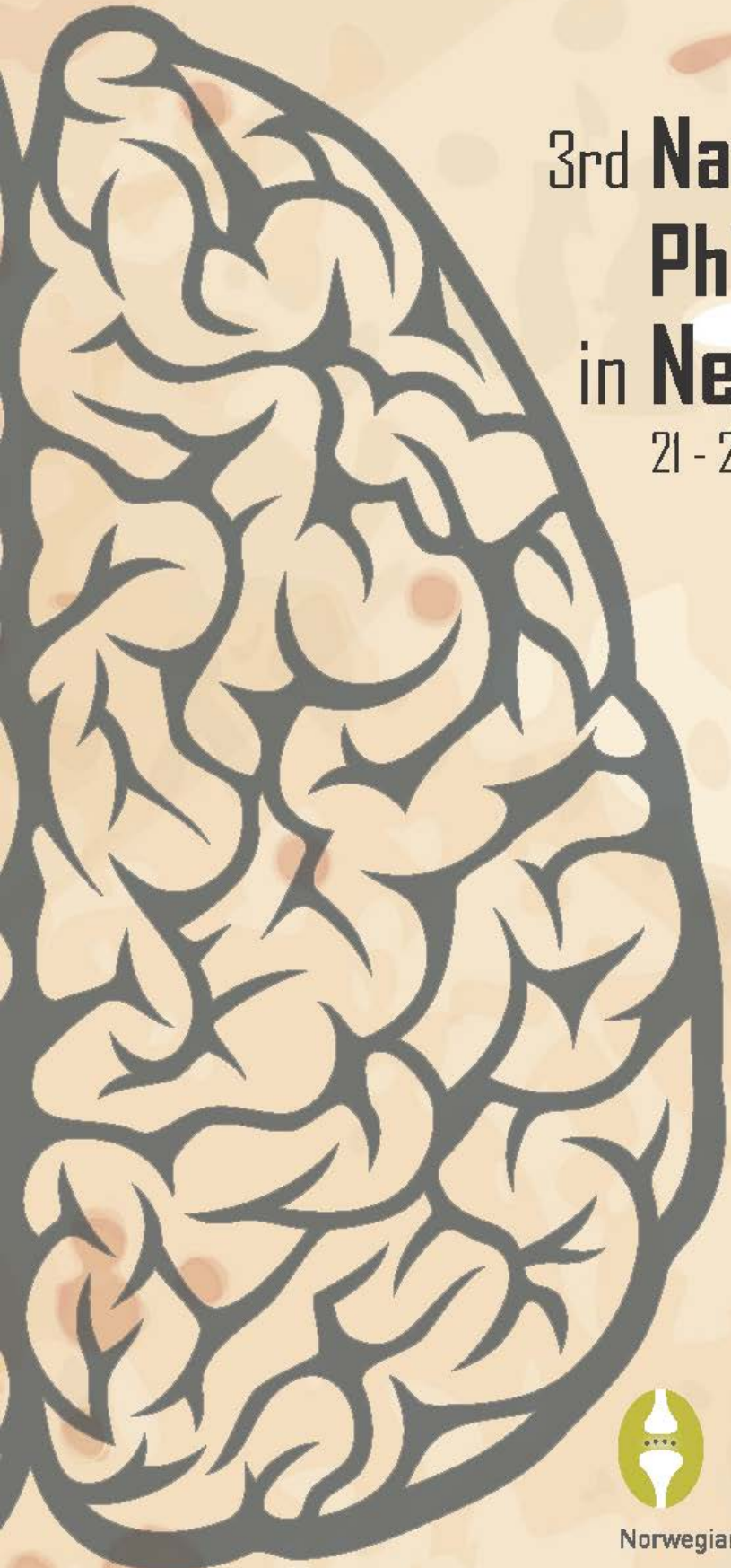

3rd National PhD Conference in Neuroscience

21 - 23 September, 2015, Sotra

Organized by

NRSN

Norwegian Research School in Neuroscience

The 3rd National PhD Conference in Neuroscience

Panorama Hotel, Sotra

21-23 September 2015

NRSN

Norwegian Research School in Neuroscience

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Preface by the organizing committee

Dear Friends and Colleagues,

We are delighted to welcome you all at the 3rd National PhD Conference in Neuroscience.

This conference runs under the auspices of the Norwegian Research School in Neuroscience (NRSN), which brings together the expertise of PhD neuroscientists from all over the world conducting their research in Norway. The NSRN PhD Neuroscience Conference is organized exclusively by PhD students, for PhD students.

The Conference Programme Committee has selected a comprehensive series of keynote lectures, workshops, various oral, poster and blitz sessions covering the entire field of neuroscience.

You will have a unique opportunity to network with PhD peers working all over Norway, enhancing your research and career development. You will be exposed to a variety of interactive educational sessions in a stimulating environment and learn about the latest scientific research and developments in the field of neuroscience. Cutting-edge studies will be presented.

This year, along with the scientific program, we have a wide range of social activities such as: yoga, jogging, fishing and networking games and leisure time during and after dinner.

On top of this, prizes will be awarded to the best oral presentation, the best poster and the best blitz presentation, 6000 NOK each, to be used for any purpose that promotes the winners research training. The "blitz" is a super brief presentation (60 seconds) where participants advertise their own poster.

We wish you a pleasant and stimulating NSRN PhD Neuroscience Conference and a great time in Sotra.

Sincerely,

The organizing committee:

Aliona Nacu, UiB
Kjetil Vikene, UiB
Rishab Chawla, UiO
Kristina Skåtun, UiO
Violeta Botellero, NTNU
Christin Berndtsson, NTNU
Abdolrahman Khezri, NMBU

Preface by the director of NRSN

To all participants of the 3rd annual meeting of Norwegian PhD students in Neuroscience,

Welcome to the third national meeting of PhD students in neuroscience, organized under the responsibility of the Norwegian Research School in Neuroscience NRSN. We, as board and administration aim to make NRSN the hub in the community of young, Norwegian-trained neuroscientists. The NRSN, funded by the Norwegian Research Council, has an annual budget of around 3 Mill NOK.

This meeting is organized *by* PhD candidates *for* PhD candidates. We had two very successful meetings already, following the same model, and we are all looking forward to this 3rd event. The philosophy behind the event is based on the concept that the organizing committee is composed of a group of dedicated PhD candidates from all partner universities, so essentially you are organizing your own meeting. This concept has been successful in other places and has recently been adopted for a European PhD meeting in Neuroscience as well (ENCOD). During or directly following the meeting *you can volunteer to be on the organizing committee for the 2016 meeting,* for which we have already started to scout a new venue.

We have used your evaluations of both previous meetings to make the event even better, allowing you to interact and socialize, get to know each other, and learn about the impressive variety and high level of Norwegian neuroscience. Looking at this year's program, I am sure this again will be a great meeting. I find it a privilege to attend this year, since after all, it is your meeting, providing you with the opportunity to interact without having your supervisors around.

In addition to the annual meeting, NRSN is working to get a training program in place, teaming with our partners in the school. We have organized a number of courses and are actively building a strong training portfolio. We had a summer-school in August in Oslo, and are planning the second one for 2016. So NRSN is alive and active, there is more to come, not only for you but also for your supervisors.

As director of NRSN, and on behalf of the board, I am very pleased with what the organizing committee has been able to establish. I thank them for their enthusiasm and all their efforts, and I like to acknowledge the important help of the NRSN administration to make this meeting become reality. Finally, I am grateful to you and your supervisors for the decision to come, and to submit an abstract and most importantly to attend and participate.

Enjoy the meeting, make good use of it, give us constructive feedback, and become an active member of NRSN.

Trondheim, August 2015

I look forward to seeing you in Bergen.

Menno Witter, PhD
Professor of Neuroscience, Director of NRSN

Program

Monday 21 September

16:15 Bus departure from Flesland airport
17:30 Arrival at Sotra
17:30-18:30 Check in, refreshments, poster mounting
18:30-18:45 **Welcome talk by Professor Menno Witter, NTNU - Scientific director NRSN**
18:45-20:00 **Opening lecture and discussion: "The scientific career "**
Ass. Prof. Emre Yaksi, NTNU and Dr. Nathalie Jurisch-Yaksi, NTNU
20:00-23:00 Dinner. Mixing and mingling.

Tuesday 22 September

07:00-08:00 Rise and shine! Optional activities: yoga, jogging, fishing.
07:00-09:00 Breakfast
09:00-10:00 **Oral session I: Genetic, molecular and cellular neurscience**
Chairs: Rishab Chawla (UiO), Abdolrahman Khezri (NMBU)

- Ane Charlotte Christensen (UiO): *"The role of extracellular matrix molecules for spatial representations and plasticity in entorhinal cortex.", p. 19.*
- Anders Lunde (UiO): *"Gene expression profiling by RNA-sequencing and immunohistochemistry of the developing vestibulospinal system.", p. 20.*
- Charlotte Jendresen (UiO): *"Heparan sulfate fragmentation lowers amyloid burden in Alzheimer disease transgenic mice.", p. 22.*
- Eirik Stamland Nilssen (NTNU): *"Local connectivity and immunoreactivity of principal cells in layer II of lateral enthorinal cortex.", p. 23.*
- Shreyas Rao (UiO): *"Upregulation of astrocity dystroglycan upon hypotonic stress.", p. 24.*

10:00-10:15 Break
10:15-11:15 **Oral session II: Clinical neuroscience**
Chairs: Aliona Nacu (UiB), Kristina Skåtun (UiO)

- Nathalia Zak (UiO): *"A longitudinal study of cortical thickness in bipolar disorder type II.", p. 27.*
- Intakhar Ahmad (UiB): *"Legumain and SLC7A5 protein in the early processes of Multiple Sclerosis (MS) pathology.", p. 29.*
- Kjetil Vikene (UiB): *"Perception of complexity in rhythm in PD.", p. 30.*
- Agnes Balint Bjørke (UiO): *"Is temporal lobe epilepsy with hippocampal sclerosis a neurodegenerative condition?", p. 31.*
- Emanuel Neto (UiB): *"Discrimination of dementia patients using novel EEG spectral features.", p. 32.*

11:15-11:30 Break
11:30-12:15 **Workshop: How to succeed with your poster presentation?**
12:15-13:30 Lunch
13:30-14:15 **Blitz session I** (PhD students with poster, 60 sec each)
14:15-15:15 **Poster session I**

15:15-15:30 Break

15:30-16:30 **Keynote lecture: "The plastic human brain"**
Professor Lutz Jäncke, Neuroscience Center Zurich

16:30-17:00 Break and light snack

17:00-18:00 **Oral session III: Cognitive neuroscience and neuropsychology**
Chairs: Kjetil Vikene (UiB), Violeta Botellero (NTNU)

- Cecilie Skaftnes (UiO): *"Deficits in inhibitory mechanisms after exposure to life-threatening events.", p. 35.*
- Magnus Holth (NTNU): *"Coupling perception, action and cognition in estimating successful contact-timing of a moving object.", p. 36.*
- Alexandra Vik (UiB): *"Changes in resting state fMRI connectivity in normal aging is associated with introspective reports of experience of memories.", p. 37.*
- Aleksander Hagen Erga (SUS): *"A population-based study of impulse control disorders in Parkinson's disease: the Norwegian ParkWest study.", p. 38.*
- Ragnhild Bø (UiO): *"Dissociated decision-making process in binge drinkers and relation to sensation seeking.", p. 40.*

18:00-20:00 Resting state (free time)

20:00-22:00 Fun 'n' fancy dinner

22:00- Social evening

Wednesday 23 September

07:00-09:00 Breakfast

09:00-09:45 **Blitz session II** (PhD students with poster, 60 sec each)

09:45-11:00 **Poster session II**

11:00-11:30 Poster demounting/check out

11:30-12:30 **Oral session IV: Systems and computational neuroscience**
Chairs: Christin Berndtsson (NTNU), Rishab Chawla (UiO)

- Benjamin Kanter (NTNU): *"Transgenic activation of medical entorhinal cortex similarly alters spatial firing properties of CA3 and CA1 place cells.", p. 43.*
- Tammo Ippen (NMBU): *"NESTML: A Domain Specific Language for Creating Neuron and Synapse Models for the NEST Simulator.", p. 44.*
- Ewelina Bartoszek (NTNU): *Brain-wide connectivity underlying habenular activity in zebrafish (danio rerio).", p. 45.*
- Andreas Solbrå (UiO). *"Novel scheme for modeling ion dynamics in 3D neural tissue.", p. 46.*
- Bartul Mimica (NTNU). *"Cognitive demand dependent changes in neural coding of self-motion in parieto-frontal circuits in rats.", p. 47.*

12:30-13:30 Lunch

13:30-14:00 **Closing session**. Awards, conclusive remarks

14:30 Bus departure for Flesland airport

16:00 Arrival at Flesland airport

Blitz- and poster presentations 22 September

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Blitz- and poster presentations 23 September

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Invited speakers

Opening lecture: Ass. Prof. Emre Yaksi and Dr. Nathalie Jurisch-Yaksi

Title: The Scientific Career

Time: Monday 21 September, 18:45-20:00

Associated Professor Emre Yaksi and his group studies information processing in neural circuits, aiming to understand the fundamental principles that underlie the development and function of neural circuits. The research focus in his group center around questions of how sensory information is integrated and processed in the brain in order to create behavior, how neural circuits interact with the sensory world and which functional rules control the assembly of these neural circuits in both the developing and the adult brain.

In order to investigate these questions, the Yaksi lab uses the chemosensory systems of the adult and larval zebrafish. Using an array of different methods, they attempt to monitor, dissect and perturb the neural circuits underlying the chemosensory input in the zebrafish brain. Emre won the EJN Young Investigator Prize for his work in 2014, and together with his wife Nathalie Jurisch-Yaksi, he recently moved his lab from Belgium to the Kavli institute in Trondheim.

Nathalie did her PhD work in Heidelberg, Germany and has held several post doc positions. She has mainly focused her research on disease models, working on the signaling pathways involved in cancer, and factors contributing to Alzheimer's disease. In addition to research, she has a keen interest in the career possibilities available to scientists.

Together Emre and Nathalie have a lot of experience working in a scientific environment and a strong interest in the different career opportunities that are available for PhDs.

Selected publications:

Karmen F, Franco LM, Wyatt C, Yaksi E. (2013) *"Neural circuits mediating olfactory-driven behavior in fish."* Front Neural Circuits. 7(62)

Dreosti E, Vendrell Llopis N, Carl M, Yaksi E, Wilson SW. (2014) "*Left-right asymmetry is required for the habenulae to respond to both visual and olfactory stimuli*." Curr Biol. 24(4)

Jetti SK, Vendrell-Llopis N, Yaksi E. (2014) *"Spontaneous activity governs olfactory representations in spatially organized habenular microcircuits."* Curr Biol. 24(4)

Jurisch-Yaksi N, Annaert W. (2013) *"Protein quality control by Rer1p in the early secretory pathway: from mechanism to implication in Alzheimer's disease."* Alzheimer's Research and Therapy. 5(61)

Invited speaker

Keynote lecture: Professor Lutz Jäncke

Title: The plastic human brain

Time: Tuesday 22 September, 15:30-16:30

Lutz Jäncke is a cognitive neuroscientist interested in cognitive and functional neuroanatomy, and is currently a professor of neuropsychology at the Department of Psychology, University of Zürich, Switzerland. He has published more than 360 original peer-reviews scientific works, and has published in such journals as Science and Nature. He has also written and edited several books in the field, both in German and English. Jäncke's research covers many different areas, from cognitive-motoric integration, spatial presence, synesthesia, to the relation between brain and music.

Not long ago neuroscientific consensus held that the lower brain and neocortical areas were immutable after development, whereas areas related to memory formation, such as the hippocampus and dentate gyrus, were highly plastic. The advent of modern brain imaging methods has enabled the study of cortical plasticity in healthy human subjects, and plastic changes have now been demonstrated not only in the brain of children, adolescents, and younger adults, but also in mid-aged adults and more recently in the elderly. Thus, the human brain is plastic throughout the entire lifespan.

In his presentation, Jäncke will summarize findings of cross-sectional and longitudinal research on cortical plasticity as uncovered in his lab, placing greater emphasis on structural and functional plasticity in one specific expert group, namely musicians.

Selected Publications

Munte, T. F., Altenmuller, E., & Jancke, L. (2002). The musician's brain as a model of neuroplasticity. Nature Reviews. Neuroscience, 3(6), 473-478.

Jancke, L., Wustenberg, T., Scheich, H., & Heinze, H. J. (2002). Phonetic perception and the temporal cortex. Neuroimage, 15(4), 733-746.

Jancke, L. (2009). The plastic human brain. Restor Neurol Neurosci, 27(5), 521-538.

Jäncke, L., Mérillat, S., Liem, F., & Hänggi, J. (2015). Brain size, sex, and the aging brain. Hum Brain Mapp, 36(1), 150-169.

Beeli, G., Esslen, M., & Jancke, L. (2005). Synaesthesia: when coloured sounds taste sweet. Nature, 434, 38.

Jäncke, L., Rogenmoser, L., Meyer, M., & Elmer, S. (2012). Pre-attentive modulation of brain responses to tones in coloured-hearing synesthetes. BMC Neuroscience, 13, 151.

Award winners 2014

Asgeir Kobro-Flatmoen
Kavli Institute for Systems Neuroscience and Centre for Neural Computation, NTNU

Winner of the award for Best Oral Presentation,
2nd National PhD Conference in Neuroscience, Stiklestad 2014.

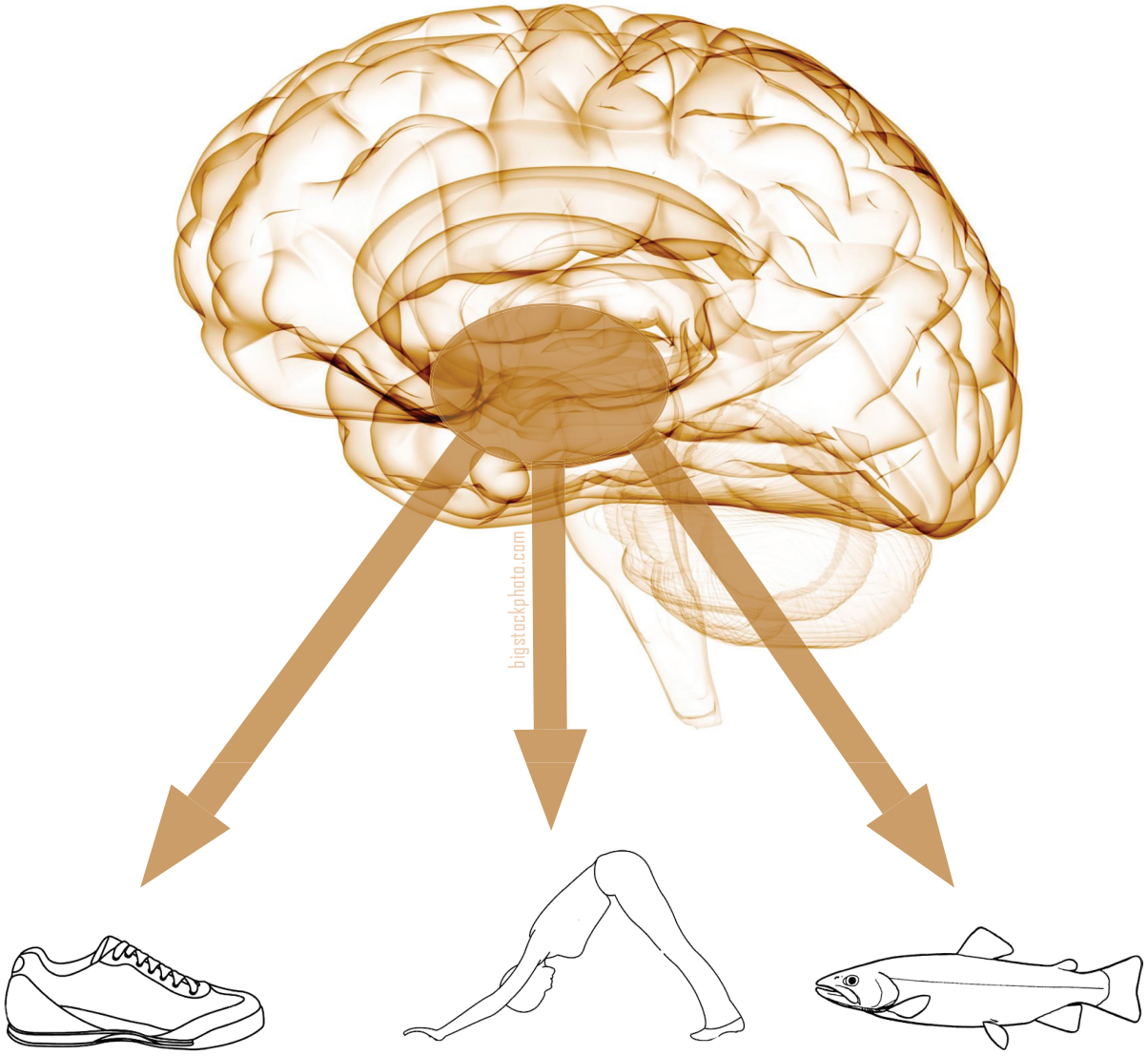
Ane Charlotte Christensen
Institute of Basic Medical Sciences, University of Oslo

Winner of the award for Best Poster Presentation,
2nd National PhD Conference in Neuroscience, Stiklestad 2014.

Ashraf Pakzad
Department of Biomedicine, University of Bergen

Winner of the award for Best Blitz Presentation,
2nd National PhD Conference in Neuroscience, Stiklestad 2014.

Activate your **Reward and Pleasure** circuitry



Go **Jogging** with Rishab

Do **Yoga** with Violeta

Go **Fishing** with Kjetil

Tuesday morning 07:00 - 08:00

Meet up at the reception

Abstracts for oral session I:

Genetic, molecular and cellular neuroscience

Abstracts are organized in the order of presentations

The role of extracellular matrix molecules for spatial representations and plasticity in entorhinal cortex

Ane Charlotte Christensen[1,2], Kristian Kinden Lensjø [2], Mikkel Lepperød [1,2], Marianne Fyhn [2], Torkel Hafting [1]

1. Institute of Basic Medical Sciences, University of Oslo
2. Department of Biosciences, University of Oslo

The hippocampus and parahippocampal areas are key players in spatial memory processing. A substantial fraction of principal neurons in the medial entorhinal cortex (MEC) are grid cells which are characterized by their multiple firing fields forming a hexagonal pattern spanning the area visited by the animal. The grid cells form stable spatial representations that are reactivated any time the animal visits the same environment. The processes of preserving existing maps and encode novel representations require both stability and plasticity. Growing evidence suggests that GABA'ergic fast spiking parvalbumin-positive (PV+) inhibitory neurons, are essential for regulation of plasticity in sensory cortices. The PV+ cells in the adult cortex are to enwrapped in perineuronal nets (PNNs) which are condensed extracellular matrix molecules. Emerging evidence suggests that perineuronal nets (PNNs) stabilize synaptic connections and restrict plasticity in the adult brain. Enzymatic degradation of PNNs with Chondroitinase ABC (chABC) induces plasticity in adults and promotes some types of learning but it remains elusive if spatial processing of the MEC is affected by degradation of PNNs. In the present study, we investigated how enzymatic degradation of PNNs affects spatial representations in the MEC in awake and behaving rats. The superficial layers of MEC are densely filled with PV+ neurons, and we show that most of them are enwrapped by PNNs. Bilateral injections of the enzyme chondroitinase ABC in the dorsal MEC were used to disrupt the nets. Extracellular recordings from single units in MEC were conducted in rats running in an open field (1x1m square box). When stable recordings of grid cells were obtained across successive recording sessions in a familiar environment, the rat was introduced to a similar box in a novel room. In animals with PNNs degraded we observed decreased spatial information of grid cells in a familiar environment. Also, the establishment of stable grid representations in novel environments was delayed, and continued to display decreased spatial correlation compared to control animals. Furthermore, analysis of local field potentials showed that disruption of PNNs lead to increased theta power in the MEC. Results from this study indicate that PNNs could be important for sustaining stable spatial representations of MEC in adult animals.

