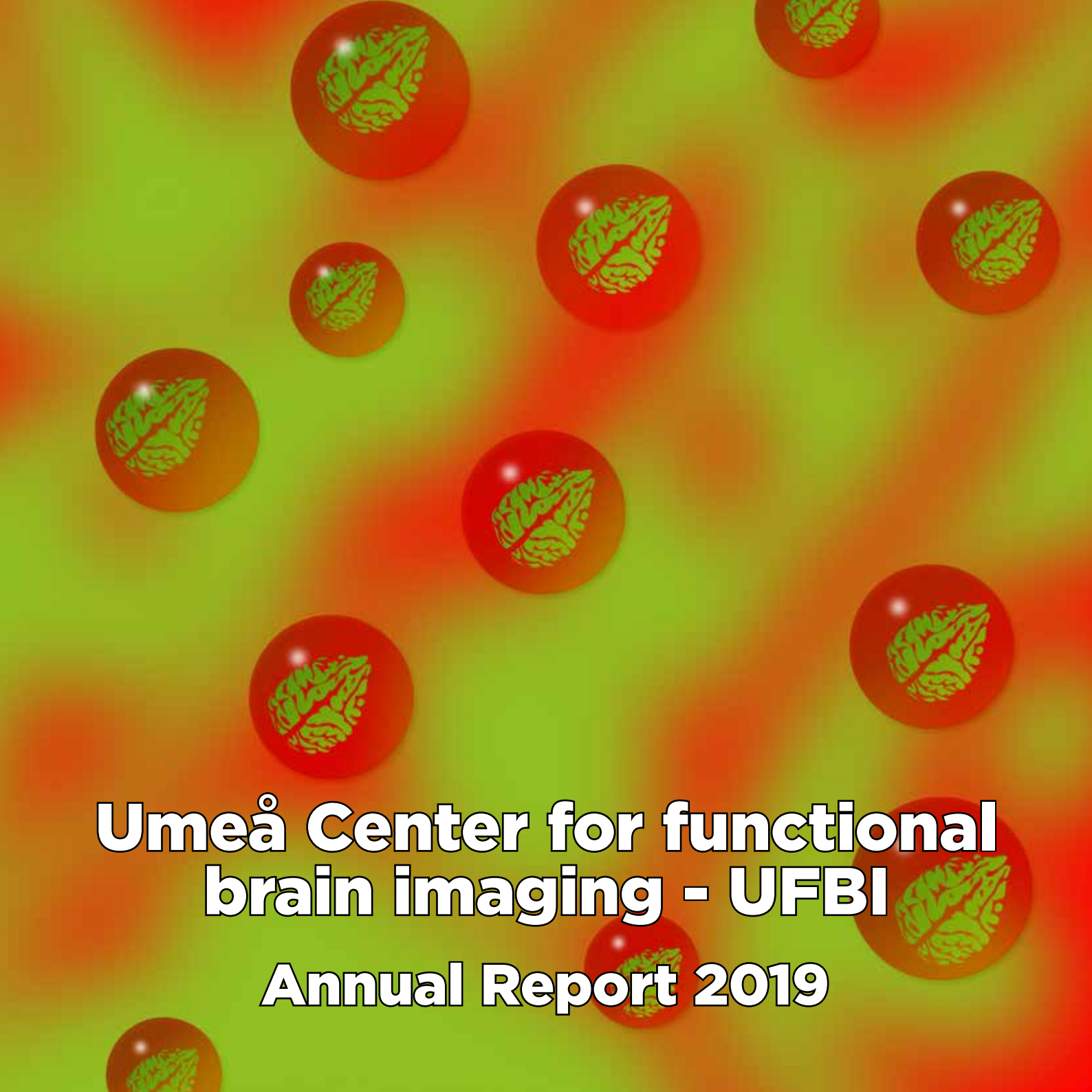

Umeå Center for functional brain imaging - UFBI

Annual Report 2019

UFBI
Umeå center for
Functional Brain Imaging

UFBI 2019 Annual Report

Editor: Lars Nyberg. **Layout:** Mikael Stiernstedt. **Cover:** Mikael Stiernstedt. **Photos:** Mikael Stiernstedt (if nothing else is specified). **Paper:** Munken Kristall 300g (cover), Munken Kristall 100g (insert).

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Welcome to the Annual Report for 2019!

I write this editorial in a hotel room in Denver, where I have presented at the 48th Annual Meeting of the INS and where I just listened to a session on international collaboration within the ENIGMA consortium. It felt nice to see the world-wide map of participating sites and note a marker very far north, representing the UFBI and Betula contributions. This is only one of several examples of our work being part of, and having an influence on, the international research community. In this report you will get several additional examples, such as many meeting presentations by UFBI researchers, organization of our own meetings with international speakers, and participation in the Lifebrain Horizon 2020 consortium (described by Sara Pudas). We also have strong links to other national research groups, not least to KI in the context of the Cobra consortium (described by Nina Karalija) and also by the recent appointment of UFBI researcher Karolina Kauppi as assistant professor at KI (in this report you can read her report from the "night train").

The scanning activities continue to be intense. In the "In short" section you will see numbers attesting to this; on both the MRI, the PET-CT, and the PET-MRI scanners. Also, you will find 25 publications from UFBI in 2019, and Anders Wåhlin zooms in on one of them. The start of new projects, such as the HIT Study described by Emma Simonsson, promises that we will have strong publications also in the years to come.

We continue to have our regular, monthly UFBI lab meetings, and they are very well attended. Many students at different levels participate, and a highlight in this year's report is the 10 PhD dissertations that in whole or in part were based on UFBI scans. Congratulations to all the new doctors!

I look forward to an interesting and stimulating 2020. With all the competent staff and scientists that work and collaborate here, it is a true pleasure to serve as the UFBI director.

Lars Nyberg, February 2020
UFBI Director (2001 - Present)

In short

In 2019 the members of UFBI produced:

25 articles

10 disserations

1005 fMRI-scans

6 PET-MR UFBI research scans

1103 clinical MRI scans

15 conference talks/posters

15 clinical fMRI-scans

140 PET-CT UFBI research scans

Research

The Umeå High-Intensity Training Study

The Umeå High-Intensity Training Study (Umeå HIT) is a randomized controlled exercise-trial with an interdisciplinary approach. With this study we are continuing the strong tradition of exercise interventions at UFBI and in this project we are teaming up with the Physiotherapy department here at Umeå University. The goal is to further explore and expand our knowledge regarding the beneficial effects of exercise among older individuals, and here we are particularly interested in high-intensity exercise. So, by turning the intensity up our aim is to evaluate the effects of short-duration supramaximal high-intensity interval training (HIT) among older adults on health factors known to decline with aging, such as cardiorespiratory fitness, metabolic processes as well as structural and functional brain changes.

