relay cells must receive inputs from only a small number of functionally similar retinal ganglion cells. However, recent studies challenged this by revealing substantial levels of retinal convergence onto relay cells. Here, we sought to identify mechanisms responsible for the assembly of such convergence. Using an unbiased transcriptomics approach and targeted mutant mice, we discovered a critical role for the synaptic adhesion molecule Leucine Rich Repeat Transmembrane Neuronal 1 (LRRTM1) in the emergence of retinothalamic convergence. Mice lacking LRRTM1 and complex retinothalamic synapses display impairment in visual behaviors, suggesting a novel role of this convergence in vision.
http://research.vtc.vt.edu/people/michael-fox-phd/
http://labs.vtc.vt.edu/fox/

The locus coeruleus - norepinephrine system in attention and effort

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The common ability to select or prioritize information while shutting out distractions are defining features of focused attention. However, as the expression *to pay attention* suggests, when we focus attention, we are spending limited cognitive currency that should be wisely invested. This *intensive* aspect of attention is related to the level of arousal, but corresponds better to the phenomenological experience of cognitive effort or mental labor rather than simply to wakefulness. The level of engagement in mentally demanding tasks has been suggested to be mediated by activity in the brain stem locus coeruleus – norepinephrine system (LC-NE), the integrity of which is compromised in normal aging and in several CNS-related diseases. I will present results from several recent and ongoing studies aiming to experimentally manipulate the activity of LC-NE system, and to describe individual differences in attention and effort.
https://www.sv.uio.no/psi/english/people/aca/thomaesp

Extracting and modeling circuits down to the neuron and synapse level in an entire brain: high throughput EM in the fruit fly

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Abstract: This talk will cover the recent technical advances that bring us to the verge of a model of the entire brain of the fruit fly, Drosophila Melanogaster, an organ of about 100,000 neurons and 100 million synapses. This task has required advances in sample preparation, electron microscopy, image alignment, computer vision techniques, manual proofreading and correction, and circuit analysis. These techniques have led to dense (every neuron and synapse) maps of portions of the fly brain, and sparse (following selected neurons) models of specific full-brain circuits. Soon to come will be dense reconstructions of a full fly brain plus the ventral nerve chord (the fly equivalent of the spinal cord). Analysis and modeling of the limited portions of the brain extracted so far have already led to advances in our understanding of fly vision, sensory integration, and olfactory memory. Possessing the entire nervous system promises us enormous help in understanding the neural basis of more complex behaviors such as navigation, sleep, courtship, aggression, and other tasks the nervous system must perform in any animal.
https://www.janelia.org/lab/scheffer-lab

Medical research and precision neuroscience at Karolinska Institutet

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"*Medicine is a science of uncertainty and an art of probability*" wrote William Osler, one of the founding fathers of modern medicine. With the development of "Precision Medicine" we are about to prove him wrong. Medicine is now transforming into real science where uncertainty gives way to precision. It is fascinating to take part in this transformation. What is needed to retain a competitive edge? We need engagement of all stakeholders: research, health care, industry, patients, ethical, legal, and societal. We need access to health and patient data. We need an integrated national program, not only isolated funding initiatives. Given this complexity we need political support. In Sweden, Life Science and Precision Medicine constitute a prioritized area for the government, most recently exemplified by the establishment of a permanent Life Science Office under the Ministry for Enterprise and Innovation. The recent white paper – "Färdplan Life Science" – identifies Precision Medicine as one of three prioritized areas.

For research groups to remain competitive in Precision Medicine, access is required to a wide range of modern technologies and -omics, including the genome, transcriptome, proteome, metabolome, connectome, microbiome, epigenome, and exposome. Few if any universities are resourceful enough to muster all these technologies. Collaboration is required. In the case of Karolinska Institutet we have engaged in a fruitful collaboration with our neighbor universities – KTH Royal Institute of Technology, Uppsala University, and Stockholm University. The SciLife Lab is run as a collaborative effort between these four universities and is a national resource with broad participation of Swedish Life Science institutions. SciLife Lab spearheads the development of Precision Medicine in several fields, not

least when it comes to comprehensive analysis of health and detailed census of cell types in the CNS and other organs. In few other fields is the benefit of translational research as evident as in the field of precision medicine.

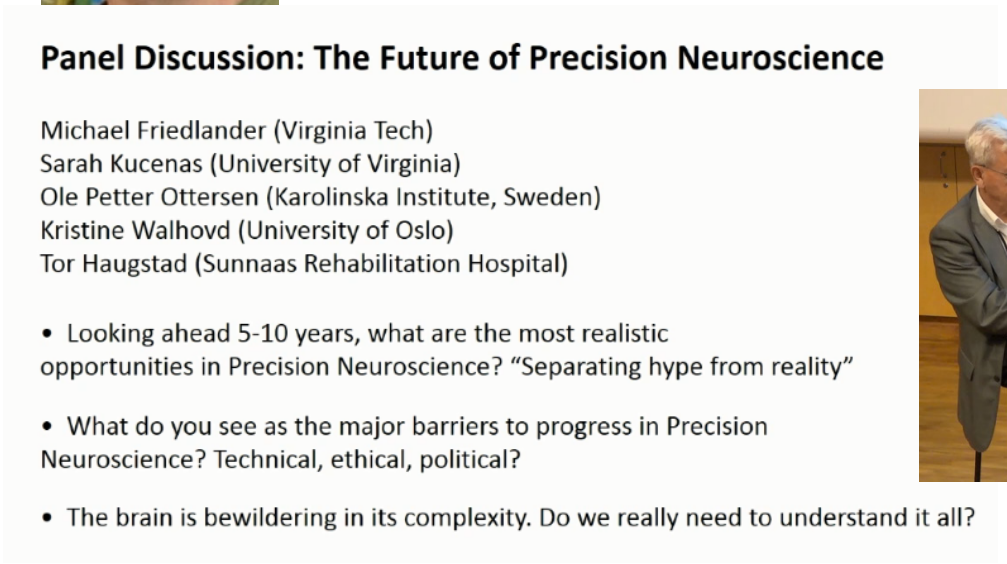
Scientists, academic leaders, politicians, and other actors must join forces to catalyze the transformation of medicine into a science that is characterized by precision rather than uncertainty. Regional, national, and international collaboration is paramount. In this context the current symposium is both timely and opportune.

https://ki.se/en/about/president-ole-petter-ottersen
https://ki.se/en/research/sharing-global-responsibilities

Panel Discussion: "Future of Precision Neuroscience"

Bramham, Friedlander, Haugstad, Kucenas, Ottersen, Walhovd, and audience
Moderation, summing up: **Clive Bramham** (President of the Norwegian Neuroscience Society)

Video recording: https://www.youtube.com/watch?v=J6c2Gd8vFCg



End of VNPN2

VNPN3 ***is planned to be organized in Virginia 20-22 May 2020 by Mike Friedlander et al.*** https://precisionneuroscience.org/