Keywords:
Molecular neuroscience
Cellular neuroscience
Systems neuroscience

Gene expression profiling by RNA-sequencing and immunohistochemistry of the developing vestibulospinal system.

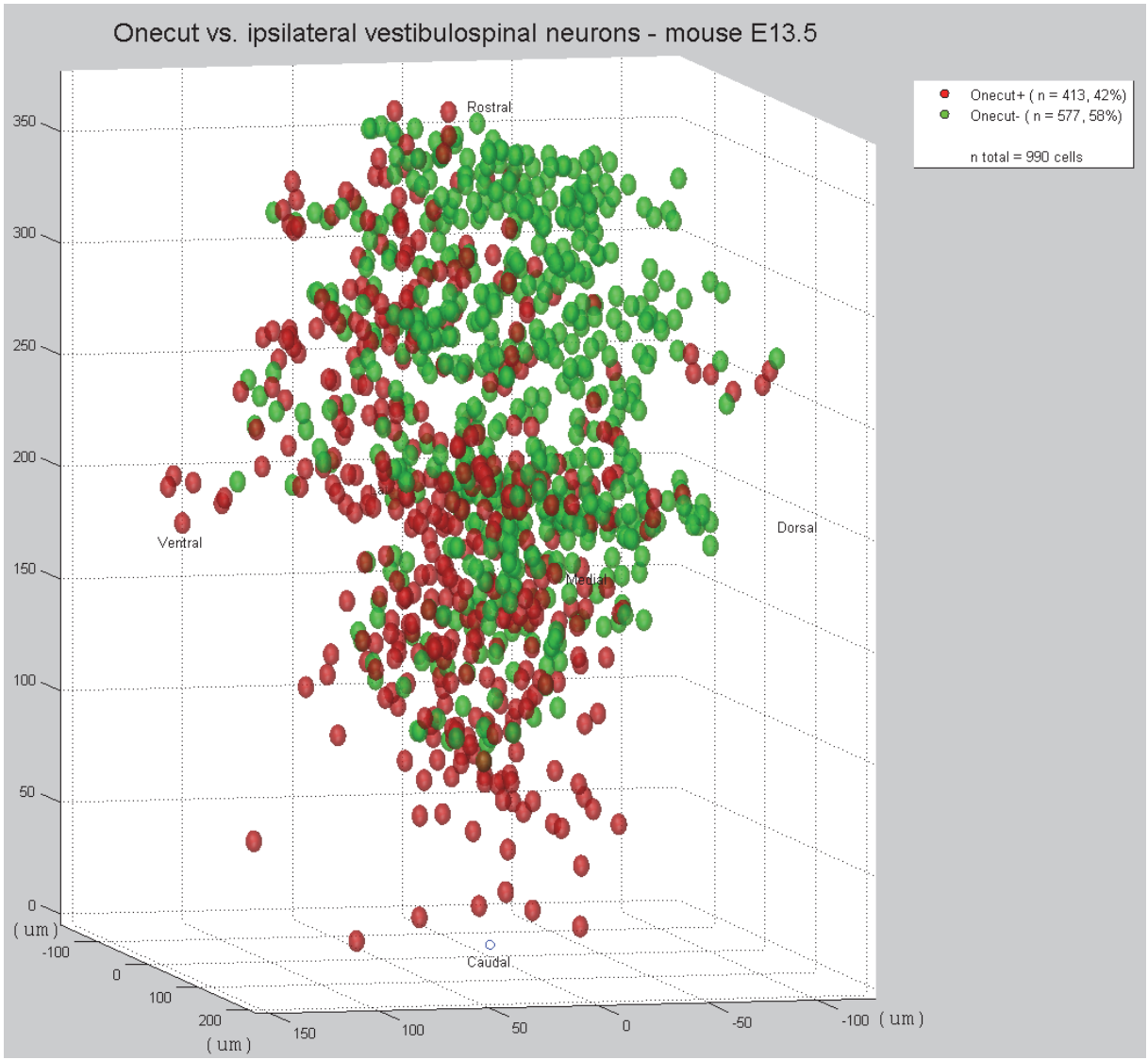
Anders Lunde[(1)], Benjamin Okaty [(2)], Joel Glover [(1)]

1. Institute of Basic Medical Sciences, University of Oslo, Norway
2. Department of Genetics, Harvard Medical School, Boston MA, USA.

The human brain is made up of about 86 billion neurons. Each neuron can connect to tens of thousands of other cells, arguably making the human brain the most complex structure in the known universe. A salient question for neuroscientists who aim to understand or model the brain concerns the classification of neurons into categories based on functional, structural, molecular and other characteristics. Estimates range from a few to one thousand for the cortex alone. Developmental neurobiology is particularly suited to answer the question of neuronal categories, and much progress has been made in the identification of neuronal subtypes by studying neuronal birth and differentiation during embryogenesis, especially by correlating differential expression of transcription factors with mature neuron phenotypes. Our work focuses on the embryonic development of an evolutionarily ancient system that helps us maintain posture and balance: the vestibulospinal system, which relays three-dimensional positional information from the inner ear to the muscles of the body. Currently this collection of some 3000 individual neurons in the mouse are known to contain different types of neurons in terms of connectivity and neurotransmitter phenotype, but this has not yet been linked to a molecular or genetic classification. In particular there is an ipsilateral (lateral vestibulospinal tract, LVST) and a distinct contralateral (contralateral medial vestibulospinal tract, cMVST) projection of the vestibulospinal system to the spinal cord. We have been isolating RNA from these two categories of vestibulospinal neurons in both mouse and chicken, and use RNA-sequencing to determine which pattern of gene expression distinguish these two sub-populations. We also label the vestibulospinal neurons retrogradely and investigate the most highly expressed transcription factors and other proteins by immunohistochemistry. With this we have begun to reveal subpopulations of vestibulospinal neurons within each of the two broad vestibulospinal neuron categories. Initial results from RNA-sequencing and immunohistochemistry of the ipsilateral LVST neurons at embryonic day 13.5 in mice have already revealed a gene whose expression appears to divide the group into two distinct subpopulations, one positioned caudo-ventrally and the other rostro-dorsally.

Keywords:
Genetic neuroscience
Systems neuroscience
Developmental neuroscience

See image on next page.



3D reconstruction of the LVST neurons in the mouse at embryonic day 13.5. Neurons positive for the transcription factor Onecut in red, and negative in green.

HEPARAN SULFATE FRAGMENTATION LOWERS AMYLOID BURDEN IN ALZHEIMER DISEASE TRANSGENIC MICE

Charlotte Jendresen[1], Hao Cui [2], Xiao Zhang [3], Israel Vlodavsky [4], Lars Nilsson [1], Jin-Ping Li [2]

1. Department of Pharmacology, University of Oslo, Norway
2. Department of Medical Biochemistry and Microbiology, University of Uppsala, Sweden
3. Department of Neuroscience and Pharmacology, University of Uppsala, Sweden
4. Cancer and Vascular Research Center Rappaport, Technion, Israel

Heparan sulfate proteoglycans (HSPGs) are complex glycoconjugates expressed in all vertebrate tissues in extracellular matrices and at cell surfaces. Amyloid deposits in Alzheimer disease (AD) brain consist mainly of amyloid-β (Aβ), but other components have been found co-localizing with Aβ, e.g. HSPGs and their heparan sulfate (HS) side chains. In vitro experiments have shown that HS/HSPGs augment Aβ aggregation. But still, the pathogenic role of HSPGs in AD brain remains unclear. Therefore, the aim of our study was to test if HS participates in Aβ-pathogenesis in vivo. Heparanase is an enzyme that fragments HS, and by overexpressing heparanase in an AβPP transgenic mouse model, we were able to investigate the effect of in vivo fragmented HS in cerebral amyloidosis. We compared neuropathologies of 15-months-old transgenic mice overexpressing both human heparanase and human AβPP with the Swedish mutation (tgHpa*Swe, n=17) with AβPP single-transgenic mice (tgSwe, n=17). Brains were examined with Congo red as well as Aβ-, HS-, and heparanase-immunohistochemistry and immunofluorescence. Sizes of HS fragments in brains were examined by gel chromatography. For AβPP-processing, Aβ and sAβPPβ levels were measured in 2.5-months-old mice by ELISAs and western blots. Heparanase was overexpressed in neurons and astrocytes in tgHpa*Swe mice in both the active and inactive forms. Heparanase-overexpression also led to fragmented cerebral HS. The tgHpa*Swe mice had significantly lower amyloid burden ($p<0.001$) and Aβ-burden ($p<0.05$) than tgSwe mice. HS-stained plaques were fainter in tgHpa*Swe than in tgSwe ($p<0.0001$) and this correlated with Aβx-42-burden ($p<0.05$). The levels of sAβPPβ, Aβx-40, and Aβx-42 in 2.5-months-old mice did not differ. In the present study, heparanase-fragmentation of HS in mouse brain was found to lower amyloid- and Aβ-burden in aged heparanase-overexpressing tgHpa*Swe mice, while AβPP-processing remained unchanged in young mice. In concordance with in vitro experiments, this suggests that HSPGs play an important role in amyloid deposition in AD by increasing aggregation of Aβ.

Keywords:
Cellular neuroscience
Neuropathology

Local connectivity and immunoreactivity of principal cells in layer II of lateral entorhinal cortex

Eirik Stamland Nilssen[(1)], Gunhild Fjeld [(1)], Menno Witter [(1)]

1. Kavli Institute for Systems Neuroscience and Centre for Neural Computation, NTNU, Trondheim

Neurons in layer II of the entorhinal cortex provide a strong input to the dentate gyrus (DG) and CA3 of the hippocampal formation. In medial entorhinal cortex (MEC), DG-projecting cells are mainly stellate cells, and positive for the molecular marker reelin but not for calbindin. Stellate cells are connected with each other almost exclusively through inhibitory interneurons. In lateral entorhinal cortex (LEC), all principal cell types (fan, pyramidal and multiform) project to the DG. Little is known about the local synaptic connectivity of these cells and their immunoreactivity. The aim of the present study was to investigate whether the principal cell local network in LEC layer II is similar to the stellate cell network in MEC, or whether monosynaptic excitatory connections prevail. Furthermore, we aimed to check if there is a correlation between cell type identity and immunoreactivity for reelin or calbindin. We carried out simultaneous whole-cell recordings in vitro of clusters of up to four neurons in LEC LII, and filled neurons with fluorescent dyes during recording and subsequently immunostained for reelin and calbindin. Neuronal morphology and immunoreactivity were assessed with confocal laser-scanning microscopy and 3D-reconstructions. The data set includes recordings of 630 pairs of principal cells, of which 105 cells were selected for immunocytochemical analysis. Among 98 three-cell and 56 four-cell clusters, direct excitatory connections were observed in nine clusters, whereas indirect inhibitory connectivity was detected only in a single cluster. Most recorded clusters contained a mix of fan, pyramidal and multiform cells, however, fan cells were most abundant. Immunostaining of the recorded cells revealed a high degree of overlap with reelin, and clearly showed that reelin-positive cells are found among fan, pyramidal and multiform cells. Furthermore, no direct connections were detected between these reelin-positive cells. Given that the majority of our recordings were from fan cells, the results indicate that direct excitatory connectivity between these cells is sparse. The low number of disynaptic inhibitory connections is surprising, and might be due to weak connectivity with inhibitory interneurons. It is more likely, however, that the three principal cell types interact with separate populations of interneurons, making it difficult to detect disynaptic inhibitory connections in our clusters containing multiple principal cell types.

Keywords:
Cellular neuroscience
Systems neuroscience

Upregulation of astrocytic dystroglycan upon hypotonic stress

Shreyas Rao[(1)], Henning Boldt [(1)], Doreen Leung [(1)], Mahmood Amiry-Moghaddam [(1)]

1. Laboratory of Molecular Neuroscience, Department of Molecular Medicine, Institute of Basic Medical Sciences, University of Oslo

Hyponatremia is a condition associated with a number of clinical complications and may cause serious consequence such as brain edema with significant mortality rate. The current treatment for hyponatremic brain edema aims at relieving the symptoms and does not prevent the formation of edema. Aquaporin-4 (AQP4), the membrane water channels anchored to perivascular astrocytic endfeet via dystrophin associated protein complex (DAPC) are known to be involved in development and resolution of hyponatremic brain edema. A previous study has shown an increased density of the perivascular AQP4 following systemic hyponatremia in rat. Although there was an increase in AQP4 protein, the levels of mRNA remained unchanged. The mechanisms involved in the increased AQP4 protein expression following hyponatremia are still not known. In this study, we exposed primary rat astrocytes to hyponatremia and analyzed the expression pattern of AQP4 and other members of DAPC. The cells were exposed to 1 or 6 hours of hyponatremia, followed by 6 or 12 hours of incubation in the normal media. Our data show a significant increase in the expression level of Dag1, the gene encoding for the transmembrane proteins alpha- and beta- dystroglycan. Expression levels of the other DAPC genes such as AQP4, dystrophin, alpha syntrophin remained unchanged. Since dystroglycan link the extracellular matrix to the intracellular cytoskeleton, we hypothesize that it is the gene regulated by the hypotonic stress and its upregulation leads to increased mobilization of AQP4 to the perivascular membrane domains.

Keywords:
Molecular neuroscience

Abstracts for oral session II:

Clinical neuroscience

Abstracts are organized in the order of presentations

A LONGITUDINAL STUDY OF CORTICAL THICKNESS IN BIPOLAR DISORDER TYPE II

Nathalia Zak[1,8], Lars T. Westlye[1,2,3], Erlend Bøen[4,8], Birgitte Boye[5,6], Per K. Hol[7], Ulrik F. Malt[2,8,9], Torbjørn Elvsåshagen[1,2,8,10]

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5. Department of Psychosocial Oncology and Rehabilitation, The Norwegian Radium Hospital
6. Deptartment of Behavioural Sciences in Medicine, University of Oslo
7. The Intervention Centre, Oslo University Hospital
8. Department of Psychosomatic Medicine, Oslo University Hospital
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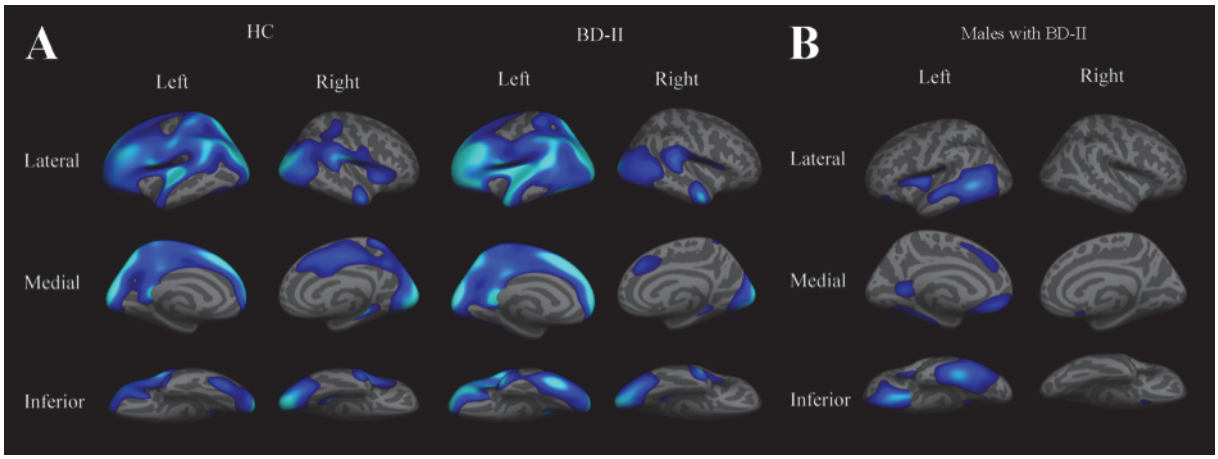
Background: Several research groups, including ours, have reported evidence for frontotemporal cortical thinning in bipolar disorder (BD). Whether cortical thinning in BD is a stable disease trait or an illness effect that might progress over time remain largely unknown. We aimed 1) to replicate cortical thinning in BD type II (BD-II) and 2) to longitudinally examine cortical thickness in healthy controls (HCs) and individuals with BD-II. **Methods:** Thirty-three HCs and 29 BD-II patients underwent 3T-MRI at time point (T)1 and 2.4 years later at T2. Cross-sectional and longitudinal analyses of thickness across the cerebral cortical mantle were performed using Freesurfer. **Results:** We found bilateral prefrontal cortical thinning in BD-II at T1, as published previously (Bipolar Disord 2013), and at T2. HCs and BD-II patients showed widespread cortical thinning from T1-T2 (Fig. A; blue color indicates thinning; $P<.05$, uncorrected). BD-II was associated with greater cortical thinning from T1-T2 than HCs in a left orbitofrontal and a left temporal cluster ($P<.05$, uncorrected), which was mainly driven by males with BD-II (Fig. B; greater thinning in male patients relative to HC men in blue; $P<.05$, uncorrected). **Conclusions:** These findings provide further support for prefrontal thinning in BD-II. The longitudinal results indicate that BD-II is associated with greater left orbitofrontal and temporal cortical thinning than HCs and that this effect may be most pronounced in male patients.

Keywords:
Clinical neuroscience
Neuroimaging

See image on next page.


A
HC
BD-II
Left
Right
Left
Right
Lateral
Medial
Inferior
B
Males with BD-II
Left
Right
Lateral
Medial
Inferior

Legumain and SLC7A5 protein in the early processes of Multiple sclerosis (MS) pathology.

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Multiple sclerosis (MS) is the most frequent cause of non-traumatic nervous system disability in young adults .No curative treatment is available for MS, but immunomodulatory therapies modify the disease course. In MS there are multi-focal inflammatory damages and loss of nerve fiber insulation (myelin) in the central nervous system (CNS), with secondary nerve fiber (axon) destruction. MS occurs in human only and there is no single animal model that incorporate all clinical and pathological features of MS. In this study, we used two animal models; experimental autoimmune encephalomyelitis (EAE) and the cuprizone model to capture two main pathogenic events of MS, inflammation and demyelination. Hightroughtput proteomic analysis was done in the brain tissue from EAE acute phase (16th day) and recovery phase (32th day) and the cuprizone late demyelination/remyelination phase (42th day). Human homologs of differentially expressed proteins were further investigated in autopsy MS tissue material. We studied their distribution by immunohistochemistry in lesions having different stages of lesion pathology, staining them for myelin proteolipid protein (PLP), human leucocyte antigen-DR (HLA-DR), glial fibrillary acidic protein (GFAP) and candidate molecules. Histochemical data showed that Legumain and SLC7A5 protein might involved in the early processes of Multiple sclerosis pathology. This preliminary finding indicates their association with early diseases activity. Further investigation in a larger autopsy material and in cerebrospinal fluid (CSF) from MS patients is ongoing, in order to characterize their role in early MS pathology.

Keywords:
Molecular neuroscience
Clinical neuroscience
Neuropathology

Perception of complexity in rhythm in PD

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Musical and specifically rhythmic therapy has beneficiary therapeutic effects on the physical symptoms in Parkinson's disease (PD). If the rhythms gets to complex, the therapeutic effect diminishes. Our hypothesis is that this is due to interactions between bottom-up perceptual and sensory systems and top-down cognitive control, where complexity in rhythm increases the total load on this two-way communication. This project (PD's=40/Controls=40) aims at contributing to the knowledge of the neurological basis for this phenomenon, through the study of the perception of rhythm of various complexi-ty in PD's (n=40, 20 female, ages 40-80) vs. controls (matched). So far we have recruited pa-tients and controls, charted their physical and mental symptoms (Unified Parkinson's disease rating scale / UPDRS), done neuropsychological tests (California Verbal Learning Tests / CVLT, STROOP, Minimal Mental State / MMS), and a music ability test (PROMS) to opti-mally match participants in different groups and trails. To establish a baseline for rhythmic complexity – and to pilot the design of the main project – we recruited approx. 100 students to part take in an online survey about their liking for and perception of levels of complexity in tailored musical stimuli at various tempi, and with differ-ent a priori levels of complexity. Our findings favour a simple computational model for com-plexity, based on cognitive load of calculable beat structures. We find clear group level scores for the rating of complexity of the stimuli, as well as individual profiles, and based on these findings, a subset of stimuli was transformed to fit pilot paradigms for both EEG and fMRI (to correlate findings between modalities). In the EEG paradigm, an Omission Evoked Potential-study, we investigated if the omission of a beat will generate different EP's depending on the position of the omission and the level of surrounding rhythmic complexity. This tells us something about early perceptual, sensory and involuntary, "non-cognitive" mechanisms. Of particular interest is MMN, P150 and P300 (early EP's). In fMRI we are looking at differences in activation in the pre-motor cortex, SMA, cerebellum and basal ganglia, as related to effects of tempo and complexity. We are also looking at other areas of cortex known to be involved in the processing of rhythmic com-plexity. It is results from these pilots we will be reporting at the conference.

Keywords:
Cognitive neuroscience and neuropsychology
Clinical neuroscience

Is temporal lobe epilepsy with hippocampal sclerosis a neurodegenerative condition?

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Introduction: Temporal lobe epilepsy (TLE) is one of the most frequent types of epilepsy. A proportion of TLE patients have a benign course while others exhibit progression, leading to repeated and pharmacoresistant seizures. Currently we do not know which factors contribute to this progression. The aim of this study is to follow the development of HS in the ipsilateral temporal lobe, as well as to identify and monitor any structural changes in the hippocampus and temporal lobe on the contralateral side, and in the brain parenchyma in general the years before surgery. **Method:** Patients operated for temporal lobe epilepsy at Rikshospitalet between 2008-2013 and with histologically proven hippocampal sclerosis (HS), are included in a retrospective study (RetroTLE). For each patient two preoperative magnetic resonance imaging (MRI) of the brain are considered: the first available MRI and the last preoperative MRI. The evaluation of these imaging studies is conducted by two experienced and independent neuroradiologists who are blinded to the scan time points. **Results:** The study material consists of 22 patients of whom 64% are women and 64% have HS with left-sided localization. Median age at surgery is 40,5 years. The time between the first available MRI and the last preoperative MRI studies used for the analysis varies between 1-8,5 years, with a median of 3,375 years. The MRI analysis has recently been initiated. The results will be available during June 2015 and presented at the 3rd National PhD Conference in Neuroscience. **Possible implications:** Current treatment of epilepsy is still only capable of preventing seizures, without affecting the underlying pathomechanisms. By characterization of clinical endophenotypes among patients with TLE and mapping of group-specific risk factors and / or biomarkers it will be possible to distinguish the clinical / radiological subgroups at an early stage. This may lead to new and individual treatment as well as preventive strategies for distinctive subgroups of TLE.