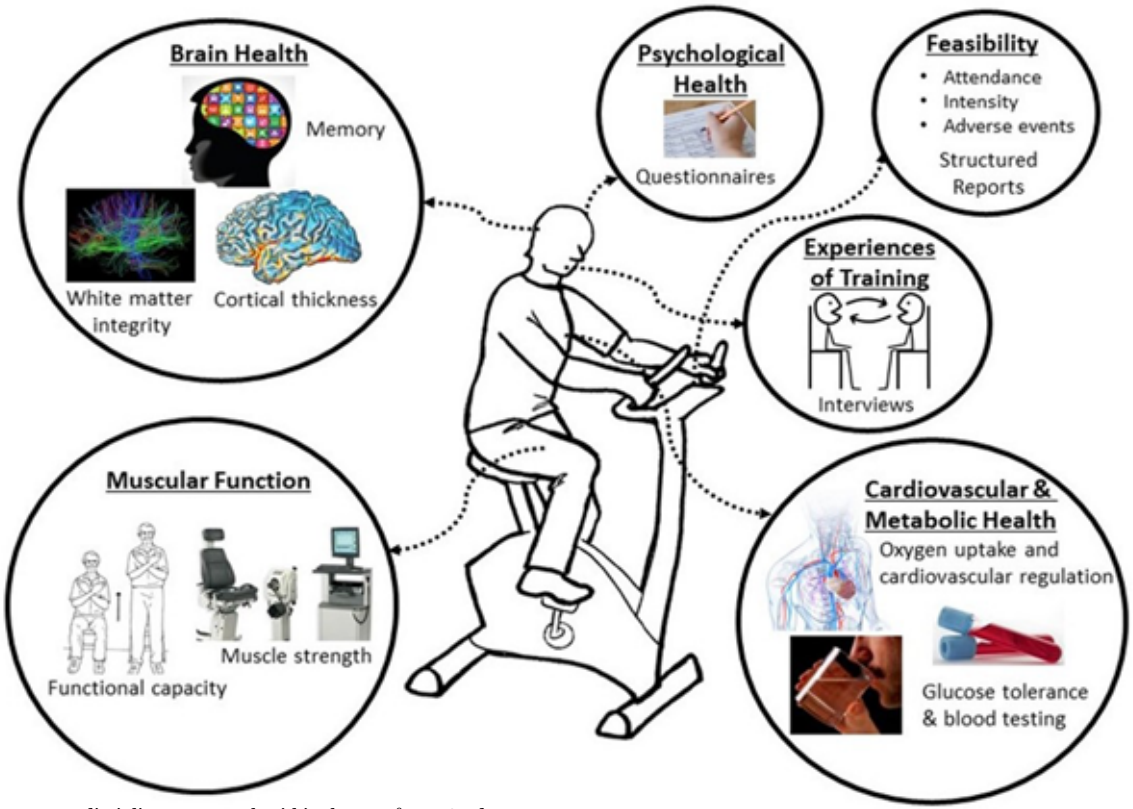
Assessment of cognitive functions derives from the test battery used in another UFBI-study, PHIBRA. We test several cognitive domains such as executive function, processing speed, episodic memory and visuospatial abilities. We also collect both structural and functional MRI, including the face/name-task from Betula, to examine hippocampal function with the paradigm of pattern separation and pattern completion. By making a link to both PHIBRA and Betula, we believe that we will have better possibilities to understand the role of exercise for healthy brain aging.

The Umeå HIT project has a parallel design consisting of two groups that differs in their aerobic exercise-protocols. The HIT-group consists of 10 repeated 6-second cycling sprints at an individualized target load around 300% of maximum aerobic power output (MAP), with 1 minute of recovery in between. The MICT-group (moderate intensity continuous training) consists of 3 x 8-minute cycling intervals in a moderate intensity (≤ 60% of MAP), which today is the more common recommendation of exercise intensity for older individuals. Both HIT- and MICT-groups exercise twice weekly for 12 weeks at IKSU in groups of 8-10 people. All sessions are being guided by an interval timer displayed on a projector and supervised by a Physiotherapist and a Sport Scientist. Some of the key factors of our HIT-protocol are the standardized pedalling cadence for all participants, while resistance is individualized (based on baseline tests of individual capacity), together with controlled and systematic adjustments of training intensity following standardized escalation criteria based on both objective and subjective measures.

On the 2nd of January 2019 I started as a PhD-student within this project and only five days later our first participants were tested. From that point it has been a busy year consisting mostly of data collection and exercise interventions. In total, we have included 68 participants (66-78 years of age, females = 38). When this text goes into print we have managed to complete 200 exercise sessions (me myself attending almost all of them) and, crazy as it may sound, to be able to control the individualized exercise intensities we have validated the watt-bikes at IKSU approximately 1700 times. I am quite confident to say that during my first year as a PhD-student at least I have become a master expert on pedalling at the cadence of 60 and 85 rpm.

Soon, all groups have completed both baseline and 3-month follow-up assessments, and during 2020 we will finish the last part of our 9-month long term follow-up. Then (finally) we get to start digging in to all of the data that we have collected and hopefully get to share some interesting results. I also look forward to finally have the time to attend the UFBI-meetings, aiming to correctly pair the faces and names of the UFBI-team!

Emma Simonsson



Interdisciplinary approach within the Umeå HIT Study. *Illustration: Nina Lindelöf*

Photo: Mattias Pettersson

A HIT-program exercise session taking place in IKSU.

Studies of the dopamine-cognition link in older adults: insights from COBRA

The dopamine (DA) system has been described as one of the most age-sensitive networks of the brain. This statement finds support from nearly 100 independent studies, demonstrating reduced DA neurons and receptors as a function of age (Karrer et al., 2017). Research has further demonstrated that attenuated DA transmission is accompanied by reduced cognitive performance. Consequently, age-related DA decline has been suggested to underlie cognitive malfunction, such as memory impairment (Bäckman et al., 2006).

On this background, the Cognition, Brain, and Aging (COBRA) study was launched by researchers at UFBI (Lars Nyberg & Katrine Riklund), Karolinska Institute (Lars Bäckman & Martin Lövdén), and the Max Planck Institute in Berlin (Ulman Lindenberger). COBRA was designed to estimate (i) longitudinal decline of the DA system and in brain structure and function, (ii) links among DA and various brain measures in relation to cognition, and (iii) effects of genetic and lifestyle factors on such relationships. The baseline data collection was finished in the summer of 2014 (n=181 healthy adults, age: 64-68 years). During 2019, a number of articles were published with findings from the cross-sectional data.

One of the most recent articles focused on associations among cardiovascular-related factors and neurocognitive status. Lesions in the white-matter is considered a manifestation of small-vessel disease and cardiovascular dysfunction. We demonstrated that DA D2-receptor levels in two brain structures central for episodic memory, the caudate and the hippocampus, were reduced in individuals with more lesions in the white matter. In individuals with large lesions, DA D2-receptors as well as episodic memory reductions were evident (see Figure). Furthermore, individuals with higher risk of cardiovascular disease (estimated as risk profiles from hypertension diagnosis, blood pressure, smoking, and body-mass index) had more lesions, but also, reduced cortical blood flow and volume, striatal D2-receptor levels, and poorer episodic memory performance (Karalija et al., 2019b). These findings highlight the importance of cardiovascular health in relation to brain maintenance at older age.