Keywords:
Clinical neuroscience

Discrimination of dementia patients using novel EEG spectral features

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This current work tests the power of specific electroencephalogram (EEG) markers for group discrimination in dementia patients. We used 343 clinical EEG datasets to extract six features that describe the undergoing EEG spectra from 114 healthy controls (NC), 114 vascular dementia (VaD) and 114 probable Alzheimer's patients (AD). We used such features in group classification applying linear discrimination analysis (LDA) with cross validation and regularization. Our results showed robustness on the classification models with moderate and good classification performances. Our results indicate that such features may be of importance for dementia group classification.

Keywords:
Cognitive neuroscience and neuropsychology
Clinical neuroscience
Neuroimaging

Abstracts for oral session III:

Cognitive neuroscience and neuropscyhology

Abstracts are organized in the order of presentations

Deficits in inhibitory mechanisms after exposure to life-threatening events

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Background: The illumination of key mechanisms in posttraumatic stress disorder (PTSD) is important for the understanding of how PTSD develops and maintains. PTSD is characterized by intrusive memories/thoughts related to the traumatic event. It is suggested that PTSD may be related to impaired reactive and/or proactive control: The inability to suppress these thoughts as they occur, or to prevent them before they occur, respectively. Accordingly, studies using tasks involving inhibition control (e.g., Stroop, Flanker, and Go/No-Go) find that PTSD patients are more prone to task interference by irrelevant distracting objects compared to healthy controls. However, it is still unclear whether poor performance on these tasks is related to impairments in proactive or reactive control. **Methods:** To investigate this further, we have examined task performance and neural activations (BOLD-fMRI) in 26 adolescents who survived the terror attack in Norway (Utøya) on the 22nd of July 2010 using the attention network task (ANT). A group of healthy, age-matched adolescents were used as comparison. Should we find a group difference in the effects of valid versus invalid cues, rather than target congruency, our findings will support the notion that impaired proactive inhibition is a key mechanism in developing and maintaining PTSD. **Behavioral Results:** The results revealed a main effect of both congruency, $F(2,50) = 2105.42$, $p < .0001$, and cue type, $F(2,50) = 173.37$, $p > .0001$. There was a significant interaction between congruency x cue type, $F(2,50) = 11.360$, $p = .002$, and cue type x group, $F(2,50) = 7.513$, $p = .009$. Follow-up analysis further revealed that the Utøya group had a smaller cue effect compared to the controls, $t(44) = 2.658$, $p = .011$. These findings support the hypothesized role of impaired preparatory mechanisms in PTSD patients. **Plans for fMRI data analysis:** In order to examine group differences in functional connectivity within the network governing proactive control, we will perform a psychophysiological interaction (PPI) analysis on the fMRI data. Thereafter, we will investigate whether strengthened functional connectivity within this network correlates negatively with PTSD symptom severity. Finding that the group differences observed from the behavioral data correspond to the functional connectivity within the networks governing proactive control will further strengthen the implied role of impaired proactive control in PTSD.

Keywords:
Cognitive neuroscience and neuropsychology
Clinical neuroscience
Neuroimaging

Coupling perception, action and cognition in estimating successful contact-timing of a moving object

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1. NTNU

Many behavioural studies on interceptive motion have been carried out, but little is still known about the neural correlates for successful contact-timing of a moving object [1]. Preparing and guiding actions into the future, involves a complex system where perception, action, and cognition are tightly coupled together. With objects moving at constant velocity, time-to-contact (ttc) is given exactly by its first order estimate (tau) [2]. With objects decelerating or accelerating the task becomes increasingly complex since humans cannot perceive velocity change as such. However Port et al. [3] suggested that the challenge of exact time-to-contact with decelerating or accelerating objects can still be solved by using tau to determine when to initiate an interceptive action. Actively incorporating behavioural events as time-locking triggers to the EEG recording [4], may help us in studying these neural correlates more specificly. The stimulus was a small car moving under three decelerating conditions horizontally on a large screen, where the final approach of the car was temporarily occluded. The adult participants controlled a vertical moving car with a joystick. The task was to move the joystick car, and intercept with the horizontally moving stimulus car in a target area. Joystick initiation data showed that participants used different strategies when they moved the joystick. One strategy was an early initiation, and gradually coupling the Tau of the joystick car with the Tau of the stimulus car. The other strategy was a late initiation, and keeping the time-to-contact from joystick initiation and car interception (crash) as constant as possible. Neural correlates for both strategies and possible tau-couplings are still unclear, but preliminary findings suggest a promising link between perception, action and neural activation in this task.

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Keywords:
Cognitive neuroscience and neuropsychology

Changes in resting state fMRI connectivity in normal aging is associated with introspective reports of experience of memories.

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3. Department of Radiology, Haukeland University Hospital, Bergen, Norway,
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Recent resting state functional magnetic resonance imaging (rsfMRI) studies have revealed age-related changes in connectivity between different brain areas. Decrease in the functional connectivity of the default mode network (DMN) has been reported in studies of healthy as well as pathological aging. Although considered to be a scan during resting state, participants may experience various inner unconstrained, stimulus independent thoughts during the scanning procedure. How this might effect the rsfMRI measurements is not thoroughly explored. In this study a post-scan semi-structured resting state questionnaire (ReSQ) was included to assess mental activity during the rsfMRI examination. The rsfMRI data were analyzed by independent component analysis (ICA) in a cohort of 84 healthy middle aged and older subjects (52-83 years). The results revealed a systematic higher functional connectivity between the anterior and posterior part of the DMN in participants reporting memories during the scan compared to those who did not. This indicates that the ReSQ may be a valuable tool to assess participants experiences during rsfMRI. Further, it illustrates that mental activity may influence functional connectivity in at least some of the DMN components. Further studies are warranted.

Keywords:
Neuroimaging

A population-based study of impulse control disorders in Parkinson's disease: the Norwegian ParkWest study

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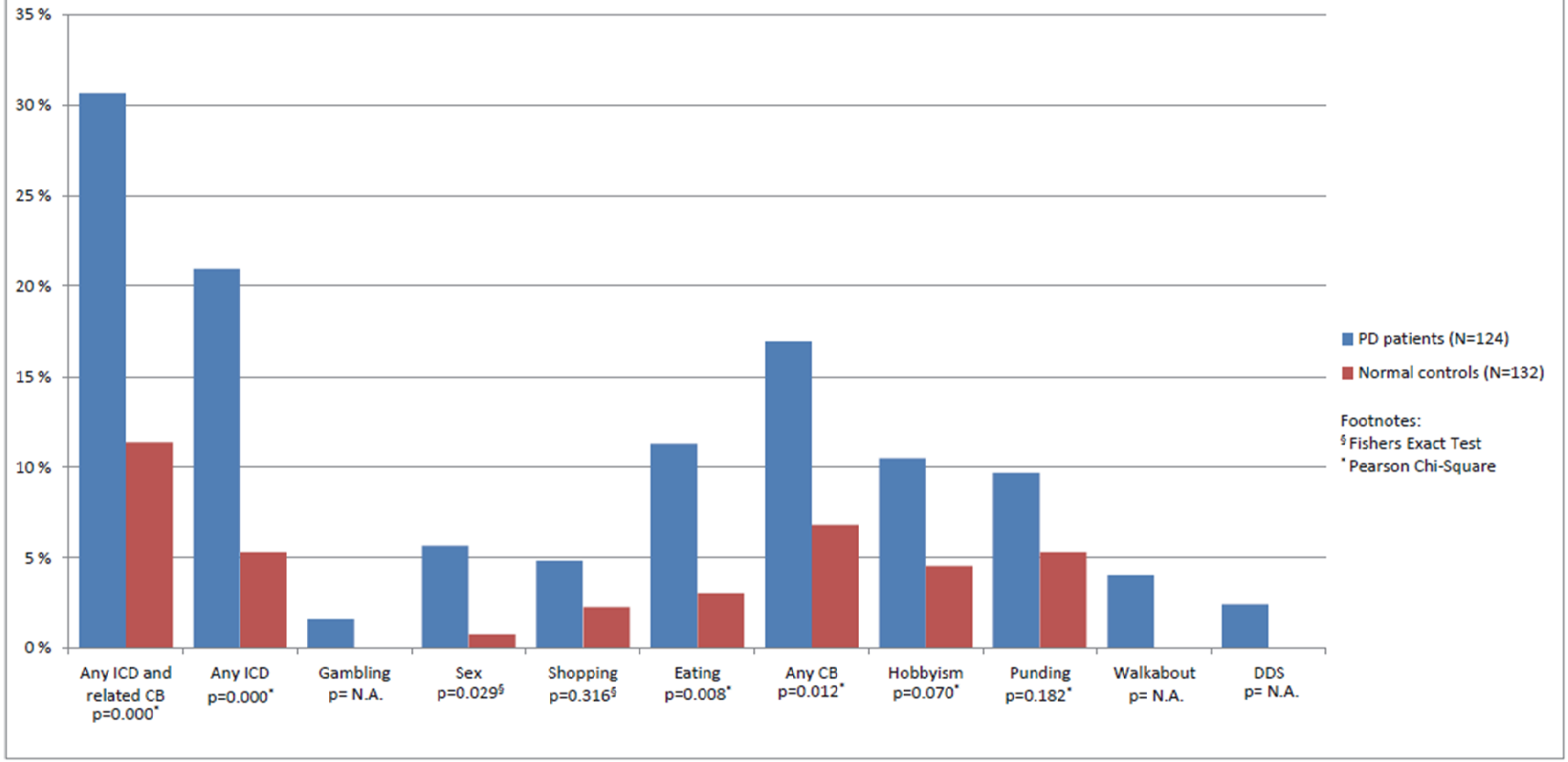
2. Department of Neurology, Haukeland University Hospital

Objectives: To determine the frequency and associated clinical, neuropsychiatric, and cognitive correlates of impulse control disorders (ICDs) in a population based cohort of patients with Parkinson disease (PD). **Methods:** We examined 125 non-demented patients with PD and 159 normal controls (NCs) recruited from the Norwegian ParkWest study. Data presented here include the first evaluation of ICDs performed during the 5-year follow-up assessment. All participants underwent a comprehensive neurological, neuropsychiatric and neuropsychological assessment. Presence of ICDs was assessed using the Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP) short form. Multivariate logistic regression analyses were performed to identify independent correlates of ICDs. **Results:** ICDs were significantly more frequent in patients (30.4%) compared with NCs (11.9%); relative risk 2.54 (95 % confidence interval 1.55 - 4.19; $p<0.001$). In multivariate logistic models, higher depressive scores (OR) and dopamine agonist (DA) treatment (OR) were associated with a higher risk of ICDs in patients with PD. We found no significant differences in neuropsychological measures of attention, executive function, memory or visuospatial skills among PD patients with and without ICDs. **Conclusions:** This population-based study demonstrates that patients with PD have a 2.5-fold increased risk of ICDs compared with demographically comparable NCs. Our results support previous findings that treatment with DA and depressive symptoms are associated with higher risk of ICDs in PD patients. However, we found no evidence of cognitive impairments in patients with ICDs.

Keywords:
Cognitive neuroscience and neuropsychology
Clinical neuroscience

See image on next page.

Figure 1. Percentage of patients and normal controls with Impulsive control disorders and compulsive behavior. Group differences indicated with significance levels.



Dissociated decision-making process in binge drinkers and relation to sensation seeking

Ragnhild Bø[1], Dag-Erik Eilertsen [1], Joël Billieux [2], Nils Inge Landrø [1]

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2. Catholic University of Louvain, Louvain-La-Neuve, Belgium

Background: Binge drinking is a risky behavior, often causing negative consequences. Also, binge drinking (heavy intermittent alcohol exposure) might cause adverse effects on the prefrontal neuronal systems implicated in decision making and impulsivity. Some studies have investigated ambiguous decision making in binge drinkers, however few have investigated decision making under risk where the probabilities are known. In this study we investigated the relative contribution of these dissociated decision making processes to binge drinking, and its association to impulsive personality traits. **Methods:** 121 heavy binge drinking (HBD) and light binge drinking (LBD) students aged 18-25 years of age was identified by means of median split of the binge drinking score derived from the Alcohol Use Questionnaire. In order to assess decision making under ambiguity and decision making under risk, they performed the Iowa Gambling task (IGT) and the Information Sampling task (IST), respectively. They also completed the short UPPS-P Impulsive Behavior Scale assessing five factors of impulsivity (negative and positive urgency, sensation seeking, lack of perservance and lack of premediation). **Results:** Compared to LBD, HBD showed impairment on the IST, but not on the IGT. On the short UPPS-P HBD also reported more impulsive behaviors in general, and behaviors related to sensation seeking in particular. The latter was negatively correlated with probability of being correct at the time of decision. **Conclusions:** Heavy binge drinkers are impulsive and impaired in decision-making under risk, but not under ambiguity. Riskier decisions were also associated to higher levels of sensation seeking. These findings might give clue to why binge drinkers continue the pattern of alcohol consumption, despite the known propensity for negative outcome.

Keywords:
Cognitive neuroscience and neuropsychology
Clinical neuroscience

Abstracts for oral session IV:

Systems and computational neuroscience

Abstracts are organized in the order of presentations

Transgenic activation of medial entorhinal cortex similarly alters spatial firing properties of CA3 and CA1 place cells

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The hippocampus is required for the encoding of episodic memory, the recollection of "what" happened, "when" it happened, and "where" it happened. Hippocampal place cells are preferentially active as an animal passes through specific locations (i.e. place fields) of a particular environment. When introduced to a novel environment, the firing rate and/or location of place fields drastically change, a process called remapping. Exactly how place cells remap remains one of the most elusive questions in our field. Our laboratory uses a transgenic mouse line expressing a mutated human muscarinic glutamate receptor (the hM3Dq DREADD) primarily in medial entorhinal cortex layer II (MECII), one of the main inputs to the hippocampus. Systemic injection of clozapine N-oxide (CNO), which only binds to hM3Dq receptors, depolarizes a subset of MECII neurons. We have previously shown that this leads to "artificial remapping" of CA1 place cells, where cells remap though the animal remains in a stable environment. Here, we show that artificial remapping is also induced in CA3 place cells. CA3 has unique recurrent connectivity and responds differently than CA1 to environmental change. Therefore, it has been proposed that CA3 may nonlinearly transform sensory input to support the complementary functions of pattern completion and pattern separation (Guzowski et al., 2004). The authors predict that relative to those of CA1, the firing properties of CA3 will change less with small changes to the environment, but will change more with large changes to the environment. We therefore hypothesized that dose-response curves measuring changes in spatial firing properties at different doses of CNO would differ between CA3 and CA1. To test this hypothesis, we injected a range of doses of CNO to simulate varying amounts of contextual change while recording from CA3 and CA1 place cells. We computed spatial correlations between rate maps of a given cell before and after CNO injection to assess the degree of remapping. Surprisingly, the dose-response curves for the two regions are quite similar. Rather than disproving the model, our results may highlight the mechanistic differences between artificial and traditional remapping. By altering the firing rate of entorhinal inputs in a stable environment, we dissociate an animal's sensory experience and the evoked neural activity to address what truly causes a place cell to remap.

Keywords:
Systems neuroscience

NESTML: A Domain Specific Language for Creating Neuron and Synapse Models for the NEST Simulator

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Neuroscientists use computer simulations as one way to research the brain and brain activity. They developed and published numerous neuron and synapse models with different levels of detail to be used in simulations of single neurons or large biological neuronal networks. Besides the neuron and synapse models, the neuroscience community has developed several simulators with different scopes and, mostly, incompatible model description languages. This makes it hard to develop and publish new neuron and synapse models and even harder to compare and verify findings across simulators, since the models must be implemented and adjusted for every simulator [1]. In this work we focus on the NEST simulator [2]. New neuron and synapse models for NEST are written as C++ classes that are embedded in the NEST infrastructure and have to comply to NEST's API. Hence, developing the model requires expert knowledge of the neuroscience context, as well as of C++ and the NEST internals. Changes to NEST's infrastructure or API might require adjusting all available neuron and synapse models, which impacts the maintainability of NEST. We tackle the issues mentioned above by designing and developing the domain specific language NESTML for the NEST simulator using the language workbench MontiCore [5, 6]. It allows modeling neuronal and synaptic components in a clean and concise syntax — based on the Python programming language, which is well-known in the neuroscience community. The model dynamics can be described textually as ordinary differential equations (ODE) in a mathematical plausible way, which allows automatic analysis and proper solver selection for the ODE. An embedded procedural language is used for detailed model behavior. The associated processing tool performs static analysis on NESTML models to check for programmatic correctness and, thus, supports neuroscientists in creating models. Furthermore, the processing tool generates efficient code for the NEST simulator and the NEST module infrastructure, which allows to easily compile and load the generated code into NEST. Models described in other languages, such as NineML [4] or NeuroML [5], can be compiled into the simple NESTML format, instead of generating platform specific code for the NEST simulator directly.

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Keywords:
Computational neuroscience and neuroinformatics

Brain-wide connectivity underlying habenular activity in zebrafish (danio rerio).

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The habenula is an evolutionarily conserved brain region associated with stress and fear response. In recent years this small brain region has started to attract a lot of attention from basic researchers to medical doctors as the habenula was shown to play important roles in addiction, depression, sleep disorders, cognition and psychosis. Due to its small size and limited accessibility in mammals, little is known about neural mechanisms related to the function of this elusive but essential brain structure. In my PhD project, I will investigate how habenular circuits are connected to the other brain regions that are known to be associated with learning and fear (e.g. hippocampus, amygdala) and how this brain-wide network modulates sensory information processing and regulates animal behavior. To achieve these goals, I will combine, functional brain imaging, optogenetic stimulation, electrophysiological recordings and anatomical tracing in the brain of a small vertebrate, the zebrafish. First, I will perform volumetric two-photon calcium imaging, in order to measure brain-wide on-going spontaneous activity in the zebrafish brain, with high spatial and temporal resolution. Later, I will use applied mathematical tools to identify those brain regions, whose activity is correlated with habenular networks. Subsequently, I will test the causality of these brain-wide connections by combining intracellular recordings of habenular neurons with optogenetic stimulation of the candidate brain regions. Here, I will adopt emerging tools for spatial and temporal control of optogenetic stimulation of the zebrafish brain. This stimulation protocol combined with intracellular recordings of habenular neurons will allow me to scan the entire zebrafish brain rapidly and map the functional inputs to the habenular neurons. In parallel, I will perform anatomical tracing experiments in order to test the anatomical wiring diagrams of brain regions that are identified as candidate habenular input regions by the optogenetic circuit mapping experiments. Finally, I will test whether electrical or optogenetic stimulation of candidate brain regions that are inputs to habenula (e.g. amygdala, hippocampus), can manipulate the olfactory responses in habenular networks. I expect that the results of my PhD project will provide a better understanding of the role of habenula circuits as part of a brain-wide network regulating animal behaviors associated with fear learning, anxiety and stress.

Keywords:
Systems neuroscience

Novel scheme for modeling ion dynamics in 3D neural tissue

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A piece of brain tissue in cortex consists of neurons (~40-45%) and glia cells/astrocytes (~40-45%) while the rest is extracellular space, that is space between the cells. One method to model the dynamics of ions in such tissue has been based on the Poisson-Nernst-Planck formalism. This is very computationally expensive and in practice it has been difficult to go beyond simulations lasting for longer than a microsecond, in volumes some micrometers across. The reason is that very small time steps are needed to describe relaxation of disturbed charges back to electroneutrality (in bulk). (The typical time scale for this relaxation is in nanoseconds.) Recently, a new electrodiffusive scheme has been developed that circumvents this problem by explicitly enforcing electroneutrality. Then simulation time steps can be increased by, say, a factor one million. The method solves the Nernst-Planck equation for electrodiffusion, but instead of finding the physically correct field (from the Poisson equation), the method finds a field such that electroneutrality is kept. This was published on at the end of last year [1] where the 1D version of this formalism was used to investigate astrocytic processes. Now we want to extend this electrodiffusive scheme to 3D. If we can develop a scheme where it is possible to simulate extracellular diffusion for a population over a timespan of several seconds, this may provide insight to long term processes, such as spreading depression. We will build the solver using the Finite Element Method solver FEniCS, developed in part at Simula Research Center. The first goal of the project is a numerical investigation into the accuracy of the method, where the novel scheme will be compared to the traditional Poisson-Nernst-Planck scheme, to check whether the method provides realistic dynamics. Then, the results of [1] and [2] will be extended to 2D and 3D. Finally, the goal would be to write the software in a reusable fashion such that others might apply their own neuron model with arbitrary morphologies and currents and calculate the extracellular diffusion effects. [1] G. Halnes et al., An Electrodiffusive Formalism for Ion Concentration Dynamics in Excitable Cells and the Extracellular Space Surrounding Them, Advances in Cognitive Neurodynamics 2015, pp 353-360 [2] G. Halnes et al., Electrodiffusive Model for Astrocytic and Neuronal Ion Concentration Dynamics, PLoS computational biology 9.12 (2013)

Keywords:
Computational neuroscience and neuroinformatics

Cognitive demand dependent changes in neural coding of self-motion in parieto-frontal circuits in rats

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Posterior parietal cortex (PPC) is a structure with complex multisensory processing capacities that has strong reciprocal connections with retrosplenial cortex, motor and premotor areas, such as medial agranular cortex (AGm). The vast majority of findings about the functions of PPC and AGm cell populations has been obtained through work on head restrained monkeys or humans. However, much can be gained by exploiting the technical strengths of the rodent preparation. Not only can rodents be trained to do tasks which would allow one to study goal-oriented motor behaviors studied in primates, but they also allow for the use of multi-tetrode drives which can sample the activity of dozens of cells simultaneously, as well as the efficient implementation of optogenetics. The research done on rodents so far seems to suggest that both PPC and AGm play a role in the planning and execution of locomotor behaviors during spatial navigation. Importantly, it was shown that PPC neurons on average showed tuning to movements a quarter of a second ahead of time and some cells coded multipart trajectories even a second in advance (Whitlock et al, 2012), while AGm neurons predicted the rat's impending orienting movement during a memory-guided task (Erlich et al, 2011). The aim of this project is to ascertain whether ensemble coding of movement intentions in parietal-premotor circuits changes depending on the presence or absence of a fixed goal during a navigational task, and to determine if the time window for future movement planning changes flexibly between the same conditions. In order to meet this objective, we plan to utilize a task design where the animal switches between exploratory (searching for a liquid reward at an unknown location) and goal-oriented (moving to a known reward location) modes of navigational behavior while it is moving through the same space. Ensembles of PPC and AGm cells will be recorded extracellularly using custom-made microdrives targeting anatomically precise coordinates with mounted silicone probes. For the purpose of analyses, the recording data will be synchronized with the animals' head and body coordinates that will be captured by a 3D infrared tracking system. If successful, our experiments would reveal whether the self-motion representations in parieto-frontal circuits change when freely exploring animals switch from exploration to goal-finding and how quickly complex movement plans emerge once a goal is established.