Human behavior is modulated by numerous factors. The scarcity of studies with multimodal designs and the limited sample sizes of in vivo DA studies (< 30 individuals at average; (Karrer et al., 2017)) have left us with gaps in knowledge for how interactions among DA integrity and other factors predict cognitive performance. Studies of genetic variation in COBRA has demonstrated that high D2-receptor availability characterizes high-performing individuals. Yet, the nature of this link depends on other factors as well, including variation in genes regulating levels of neurotrophic factors (Papenberg et al., 2019a) and endogenous DA (Karalija et al., 2019a; Papenberg et al., 2019b). These and other COBRA findings are all important insights, especially when considering that e.g. studies of genetic variation are rare due to the lack of statistical power of in vivo DA studies.

The 5-year follow-up data collection for COBRA was finished in early summer of 2019. In the near future, we will be able to provide the first longitudinal analyses that will test the accuracy of cross-sectional estimates of annual DA decline rate and the hypothesized link to cognitive decline in aging.

Nina Karalija

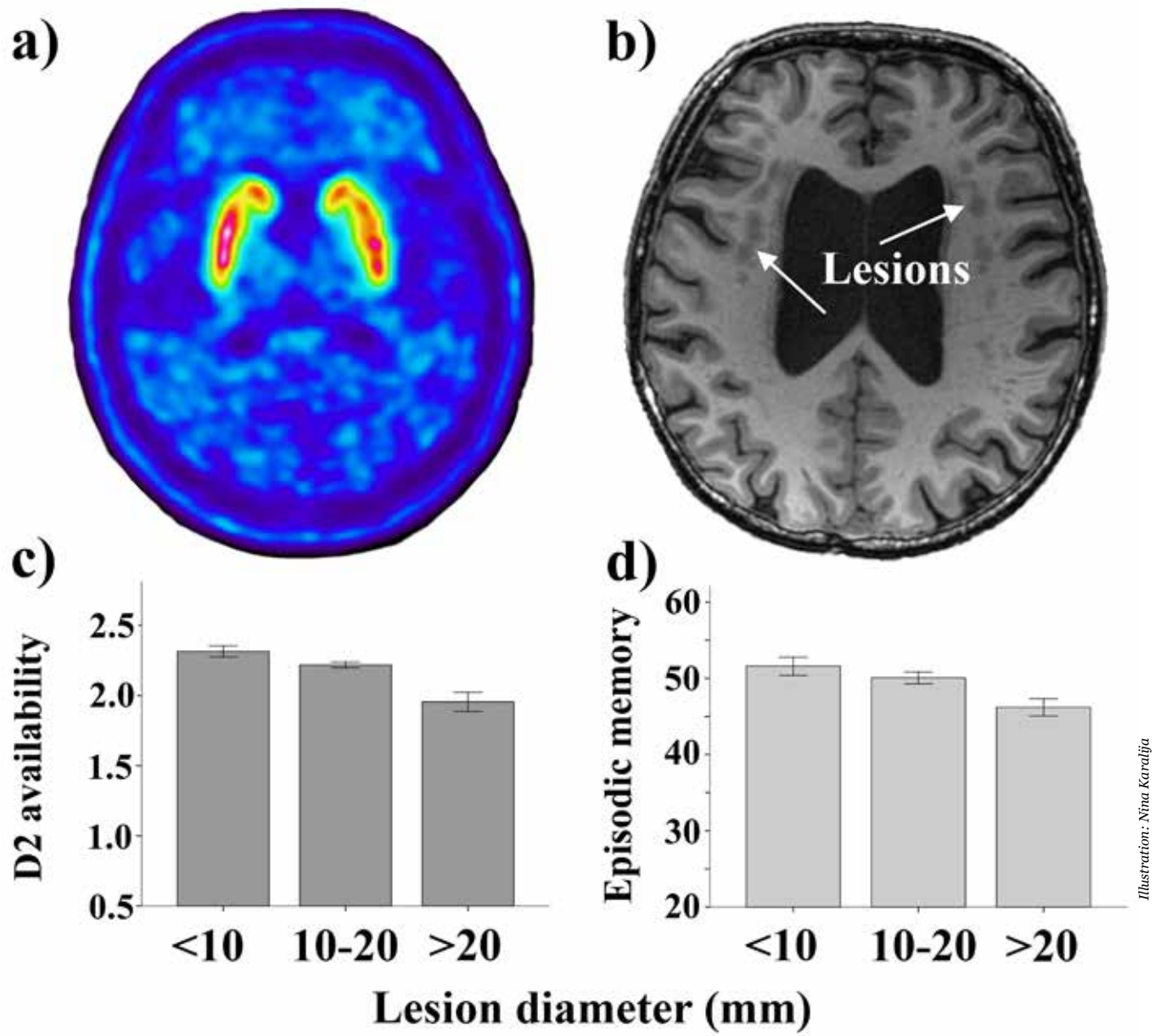


Illustration: Nina Karadija

Positron emission tomography with the ligand 11C-raclopride and magnetic resonance imaging was performed to assess D2-receptor availability (a, high uptake is illustrated with red/yellow), and lesions in the white-matter (b). Increased lesion burden was associated with reduced caudate D2-receptor availability (c) and episodic memory performance (d).

Zooming in

At the heart of cognitive functioning in aging

Wåhlin, A. & Nyberg, L. (2019). At the Heart of Cognitive Functioning in Aging. Trends in Cognitive Sciences, 23(9), 717–720.

Multiple lines of evidence highlight that vascular health plays an important role in brain aging. Hypertension and pulse pressure increase risk of cognitive decline and dementia and fragments of injured capillary cells are found in the cerebrospinal fluid in dementia patients early in the disease course.

In our forum article "at the heart of cognitive functioning in aging" (Wåhlin and Nyberg, Trends in Cognitive Science, 2019) we integrate recent literature and propose a model that brings together a plethora of observations that we think collectively reveal a chain-of-events that starts with the heart and great vessels and ends at cognitive abilities that might be early affected. We also describe a series of imaging experiments that could be used to address particular hypotheses postulated by the model.

With aging and accumulation of vascular risk factors the arterial system deteriorates and threatens the brain by multiple harmful mechanisms. A relatively unexplored pathway involves the changes that occur in blood flow dynamics over the cardiac-cycle. As arteries become stiffer it alters the flow in more distal vasculature to become less smooth. Such exposure to aberrant flows and pressures can contribute to the age-dependent breakdown of the highly specialized brain capillary. The capillary blood-brain barrier consists of a layer of tightly connected endothelial cells that restricts passage of blood derived pathogens to the brain tissue. Surrounding the endothelial layer are pericyte cells that only recently have been shown to regulate capillary responses to neural activity and initiate, by upstream signal propagation, the vascular responses in arterioles. This arrangement of cells is damaged if the capillary pulse pressure becomes too large. Specifically, animal experiments have revealed that such aberrant forces cause the blood brain-barrier to become leaky, and that the vascular regulation capacity is compromised. Perhaps owing to proximity to large feeding vessels, the hippocampus vasculature appears particularly sensitive to such increased blood flow velocity amplitudes.