Keywords:
Systems neuroscience

Abstracts for blitz and poster sessions
22 September

Abstracts are organized in the order of presentations

Ventral hippocampal encoding of non-spatial information: preliminary results

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While precise spatial firing fields is a hallmark of pyramidal cells in the dorsal part of the hippocampus, it is still unresolved whether the large-scale place fields in the ventral cell population are modulated by visuospatial input, or if the cells respond to something else. To answer if the ventral cells encode non-spatial information, as spatial selectivity is lost, we recorded cells along the longitudinal axis of the hippocampus in rats that experienced changes in contextual valence rather than visuospatial changes. Several lines of evidence suggest emotional valence to be represented in the ventral hippocampus. Gene expression, anatomical connections, electrophysiological recordings and functional data in unison suggest a ventral hippocampal involvement in stress responses. While the dorsal hippocampus is required to solve vision-based navigation tasks, the ventral hippocampus seems to have a role in innate fear responses. Dorsal hippocampal place fields respond and re-map to non-spatial stimuli, such as odors. One hypothesis is that the ventral hippocampus is responsible for remapping even of dorsal firing fields. The ventral cells could also help generalize learned experiences to similar situations. Larger place fields in the intermediate hippocampus could be a mere reflection of increasing grid spacing in the MEC, but we do not know if this applies to the very ventral part of the hippocampus. In the current experiment, we investigate how dorsal and ventral hippocampal cells change their coding when emotional valence of the environment is changed. Single hippocampal units were recorded in Long-Evans rats while an emotional change was evocated by applying white noise (90 dB) or the scent of a natural predator to a costume made environment (a 70 cm x 70 cm ventilated box).

Keywords:
Cellular neuroscience
Systems neuroscience

Ischemic Stroke in the Young

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Background: TOAST and ASCOD classifications of causes of ischemic stroke have been internationally used since 1993 and 2013. The reason for the development of the ASCOD classification was the high rate of "unknown cause of stroke" despite a "high-tech" diagnostic work-up. Both classification systems use the 50% level of a stenosis as border for the fefinition of atherosclerosis or no-atherosclerosis. However, cardiologic research over the last years has emphasised the importance of unstable minor plaques rather than the degree of stenosis as causes, leading to an infarction. **Methods:** At the end of the 5-year of inclusion in NOR-SYS on August 31rst, 2015, about 400 patients at age 15 to 60 years, will be included. Causes of the acute ischemic stroke have been sub-typed by TOAST with the five following classifications of causes of stroke that have been used for many years: 1) Large-artery atherosclerosis, 2) Cardioembolism, 3) Small-vessel occlusion, 4) Other determined causes and 5) Undetermined causes. ASCOD is the abbreviation for the five main causes of ischemic stroke: Atherosclerosis, Small-vessel occlusion, Cardioembolism, Other determined causes and Dissection. In the TOAST classification, dissection is categorized as other determined cause. The problem of unknown causes of stroke in TOAST is tried to be kept to a minimum by the ASCOD classification. ASCOD uses the following numbers to increase other important information: 1= definitely a potential cause of the ischemic stroke, 2= uncertain cause, 3= the cause is present but is found unlikely, 0 = cause is not present, 9 = insufficient work-up. New classification after ASCOD will be done by the PhD-candidate and she will relate the TOAST and ASCOD results of causes of stroke to the ultrasound research protocol findings. **Hypotheses:** The unknown causes of stroke in the TOAST classification are still expected to occur in about 35% of our young patients, despite a better and extended diagnostic work-up. For ASCOD, we expect similar results as found in a first comparison of 103 patients with good interrater agreement and first results from other patient populations that show high prevalence of atherosclerosis. Minor atherosclerosis with stenosis < 50% is quite equally distributed among all causes of stroke apart from the large-artery atherosclerosis. Minor atherosclerosis is a common disease of the arteries in young ischemic stroke patients.

Keywords:
Clinical neuroscience

Functional development of neural circuits associated with aversive learning in zebrafish brain

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How does brain relates an unpleasent experience with sensory information (visual, olfactory) from the external world and convert it into learned fear response? One interesting brain area that is involved in this complex process is the Habenula (Hb). The Hb is associated with various important behaviors such as social interaction, reproduction, fear and aggression [Reference]. It is present in virtually all vertebrates, including those that seemingly lack cognitive functions, indicating its important role in survival through a relatively simple mechanism. However, it is just recently that the underlying neural networks and its functional mechanisms are starting to be understood. Previous work in our laboratory has indicated the importance of spontaneous activity in the zebrafish Hb. It has been suggested that this brain structure functions as a switchboard-like hub for the execution of different behaviours. Spontaneous activity of the Hb network could therefor represent its functional architecture. In this project, the anatomical and functional changes in habenular networks of zebrafish during development are investigated. Recently developed techniques, such as two-photon calcium imaging, light-sheet microscopy and electrophysiology, will be implemented in this research. It is expected that the outcomes of this study will give a better insight in how spontaneous activity gets established in Hb. This will enable further unravelling of the mechanisms of how information is received and processed in the brain and how it can lead to specific learned or innate behaviours.

Keywords:
Cellular neuroscience
Systems neuroscience
Developmental neuroscience

Subcortical volumes in children at early school age relate to preterm birth and very low birth weight

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BACKGROUND: Preterm birth is a worldwide problem, affecting 15 million newborns each year and burdening many survivors with lifelong physical, cognitive, and psychological challenges. Individuals born preterm with very low birth weight (VLBW: birth weight ≤1500 grams) are at an increased risk of perinatal brain injury and neurodevelopmental and cognitive problems. Cerebral white matter injury and neuronal and axonal abnormalities are considered the dominant neuropathologies in preterm-born infants and are believed to underlie many of these cognitive deficits. OBJECTIVE: We investigated group differences in subcortical brain structure volumes between VLBW children and controls, as well as possible relationships between brain structure and IQ scores, birth weight, and gestational age. DESIGN/METHODS: 103 term-born children participating in the Norwegian Mother and Child Cohort Study and 37 VLBW children born between 2001 and 2007 underwent 1.5 T MRI and age-appropriate cognitive testing with Wechsler tests (mean age=8 years). We used FreeSurfer software version 5.3.0 to extract volumes of subcortical structures and the general linear model for between-group analyses of subcortical volumes and partial correlations for morphometric data and IQ scores. Morphometry analyses were controlled for age at scan, sex, and estimated total intracranial volume. RESULTS: Compared to controls, the VLBW group had reduced volumes of thalamus, right globus pallidus, right hippocampus, cortical white matter, and brain stem, while the ventricular system was enlarged. Uncorrected IQ scores were significantly lower ($p<0.001$) in the VLBW group (mean=98.6; SD 9.7) than in controls (mean=108.1; SD 13.6). Among all participants, IQ score correlated significantly with volumes in cortical white matter, both thalami, right hippocampus, and right ventral DC; only in right hippocampus among controls; and no correlations found in the VLBW group. Birth weight among all subjects and gestational age among VLBW subjects also correlated ($p<0.05$) with several subcortical volumes. CONCLUSIONS: Volumes of specific subcortical structures in both hemispheres are associated with very low birth weight and preterm birth. These persistent structural differences may be due to perinatal brain injury, and their relationship to emergent cognitive, behavioral, and mental health outcomes merits further evaluation.

Keywords:
Cognitive neuroscience and neuropsychology
Developmental neuroscience
Neuroimaging

Electrophysiological markers of human consciousness

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Consciousness is necessary for human experience of reality. However, it disappears every night when we drift into dreamless sleep, and effortlessly reappears when we wake up. Understanding how a lump of matter can generate subjective experience has long been a quest in the realm of philosophy, but in the last decades, scientific theories of consciousness have been developed. To test their predictions, researchers have developed methods for probing brain activity in states of varying degree and form of consciousness – in awake, sleeping or anesthetized volunteers, as well as patients with disorders of consciousness (DOC). We aim to test some of the most promising methods, and compare them to aid in the fundamental understanding of consciousness. In collaboration with experts in the field, we also aim to develop these methods further, making them useful for the diagnosis of state and prognosis in patients suffering from DOC. If these methods do indeed quantify the level of consciousness in humans, we hypothesize that they will covary in a predictable manner under controlled experiments with human subjects in different states of consciousness. To test this, we will focus on two methods for probing the level of consciousness in human subjects, developed to test specific theoretical predictions. A technique developed to probe the integration and differentiation of the brain activity – two properties predicted to be necessary for conscious systems by G. Tononi's Integrated Information Theory – uses transcranial magnetic stimulation (TMS) to perturb the brain state in a controlled way, and EEG to measure how this perturbation propagates through the brain. Using the signals recorded, it is possible to calculate the Perturbational Complexity Index, which has been shown to reliably separate the conscious from the unconscious at the level of individuals. Another technique uses event related potentials (ERP), and measures the properties of the P3b component. This component is hypothesized to be necessary for global ignition of a large scale, recurrent network of neurons, predicted to be necessary for consciousness by the Global Neuronal Workspace theory. By comparing (and further developing) these two methods and testing theoretical predictions, on subjects in a wide variety of conscious states, we hope to deliver clinical tools for diagnosis of a very vulnerable group of patients, while at the same time learning more about the physical underpinnings of consciousness.

Keywords:
Clinical neuroscience
Neuroimaging
Neurophilosophy

Light--activated nanoparticles for targeted release of small inhibitory RNAs to specific neuron populations in vivo

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The ultimate aim of the project is to control the gene expression of endogenous neurons and of stem cell-derived neurons introduced into damaged brains and spinal cords via controlled delivery of si-RNA molecules to the mentioned neurons. Striking advances have been made in recent years in the areas of developmental neuroscience and the potential for stem cell-based treatment of neurological diseases.This is in large part based on the increasing power of high throughput gene sequencing technology to provide comprehensive gene expression and epigenetic profiles of selected cell populations. The use of small RNA molecules represents a powerful technology for selective gene knockdown and activation. However, there are 2 limitations to the use of small RNA molecules for studies of normal and pathophysiological processes and for the potential treatment of neurological diseases. first, the lack of temporal control of the manipulation; and the second, the specificity with which they can be delivered to selected neuron populations. Typically, small RNAs are introduced through electroporation or viral transduction. This is trivial for neurons in culture, but more challenging for neurons in vivo. To overcome the two-pronged problem of temporal control and target neuron selectivity, we propose to combine the recently developed approach of photosensitive small RNA caging with a non-viral nanodelivery system developed nearly 30 years ago by Joel Glover. For providing temporal control of the manipulation, we will develop caged small RNA molecules by a photosensitive moiety that contains bonds that can be broken by a pulse of light of a specific wavelength. As a non-viral nanodelivery system we will utilize modified fluorescent dextran nanoparticles conjugated to mentioned photocleavable protecting group installed on si-RNA. These photoliable caged si-RNA can be restricted to specific neuron subpopulation and be activated by delivering of light pulses via fiberoptic probes. This approach will only involve the standard invasive procedure, which already is used in neurosurgery for the stereotaxic placement of electrodes into the brain and spinal cord. This process does not involve the use of viruses or any permanent gene modification. If this approach is successful, it will provide a way to manipulate gene expression in specific neuron populations in human patients.

Keywords:
Molecular neuroscience

Grid synchronization in merged space

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Introduction: Natural environments are compartmentalized and likely represented by multiple local maps stitched together at salient landmarks (Derdikman et al., 2009). In this project, we focus on the mechanisms for generating one coherent global map from discrete local fragments. **Methods:** We trained rats in two rectangular compartments A and B (each 1x2m) separated by a wall. Once two distinct maps were established we removed the wall, allowing the rat to explore the merged open square box (2x2m). In order to reveal the contribution of the initial representations to the global grid pattern in the entire environment we first performed a sliding-box correlation analysis approach to assess local similarity between maps. We are currently testing the change in local periodicity across the entire environment, in addition to comparing real field locations to expected field locations of extended A and B maps. **Results:** We observed that the open field grid pattern was not generated de novo, but similar to either one or both of the rectangular maps A and B. The open field grid pattern could be an extension of one map or a complex fusion of the A and B maps. Fusions could be achieved globally by phase shifting the A and B maps relative to each other or locally by merging the maps at the transition in the center of the box. The type of response was specific to grid modules and global and local fusions could occur simultaneously. Fusion responses required successive visits to the merged environment. The data suggest so far that distinct grid maps for large environments get synchronized both globally and locally, that the effects depend on experience, and that the type of response depends on grid scale. **References:** Derdikman, D., Whitlock, J.R., Tsao, A., Fyhn, M., Hafting, T., Moser, M.B., and Moser, E.I. (2009). Fragmentation of grid cell maps in a multicompartment environment. Nat. Neurosci. 12, 1325–1332.

Keywords:
Systems neuroscience

Inhibition and the serotonin transporter (5-HTTLPR) genotypes in adolescent Chronic Fatigue Syndrome and comparison group

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Introduction. Chronic fatigue syndrome (CFS) in adolescents is associated with deficits in cognitive function. Previous studies have linked a polymorphism in the promoter region (5-HTTLPR) of the human serotonin transporter gene (SLC6A4) with variations in cognitive inhibitory control. Two common alleles, a short S and a long L allele consisting of 14 and 16 copies of a 20 to 23 nucleotide repeat cassette, have been described. In addition, the promoter region of the serotonin gene also contains a single nucleotide polymorphism (SNP) A>G (rs25531). The primary aim of this investigation was to compare the genotype-cognition interaction effect between adolescents with CFS and healthy controls (ages 12–18 years). **Method.** Participants included 119 adolescent CFS patients and 37 controls, which underwent genotyping and cognitive evaluation using color word interference tasks (CWIT) from D-KEFS test battery. Independent two-sample t-test was used to assess between-groups differences on inhibition performance. One-way ANOVAs were conducted to explore possible differences within-groups for age, disease duration, symptom scales and inhibition measure across 5-HTTLPR genotype combined with the A>G SNP. Simple planned contrasts were performed to test the dose effects of low expressive alleles across genotypes. Finally, a linear regression analysis was used to explore the relationships of inhibition performance, group and dose effects of low expressive alleles. **Results.** A deficit in cognitive inhibition was observed in the patients. However, the genotype-cognition effect was found only in the control group. **Discussion.** These data show that the influence of variations in the serotonergic system on cognitive inhibitory control was not observed in adolescent CFS patients. Without the well-known genotype-cognition effect in the CFS group, it suggests that other factors must explain the cognitive deficits in this group and 'overrule' the impact of genes.

Keywords:
Genetic neuroscience
Cognitive neuroscience and neuropsychology
Clinical neuroscience

See image on next page.

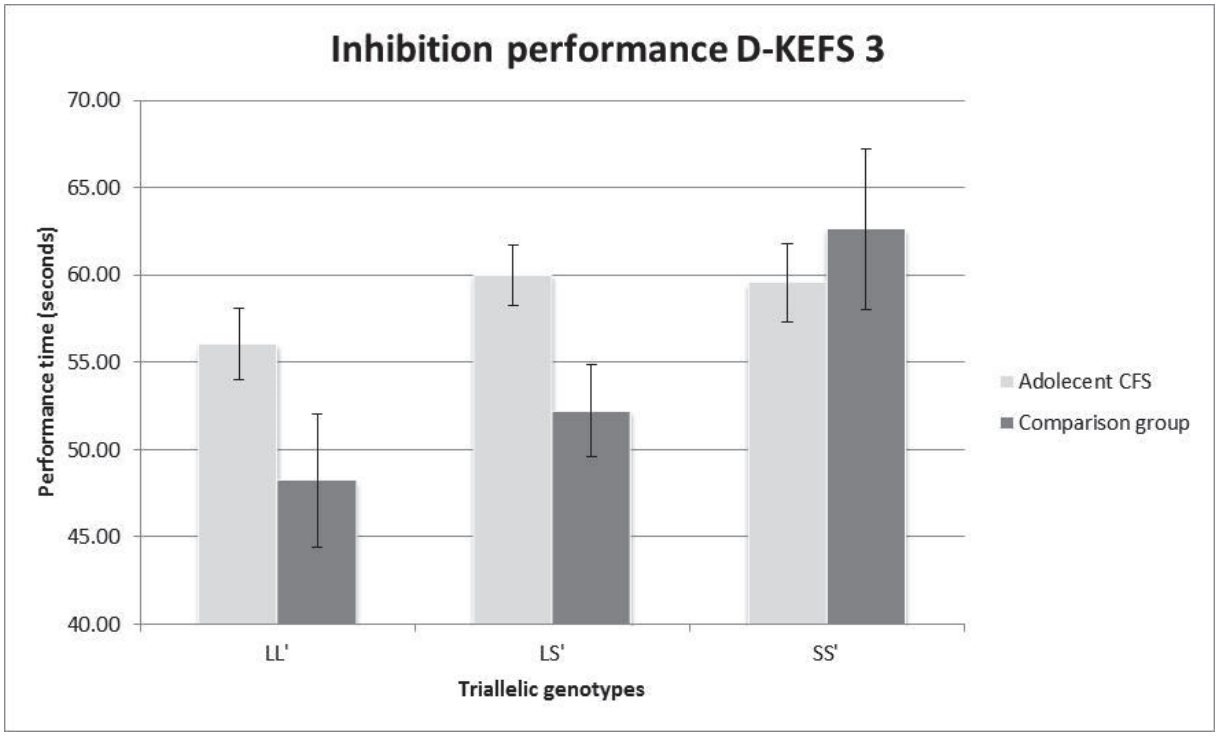

Figure 1: Mean inhibition time (seconds) for 119 adolescent CFS patients and 37 comparison subjects. Number of low expressive alleles: LL' (high leveled RNA transcription), LS' (intermediate leveled) and SS' (low leveled). Error bars: SEM.

Roles of cortical feedback in Lateral Geniculate Nucleus

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In order to understand how the brain works it is necessary to assimilate the wealth of data that has been accumulated over the past century and build biologically accurate models of the brain. A well-suited candidate for mathematical modeling is the early visual pathway, including the retina, lateral geniculate nucleus (LGN) and primary visual cortex (V1). All these early parts of the visual system are quite well mapped out both in terms of physiological properties of the neurons and synaptic connectivity patterns, making them excellent candidates for development of well-constrained mathematical models. A striking feature of the organization of the early visual pathway is the significant feedback from layer 6 in V1 to cells in the dorsal LGN. Our main objective is to understand what this massive feedback from cortex to LGN really does with the information transmitted from LGN to cortex. To understand the functional role of the cortico-thalamic pathway during sensory processing, we will in parallel with experiments model how the input control the information-flow in LGN. A first project will be on expanding a firing rate model (extended difference-of-Gaussians model) for the relay cells in LGN of rat, explicitly accounting for the inhibitory action of interneurons on relay cells and cortico-thalamic loop effects. An important part of this project will be to introduce short-term plasticity in the model, since it is well established that mechanisms for synaptic short-term plasticity, like synaptic facilitation, have an important role in the cortical regulation. In addition, the model will be used to explore the visual features represented in the LGN, which generally is thought to encode simple center-surround receptive fields. However, recent evidence suggests that mouse LGN has a more diverse visual features, including direction and orientation selectivity. These possible features will be studied using our network model. In the next project we will use the obtained overall behavior in the firing rate model from the first project as a guideline to develop a more detailed network model for LGN, consisting of a compartmental model for the relay cells and interneurons. Using the network we will explore how the input to LGN, including the cortical feedback, changes the state of the interneurons (bursting vs. tonic mode), that further shapes the response properties of the relay cell projections to visual cortex.

Keywords:
Computational neuroscience and neuroinformatics

Subcellular distribution of aquaporin-4 in the human cortex: a study using immunogold electron microscopy

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Aquaporin-4 (AQP4), the most abundant water channel in brain, plays a crucial role in brain water homeostasis. In mice, AQP4 expression is restricted to ependymal cells and astrocytes, being highly concentrated in astrocytic endfoot membranes at the brain-blood and brain-cerebrospinal fluid interfaces. The subcellular distribution of AQP4 in the human cortex is poorly characterized. Here we performed a high resolution immunogold analysis of AQP4 expression in non-lesional cortical tissue resected from 12 patients with temporal lobe epilepsy (n=9), aneurism (n=2) or tumor (n=1), and compared data with those obtained in adult mice. Immediately after resection the tissue was immersed into a fixative containing 4% paraformaldehyde and 0.25% glutaraldehyde. Tissue blocks were subjected to freeze substitution, embedded in Lowicryl HM20 resin and processed for postembedding immunogold cytochemistry. In human subjects the AQP4 distribution pattern mimicked that of mice, but showed much higher immunogold labeling densities over perivascular astrocytic endfoot membranes. We present AQP4 immunogold data for endfeet at different segments of the vasculature and will compare AQP4 polarization between the two species.

Keywords:
Neuropathology

Development and validation of specific ELISAs for Medaka (Oryzias latipes) gonadotropins Lh (luteinizing hormone) and Fsh (follicle-stimulating hormone) using recombinant proteins

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Vertebrate puberty and sexual maturation is regulated primarily through the endocrine system known as the hypothalamo-pituitary-gonad (HPG) axis, of which Fsh and Lh play integral parts. Fsh and Lh belong to a large family of cysteine knot-forming polypeptide glycoproteins with non-covalently linked heterodimers between a common glycoprotein α-subunit (Gpa), and a β-subunit that is hormone-specific (Fshb and Lhb). There are indications that these hormones play important roles also during early development, although detailed functions and underlying mechanisms have not been described. As a tool to investigate the function of early pituitary gonadotropin expression, we are developing specific and homologous competitive enzyme-linked immunosorbent assays (ELISA) to quantify Fsh and Lh protein levels in medaka pituitary and plasma, including development of antisera against the two hormones. Plasmids containing Gpa , Lhb, Fshb, or single-chain Lhab or Fshab were expressed using the methylotrophic yeast Pichia pastoris. Hormone production in P. pastoris in 1 l cultures over 3 days (large production of recombinant protein) resulted in 2,357 mg of highly purified medaka Lhb and 4,168 mg highly purified medaka Fshb, both based on one-step nickel batch purification. Western blot analysis using his-hrp antibody showed bands with expected sizes of 15 kDa for Lhb and 12.5 kDa for Fshb. Specific antisera were raised in rabbits, using three injections of purified protein in 0,9 % NaCl and emulsified with complete Freund adjuvant at 3-wk intervals. Gpa will be joined with medaka Lhb or Fshb mature protein-coding sequences to form a fusion gene that encodes a “tethered" polypeptide, in which the gonadotropin β-subunit forms the N-terminal part and the α-subunit forms the C-terminal part. We are currently producing Lhab and Fshab single-chain peptides in P. pastoris to be used as standards in the specific ELISAs and for characterization in ligand-Lhr/Fshr receptor-binding studies. The validated assays for medaka Fsh and Lh will be important tools to reveal the functional roles of these hormones during different stages of medaka reproductive development.