Old individuals with cognitive impairment display a leaky blood-brain barrier in the hippocampus as well as cerebrospinal fluid protein pathology indicative of pericyte loss. Inspired by in vitro and animal studies, we think that such damage in humans can be a consequence of accumulated vascular risk factors causing vascular remodeling and excessively violent blood flow velocities in the capillaries. Hippocampal pericyte loss should be particularly damaging to episodic memory since episodic memory relies on specialized circuitry in the hippocampus and since that circuitry operates in a manner that requires sustained pericyte-dependent vascular upregulation to support its metabolically demanding processes. Therefore, we think that future studies should zoom in on the links between vascular factors, arterial hemodynamics and hippocampus-dependent episodic memory, and structural and functional markers of hippocampal integrity.

To follow up the outlined model we are now in the process of developing and applying methodology that enables accurate estimations on the hemodynamics in cerebral vasculature. In a recent publication

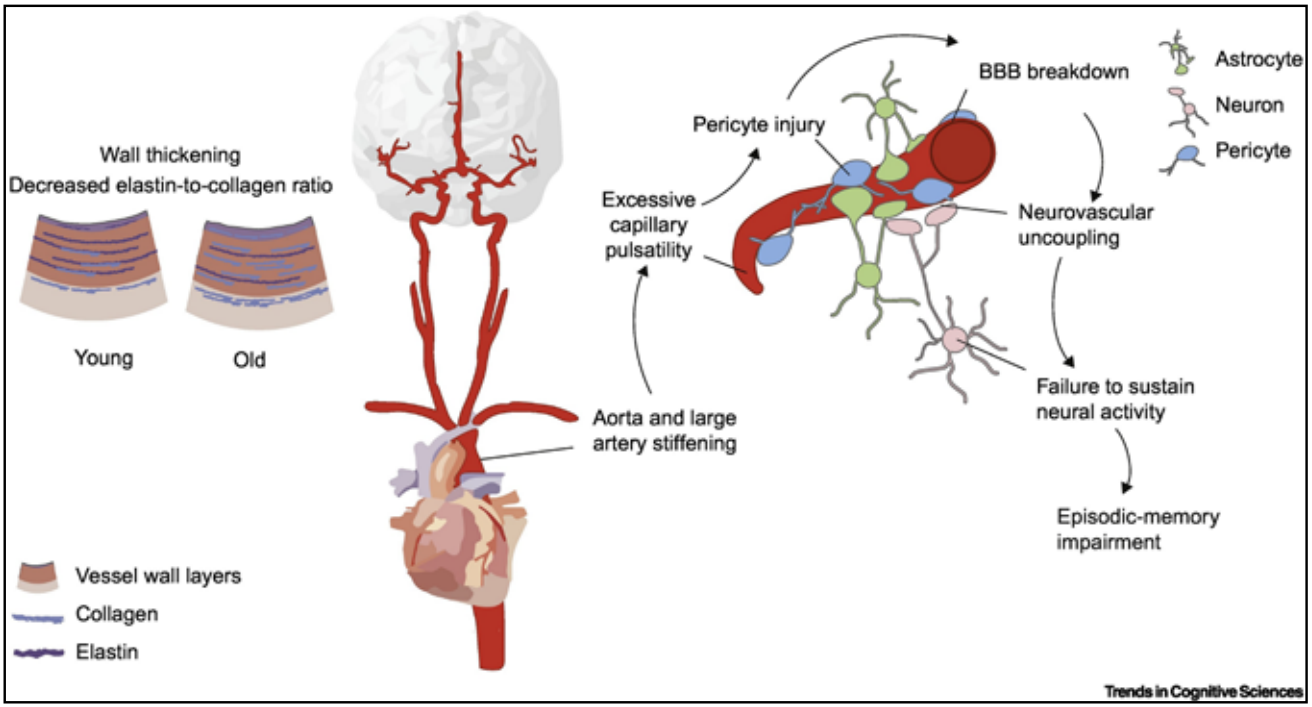


Illustration: Anders Wåhlin

(Vikner et al., Journal of Cerebral Blood Flow and Metabolism, 2019) we describe a 4D flow MRI approach of characterizing blood flow in vessels too small for conventional post-processing. The methodology boosts signal to noise ratio by applying signal averaging in the longitudinal direction of tortious small arteries, and by combining data from similarly sized arteries into one composite measure.

Hopefully such novel approaches can help to determine how changes to the arteries may trigger brain deterioration. In addition, the vascular abnormalities outlined in our model presumably develop over a long time period, so methodology enabling early detection will be instrumental in order to be able to initiate interventions in time.

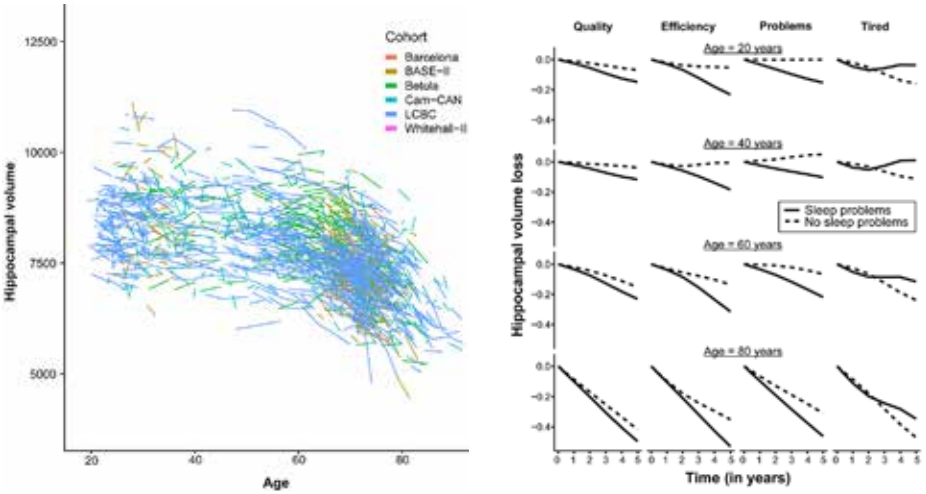
Anders Wåhlin

Lifebrain collaboration progress

UFBI participates in the Lifebrain consortium, funded by EU's Horizon 2020 programme. This collaborative effort between eight universities and research centers across Europe aims at unravelling environmental-, lifestyle-, and social determinants of brain, cognitive and mental health across the human lifespan. During 2019, UFBI participated in two published Lifebrain studies. The first targeted the important lifestyle factor sleep, and its potential impact on atrophy in the hippocampus, an important brain structure for our long-term memory ability – especially as we age. The study combined data from six European study cohorts where the 1 299 participants, aged 18-90 years, had both provided self-reported assessments of various aspects of their sleeping habits, and had structural MRIs on one or multiple occasions. The results showed that accelerated hippocampus volume loss over time was related to several aspects of sleep, particularly to worse sleep quality and efficiency, and more self-reported sleep problems, and to a lesser extent to daytime tiredness. While significant, the effect of sleep was relatively modest in magnitude, and did not differ across different parts of the lifespan (see Figure below).