Keywords:
Developmental neuroscience
Neuroimaging

Political attitude and fear of death

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Background: It is well established in social psychology that conservatives have problems to cope death and uncertainity [Jost 2003]. Reminding fear of death can change attitude and behaviour [Pyszczynski 2006]. These cognitive patterns are mirrored in brain structures of conservatives and liberals [Kanai 2011]. Recognizing different cognitive patterns and the brain structures they are based on might be important, both in political and clinical psychology. **Aim:** This project has three goals: (1) To establish a liberal/conservatism score feasible for Norwegian participants (2) To identify specific cognitive patterns regarding death in Norwegian conservatives and liberals. (3) To investigate brain activation patterns in right amygdala and anterior cingulate cortex in liberals and conservatives confronted with death **Methods:** (1) Existing American conservatism scores will be used as a base to develop a Norwegian Conservatism score. Preliminary results will be presented on the poster (2) In a qualitative approach Norwegian conservatives and liberals will be included in an interview study to identify relevant associations and coping methods. (3) In a fMRI study, liberal and conservative participants will be primed to reflect on death (or with a control condition remembering a dentist treatment, according to [Pyszczynski 2006]). They will then be confronted in a block design with different images related to death and dying. Activation patterns in amygdala and anterior cingulate cortex will be investigated. **Results:** This is a research project in an early stage. First results of the conservatism score and the interview study will be presented.

Keywords:
Cognitive neuroscience and neuropsychology
Neuroimaging

Allelic Imbalance of Gene Expression of Multiple Sclerosis Susceptibility Genes IKZF3 and IQGAP1 in Human Peripheral Blood

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Introduction: Multiple sclerosis (MS) is a chronic inflammatory, demyelinating disease of central nervous system. The cause of MS is largely unknown, but genetic and environmental factors, as well as interaction of these contribute to disease development. Recent genome-wide studies have revealed 110 single nucleotide polymorphisms (SNPs) associated with susceptibility to MS, but their functional contribution to disease development is not known. **Methods:** Measure of relative expression levels from two SNP alleles of a gene in the same sample is a powerful approach for identification of cis-acting regulatory variants. We selected three genes, CD69, IKZF3 and IQGAP1, with an MS associated SNP in their coding region or in complete linkage disequilibrium (LD) with a coding SNP and performed allele-specific expression analyses in whole blood samples from individuals heterozygous for the studied SNPs using TaqMan technology. **Results:** Allelic imbalance was consistently observed for rs907091 in IKZF3 and rs11609 in IQGAP1, which are in strong LD with the MS associated rs12946510 and rs3539, respectively. The MS risk alleles of the respective SNPs correlated with increased IKZF3 and reduced IQGAP1 expression. Individuals homozygous for the risk allele of rs11609 had a significantly reduced IQGAP1 expression compared to individuals homozygous for the protective allele. **Discussion:** Our data indicate a possible gene regulatory role for MS-associated IKZF3 and IQGAP1 gene variants. This study highlights the usefulness of allele-specific expression measurements to identify disease-associated SNPs or SNPs in LD with gene variants with cis-acting regulatory properties. This study may provide a functional mechanism behind the MS-association SNPs nearIQGAP1 and IKZF3.

Keywords:
Genetic neuroscience
Molecular neuroscience
Clinical neuroscience

MuSK antibody status in AChR negative myasthenia gravis patients

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Background: Myasthenia gravis is a kind of autoimmune disease characterized by the antibody-mediated destruction in neuromuscular junction. Acetylcholine receptor (AChR) antibody has been found in more than 80% of all MG patients. Besides, muscle-specific kinase (MuSK) antibodies were found in some of AChR antibody-negative MG patients and often showed a more severe clinical manifestation. Previous study showed a low percentage of MuSK antibody in Norwegian MG patients (0% in previous study). However, the MuSK antibody status in East Asian MG patients is still not well illustrated. **Subjects and method:** 59 generalized AChR antibody-negative MG patients were tested anti-MuSK antibody by radioimmunoassay (RIA). All the patients were Han Chinese population origin. Clinical information includes gender, age of onset, thymus status and bulbar muscle involved or not. **Results:** 11 patients of all the 58 patients were found MuSK antibody. 48 patients were MuSK antibody-negative. No significant differences were found in gender, onset age between patients with and without MuSK antibodies (P>0.05). However, MuSK antibody-positive patients have a higher proportion of bulbar muscle involvement (10/11, 90.9%) than MuSK antibody negative MG patients (17/48, 35.4%)(P=0.001,OR=18.2). **Conclusion:** The percentage of MuSK antibody in Chinese MG patients was higher than Norwegian MG patients. The detection of MuSK antibody predicts a more severe clinical manifestation.

Keywords:
Clinical neuroscience

Executive functioning in survivors of pediatric brain tumors

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Introduction: Survivors of pediatric brain tumors (PBTs) often experience serious long-term difficulties in educational, vocational, social and emotional functioning. These problems can be linked to impairments of executive functions (EF); a subgroup of cognitive skills that control cognition, emotion and behaviour. **Aim:** This population-based study aims to investigate long-term effects in executive functioning (EF) in survivors of pediatric brain tumors (PBTs), and how this relates to difficulties in educational, vocational, social and emotional functioning. **Also to be focused on:** a. How do limitations in EF vary as a consequence of tumor location, treatment factors and age at treatment? b. To which degree is EF stable over time, i.e. according to measurements at 1, 2 and 5 years after treatment is ended and present time? c. How is impaired EF related to general intellectual ability and other specific areas of cognitive functioning? d. How are self-reports and informant reports related to results on test measures of EF? **Methods:** We aim to recruit a research group consisting of PBT-survivors from all of Norway, aged 13 to 30, who have been treated for PBT during the first 16 years of life and during 1990-2012, and whose treatment has been completed no later than 2 years prior to the survey. We plan to recruit a healthy control group, all matched for age and gender. Data will be collected from questionnaires from both groups, as well as from results from neuropsychological testing at 1, 2 and 5 years after treatment is ended and at present time. **Possible implications of the study:** The results from this project yield important information on EF and the functioning of the brain in a developmental perspective, and contribute to the understanding of how this form of brain damage effects cognitive functioning. Moreover, this knowledge may in turn form a basis for advising health and educational professionals on suitable strategies in the follow-up process.

Keywords:
Cognitive neuroscience and neuropsychology

Role of RNA-induced silencing complex in normal brain and during LTP

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Introduction: Long-lasting changes in synaptic connectivity require one or more bursts of protein synthesis involving gene transcription and protein translation. MicroRNAs and the associated RNA-induced silencing complex (RISC) are excellent candidates for the local control mechanisms that are probably essential for changes in synaptic strength and other forms of neuronal plasticity Several lines of evidence implicate the RISC as a target for reversible regulation of microRNA activity. However, the protein composition and regulation of the RISC during synaptic plasticity in the adult brain is little understood. **Methods:** We used immunoprecipitation of Argonaute 2 (Ago2), to isolate protein partners of the RISC in native brain tissue. In a complementary approach we pulled down native Ago2 using a GST-tagged GW182 peptide. The immunoprecipitated and affinity-purified samples were analyzed with mass-spectrometry and Western blot. We then performed the same analysis in total lysates of dentate gyrus after HFS. **Results:** Our results indicate a difference between endogenous RISC in the rat brain and cell-specific RISC from HEK-cells and other cell-lines. Association of Dicer, GW182, and MOV10 with Ago2 in brain tissue (neocortex, hippocampus, and dentate gyrus) is highly variable yet these proteins are reliably detected in HEK cells stably expressing Ago2-GFP. Furthermore, we find quantitative changes in RISC proteins associated with Ago2 in response to LTP in the dentate gyrus of adult rat. We observe a significant decrease in MOV10 after LTP induction and we find bidirectional changes in DDX6 association with Ago2 in response to LTP. **Discussion:** Despite intensive research the mechanisms of target recognition and RNA cleavage by RISC remain unknown. Perhaps the association between Ago2 and RISC is transient in nature, so that under physiological conditions most of Ago2 is not bound to GW182 at a given time. **Conclusion:** Our results suggest that brain RISC is in fact different from canonical RISC characterized from other tissues. LTP-induction is associated with changes in the protein composition of RISC. These changes are activity-dependent and involve both NMDA receptor-dependent and independent mechanisms.

Keywords:
Molecular neuroscience

Status epilepticus in glioma

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Introduction: Up to 85% of patients with low grade glioma and up to 60 % of patients with high grade glioma develop epilepsy at some time during the course of disease.Status epilepticus(SE) is defined a seizure that persists for a sufficient length of time or is repeated frequently enough that recovery between attacks does not occur. **Material and methods:** Patients with SE and glioma were identified from a prospective clinical observational study of patients with glioma WHO grade II-IV and one or more epileptic seizures during the course of disease.Eligible patients admitted to the Departments of Neurology at Haukeland University hospital in Bergen, Hordaland county and the Central Hospital in Førde, Sogn and Fjordane county, have been included consecutively from 2009.For tumor classification, the patients are grouped as either low grade glioma (LGG) (astrocytoma and oligodendroglioma of WHO grade II) or high grade glioma (HGG). **Results:** We identified 31 SE in 20 patients. The seizures were secondary generalized in 45.2%, focal in 29% and complex focal in 25.8%. The majority (41.9 %) had a duration of $> 1 < 5$ hours, of which 61.5 % were glioblastoma, the most aggressive type of glioma. First line treatment was sufficient in almost half of SE. Repeated SE was seen in seven of the 20 patients (35%). Sequelae were present in 15/31 SE (48%); in 38% when unrelated to progression and in 70% when related to progression.Six of the patients died within six months after SE, all of which had tumor progression as trigger factor of SE. **Discussion:** The majority of SE in our study occurring in HGG was unexpected. In marked contrast to tumor associated epilepsy, which is more common in LGG, the risk of tumor associated SE appears to be directly proportional to tumor grade.We found a trend that patients with SE requiring no treatment, or only first or second line treatment had less sequelae than treatment refractory SE.The association between level of treatment and outcome might be explained by the fact that SE with a long duration, which carries a poorer prognosis, also required more treatment. **Conclusion:** We found that SE was more frequent in patients with HGG and that the seizures mostly were secondary generalized.SE due to glioma was as responsive to first and second line treatment as SE in general, and did not recur in most patients.SE in glioma should be treated aggressively as patients usually respond to treatment and lengthy SE is associated with poor outcome.

Keywords:
Clinical neuroscience

Exchange factors directly activated by cAMP (Epac) are crucial for acute stress responses in mice

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Introduction: Among the multitude of functions of the intracellular second messenger cAMP, is the regulation of the hypothalamic-pituitary-adrenal (HPA) axis during the acute stress response. Although the bulk of cAMP signaling activity is conveyed through protein kinase A, the current study presents data implicating the exchange factors directly activated by cAMP (Epac1 and Epac2) in the regulation of acute stress response in mice. **Methods:** In the current study, male and female Epac1/2 Knockout mice were subjected to a 30-minute acute stress regimen followed by different periods of recovery. Following stress induction, serum corticosterone and the expression of factors implicated in HPA axis regulation were determined. To evaluate the integrity of the HPA axis negative feedback response to stress induced corticosterone, dexamethasone was injected intraperitoneally in Epac1/2 knockout mice, followed by corticosterone measurements 6 hours later. **Results and Discussion:** Prior to the acute stress induction, compared to wild-type mice, the basal levels of corticosterone did not significantly differ as a consequence of deleting Epac1/2 in either male or female mice. Interestingly however, female, but not male Epac1/2 knockout mice exhibited altered corticosterone levels at 0h and 0.5h following acute restraint stress, suggesting a sex specific phenotype. These altered CORT levels were associated with a delayed increase in pituitary glucocorticoid receptor mRNA expression, along with abnormal hippocampal glucocorticoid receptor protein levels. Additionally, mRNA levels of the adrenal nuclear receptor nerve growth factor inducible clone B (Ngfi-B), which is a cAMP-inducible immediate early gene known to regulate central enzymatic reactions in steroidogenesis, were altered in female mice lacking Epac at 0h and 0.5h after acute restraint stress. However, the pituitary negative feedback response to exogenous dexamethasone was normal in mice deleted for Epac. **Conclusion:** This study demonstrates the contributions of Epac in the regulation of PKA-independent cAMP induced stress responses at the different levels of HPA-axis.

Keywords:
Molecular neuroscience
Cellular neuroscience
Systems neuroscience

Effects of electroconvulsive therapy on metabolites in the brain: a prospective case-control study

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Introduction: Major depression reduces quality of life, and can in some cases lead to suicide. Electroconvulsive therapy (ECT) may be used in cases where traditional treatment shows no effect. ECT is controversial, but is by many clinicians considered the best treatment for acute, major depression. The fact that mechanisms behind both ECT and depression are unknown makes this a valuable area for further research. **Problem statement:** The aim of this study is to investigate acute and long-term effects of ECT on metabolites in the human brain using Magnetic Resonance Spectroscopy (MRS). **Approach / design:** The study consists of one patient group (n=40) and two control groups: 1) patients undergoing electrical cardioversion for atrial fibrillation (n=15) and 2) healthy controls not treated with ECT (n=15). Group 1 is given a similar anesthetic as the patient group before cardioversion. This anesthetic might influence the results. Currently 15 patients and 5 controls are included in the study. MR of the brain is acquired immediately before and after the first ECT, after ended treatment (3 sessions per week for 3-6 weeks) and at six months follow up. Group 1 is only scanned before and after cardioversion. The study is approved by REC. **Methods:** Imaging will be performed at a 3T GE Signa HDxt MR system with a 8 channel head coil, but most of the subjects will be scanned on a 3T GE Discovery 750 MR system with a 32 channel head coil. For H-MRS (hydrogen-magnetic resonance spectroscopy) both single-voxel point resolved spectroscopy, SV PRESS and a spectral editing method, MEGA-PRESS are used. The SV PRESS voxel measures 2x2x2 cm^3 and placement alternates between the right and left anterior cingulate cortex (ACC). LCModel Software is used for data-analysis. **Discussion:** This study aims at increasing the understanding of ECT and depression, by using a novel approach: Yet no study has used a control group that uses a similar anesthetic, to rule out the role of this substance, or a control group that is treated with electroshock to the chest. This project might help us understand both ECT and depression in a better way.

Keywords:
Molecular neuroscience
Clinical neuroscience
Neuroimaging

Septal inactivation of grid cells

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A normally functioning brain operates through a delicate balance between excitation and inhibition. Increasing evidence points to the inhibitory neurons critical role in neurological disorders and psychiatric diseases, e.g. reduction of parvalbumin positive (PV+) inhibitory neurons are associated with schizophrenia. Accumulating evidence suggests PV+ neurons to control critical period plasticity in local neuronal networks and to be involved in mechanisms of learning and memory. Furthermore, the PV+ neurons have been suggested as the main local source of generating high frequency brain oscillations. However, how these processes contribute formation of spatial related memories still remains elusive. The medial septum (MS) of the basal forebrain is believed to be the main theta rhythm generator both for the hippocampus and the medial entorhinal cortex (MEC). The GABAergic projections from MS synapse onto inhibitory interneurons and mainly putative PV+ cells in the MEC. These projections are believed to generate the theta rhythm in principal cells and synchronize inhibitory cells in gamma rhythm through disinhibition (Gonzalez-Sulser et al., 2014). Inactivation of the MS impair the grid cell representation of space bringing forth a prominent indication of the MS as an instrumental modulatory device for memory representation of space. However, entorhinal theta oscillations may depend on hippocampal output (Bonnevie et al., 2013) and inactivation of MS causes a large reduction of both firing rates and theta oscillations in hippocampus (Koenig et al., 2011). Thus, it remains elusive if the disintegration of the grid fields were due to MS inactivation or termination of hippocampal theta. We will use cell-specific expression of light sensitive proteins to optically manipulate projecting MS axons and PV+ cells in the MEC. This method has previously shown promising when testing the causal relationship between the precise spike timing of PV+ neurons and cell specific gamma oscillations. Using large-scale extracellular recordings, we will directly assess the effect of these manipulations on the spatial specific neural network in MEC of behaving animals. To obtain a deeper understanding of the complexity of neural network processes, computational models will be developed and later verified using experimental data. If successful, these models will predict and drive forward our understanding of the neural processes underlying spatial navigation and memory processing.

Keywords:
Systems neuroscience
Computational neuroscience and neuroinformatics

Postsynaptic targets of characteristic inputs to the twin entorhinal cortical networks

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The entorhinal cortex is a twin structure which can be divided into a lateral (LEC) and a medial part (MEC) whose projections to the hippocampus originate from the same layers and cell types, and show an overall striking similar distribution in the hippocampus. Yet, their inputs differ significantely. The majority of sources to MEC originate in areas that are components of the navigational network in the brain providing spatiovisual inputs (presubiculum, parasubiculum, retrosplenial and postrhinal cortices) and the main inputs to LEC arise from a group of cortical domains transmitting information about objects, context, or ongoing events in the environment (olfactory, perirhinal, insular, and frontal cortices). We can distinguish an analogous pattern of laminar distribution in superficial layers of the perirhinal inputs to LEC and the postrhinal inputs to MEC. However, those inputs differ significantly as postrhinal ones stimulate MEC but perirhinal ones to LEC feature a very strong inhibitory component relieved solely by co-activation of conjunctive inputs coming from the amygdala, the postrhinal cortex or other cortical parts. Actually, the object-selective firing of LEC neurons, likely reflecting a response from relieving perirhinal inhibition, strongly contrasts with the continuous influx of spatially relevant information provided by MEC grid cell. This would suggest that a subtle and intrinsic balance between inhibition and excitation within the input pathways are mediated by distinct postsynaptic targets. The objective is to determine whether the postsynaptic targets in superficial layers of sets of comparable inputs to MEC and to LEC, are different and whether differences in postsynaptic targets through which inputs impinge on overall similar network architectures cause functionally different outcomes. So far, we have used tracing experiments, intracellular filling and subsequent confocal analysis but the postsynaptic cell types remain to be established as either principal neurons or interneurons.

Keywords:
Systems neuroscience

Increased IMT in young stroke patients – a marker of genetic risk? - the Norwegian Stroke in the Young Study (NOR-SYS)

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Objectives: Family history (FH) is a risk factor for cardiovascular disease (CVD). We aim to analyze the effect of genetic risk on carotid intima-media thickness (cIMT) in young ischemic stroke patients. **Methods:** FH of CVD in first-degree relatives (FDRs) of ischemic stroke patients ≤60yrs was assessed using a standardized interview. Carotid ultrasound was performed and far wall IMT was registered in three carotid artery segments, representing the common carotid (CCA), carotid bifurcation (BIF) and internal carotid artery (ICA). IMT measurements were compared between FH+ and FH- groups and stepwise backward regression analyses were performed to identify factors associated with increased IMT. The FH groups were categorized by 15y age intervals to enable within age-group analyses. **Results:** During the study period 332 patients were enrolled, of which 229 (69%) were males and 204 (61%) reported FH of CVD in ≥1 FDRs. There were 21, 61 and 250 in the 15-29y, 30-44y and 45-60y age categories, respectively. Mean cIMT in the FH+ group was higher in all carotid segments (all $p<0.01$). Regression analyses adjusting for risk factors revealed age as the most important predictor of cIMT. Age and FH interacted significantly with ICA-IMT ($p < 0.001$). Showing FH was associated with increased ICA-IMT in patients aged <45y but not patients >45y ($p = 0.001$ and $p =0.061$). **Conclusions:** FH of CVD is associated with higher ICA-IMT in young patients. ICA-IMT is a valuable measurement in young patients, indicating increased genetic risk for CVD, especially stroke. FH is neither associated with increased IMT in middle-aged patients nor with IMT in the CCA or BIF at any age.

Keywords:
Clinical neuroscience
Neuroimaging

Characterization of cellular reactions during adaptive plasticity after spinal cord injury in the neonatal mouse

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An important phenomenon that occurs following spinal cord injury in rodents is adaptive plasticity, wherein spinal networks form novel connections that contribute to functional recovery. If adaptive plasticity can be harnessed (and maladaptive plasticity avoided), it could provide a new platform for clinical treatment. We have earlier shown that neonatal spinal cord injured (SCI) mice exhibit more functional recovery than reported in adult SCI mice, and demonstrated that during recovery unconventional synaptic connections are formed from descending pathways to spinal MNs (Boulland et al 2013). We have since, begun to characterize the cellular reactions that occur during behavioral recovery. We have focused on cell proliferation, synaptic density, and target neuron number. **Methods:** Thoracic spinal cord compression was performed with a modified aneurysm clip. EdU was injected i.p. daily from 1 to 8 days post-injury. L1 and L2 MNs were labeled retrogradely and counted or stained for presynaptic terminals using anti-synaptophysin-1, VGLUT-1, VGLUT-2 and VGAT. Specific cell types were identified by immunolabelling with NeuN, ChAT, GFAP and Iba1, and EdU+ proportions were determined. **Results:** 8 days post injury there is a complete loss of neurons at the compression epicenter, and a reduction of neuron number by a factor of 3 within the more distal parts of the compressed segment. Despite this dramatic loss, there was about a 30% increase in the number of EdU+ cells compared to controls, and these included Iba1+ cells (microglia). There was a 6-fold reduction in synaptic terminals on lumbar MNs 1 day post-injury, but this normalized by 8 days post-injury. During this time, there was no change in the number of lumbar MNs as a consequence of thoracic injury. We conclude that behavioral recovery in the neonatal mouse following thoracic compression injury is primarily due to the recovery of lost synapses, probably paralleled by reorganization of synaptic connections, and not due to compensatory neurogenesis. We are therefore now focusing on the balance between the excitatory and inhibitory synapses on lumbar MNs and on plasticity of the descending and ascending fibers through the compression epicenter during behavioral recovery.