Another important aim of Lifebrain is to investigate the general public's perceptions about their brains and about brain health, in order to inform authorities that develop public policy recommendations for helping people to better take care of their brains. As a first step towards this aim a recent Lifebrain study reported findings from in-depth individual interviews with 44 participants aged 18-70+ from Lifebrain's study cohorts in Spain, Norway, Germany, and the United Kingdom. The study showed that the interviewed participants generally did not focus much on their brain health, and felt uncertain of how to best maintain it. However, the participants did express interest in learning more about brain health and about half of them were even interested in taking personalized brain health tests for risk of developing neurological diseases. Many participants stated willingness to make lifestyle changes to maintain brain health, if they knew that they were at increased risk for developing brain disease, but desired personal guidance in doing so, and emphasized the importance of knowing that the lifestyle change was backed by scientific evidence. These findings stress the importance of health authorities making scientific knowledge on brain health easily available to the public.

Sara Pudas



Left panel shows age-related hippocampal volume across all participating research sites (y-axis indicates hippocampal volume, x-axis indicates age). Right panel shows the effect of self-reported sleep problems on intra-individual volume loss across 5-years of follow-up in four different age groups.

Illustrations: Øystein Sørensen

Thoughts from the night train

In October 2019 I started a part-time position as an assistant professor at Karolinska Institutet, Dep. of Medical Epidemiology and Biostatistics (MEB). Since then, I share my time between Umeå University (IMB) and KI. Such shared position fits nicely into my translational line of research, where I use and integrate methods from several domains of research, including brain imaging, population genetics, epidemiology/ cohort studies, and systems biology. The two institutions complement each other nicely; while UFBI constitutes an excellent platform for brain imaging research, MEB is a strong research environment for human population genetics and epidemiology. As a MEB researcher, I have access to valuable analytical and technical support in biostatistics and genetics that I can also use for guidance when dealing with the genetics data I work with in Umeå. I also find it highly stimulating to move between those two different research environments, where people have diverse background and competence profiles.

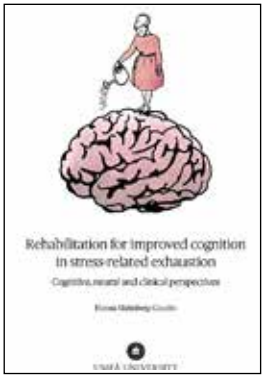
Broadly, my research concerns the genetics and biological mechanisms of cognitive impairments in aging and neuropsychiatric diseases, primarily schizophrenia and Alzheimer's disease. I study how gene variants or genetic scores associated to complex diseases and trait impact endophenotypes of the disease and phenotypes that may be genetically related, for example cognitive test performance, biomarkers and clinical data – as well as underlying brain function and structure. I also study the biological relatedness of diseases and traits through gene networks, and explore how disease genetics can be used to inform the selection of candidates for new drugs target, or for personalized medicine. The results from those studies also have potential for follow-up using brain imaging and behavioural data. In Umeå, I work with genetic, imaging and cognitive data primarily from the Betula project together with my PhD student Elise Koch and my postdoc Sofia Håglin. Elise is currently using the Betula fMRI data to study how schizophrenia genetics impact memory related brain functioning, and Sofia is studying genetics of Alzheimer's disease and hippocampal functioning. These projects will be linked to studies of how disease genetics impact cognitive decline in Betula, as well as biological aging markers of disease genetics. At MEB, I am now recruiting a postdoc that will work with longitudinal data on cognitive and biological aging from the Swedish twin registry. When possible, I aim to run analyses in both Betula and the twin registry for replication purposes.

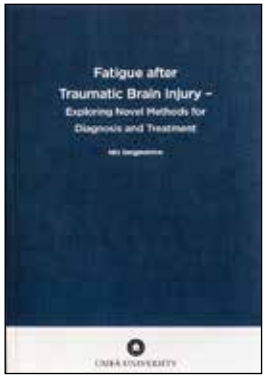
Another advantage with the shared position is that it opens up for more collaborations in general. Every now and then I support and collaborate with researchers that are interested in incorporating genetic analyses in their projects, both within UFBI, Betula, and with others at IMB. Communicating in person rather than through email is always easier, and I am happy to find that the new position has already enabled me to meet up with researchers in Stockholm that are interested in genetics of brain imaging phenotypes in Betula to provide guidance and ideas. I hope there will be more such opportunities for my presence in Stockholm to benefit also others in the community, and that my affiliation to MEB will enhance the genetics research within Betula, and the 'imaging genetics' research in UFBI!

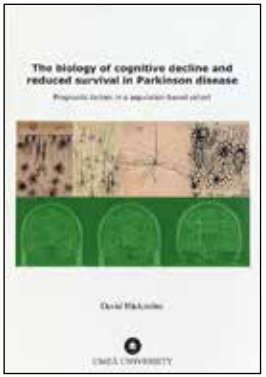
Karolina Kauppi

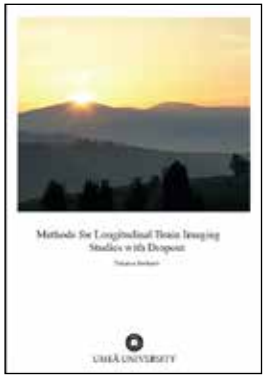
Dissertations

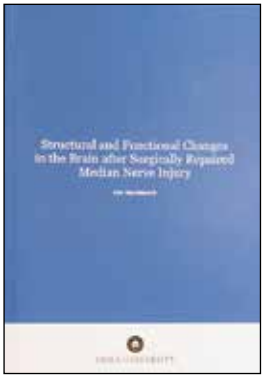
2019 was a record year when it comes to the number of dissertations that originated or was in some way connected to UFBI. Eight of them were based here at Umeå University and two were from Karolinska Institute (that in part used data that was collected here in Umeå, as well as beeing co-supervised by Lars Nyberg). In this section, you can read some thoughts, experiences and reflections that the PhD-students have had during their journey. For a list of all dissertations, see page 22.

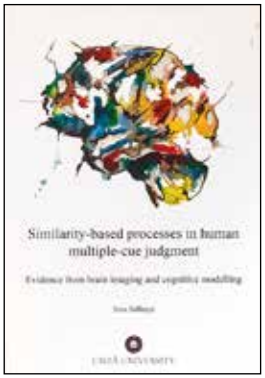


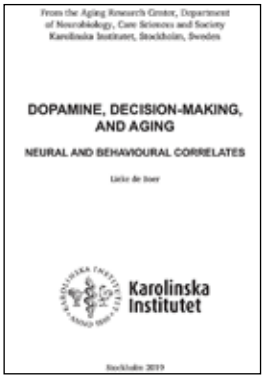


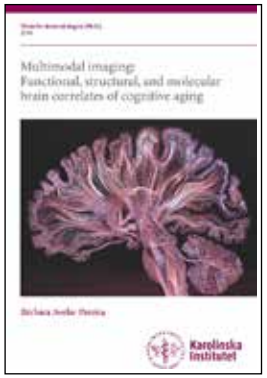












Fatigue after traumatic brain injury

During 2012 we started to plan a clinical project at the Neuro-rehabilitation clinic at the Northern University Hospital where I had been working as a psychologist for a few years. At start of the study in 2013 I had the possibility of starting my new career as a PhD student, a decision that would take me on an unforgettable journey.