Keywords:
Cellular neuroscience
Developmental neuroscience

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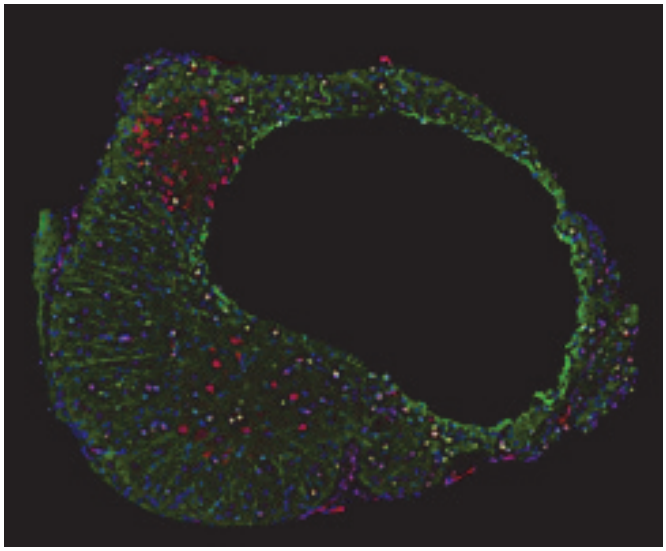

Transverse section of an injured spinal cord. Green: GFAP-labeling Red: NeuN-labeling White: EdU-labeling Blue: Hoechst-labeling

The localization and function of Arc in the neuronal cell nucleus

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Long-term memory relies on lasting changes in synaptic connectivity; modifications dependent on new gene expression and protein synthesis. Dysfunction of synaptic plasticity is implicated in a range of disorders eg. Alzheimer's disease, mental retardation, chronic pain states. Activity-regulated cytoskeleton-associated protein (Arc) is rapidly induced upon neuronal activity. Arc transcription, translation and function provides a finely-tuned system for converting neuronal activity patterns into protein synthesis-dependent synaptic plasticity and memory storage. Two new nuclear binding partners of Arc has been suggested; PTB-associated splicing factor (PSF) and Serine/arginine repetitive matrix 2 (SRRM2). They are linked to RNA splicing and editing and could therefore be involved in the control of neuronal-specific splicing events occurring at particular stages of neuronal differentiation and maturation. The overall aim is to further elucidate the function of the Arc protein in the nucleus. A major goal was to determine whether Arc protein colocalizes with putative binding partners identified by biochemical techniques. Specifically, we examined colocalization of Arc with PSF and SRRM2 in the neuronal nucleus. In vitro rat hippocampal neuronal cell cultures, were stimulated by BDNF and fluorescently stained against Arc, PSF and SRRM2. Confocal images were then acquired and rendered in Bitplane Imaris. Colocalization was performed in Bitplane Imaris Coloc module and statistical analysis was made in Microsoft Excel. BDNF treatment led to increase in Arc protein expression. A very low colocalization between Arc and PSF was found in the control experiments, which increased upon BDNF stimulation with about 20%. Although the colocalization of Arc and SRRM2 puncta was very low, Arc puncta seemed to mainly associate with the surface of SRRM2 structure. This data might suggest a novel function of Arc related to its interaction with paraspeckle proteins. This functional relationship is only tentative as there is no previous work associating Arc to the splicing machinery. By researching Arc's function and binding partners, neuronal synaptic plasticity can be further understood. The presented work is part of a major project in collaboration with Department of Biomedicine and KGJebsen Centre for Research on Neuropsychiatric Disorders, University of Bergen, Department of Neurology, Haukeland University Hospital and Nencki Institute of Experimantal Biology in Warsaw.

Keywords:
Molecular neuroscience
Cellular neuroscience
Neuroimaging

Effects of Music Training on Cortical Plasticity within Cognitive Rehabilitation of TBI Patients

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Musical training has emerged as a useful framework for the investigation of training-related plasticity in the human brain. This study explores the effects of playing the piano on traumatic brain injury (TBI) patients with cognitive deficits. The aim of the intervention is to restore the cognitive function following TBI. 8 weeks piano-tuitioin protocol has been designed to address the question if this approach may stimulate neural networks in re-routing neural connections and link up impaired networks and thus restore the cognitive deficits. 3 groups were recruited for the study. One music-training TBI patient group with cognitive impairment, one healthy control group with music and one healthy control group without music as a baseline control group. Pre-post assessment consisted of neuropsychological tests and fMRI scanning. We performed an ANOVA repeated measure analyse for the three groups on results from the neuropsychological tests. The CVLT test-results revealed a clear significant effect of musical training on cognitive enhanced performance. In analysing fMRI data we found a significant change in orbifrontal cortex in both music-training groups, no change in the baseline control group. Orbifrontal cortex controls learning,executive functioning and social interaction. Additional information from interviews of the TBI group pre-post intervention, support the aim of musical training effect of cognitive enhancement. The key findings of this study are the clear evidence for training-related neuroplasticity, a causal relationship between musical training and reorganization of neural networks and thus enhanced cognitive performance.

Keywords:
Cognitive neuroscience and neuropsychology

Monosynaptic inputs to cells in deep layers of the lateral entorhinal cortex revealed through cre-dependent rabies tracing

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Because of its importance in memory, the anatomy and function of the parahippocampal region (PHR) has been extensively studied. The PHR, and more specifically the entorhinal cortex (EC) was for a long time viewed as a passive relay structure for the hippocampal formation (HF). This view of the EC has rapidly become antiquated as more and more functional and anatomical data suggest that the EC provides essential information and processing to the cortico-hippocampal circuit. Several types of spatially tuned neurons have been found in the medial entorhinal cortex (MEC), indicating its relevance in spatial navigation and memory processing. Conversely, less is known about the function of its lateral counterpart, the lateral entorhinal cortex (LEC). It has been shown to be involved in memory processes, but only weakly spatially modulated cells have been found. The superficial layers of EC receive information from several brain regions and give rise to the main input to HF, the perforant path projection. In contrast, cells in deep layers receive input from the HF, have their dendrites extending up to the superficial layers and have also been shown to both receive input from, and project out to cortex. Therefore, the deep layers of EC have the potential to serve as an integrator, processing not only the information from the HF, but also the cortical and subcortical information coming into both superficial and deep layers of EC. The majority of anatomical studies on EC have used conventional tract tracing techniques with a focus on rat anatomy. However with the emergence of transgenic mice and complementary viral techniques it is possible to provide a more targeted, cell-specific investigation of connectivity. Moreover, as more behavioral and functional studies are done using transgenic mice, knowledge of the mouse anatomy is essential. In this study we utilized the Ntsr1-cre mouse line in combination with a cre-dependent AAV helper virus and G-protein deleted rabies virus. This allowed us to specifically dissect out the inputs to cells in deep layers of LEC. Our data show monosynaptic inputs to cells in deep layers of DLE from several regions, including piriform cortex, the hippocampal formation, putative auditory cortex, and several amygdaloid nuclei.

Keywords:
Systems neuroscience

Transgenic activation of MEC LII results in similar changes in the firing properties of CA1 place cells across distinct environments.

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The hippocampus is critical for episodic memory. The spatial component of episodic memory is thought to be encoded by place cells, which fire in specific locations of the environment. Environmental novelty causes place cells to change their firing rate and/or firing location, a process called remapping. Remarkably, there is no discernible relationship between the firing fields of a particular cell in two distinct environments. The medial entorhinal cortex (MEC), the major input to the hippocampus, contains several cell types with spatial receptive fields, including grid, head direction, and border cells. The relationship between upstream MEC neurons and remapping of downstream hippocampal neurons is still unclear. In order to address this question, we used the tTA-tetO system to express an hM3Dq DREADD (Designer Receptors Exclusively Activated by Designer Drugs) in MEC layer II. The hM3Dq is a modified muscarinic G-protein coupled receptor exclusively activated by an otherwise inert ligand, clozapine-N-oxide (CNO). Previous electrophysiological recordings in our lab demonstrated that systemic injection of CNO increases the firing rate of neurons in layer II of the MEC and causes grid fields to expand without changing the grid vertices. However, CNO-induced activation of MEC LII neurons produces drastic changes in place fields ("artificial remapping") of downstream CA1 pyramidal neurons. Multiple transgenic activations of the same entorhinal inputs via multiple CNO injections leads to the same hippocampal network response, suggesting that artificial remapping may be a hard-wired network response. To investigate whether transgenic activation of the same set of MEC LII neurons has a similar effect on two distinct receptive fields of the same CA1 place cell, we recorded activity in CA1 while mice explored two distinct environments before and after the administration of CNO. In contrast to remapping induced by changes in the animal's experience, our preliminary results suggest that there is a discernible relationship between firing rate changes in distinct environments following transgenic activation of MEC LII. These results not only provide further support for the idea that artificial remapping in response to transgenic activation of MEC LII is a hard-wired network response, but also raise the question of how known changes in input are interpreted by the hippocampal-entorhinal network.

Keywords:
Systems neuroscience

Abstracts for blitz and poster sessions
23 September

Abstracts are organized in the order of presentations

Cognition, Emotion and Behavior in Children with Tourette's Syndrome and Children with ADHD-Combined Subtype

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7. Sobell Department of Movement Disorders, Institute of Neurology, London, UK

Objective: This follow-up study investigates whether changes in cognitive control, focused attention and decision-making in children and adolescents with Tourette's Syndrome (TS) or Attention-Deficit/Hyperactivity Disorder-Combined subtype (ADHD-C) were associated with changes in anxiety and depression symptoms and/or emotional behavior difficulties. **Method:** 19 children with TS, 33 with ADHD-C, and 50 typically developing children (TDC) were examined with a battery of psychometric measures and rating forms at baseline and two-years later. **Results:** All three groups improved in measures of cognitive control over time, whereas only the TDC improved in focused attention. In the decision-making task, none of the groups improved in overall advantageous decision-making; however, the children with TS preferred a safer strategy in selecting advantageous choices than the children with ADHD-C and the TDC at T2. Children with ADHD-C and with TS showed higher symptoms of anxiety and depression and more emotional behavior difficulties compared with TDC at both time points. Finally, children with ADHD-C self-reported more depression symptoms than those with TS at both assessments. For the TS group, safer decision-making was related to more control over emotional behavior difficulties. **Conclusions:** More efficient control over core cognitive processes was not associated with fewer symptoms of anxiety or depression or increased control over emotional behavior in children with TS or ADHD-C. This study emphasizes the importance of addressing symptoms of anxiety and depression in children with TS or ADHD-C, and that children with TS or ADHD-C likely differ in their sensitivity to reinforcement contingencies.

Keywords:
Cognitive neuroscience and neuropsychology

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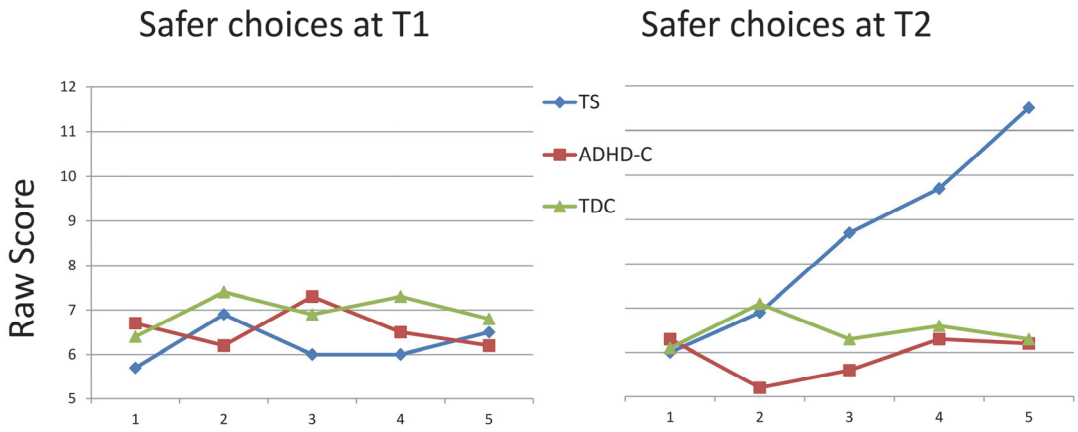

Figure 1. Rates of selecting an advantageous, less risky alternative, across 5 blocks of trials at T1 and T2. The 'safer' choice tendency in the TS group at T2 involves a preference for frequent, lower-level losses compared to a less frequent higher-level loss alternative.

ANALYZING MICROGLIAL AMYLOID BETA (Aβ) CLEARANCE IN AβPP TRANSGENIC MICE WITH A MID-DOMAIN Aβ-ANTIBODY

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Introduction: The pathological hallmarks of Alzheimer Disease (AD) brain are neurodegeneration and brain atrophy in the presence of extracellular amyloid-β (Aβ) deposits (plaques) and intracellular neurofibrillary tangles (NFTs). Aβ plaques are thought to form due to an imbalance in the production and clearance of Aβ peptides. While Aβ plaque formation is a well-studied aspect of AD pathogenesis, mechanisms of Aβ clearance are still fairly unknown. Microglial/brain macrophage uptake and degradation of Aβ peptides has been demonstrated in vitro, but its relevance in vivo remains controversial. New techniques and tools to examine Aβ clearance in brain is much needed. Mid-domain Aβ-antibodies were developed allowing detection of Aβ fragments, and one of these used to study brain macrophage uptake of Aβ in transgenic Arctic Swedish (tgArcSwe) mice. **Methods:** A new mid-domain Aβ-antibody was characterized with dot-blot, epitope mapping and ELISA. Brain sections of tgArcSwe mice was used for immunofluorescent and immunogold staining at the light and ultrastructural microscopic level respectively. Brain macrophages were identified by immunfluorescent co-staining with microglial markers. **Results:** Mid-domain antibodies were developed as tools to investigate degradation products of Aβ in vitro and in transgenic models of AD. Antibodies were raised and affinity-purified against the Aβ 21-34 amino acid sequence, but the binding domain was more restricted. By use of a mid-domain antibody we detected Aβ-fragments in brain macrophages in both transmission electron microscopic data (2-D) and at the light microscopic level (3-D). **Conclusions:** Here we describe the in vitro characteristics of a mid-domain Aβ-antibody that could become useful for further analysis of enzymatic Aβ-degradation and clearance in vitro and in vivo. Our data show uptake of Aβ in vivo in transgenic mice, confirming a role of microglia/macrophages in Aβ-clearance.

Keywords:
Cellular neuroscience
Neuropathology

An EEG study of the development of perception of optic flow in infants

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Introduction: The present study used high-density EEG to record evoked activity in response to simulated visual motion in two different speeds and two different directions. **Methods:** Three different groups were tested: infants at 4-5 months, infants at 8-10 months, and adults. The participants were shown an optic flow pattern consisting of a virtual road with moving poles at either side of it, simulating forward self-motion at two different driving speeds (20 and 50 km/h) and two directions (forwards and backwards). **Results:** Infants at 8-10 months showed lower N2 latencies, in response to the low speeds, than the infants at 4-5 months, but the two infants groups displayed relatively high N2 latencies in response to the highest speed. The adults showed the lowest N2 latencies in all conditions, compared to the infant groups (see Figure 1). Significant differences between low and high speed were found in the group of infants at 8-10 months and in the adult group. No differences were found between any conditions in the youngest infant group. **Discussion:** All infants in the second group had crawling experience at the time of testing, and this might help explain the lower latencies seen in the low speed condition. These lower latencies at the lowest speed shown by the oldest infants indicate a more developed neurobiological system, compared to the younger infants, possibly as a result of increased myelination of connecting fibres, improving visual motion detection. The 4- to 5-month-old infants that were not able to separate between any of the motion conditions had no experience with self-produced locomotion. The relatively high latencies, in both infant groups, in response to the high speeds indicate that the relatively high speeds used in this study were considered by both infant groups more complex than the lower speeds. This shows that the motion sensitive areas continue to develop through infancy and childhood, resulting in more efficient and faster processing of higher speeds of visual motion. Adults also had higher latencies in response to the higher speeds, which shows that these speeds were considered as more complex for them as well, compared to the lower speeds.

Keywords:
Cognitive neuroscience and neuropsychology
Developmental neuroscience

See image on next page.

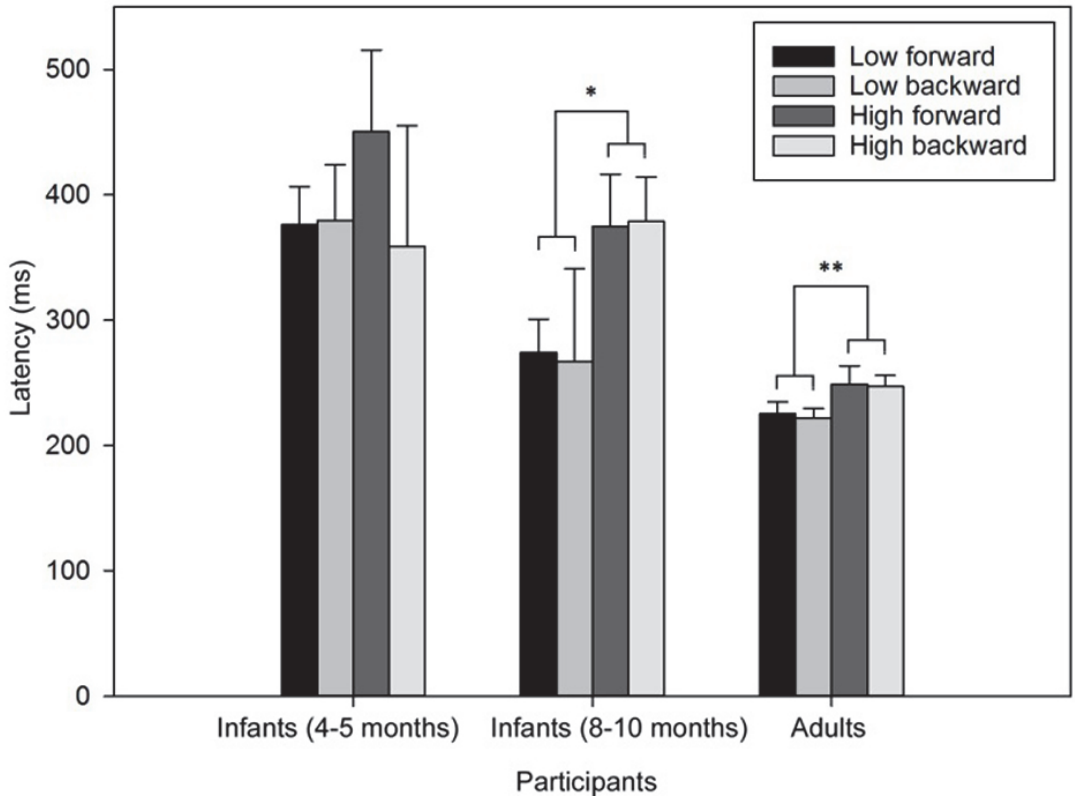

*Figure 1. Mean peak latencies (with SD) in the three groups (4/5-month-olds, 8/10-month-olds, and adults) for the two different speeds and motion directions. *Significant at p<0.01. **Significant at p<0.001.*

The role of intrahippocampal growth hormone in spatial memory

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Low levels of growth hormone (GH) and insulin-like growth factor (IGF) are seen in ageing and endocrine disturbances, and are associated with cognitive deficits. Memory can be enhanced or impaired in animals by manipulating the GH/IGF axis, but the mechanisms behind are poorly understood. In the current study, we used viral transfections to reduce or enhance GH levels locally in the hippocampus. The hippocampus is a natural target as it contains receptors for several ligands along the GH/IGF axis, and also has local production of GH. Moreover, GH-stimulating receptor (GHSR) and IGF receptors can modulate long-term potentiation, neurogenesis and memory consolidation after local stimulation in the hippocampus. In our model, we transfected the dorsal hippocampus of Long Evans rats with recombinant adeno-associated virus (rAAV) expressing GH, mutated GH (mGH) or only green fluorescent protein (GFP). The AVV infection allows for chronic elevation (AAV GH) or inhibition (AAV mGH) of GH. The rats were tested in a displaced object task and a water maze task. The results indicate that the viral transfections affect learning and memory by acting locally in the hippocampus. Further experiments will be performed to explore which parts of the memory processing that are affected most severely by GH manipulation. Understanding actions of GH in brain can give insight to why cognitive decline often follows ageing, as GH levels are dramatically reduced in ageing across several species.

Keywords:
Molecular neuroscience
Cellular neuroscience
Systems neuroscience

Monosynaptic tracing of inputs to PV interneurons in the medial and lateral entorhinal cortices

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Parvalbumin (PV) cells make up one of the largest populations of interneurons in the brain. Small and large basket cells as well as chandelier cells and several other morphological subgroups of interneurons have proved to be PV expressing. PV cells have fast-spiking electrophysiological profiles, and the basket cells in particular are known to have a profound effect on the local networks providing strong inhibition to the somata of surrounding principal cells. In the medial entorhinal cortex (MEC), it was shown that fast-spiking interneurons di-synaptically connect stellate cells in LII, and that these principal neurons do not contact each other directly (Couey et al, Nat. Neurosci. 16:318). Whether the same is true for the lateral entorhinal cortex (LEC) is unknown. In view of the unique properties of PV interneurons and their seemingly central role in the entorhinal local network, we have assessed the monosynaptic inputs of PV cells in both the medial and lateral subdivisions of the entorhinal cortex. We used monosynaptic retrograde tracing using a G-protein deleted rabies virus and a PV-cre transgenic mouse line. The PV interneurons in the entorhinal cortex all seem to receive substantial input from the hippocampus and a number of neocortical areas, as well as from selected subcortical areas such as the thalamus, the amygdala and the medial septal complex. In general, the inputs resemble what has been observed in studies using conventional retrograde tracers. PV cells in the LEC receive stronger cortical inputs than those in the MEC, on average each LEC starter cell receives 37,3 cortical connections, while MEC starter cells on average receive 16,3 inputs per starter cell. On the other hand, PV cells in the MEC receive heavier input from the hippocampus than do LEC PV cells (6,2 inputs, and 3,6 inputs per starter cell respectively). The rabies tracing also provides a unique opportunity to look at interconnectivity within the LEC and MEC. The data indicate that LEC has substantially more connections between PV cells and the remainder of the cell population, compared to the MEC (26,3 connections per starter cell in the LEC, compared to 4,9 connections per starter cell in the MEC). In conclusion, the PV interneuron specific retrograde tracing corroborates previous retrograde tracer studies, and the neocortical and hippocampal inputs to PV cells resemble those of the total neuronal population in the two areas.

Keywords:
Cellular neuroscience
Systems neuroscience

Convergence of retrosplenial and subicular inputs on principal neurons of deep medial entorhinal cortex

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As part of our ongoing investigations of the neuronal networks that enable spatial processing, we are interested in clarifying the role of the retrosplenial cortex (RSC) and its relations with the hippocampal region. The RSC projects densely to the deep layers of the medial entorhinal cortex (MEC), whose superficial layers provide the main cortical input to the hippocampal formation, including the subiculum. The subiculum provides a reciprocal projection, targeting the deep layers of MEC. We characterized principal neurons of the deep MEC that receive input from both RSC and subiculum and additionally provide axon collaterals to the superficial layers of MEC by using a triple neuroanatomical tracing technique together with confocal laser scanning microscopy (CLSM). We injected a retrograde tracer, Fast Blue, into the superficial layers of MEC and injected the anterograde tracers PHA-L or BDA into the RSC and subiculum. After transcardial perfusion and sectioning, retrogradely Fast Blue-labelled neurons in deep layers of MEC which were located within both the anterogradely labelled plexuses were intracellularly filled with Alexa 568 fluorescent dye and analysed using confocal microscopy. Subsequently, we reconstructed neurons in 3D based on confocal image-stacks using Amira software. Twenty-seven superficially projecting neurons in layer V displayed putative contacts with both retrosplenial and subicular inputs. Further analyses indicated that most of the putative synaptic contacts for both inputs were located and intermingled on the same parts of single dendrites. Currently, we aim to corroborate the existence of functionally convergent input using electrophysiological approaches. We inject AAV-viruses expressing channelrhodopsin and eYFP or mCherry into the RSC, allowing us to stimulate retrosplenial axonal fibers in deep MEC optogenetically in vitro, while conducting whole cell patch clamp recording from deep MEC neurons. In addition, we stimulate the subiculum using an electrode while recording from the same neurons.

Keywords:
Cellular neuroscience
Systems neuroscience

Early neurological worsening in acute ischaemic stroke patients

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Background: The prevalence of neurological worsening in acute ischaemic stroke patients varies between 13%-38%. **Aims:** We focused our study on neurological worsening during the first 9 hours in acute ischaemic stroke patients admitted to our stroke unit ≤ 3 hours after symptoms onset, because these first hours are critical as to recanalization and possible progression of infarction. Increasing ischemia due to late recanalization may be important in the early stages, while other factors are important more than 6-9 hours after ischaemic stroke onset. **Methods:** All acute cerebral infarction admitted to the Stroke Unit, Department of Neurology, Haukeland University Hospital between February 2006 and February 2013, were prospectively registered The Bergen NORSTROKE Registry. The National Institute of Health Stroke Scale (NIHSS) was used to assess stroke severity. Early neurological worsening was defined as NIHSS score increase ≥4 NIHSS points within 9 hours of symptom onset compared to NIHSS score within 3 hours of symptom onset. Patients with early neurological worsening were compared to patients with unchanged or improved NIHSS scores. **Results**: Of the 2484 patients admitted with ischaemic stroke, 552 patients had NIHSS score within 3 hours of symptom onset, and 44 (8.0%) experienced early neurological worsening. Patients in the worsening group continued to get worse during the first 9 hours after symptoms onset with NIHSS score 11.8 between 3-6 hours, 13.4 between 6-9 hours and 14.2 between 9-12 hours after stroke onset (all $p < .001$). Early neurological worsening was associated with low body temperature on admission, proximal MCA occlusion, ipsilateral internal carotid artery stenosis >50% or occlusion, higher NIHSS day 7 and higher mortality within day 7. **Conclusions:** Early neurological worsening has serious consequences for the short term outcome for patients with acute ischaemic stroke and leads to significant morbidity and mortality.

Keywords:
Clinical neuroscience

Action Planning and Action Observation in posterior parietal cortex in mice

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A fundamental question in the field of neuroscience is the elucidation of neural mechanisms underlying purposeful voluntary movements. Although the primary motor cortex is responsible for generating neural impulses that control movement execution, intention (planning) of the movement occurs across several brain areas including posterior parietal cortex (PPC), which has diverse sensory and motor inputs. PPC functions both in polymodal sensory association as well as in sensorimotor transformations dedicated to certain motor effectors. It has also been found that PPC contains subsets of neurons which discharge both when an animal performs a given motor act and when it observes a similar motor act done by other individual. These neurons are called “mirror neurons”, and are thought to provide a physiological mechanism which links action perception and action execution. The presence of mirror cells in PPC has been demonstrated in both primates and humans, but our knowledge of the biological basis of the mirror mechanism is constrained by the technical limitations inherent to human and primate research. The demonstration of mirror cells in a lower, genetically-tractable model system such as the mouse would be hugely advantageous since it would open the door to study the mirror system using the modern molecular tools of systems neuroscience. To determine if mirror neurons are present in mice we will conduct in vivo calcium imaging in mouse PPC using a miniature fluorescent microscope, which permits the study of relatively large ensembles (100-200 cells) simultaneously. In the first step of this task a freely-moving animal will repeatedly perform a pellet-reaching task, which requires the animal to reach through a slit, grasp a pellet and eat it. In the second step of the task the same animal will be head-restrained and observe the same pellet-reaching task performed by a familiar conspecific located in very close (10cm) proximity. We will perform calcium imaging through both phases of the task, allowing us to compare the activity patterns during both action execution and action observation. Our results will potentially provide a first-time glimpse of sensory-motor mirror matching at the neuronal population level; if successful these experiments would offer compelling evidence for the subsequent systematic investigation of the mammalian mirror system.

Keywords:
Systems neuroscience

Aberrant thalamic functional connectivity in schizophrenia and bipolar disorder

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Introduction: The thalamus is a highly connected hub region, which relays, integrates and modifies sensory and cortical information. Both core clinical characteristics and previous brain imaging studies have implicated thalamic dysfunction in schizophrenia, and emerging resting state functional MRI studies point to an increased connectivity with somatomotor regions and decreased connectivity with the frontal lobe. However, thalamic functional connectivity in bipolar disorder and how it overlaps with schizophrenia remains unclear, and subthalamic nuclei may be affected differentially. **Method:** We collected resting-state functional MRI data from patients with schizophrenia (n=96), bipolar disorder (n=57), and healthy controls (n=280). Independent component analysis was run on the whole brain and on the thalamus to investigate thalamic functional connectivity both as a whole structure and divided into subregions. Structural analyses of the thalamus encompassing shape, volume, and voxel based morphometry for gray matter were also performed. Group differences were evaluated voxel-wise using permutation testing. **Results:** We found reduced thalamic connectivity in both patient groups compared to controls, with stronger effects in schizophrenia, with only minor structural differences. Thalamocortical analyses showed increased connectivity with the somatomotor network and reduced correlations with several other networks in both patient groups, with more networks affected in schizophrenia. Subthalamic analysis showed subregions to have increased connectivity with somatomotor and sensory regions and decreased connectivity with frontal lobe in schizophrenia, though not in bipolar disorder. **Discussion:** These findings point to aberrant thalamic functional connectivity with several cortical regions in schizophrenia, with only a few affected in bipolar disorder, highlighting the thalamus as a key region in abnormal network connectivity in psychotic disorders.

Keywords:
Clinical neuroscience
Neuroimaging

Pro-social behaviour in rats – Influencing helping behaviour

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Introduction: Pro social behaviour, and empathy, are important factors to make modern society work. Empathy enables organisms to recognize the emotional behaviour of others. Pro-social behaviour is closely related to empathy. From studies using fMRI, and investigation into social behaviour of infants, there is support for a biological substrate for empathy. This PhD project will make use of the pro-sociality/empathy model animal first published in the paper from 2011 by I. Bartal and colleagues (Bartal, Decety, & Mason, 2011). The authors investigated helping behaviour where a free rat released a trapped rat from a restrainer. With this PhD project, we aim to look into possible influencing factors for such helping behaviour. **Method:** A small plexiglass restrainer is placed in the center of a 0,5*0,5m styrene acrylonitrile resin (clear plastic glass) arena. Cagemate rats will be trained to open the restrainer and release the other rat from the entrapment. See illustration 1. During both training/habituation and the experimental phase we will record and analyze movement and exploration. High frequency, 22kHz alarm call, will also be recorded. Movement and exploration, frequency of opening, latency before opening, and the number of alarm calls will be compared between the rats in this project. **Experiments and preliminary hypotheses:** *Experiment 1:* The independent variable here will be an increase of illumination. This is presumed to cause stress in rats, and we will measure the change in behaviour. H0: Increase of illumination will not noticeably affect the rats' helping behaviour. H1: Increase of illumination will negatively affect the rats' helping behaviour. *Experiment 2:* The independent variable here is oxytocin intervention. Oxytocin is presumed to influence social behaviour in rats. After oxytocin has been administrated to one group of rats, their behaviour will be examined. H0: Oxytocin intervention will not noticeably affect the rats' helping behaviour. H1: Oxytocin intervention will positively affect the rats' helping behaviour.

Keywords:
Cognitive neuroscience and neuropsychology

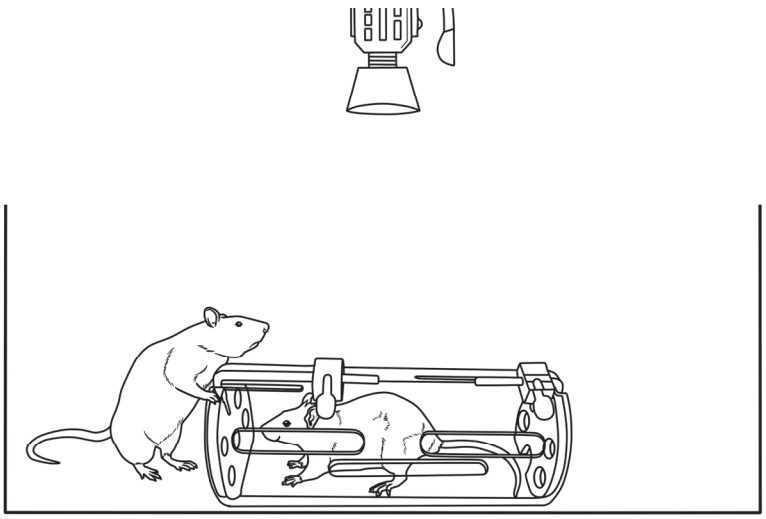

*Illustration 1 Two cagemate rats are inside of a plastic glass arena measuring 0.5*0.5m. The free rat is trained to open a door which will release the trapped rat. Video and high frequency alarm calls are recorded during the experiments for analysis.*

Investigating the implication of human-specific methylated regions in complex disorders

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A recent paper by Gokhman et al,2014 provides the first clues of the putative role of epigenetics in the origins of Homo sapiens. Using a novel methodology, the ancient methylome of Neanderthals and Denisovans was resurrected and variations in the regions methylated with modern humans were determined. The present project, as part of a doctoral thesis will seek to build upon this result by testing these differentially methylated regions (DMRs) between humans and Neanderthals, humans and Denisovans for enrichment of association with various complex traits like height, weight and body-mass-index (BMI) as well as complex diseases including but not limited to schizophrenia and bipolar disorder. The DMRs which are depicted as chromosome coordinates will be investigated for overlap and/or linkage disequilibrium (LD) with regions previously identified to be associated with schizophrenia, bipolar disorder, BMI, height and other related traits. To determine if these regions associate with various phenotypes, we will use a method developed by Schork et al, 2013 which measures the enrichment of association of specific genomic categories in genome wide association studies (GWAS) and boosts the power of existing GWAS to identify novel variants by using a covariate modulating FDR method. The results are expected to provide new insights into the role of DMRs in complex diseases in modern day humans.

Keywords:
Genetic neuroscience

The role of 14-3-3 proteins in regulation of tyrosine hydroxylase

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Protein-protein interactions (PPIs) provide the backbone of signaling networks as cell signaling provide the backbone of neuronal communication and behavior. Many efforts have been made to map the PPI networks associated with human diseases. Despite these efforts, very little data exists for proteins associated with common neurodevelopmental disorders. Interestingly, proteins of the 14-3-3 family are shown to be highly involved in these pathways. These proteins are highly interconnected network nodes (nub proteins) with >100 described binding partners. The PPI of 14-3-3 proteins is controlled by Ser/Thr phosphorylation, which makes them important effectors of cell signaling processes through a variety of mechanisms involving a plethora of cellular processes. The 14-3-3 proteins are a highly conserved protein family, counting seven mammalian isoforms (β, γ, Ɛ, η, σ, τ and ζ), highly abundant in the nervous system. The different isoforms can form homo- and heterodimers and function as binding partners to many cellular proteins. One of the first discovered targets for 14-3-3s was tyrosine hydroxylase (TH), a key regulatory enzyme of catecholamine (CA) biosynthesis. Phosphorylation of TH is an important regulatory mechanism for the maintenance of CA levels in tissues. Previous studies showed that 14-3-3s are involved in regulation of tyrosine hydroxylase by increasing the activity of enzyme and inhibition of enzyme dephosphorylation but the clear mechanism of these regulations are not clear yet. As there are several isoforms of 14-3-3 and they may form both homo- and heterodimers, we wanted to examine the effect of different 14-3-3 proteins on the regulation of tyrosine hydroxylase (TH). We investigated the regulation of TH phosphorylation and activity as these are important regulatory mechanisms for catecholamine biosynthesis. In addition, we will investigate the cellular regulation of TH by different 14-3-3 proteins and their impact on the interaction of TH with other binding partners.

Keywords:
Molecular neuroscience

Genome-wide analyses of self-reported aggressive behavior in attention-deficit hyperactivity disorder

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Aggressive behaviour is an evolutionary conserved trait that can also be harmful to individuals and society. With a heritability of 50%, genetics plays an important role in the development of aggressive behavior. As the molecular genetics of aggressive behavior remains largely unknown and it is often comorbid with neuropsychiatric disorders, we performed a genome-wide association (GWA) analysis of aggressiveness in European adults with attention deficit hyperactivity disorder (aADHD). We derived the measure of aggressive behavior from the Wender Utah rating scale (WURS) in 1060 aADHD patients recruited from Germany, Norway and Spain. Given that WURS reflects recalled childhood experiences, genetic contributors to aggression identified in adults were meta-analysed with a childhood ADHD sample of 769 children from International Multicentre ADHD Genetics (IMAGE) study. Gene-based and pathway analyses were performed to gain insight into cumulative genetic effects and biological processes behind aggressiveness in ADHD. No single polymorphism reached genome-wide significance. The strongest signal was observed at rs10826548 on chromosome 10 (beta = -1.66, standard error (SE) = 0.34, p-value = 1.07E-06), closely followed by rs35974940 in neurotrimin (NTM) gene (beta = 3.23, SE = 0.67, p-value = 1.26E-06). Pathway analysis implicated the NF-kappa-B transcription regulating protein complex (p=7.16E-04). Taken together with previous findings, our results point to a spectrum of biological mechanisms, such as cell adhesion, transcription regulation and inflammation, underlying aggressiveness in ADHD and providing targets for further genetic exploration of this complex trait across the traditional diagnostic boundaries of psychiatric disorders.

Keywords:
Genetic neuroscience
Molecular neuroscience
Cellular neuroscience

Morphine effects on reward processing in healthy humans: an fMRI study

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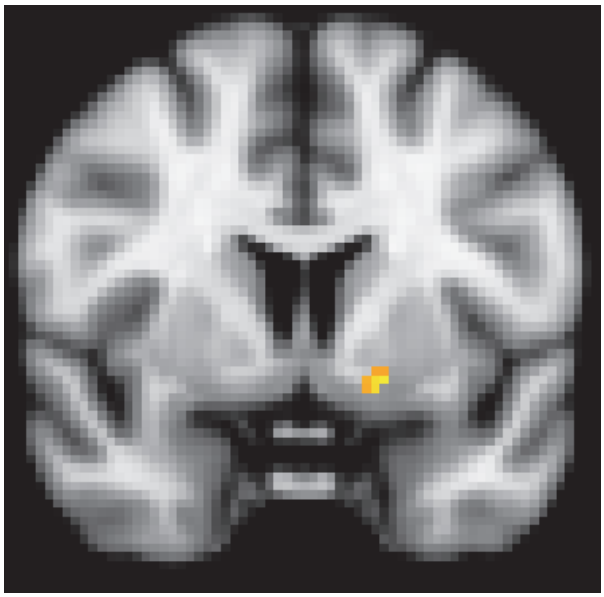
The mu-opioid receptor (MOR) system is central to reward and pain relief across species. In rodents, injection of MORs into the striatum amplifies hedonic responses to and/or motivation for rewards. In humans, opioid agonists can induce euphoria, whereas antagonists reduce food reward. The mesolimbic reward system is rich in MORs. One established task to assess reward associated human brain activity is the monetary incentive delay (MID) task (Knutson et al., 2000). This task allows for parsing anticipatory and consummatory phases of reward. MID task activity has been shown to be sensitive to pharmacological manipulation of the dopamine and serotonin systems. In a current, ongoing fMRI study we investigate the role of MOR agonism in reward processing in healthy humans. We predicted that MOR agonism would be associated with an increase in BOLD activation to reward in the striatum. In a within-subjects, counter-balanced, double-blind design, 11 healthy volunteers received a single dose of a MOR agonist (morphine 10 mg per oral) or placebo on two separate days. 60-90 minutes post-drug administration, participants performed the MID task during fMRI. The morphine dose was chosen to activate MORs without causing sedation or euphoria. Indeed, t-tests revealed no significant differences between drug conditions on subjective reports of drug effect (M>P, p=.91), feeling high or good (M>P, p=.47, p=.89). Results from other control measures (motor coordination, respiration, and a visual checkerboard fMRI) showed no significant effects of drug condition, indicating that differences in task-related BOLD were not confounded by general drug effects on performance. In line with previous research, our preliminary results show significant activity in the ventral striatum during the anticipation and delivery of monetary rewards. Analyses of a priori regions of interest (ROIs) show an effect of cue valence on mean signal change in the ventral putamen bilaterally during anticipation of reward. The ventral striatum (putamen and NAc bilaterally) was also significantly more activated during successful trials than non-successful trials (reward outcome). Preliminary evidence using small volume correction revealed higher activation in the left ventral putamen in the morphine condition for the contrast of successful versus non-successful outcomes. Current preliminary results support a role for μ-opioids in reward processing in the striatum of the healthy brain.

Keywords:
Cognitive neuroscience and neuropsychology
Neuroimaging

See image on next page.



Voxels activated in the contrast morphine > placebo for successful vs. unsuccessful outcome, identified using small volume correction inside the left putamen (MNI coordinates: -15, 9, -6; a priori ROI). Maximum Z-score = 3.2, p<0.05.

Predicting electrical potentials (EEG) and magnetic fields (MEG) from reconstructed nerve cells

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Recording of the extracellular voltage by inserting electrodes in neural tissue is one of the main tools for measuring brain activity. Traditionally, the focus has been on extracting action potentials from the background voltage fluctuations (local field potential, LFP) that reflect a complicated orchestra of membrane potential changes in nearby cells (Buzsaki et al. Nat. Rev. Neurosci. 2012, Einevoll et al. Nat. Rev. Neurosci. 2013). Once the spikes are extracted, the rest of the LFP signal has traditionally been discarded because the biophysical properties of the dendrites and the connectivity were too poorly understood to make much sense of the LFP signal. In the past, it was thought that neuronal dendrites were passive and that active processing of synaptic inputs occurred in the soma. However, the last two decades have revealed a richer repertoire of dendritic processing. Now we know that there are also large and slow potentials occurring in the distal dendrites of pyramidal neurons, called 'dendritic spikes' (Major et al. Ann. Rev. Neurosci. 2013). These are thought to be important events that dramatically enhance the output of the cell and are thought to be important for learning and memory by regulating synaptic strength. Because there is a large Ca^{2+} influx during a dendritic spike, it is possible to use microscopy and Ca^{2+} indicators to monitor these events. These microscopy techniques are restricted unfortunately to behavior in head-fixed animals (Xu et al. Nature 2014). Ideally, it is desirable to be able to record dendritic spikes in freely moving animals. It may be possible however, that dendritic spikes can be resolved by extracellular recordings if one knew what it's 'signature' was in the LFP. To date this extracellular signature is unknown. The goal of this project is to perform simulations using realistic models of cortical pyramidal neurons, simulate dendritic spikes and study their 'signature' in the simulated LFP. We will use software such as NEURON, NEST and LFPy for this purpose. Once we have a thorough understanding of this signature, we will develop the tools to extract dendritic spike events from experimentally obtained LFP recordings in awake freely foraging mice. Thus our bold ambition is to develop an algorithm that isolates not only somatic spikes but also dendritic spikes from extracellular voltage recordings. We present the current state of the project and its future prospects.

Keywords:
Computational neuroscience and neuroinformatics

BEHAVIOURAL EFFECTS OF MULTISIZED GOLD NANOPARTICLES IN ZEBRAFISH EMBRYOS AND LARVAE

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Nanoparticles are particles with at least one dimension between 1 and 100 nm. Due to their unique properties, gold nanoparticles (AuNPs) are used for drug delivery, diagnostics and cellular imaging, but there are concerns they interfere with neuronal development. In this study, we tested for potential neurotoxic effects of AuNPs by analyzing behavioral changes in zebrafish (Danio rerio) embryos and larvae. We injected three different sizes of AuNPs (20, 40 and 80 nm) into both embryos at 2-4 h post fertilization (hpf), and larvae at 72 hpf. The AuNPs were delivered into the yolk sack of the embryos and the duct of Cuvier (i.e. the blood stream) in the larvae. Five concentrations of each AuNPs were tested in triplicate (1000, 500, 100, 50 and 10 μg/ml), all of which were below the lethal dose. Changes in behavior are a good indicator of neurotoxicity. Therefore, we used an automatic tracking system to analyze the distance travelled and time spent active in 96 hpf zebrafish. These endpoints were tested under light-dark-light photo regimes. In addition, we monitored motorneuron development using whole-mount immunohistochemistry staining for α-AT. We found that embryos injected with all three AuNP sizes showed reduced locomotor activity during the dark phase, but there was no effect in the light phase. These reductions were concentration dependent, whereby the highest doses resulted in the lowest movement. We did not find any significant interaction of AuNP size on the reduction in locomotor activity. In contrast, we found no clear response patterns in larvae injected with AuNPs at 72hpf. Here, some concentrations increased, whereas others decreased, activity levels. The results of the motoneurons development are forthcoming. These results show that AuNPs have an effect on zebrafish behavior. As the behavioral effects were more apparent and consistent following the earlier exposure window, i.e. embryos, this suggests AuNPs may interfere with the early stages of neurological development.

Keywords:
Developmental neuroscience
Neuropathology

Investigating the instantaneous transition from non-estrus to estrus in devocalized as well as vocalizing hormone-treated, ovariectomized rats housed in a semi-natural environment

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Previous studies in intact females revealed a sudden change in behavior immediately preceding the first lordosis displayed during estrus. The purpose of the present study was to determine how this sudden change occurs in ovariectomized females after sequential estrogen-progesterone treatment, and if vocalizations played a role in this transition. Five groups of 7 rats (3 males and 4 females) were housed in a semi-natural environment for 8 days. Some of the individuals were devocalized prior to experiment. Females were injected with 18 µg/kg of estradiol benzoate 48 h prior to observation and with 1 mg/rat of progesterone 4 h before observations. Socio-sexual behaviors during the 8 minutes preceding the first lordosis of each female and the 8 minutes following it were recorded. Most of the behavioral changes happened during the last minute of the pre-estrus. During the 10 last seconds of this last minute, females demonstrated an increase in paracopulatory behaviors including ear wiggling, running and darting. These behaviors were the only ones found to increase before the first lordosis. Among the last behavior performed by each female before the first lordosis, we found that 50% were paracopulatory, 33,3% sniffing and 16,7% nose-off or rejection. This pattern was found both in vocalizing and devocalized females. Also, 75% of the last behaviors were directed toward the male to whom the first lordosis was going to be displayed. Finally, the first lordosis of devocalized females appeared at the same moment that the ones of vocalizing females. In a semi-natural environment in which female herself determines whether to copulate or not, the behavioral transition from non-estrus to estrus not only is instantaneous rather than gradual, but also seems unpredictable until 10sec before the first lordosis. Because this pattern exists both in intact females and in females with induced estrus, we can conclude that the behavioral changes observed are not directly related to momentaneous changes in hormones levels. Moreover, since we did not found any behavioral difference between devocalized and vocalizing females, we can hypothesize that vocalizations do not modify male-female interactions, and especially are not involved in females attractiveness.

Keywords:
Cognitive neuroscience and neuropsychology

Relative frequencies of TOAST stroke subtype

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Introduction: Atherosclerosis, cardiac embolism and small vessel disease are the most common causes of cerebral infarction. **Objective:** We hypothesized that the relative frequencies of these causes are age dependent. **Methods:** We included all consecutive patients with acute cerebral infarction admitted to the Stroke Unit, Department of Neurology, Haukeland University Hospital between 2006 and 2012, age 15-100 years and residency in Hordaland country, Norway. Aetiology of ischaemic stroke was defined by the TOAST criteria as large-artery atherosclerosis, cardio-embolism, small vessel disease, other, and unknown. The study patients were divided in three major age groups: young (15-49 years old), middle age (50-74 years old) and elderly (≥75 years old). Relative frequencies of TOAST subgroups are displayed by mean of the lowess function. Correlation analyses were performed post hoc based on the lowess analyses adjusting for age. **Results:** In total, 2217 patients with acute cerebral infarction were included. Mean age 70.8 years (SD14.9), 1274 females (57.5%) 943 males (42.5%). 205 patients under 50 years old. Cardiac embolism is frequent among the very young and the elderly patients. Atherosclerosis declines among the very elderly. Small vessel disease is most frequent among middle age patients. This probably reflects different age dependent pathophysiological mechanisms in TOAST subgroups. C**onclusion:** Relative frequencies of TOAST subgroups are age dependent.