The first study was a randomized, double-blinded, placebo-controlled clinical trial of monoaminergic stabilizer OSU6162, aimed at fatigue after traumatic brain injury. Study II investigated whether functional magnetic resonance imaging could be used to capture post traumatic brain injury fatigue. In study III, we used what we had learned from study I and II, and examined the effects of OSU6162 on functional magnetic resonance imaging data in yet another clinical trial. Finally, study IV investigated the relationship between damage in white matter of the brain, so called white matter hyperintensities, and fatigue or cognitive dysfunction after traumatic brain injury.

After almost 6 years as a PhD student, shared with time for work at the clinic, parental leave, and teaching, I finally reached the day of thesis defense. February 8 2019 was a really enjoyable day, much due to excellent opposition from Professor Jan Lexell of University of Uppsala.

I have been really fortunate to work with a really interesting project during my PhD years, together with competent and encouraging people from different research groups such as the Healthy Ageing Initiative and UFBI, as well as the Dep. of Community Medicine and Rehabilitation and the Dep. of Psychology at Umeå University. As for now, I will continue working as a clinical psychologist at the Neurorehabilitation Clinic, and start working as a senior lecturer of psychology at the Dep. of Psychology, while trying to continue my research. We have just started up a project that will investigate fatigue and cognition in patients with long term pain at the Dep. of Community Medicine and Rehabilitation. For now we have only included behavioural and medical assessments, but the aim is to also include both functional and structural neuroimaging in this project.

Nils Berginström

Similarity-based processes in human multiple-cue judgment

Back when I started my PhD, knowledge about the neurocognitive mechanisms underlying human multiple-cue judgment was limited. One important question that was especially difficult to answer based on behavioural data alone was the role for similarity-based processes in human multiple-cue judgment. Similarity to previous similar situations was hypothesized to always have an influence on the judgment process, even when we utilize rules and logic. The aim of my PhD was to investigate the role of similarity-based processes in human multiple-cue judgment, using a combination of behavioural methods, fMRI and cognitive modelling.

After years of intense studies, it was time to defend my thesis entitled ”Similarity-based processes in human multiple-cue judgment: Evidence from brain imaging and cognitive modelling”. I don´t even have words to describe my pre-defense anxiety, but when June 14 arrived, I was surprisingly calm. My opponent, Professor Alan Sanfey from the Donders Institute did an excellent job posing both tricky and interesting questions, and I somehow even managed to forget about the crowd that listened to our discussion. In all, the occasion was more fun and rewarding than I ever had imagined it to be!

Looking back on the past years, I appreciate the possibility to be part of an interdisciplinary research team and the stimulating research environment at UFBI. The time I spent at UFBI have been extremely valuable, and it has certainly shaped me as a researcher. I was lucky enough to get appointed as a post-doc researcher in cognitive neuroscience at the department of Applied Educational Science at Umeå University just a few days after my defence. I now investigate the neurocognitive correlates to the boost of learning following retrieval practice compared to typical repetition; a phenomenon referred to as the testing effect. I will continue to do research in collaboration with UFBI, and I look forward to the years to come.

Sara Stillesjö

Rehabilitation for improved cognition in stress-related exhaustion: cognitive, neural and clinical perspectives

In my PhD project, we investigated the effects of cognitive and aerobic training for persons with stress-related exhaustion disorder from a cognitive, neural and clinical perspective. The project was based on the Rehabilitation for Improved Cognition (RECO)-study, a randomized controlled trial conducted in collaboration with the Stress Rehabilitation Clinic at the University Hospital in Umeå. This was a very exciting project for me to be a part of, as it meant I got the opportunity to combine my two primary interests as a researcher and a psychologist: stress-related illness and neuropsychology.

Before my defense, my colleagues told me to enjoy this special day and that they themselves had found the defense a fun experience. I was sure this would not be the case for me, and was mainly focused on making it through the day. But of course, my colleagues were right – it was a very special experience and I really enjoyed discussing my research with my excellent opponent, Professor Ingibjorg Jonsdottir from the Institute of Stress Medicine.

The years as a PhD student have been very memorable and I have enjoyed coming to work every day. Much of this is thanks to my inspiring supervisors, Anna Stigsdotter Neely and CJ Boraxbekk. Through CJ, I also got in contact with the stimulating research environment at UFBI. At the moment, I am working as a post doc at the Department of Psychiatry, University of Melbourne. Here, I will continue working with developing, evaluating and studying the mechanisms of cognition-oriented treatments, with a specific focus on combining cognitive and aerobic training.

Hanna Malmberg Gavelin

Multimodal imaging: Functional, structural, and molecular brain correlates of cognitive aging

I defended my thesis in the fall of 2019 at Karolinska Institutet (KI). For my PhD project I measured different brain parameters and investigated how these relate to each other and are linked to cognition. Working on these topics was a genuine pleasure, despite all the ups and downs that come with doing science. Even now, I'm very grateful that this is what I'm paid to do. I also had the privilege of being affiliated to both KI and the UFBI, which allowed me to keep learning new neuroimaging and statistical analyses and get input from scientists with different skill sets. What I remember best from my trips to Umeå is how friendly and welcoming everyone was, including strangers who helped me find my way on campus when I got lost (which happened on a semifrequent basis).

My supervisors told me that I should enjoy my doctoral defense as much as possible, which, at the time, I took with a bit of skepticism. But they were spot on. Although I recall being ill and sort of sounding like Tom Waits, it was very cool to have others interested in discussing my work with me.

As I don't particularly mind cold weather and darkness during the winter, I've always found Umeå a charming city and hope to come by more often in the future. As for the now, I will still be working with KI and UFBI, but will also start a postdoctoral position at Stanford University early next year.

Barbara Avelar Pereira

A new method of investigation can improve the diagnostic accuracy in patients with carotid stenosis

In my thesis we have been investigating cerebral blood flow using an MRI sequence called phase contrast MRI (PCMRI). The first part of my thesis (1st and 2nd paper) described the normal cerebral blood flow rate (BFR), its distribution and pulsatility in healthy subjects. The data were presented according to age and sex. These results were important as they can improve our understanding of the pathological changes in BFR that can occur in patients with stroke.

Further, using a newer PCMRI method called 4D PCMRI, we investigated how a carotid stenosis affects cerebral blood flow and its distribution. We found that the distribution is affected and that compensatory mechanisms, such as collateral pathways, are activated. After carotid endarterectomy, BFR distribution became normalized and similar to that of healthy subjects. By studying cerebral hemodynamics using BFR instead of surrogate markers such as blood flow velocity, we get a better understanding of the hemodynamics and the compensatory mechanisms that occur in the cerebral arteries.

Finally, it was time for me to defend my thesis. My daughter Dina (who was 6 years old at the time) helped me with the "nailing" up of my thesis on the university wall. Dina and my co-author Anders Wåhlin´s daughter Hedvig handled the hammer and nail perfectly together. My biggest idol in my field of research, Professor Sepideh Amin-Hanjani from the university of Illinois, was my opponent. Meeting her was truly a dream come true for me. My biggest concern for the big day, however, was whether or not my newborn daughter Sofia would become hungry while I was defending. However, she managed to sleep for 3.5h while being carried around in a "baby Björn" by my husband. What a perfect day it was!

Laleh Zarrinkoob

Dopamine, aging, and decision-making: neural and behavioural correlates

I studied the role of the dopamine system in decision-making. Because the number of dopamine producing cells and receptors in the brain decreases as people get older, aging provides a good context to study the role of dopamine in different cognitive processes. Decision-making (choosing the best alternative among a set of options, and updating your preferences based on the reward you get) is one such process. We have done some of the first studies that combine positron emission tomography (PET), functional magnetic resonance imaging (fMRI) and computational modelling of decision-making tasks to elucidate the role of dopamine.

We found that an important difference between older and younger people when it comes to decision-making is how strongly the activity in the prefrontal cortex reflects the value of the alternative that people will choose. When this neural signal was strong, people did well on the task. When this signal was less strong, they did poorly. Older people showed a weaker signal than younger people, so we think that is why they performed poorly in comparison to younger people. We also found that dopaminergic and microstructural integrity of neural pathways in the brain were crucially important for this neural signal to emerge. So the brain deterioration as you get older may lead to a weaker value signal, which leads to worse performance. Another main finding was that while learning action-outcome contingencies, the extent to which you learn more from rewarded actions compared to rewarded inactions, was related to dopamine D1 receptors in the dorsal striatum. This is an area in the brain important for action selection and motor execution. This was the same for young and older people.

We now understand a little more about how the small changes that occur in the brain as people age may contribute to the ability to successfully learn how to adapt one's behaviour to the environment. This is important for people in old age, and may point to a target for the treatment of cognitive and behavioural problems in the future.

Lieke de Boer

The biology of cognitive decline and reduced survival in Parkinson disease

A winterly Friday in February 2019, my doctoral studies "suddenly" came to an end, and I defended my thesis about cognitive functions and survival in Parkinson's disease. It was an exhilarating day, in part due to my excellent opponent Professor Jan Aasly, from Trondheim, Norway, who made it joyful to discuss the work in front of an audience, in part because of the tangible feeling of gratification for the opportunity to work in clinical neuroscience that I had enjoyed during the preceding 6 years.

My thesis investigated clinical, neurobiological and genetic factors of importance for the prognosis (especially concerning cognitive function and survival) in Parkinson's disease (PD), Multiple System Atrophy and Progressive Supranuclear Palsy. We made several findings during the population-based, prospective project. PD patients with mild cognitive impairment (MCI) at baseline had a 2.2 times increased risk of death during the following years, compared to the general Swedish population, while PD patients with normal cognitive function had a normal survival. Hyposmia and mild inflammation were associated with a shorter lifespan. Factors that predicted dementia and cognitive decline in PD, especially in attention and episodic memory, were decreased Beta-amyloid and increased neurofilaments in the cerebrospinal fluid and low extrastriatal dopamine D2 receptor availability (as measured by a functional DRD2-gene polymorphism). One part of the project was diffusion tensor imaging.

At the same time that I was working with the thesis, I worked with PD patients clinically as the responsible physician and completed my specialty training in neurology. This meant a lot of work, but meeting persons with neurological diseases is often a humbling experience, and makes you realize what having a brain is actually good for, in a very concrete way!

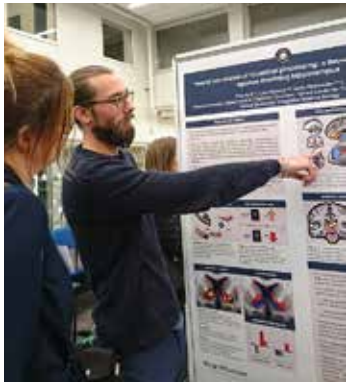
After the dissertation, I have received a 2-year post-doc grant from hjärnfonden and am actively working with or planning research in cellular and clinical neurobiology and post mortem examination of parkinsonian brains. I also have an interest in imaging of working memory training in PD and imaging in neurological diseases in general.

Although my career in UFBI to date was brief, I am interested to uphold a bridge between UFBI and patients in the hospital. A nice thing about clinical neuroscience is that while you try to elucidate some of the fascinating underpinnings of the human brain you can, at the same time, work with science for the benefit of those affected by disease.

David Bäckström

Meetings and seminars

A multidisciplinary research environment, a multi-faceted research agenda, and a growing research group make structured interaction platforms indispensable. To this end we have monthly lab meetings where project plans, experimental designs, analysis strategies, results and articles are discussed in an informal setting to benefit from the whole brain trust of UFBI. In addition to these meetings we also have an annual UFBI lab day. This year it was held on June 18, were we had the pleasure of having Fabienne Collette from the University of Liege as a guest speaker. Our members also gave presentations on their different projects, with subjects spanning from conscious/nonconscious visual perception to high intensity training and brain health, to mention a few of the contributions. During the fall the Swedish Cognitive Science Society held their annual meeting in Umeå, where several speakers and attendees from UFBI was present as speakers as well as presenting posters. Besides in-house meetings, members of UFBI usually attend several meetings and conferences each year held in, and outside Sweden. A list of attended conferences and given talks is shown on page 22.



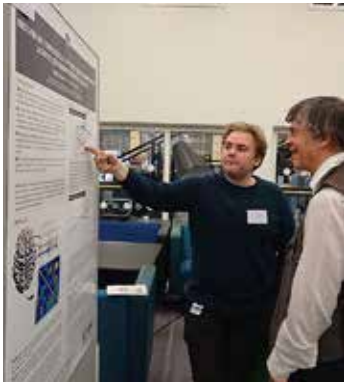


Photo: Sara Pudas

Photo: Sara Pudas

Top: Fabienne Collette (left) and Tiziana Pedale (right) presenting at the UFBI lab day.
Bottom: Filip Grill (left), Linnea Karlsson Wirebring (middle), Robin Pedersen (right) at the Swecog conference in Umeå November 2019.

Media

Members and projects from UFBI often appear in the general media. During 2019, the article “At the Heart of Cognitive Functioning in Aging“ in TiCS (see Zooming in, on page 10-11) got a lot of coverage in Sweden, Germany as well as other countries. Below you can se some examples of UFBI in the media.

eurekalert.org

orebronyheter.com

neurologiisverige.se

Neurologi i Sverige, “Trötthet efter traumatisk skallskada”, article by Nils Berginström, 2019-10-08.

Sveriges Radio P4 Västerbotten, Lars Nyberg in interview, ”Professor Lars Nyberg om minnet och lokalsinnet”, 2019-08-27.

Sveriges Radio P4 Västerbotten, Lars Nyberg in interview, “Stela blodkärl ger sämre minne”, 2019-08-21.

Örebro nyheter, news article on the publication in Trends in Cognitive Sciences “At the Heart of Cognitive Functioning in Aging”, 2019-08-21.

EurekAlert (AAAS), news article on the publication in Trends in Cognitive Sciences “At the Heart of Cognitive Functioning in Aging”, 2019-08-20.

Pressetext.com, news article on the publication in Trends in Cognitive Sciences “At the Heart of Cognitive Functioning in Aging”, 2019-08-20.

Tidningen Syre, news article on the publication in Trends in Cognitive Sciences “At the Heart of Cognitive Functioning in Aging”, 2019-08-20.

umu.se, ”Brain takes a beating as arteries age”, news on the article ”At the Heart of Cognitive Functioning in Aging” published in Trends in Cognitive Sciences, 2019-08-16.