Keywords:
Clinical neuroscience

A study of interaction between the plasticity related protein Arc and its major regulator ERK

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Background: The immediate-early gene Arc is an important modulator in long-term synaptic plasticity and memory formation. Arc plays a role in both synaptic strengthening, synaptic weakening and homeostatic scaling. What determines when, where and with what Arc interacts? Extracellular signal-regulated kinase (ERK) serves as a regulator of Arc expression. We suggest that post-translational modifications of Arc by ERK contribute to further regulation of Arc function. **Methods:** The methodical apporach for studying arc regulation by ERK involves direct binding studies by surface plasmon resonance (SPR), functional studies in neurons and structural studies of Arc by SAXS. Imaging experiments by FRET are in progress. **Preliminary results:** Data from SPR indicates that there is a direct interaction between Arc and ERK. It seems as Arc has a DEF-domain which interacts with a specific binding site within ERK. Studies of GFP-Arc in neurons show a trend where phospho-mimicking and phospho-deficient Arc localize differently between the nucleus and cytosol following stimulation. **Discussion:** We have validated three of five novel ERK phosphorylation sites on Arc in vitro and hypothesize that Arc phosphorylation might serve as a molecular modulator which acts as a "switch" on Arc function. Arc has been suggested to have a basic N-terminal, acidic C-terminal and an unstructured middle region (Myrum et al., 2015). The predicted DEF-domain within Arc, based on in silico analysis and studies in our lab, is present within the middle of the protein. Thus, the instant structure of Arc might determine whether Arc and ERK interacts, and consequently whether Arc is phosphorylated.

Keywords:
Molecular neuroscience

Assessing treatment-induced post-stroke neuroplasticity using multimodal MRI

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A stroke is a loss of brain function due to insufficient blood supply to the brain caused by a lack of blood flow (ischemia) due to blockage (thrombosis, embolism) or leakage (hemorrhage). Impaired cognitive functions following stroke is common, yet effective rehabilitation programs are lacking. Previous studies combining cognitive training and transcranial direct current stimulation (tDCS) have shown promising results, but the mechanisms and the clinical utility remain unclear. With the ultimate goal of improving the rehabilitation and treatment programs, the aims of this randomized, controlled clinical trial is to evaluate the utility, efficacy and mechanisms of tDCS as a non-invasive and targeted method for increasing recovery after stroke. The present study comprises 3 parts: (A) Baseline, incl. clinical and cognitive assessments and multimodal MRI, (B) Intervention period of 6 weeks incl. cognitive training combined with tDCS (active or sham stimulation), and (C) Follow-up, incl. clinical and cognitive assessments and multimodal MRI. This longitudinal design will allow us to assess both the cognitive efficacy and the candidate neuronal mechanisms of tDCS in a patient-oriented clinical rehabilitation setting. Our project targets patients between 3 to 12 months post-stroke (n = 60) allowing enough time for spontaneous recovery, yet targeting a critical time window for recovery. More specifically, the following research questions will be addressed: (1) Does tDCS improve cognition and induce neuroplastic changes in corresponding brain networks in stroke patients? (2) Does tDCS enhance the effects of existing cognitive rehabilitation on long-term functional and clinical recovery after stroke? (3) Are cognitive and clinical benefits of tDCS in stroke survivors reflected in prospective neuroimaging indices of neuroplasticity?

Keywords:
Cognitive neuroscience and neuropsychology
Clinical neuroscience
Neuroimaging

High-frequency heart rate variability is associated with Catechol-O-methyltransferase mRNA levels in blood of Chronic Fatigue Syndrome Adolescents

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Catechol-O-methyltransferase (COMT) performs the metabolism of catecholamines and has vital contribution in regulation of autonomic nervous system. Chronic Fatigue Syndrome (CFS) is a long-lasting condition (more than 6 months) with unknown aetiologies. Some association studies have suggested the link between CFS and genetic polymorphisms. Moreover, underlying pathologies of CFS may stem from a neurological dysfunction that lead to persistent physical fatigue, pain and other symptoms. In order to see potential brain-body interactions driven by genetic factors that may explain disease mechanism of CFS, we analysed COMT gene expression in blood of CFS patients versus healthy control. Three COMT genotypes of one common polymorphism, rs4680 (Val158Met) and their mRNAs levels at baseline plus 30-week follow up were analysed using conventional and quantitative polymerase chain reactions (PCR) subsequently. In this report, we show that COMT expression is correlated positively with high-frequency heart rate variability (HF-RRI) at baseline. As HF-RRI is an index for parasympathetic nervous activity and COMT is an important modulator in the prefrontal cortex of the brain, this correlation may reveal more about cardiovascular neural regulation in CFS pathophysiology

Keywords:
Molecular neuroscience

Synaptotagmin I is down-regulated in the cytoplasm of CA3 area of rat hippocampus in chronic medial temporal lobe epilepsy

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Epilepsy is a common neurodegenerative disease that induces brain cell death. However, surviving neurons may show synaptic plastic changes, which may either protect against further degeneration, or may further aggravate the condition. Either way, surviving synapses hold information crucial to understanding the diseased brain. We, accordingly, investigated synapses which have survived brain cell death. We examined SNARE proteins (synaptotagmin I, SNAP-25, syntaxin-1 and VAMP2) in chronic medial temporal lobe epilepsy (MTLE) using a kainic acid (KA)-induced animal model of chronic MTLE (eight weeks after first chronic MTLE). Western blotting technique was used to examine these proteins in synaptic fractions (synaptosomes) of the hippocampus. In addition, immunogold electron microscopy was used for synaptotagmin I in glutamatergic synapses of the stratum radiatum of the CA1 and the CA3 areas of the hippocampus. Statistical analysis of the results indicated a significant down-regulation in synaptotagmin I and a significant up-regulation in VAMP2 in the chronic MTLE groups. Due to the highly significant reduction observed for synaptotagmin I as well as its role as a Ca2+-sensor, quantitative immunogold electron microscopy analysis was carried out to determine the sub-synaptic sites for this reduction. Synaptotagmin I was significantly reduced in the pre- and postsynaptic cytoplasm of CA3 area synapses. The reduction in synaptic concentrations of synaptotagmin I in the hippocampus points to an adaptive or protective measure in surviving neurons and their synapses following the initiation and spread of the seizure. These findings will be useful in understanding the molecular mechanisms underlying chronic MTLE.

Keywords:
Molecular neuroscience
Cellular neuroscience
Neuropathology

Parameter estimation and uncertainty quantification in multicompartmental neural models.

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A generic problem in computational neuroscience is to determine model parameters and uncertainties for a given model. A particular challenging feature of biological systems is that the model parameters often are regulated by the living system itself. This means that the system changes the model parameters with time. One example is the parameter describing the area density of different ion channels. This parameter is typically assumed when doing biophysical detailed neuron modeling, which has the effect of increasing uncertainties in the model. The ion channels consist of proteins, and the production of such proteins is somehow self-regulated by the system itself, presumably to maintain the firing properties of the neuron. Thus the model parameter is continuously changing. One method for estimating uncertainties in models containing parameters that can be represented by probability distributions, is polynomial chaos, a fairly recently developed mathematical framework. It is much faster than the standard Monte Carlo methods used for uncertainty quantification as long as the number of parameters is small, less than 20, which is the case for many, if not most neuroscientific models. Polynomial chaos will therefore be the method of choice when looking at uncertainties and its robustness and efficiency on uncertainty quantification for neuroscientific models will be examined. The plan is to first examine a simple biological system, the multicompartmental model for interneurons in the dorsal Lateral Geniculate Nucleus (dLGN) (Halnes et al, PloS Comp Biol, 2011), with uncertain constant parameters. The goal is to modify and enhance the conclusions in the paper by Halnes et al by quantifying the statistical uncertainties in both the model and parameters. The project then expands to examine uncertainties in a generalized class of problems containing time dependent uncertain parameters, regulated by the system itself. To solve this problem a method for modeling these kind of uncertainties in a generic way must be developed. The overall goal is to develop a toolbox for performing such uncertainty quantification on a wide variety of neuroscientific models.

Keywords:
Computational neuroscience and neuroinformatics

Intrathecal synthesis of IgM in RRMS: comparison of biological parameters and mathematical formulae

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Background: We have previously investigated the association between confirmed relapsing-remitting multiple sclerosis (RRMS) patients and levels of CSF IgM to SNOcys compared to controls. Around 70% of MS patients showed elevated levels of the antibody, with no detection in any controls. There was also an inverse correlation between anti-SNOcys levels and relapse onset, indicating a potential use as a biomarker in clinical practice. The present data examine the presence or absence of oligoclonal bands of IgM in RRMS and controls. We have also compared various mathematical formulae for calculating the intrathecal synthesis of IgM in RRMS versus controls, and compare these derived results with our antibody biomarker. **Methods:** CSF from patients with clinically-definite RRMS (n=18), was compared with CSF from patients with mild neurological symptoms (N=14). Total IgM and anti-SNOcys IgM were determined in CSF and serum using ELISA techniques and immunoturbidity. Oligoclonal bands of IgM were demonstrated in CSF and serum by isoelectric focusing and immunodetection. Sensitivity, specificity and receiver operating characteristic (ROC) plots were created to examine the ability of these parameters to accurately distinguish patients with RRMS from controls. The results were compared with those achieved by accepted mathematical formulae. **Results and Conclusions:** In this small study, the presence of even one extra oligoclonal band of IgM in CSF gave the best separation of RRMS from controls. If a cut-off of two bands was applied, several false negatives arose, though no false positives, suggesting the application of two extra bands might be too stringent. The IgM index was the most accurate of the mathematical formulae, which can be more easily applied if the demonstration of oligoclonal bands of IgM is not possible. The demonstration of at least one extra oligoclonal band in CSF may be a useful extra diagnostic tool for MS.

Keywords:
Molecular neuroscience
Clinical neuroscience

Removal of perineuronal nets in the visual cortex leads to a reduced inhibition and mimics critical period plasticity

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During postnatal development, the sensory cortices undergo a period of heightened plasticity. In primary visual cortex (V1), this critical period (CP) is initiated by the maturation of parvalbumin expressing (PV+) inhibitory neurons. Towards the closure of the CP the PV+ cells become enwrapped in a dense extracellular matrix called perineuronal nets (PNNs) which contributes to restriction of plasticity in the adult. The PNNs are thought to act out this function by stabilizing synaptic connections and facilitating the high spiking activity of PV+ cells. Removing the PNNs in adult animals with the enzyme Chondroitinase ABC (chABC) restores plasticity levels comparable to that of juveniles. It remains unknown how the PNN degradation allows for plasticity, and how individual neurons change over time during activity-dependent plasticity. We addressed this by degrading PNNs in V1 of adult rats (by local injections of chABC) and conducted extracellular recordings in freely moving animals of single-unit and ensemble activity using chronically implanted tetrodes. Degradation of the PNNs caused a reduction in activity of putative inhibitory neurons and a subsequent increase in activity of putative excitatory neurons. This held true both in the spontaneous and visually evoked states. In order to induce activity-dependent plasticity we used monocular deprivation (MD) for five days. In chABC treated animals, this produced a shift in OD while no effect was seen in controls. Longitudinal recordings of the same neurons revealed dramatic effects of MD, and a difference in time-course for plasticity between neurons in the ipsi –and contralateral hemispheres to the deprived eye. Recordings in adult controls showed a period of homeostatic regulation of activity within the first 48 hours of MD, before the activity stabilized at baseline levels. We also investigated how the local field potential (LFP) was affected by MD. The MD did not affect LFP in control animals, but immediately induced activity in the gamma-band (55-60 Hz) in chABC treated animals. This persisted for at least 30 minutes after eye closure, and could not be detected at any later point. In summary, degrading the PNN in adult rats mimics CP plasticity by shifting the inhibition-excitation balance. A brief period of sensory deprivation after PNN removal causes profound changes in neuronal activity, while adult controls display a brief period of homeostatic regulation of activity.

Keywords:
Molecular neuroscience
Systems neuroscience

Cerebellar volumes and psychiatric disorders in VLBW adolescents

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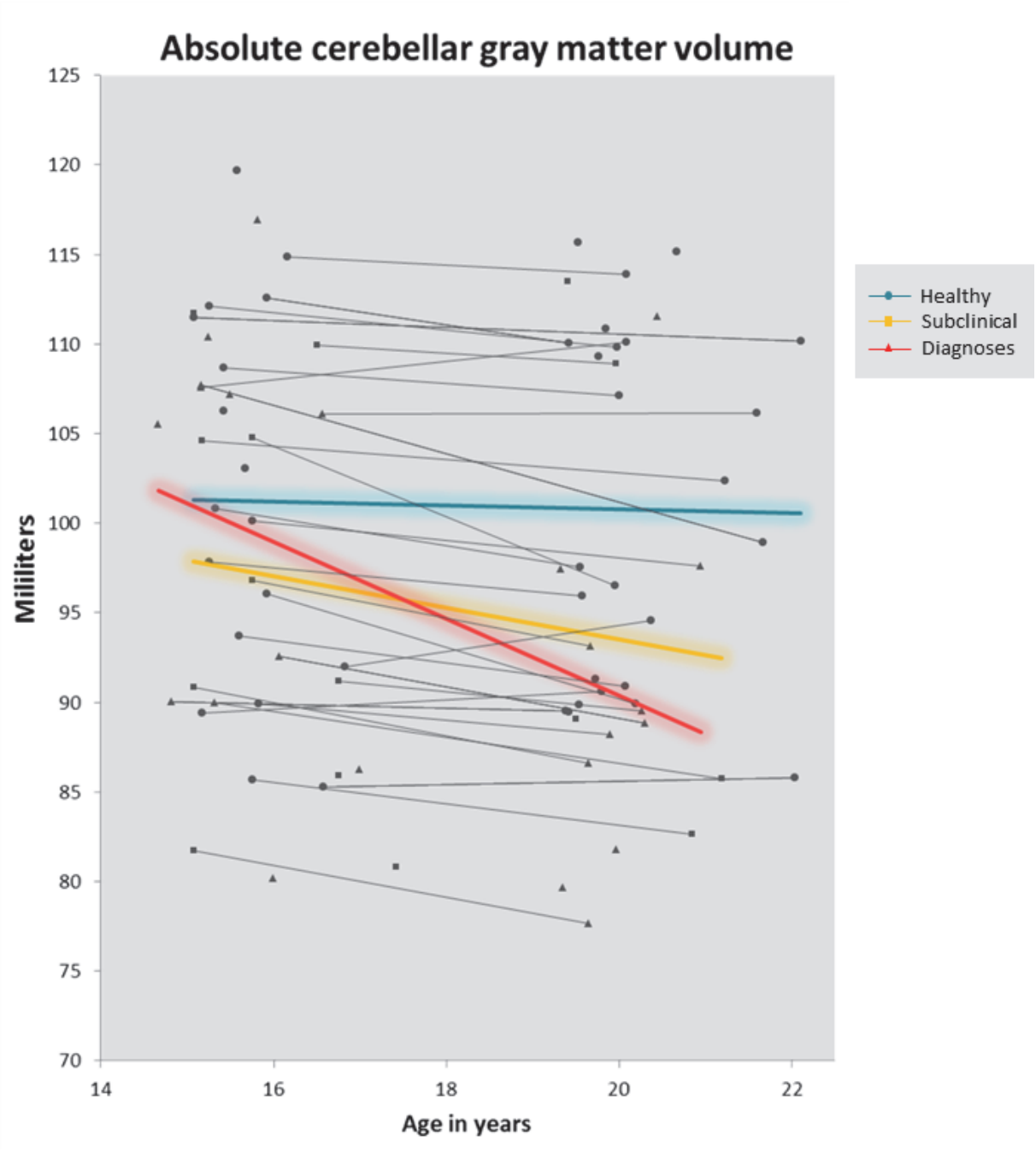
Background: Premature birth poses a risk for cerebellar injury. The cerebellum has been linked to psychiatric disorders. Higher rates of psychiatric disorders have been reported in adolescents born preterm. **Aim:** To assess whether psychiatric symptoms and diagnoses are associated with deviations in cerebellar grey and white matter (GM, WM) volume in very low birth weight (VLBW) adolescents. **Design/Methods:** Forty VLBW (birth weight ≤1500g) and 56 term born control adolescents were assessed at 14 years of age, and 44 VLBW and 60 controls were assessed at 19 years of age. Psychiatric diagnoses were assessed with diagnostic interview (Schedule for Affective Disorders and Schizophrenia for School-Age Children) and categorized in three levels: diagnosis, subclinical diagnosis (symptoms ≥75% of diagnostic criteria), and healthy. Cerebellar volumes were obtained using an automated MRI segmentation technique (Freesurfer). Associations between psychiatric diagnoses and cerebellar volumes were calculated by ordinal logistic regression. Analyses were adjusted for age, gender and total intracranial volume. Longitudinal associations were calculated with mixed linear models correcting for gender and total intracranial volume. **Results:** VLBW had higher rates of psychiatric diagnoses than controls both at 14 and 19 years, and more subclinical diagnoses at 14 years. They also had smaller cerebellar WM volumes than controls at both time points. In the VLBW group at 14 years of age, having higher rates of psychiatric diagnoses and subclinical diagnoses was associated with smaller left cerebellar WM volume OR=1.42 (1.001 to 2.006) p=0.047 per 1 ml decrease in volume. At 19 years, having higher of rates psychiatric diagnoses and subclinical diagnoses was associated with smaller cerebellar WM and GM volume (left WM OR=1.88 (1.041 to 3.380) p=0.036, right WM OR=2.33 (1.168 to 4.655) p=0.016, left GM OR=1.33 (1.083 to 1.626) p=0.006, right GM OR=1.29 (1.064 to 1.561) p=0.010 per 1 ml decrease in volume). There was a trend of association between having more psychiatric diagnoses and subclinical diagnoses with the reduction of cerebellar GM over time. **Conclusion:** Psychiatric diagnoses in VLBW adolescents seem to be associated with smaller cerebellar WM volume, and possibly with cerebellar GM loss over time.

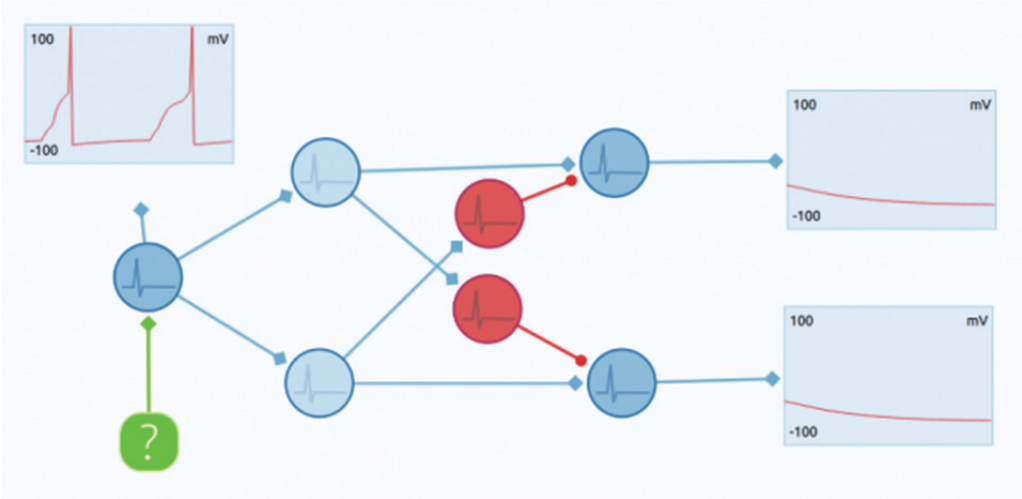
Keywords:
Clinical neuroscience
Developmental neuroscience

See image on next page.



Cerebellar gray matter volume change from 14 to 19 years of age in VLBW according to diagnostic severity. VLBW: Very low birth weight.

Neuronify: Neural networks in an app



At this year's conference, we present Neuronify, an app that runs simulations of neural networks on mobile phones, tablets and laptops.

Neuronify is an educational tool meant to give intuition for how neurons and neural networks behave. You can use it to combine neurons with different connections, just like the ones we have in our brain, and explore how changes on single cells lead to behavioral changes in important networks.

To build and explore neural networks, you drag neurons and measurement devices onto the screen. In addition, the app comes with several ready-made simulations for inspiration.

We aim to provide a low entry point to simulation-based neuroscience. Most undergraduate students don't have the computational experience to create their own neural simulator. These students should also have the opportunity to build up their intuition by experimenting with neural phenomena.

Neuronify is based on an integrate-and-fire model of neurons. This is one of the simplest models of neurons that exist. It focuses on the spike timing of a neuron and ignores the details of the action potential dynamics. These neurons are modelled as simple RC circuits. When the membrane potential is above a certain threshold, a spike is generated and the voltage is reset to its resting potential. This spike then signals other neurons through its synapses.

Neuronify will soon be available on App Store and Google Play. While it is still in heavy development, an early preview is available for Windows, Linux and OS X at cinpla.org/neuronify/

Svenn-Arne Dragly, Andreas Solbrå, Simen Tennøe, Milad Mobarhan
Centre for Integrative Neuroscience, University of Oslo

The Norwegian Research School in Neuroscience (NRSN) was established in 2013 in order to coordinate and improve neuroscience training activities that are available for PhD candidates in Norway. Our aim is to help YOU achieve high-quality research training in your own area of specialization and hereby get the most out of your PhD project.

NRSN is a collaboration between four universities, Norwegian University of Science and Technology (NTNU), University of Oslo (UiO), University of Bergen (UiB) and Norwegian University of Life Sciences (NMBU), that all contribute with their specific expertise to provide a broad and diverse neuroscience training program. Courses are organized as condensed courses or modules and are available for all PhD candidates in Norway. NRSN also offers travel- and accommodation grants for members who participate in external courses, and organizes events such as the annual PhD conference to stimulate national networking and interdisciplinary exchange.

Membership in NRSN is open to all neuroscience PhD candidates who are working at a Norwegian institution, including research program medical students. The primary target group is PhD candidates from the partner institutions (NTNU, UiO, UiB, NMBU), but also candidates from other Norwegian institutions working in relevant fields are eligible.

As a member of NRSN you have access to all NRSN activities and will benefit from our various grants:

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- **Annual conference** – organized by and for PhD candidates
- **Summer school** – intensive, targeted courses with international faculty
- **Training in transferable skills** – courses in e.g., scientific writing, innovation, communication
- **Travel- and accommodation grants** – available to all members who participate in our activities
- **Funding for course organizers** – development of new PhD courses and seminars

Our activities should be seen as a supplement to the existing PhD programs at the partner institutions. Registered members keep all formal affiliations to their own university, and the candidate's own university is responsible for the formal approval of a course into the educational component of the PhD degree.

NRSN is funded by the Research Council of Norway. The daily management is hosted by the Faculty of Medicine, NTNU. All partner institutions are represented in the NRSN Board.

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