Sveriges Radio, Sisuradio, “The brain can do well when you challenge it by learning new things”, radio interview with Sara Pudas, 2019-04-16.

Västerbottens-kuriren, “Utbärnda blir bättre med hjälp av träning” article on Hanna Malmberg-Gavelin’s dissertation, 2019-04-15.

Sveriges Radio P1, Johan Eriksson in the radioshow The philosophy room, theme ”Minnet och jag”, 2019-03-24.

Publications

The list below is focused on journal articles, book chapters, doctoral theses and conference presentations that were based on structural/ functional MRI data and/or PET data collected within UFBI. In addition, other relevant work produced by UFBI members is listed.

Original articles

Berginström, N., Nordström, P., Ekman, U., Eriksson, J., Nyberg, L., & Nordström, A. (2019). Pharmaco-fMRI in Patients With Traumatic Brain Injury. Journal of Head Trauma Rehabilitation, 34(3), 189–198.

de Boer, L., Axelsson, J., Chowdhury, R., Riklund, K., Dolan, R. J., Nyberg, L., Bäckman, L. & Guitart-Masip, M. (2019). Dorsal striatal dopamine D1 receptor availability predicts an instrumental bias in action learning. Proceedings of the National Academy of Sciences, 116(1), 261–270.

Dunås, T., Holmgren, M., Wåhlin, A., Malm, J., & Eklund, A. (2019). Accuracy of blood flow assessment in cerebral arteries with 4D flow MRI: Evaluation with three segmentation methods. Journal of Magnetic Resonance Imaging, 50(2), 511–518.

Fjell,M.A., ..., Pudas, S., ... Nyberg, L., ... Walhovd, K. (2019). Self-reported sleep relates to hippocampal atrophy across the adult lifespan – results from the Lifebrain consortium. Sleep.

Friedman, B. B., Suri, S., Solé-Padullés, C., Düzel, S., Drevon, C. A., Baaré, W. F. C., ... Budin-Ljøsne, I. (2019). Are People Ready for Personalized Brain Health? Perspectives of Research Participants in the Lifebrain Consortium. The Gerontologist.

Holmgren, M., Wåhlin, A., Dunås, T., Malm, J., & Eklund, A. (2019). Assessment of Cerebral Blood Flow Pulsatility and Cerebral Arterial Compliance With 4D Flow MRI. Journal of Magnetic Resonance Imaging, 1–10.

Jonasson, L., Nyberg, L., Axelsson, J., Kramer, A. F., Riklund, K., & Boraxbekk, C.-J. (2019). Higher striatal D2-receptor availability in aerobically fit older adults but non-selective intervention effects after aerobic versus resistance training. NeuroImage, 202(15 November).

Karalija, N., Jonassson, L., Johansson, J., Papenberg, G., Salami, A., Andersson, M., Riklund, K., Nyberg, L. & Boraxbekk, C.-J. (2019). High long-term test–retest reliability for extrastriatal 11 C-raclopride binding in healthy older adults. Journal of Cerebral Blood Flow & Metabolism, 0271678X1987477.

Karalija, N., Papenberg, G., Wåhlin, A., Johansson, J., Andersson, M., Axelsson, J., Riklund, K., Lövdén, M., Lindenberger, U., Bäckman, L. & Nyberg, L. (2019). C957T-mediated variation in ligand affinity affects the association between 11C-raclopride binding potential and cognition. Journal of Cognitive Neuroscience, 31(2).

Karalija, N., Wåhlin, A., Ek, J., Rieckmann, A., Papenberg, G., Salami, A., ... & Nyberg, L. (2019). Cardiovascular factors are related to dopamine integrity and cognition in aging. Annals of Clinical and Translational Neurology, 6(11), 2291–2303.

Kaufmann, T., ..., Nyberg, L., ..., Westlye, L. T. (2019). Common brain disorders are associated with heritable patterns of apparent aging of the brain. Nature Neuroscience, 22(10), 1617–1623.

Nyberg, L., Andersson, M., Lundquist, A., Salami, A., & Wåhlin, A. (2019). Frontal Contribution to Hippocampal Hyperactivity During Memory Encoding in Aging. Frontiers in Molecular Neuroscience, 12.

Papenberg, G., Jonasson, L., Karalija, N., Johansson, J., Köhncke, Y., Salami, A., Andersson, M., Axelsson, J., Wåhlin, A., Riklund, K., Lindenberger, U., Lövdén, M., Nyberg, L. & Bäckman, L. (2019). Mapping the landscape of human dopamine D2/3 receptors with [11C] raclopride. Brain Structure and Function.

Papenberg, G., Karalija, N., Salami, A., Andersson, M., Axelsson, J., Riklund, K., Lindenberger, U., Nyberg, L. & Bäckman, L. (2019). The Influence of Hippocampal Dopamine D2 Receptors on Episodic Memory Is Modulated by BDNF and KIBRA Polymorphisms. Journal of Cognitive Neuroscience, 31(9), 1422–1429.

Papenberg, G., Karalija, N., Salami, A., Rieckmann, A., Andersson, M., Axelsson, J., Riklund, K., Lindenberger, U., Lövdén, M., Nyberg, L. & Bäckman, L. (2019). Balance between Transmitter Availability and Dopamine D2 Receptors in Prefrontal Cortex Influences Memory Functioning. Cerebral Cortex.

Salami, A., Garrett, D. D., Wåhlin, A., Rieckmann, A., Papenberg, G., Karalija, N., Jonasson, L., Andersson, M., Axelsson, J., Johansson, J., Riklund, K., Lövdén, M., Lindenberger, U., Bäckman, L. & Nyberg, L. (2019). Dopamine D2/3 Binding Potential Modulates Neural Signatures of Working Memory in a Load-Dependent Fashion. Journal of Neuroscience, 39(3), 537–547.

Satizabal, C. L., ... Andersson, M., ..., Nyberg, L., ... Ikram, M. A. (2019). Genetic architecture of subcortical brain structures in 38,851 individuals. Nature Genetics, 51(11), 1624–1636.

Sjöberg, R. L., Stålnacke, M., Andersson, M., & Eriksson, J. (2019). The supplementary motor area syndrome and cognitive control. Neuropsychologia, 129, 141–145.

Stillesjö, S., Nyberg, L., & Wirebring, L. K. (2019). Building Memory Representations for Exemplar-Based Judgment: A Role for Ventral Precuneus. Frontiers in Human Neuroscience, 13.

Vikner, T., Nyberg, L., Holmgren, M., Malm, J., Eklund, A., & Wåhlin, A. (2019). Characterizing pulsatility in distal cerebral arteries using 4D flow MRI. Journal of Cerebral Blood Flow & Metabolism,

van der Meer, D., ..., Andersson, M., ..., Nyberg, L., ... Andreassen, O. A. (2019). Association of Copy Number Variation of the 15q11.2 BP1-BP2 Region With Cortical and Subcortical Morphology and Cognition. JAMA Psychiatry, 1.

Wåhlin, A., & Nyberg, L. (2019). At the Heart of Cognitive Functioning in Aging. Trends in Cognitive Sciences, 23(9), 717–720.

Zarrinkoob, L., Wåhlin, A., Ambarki, K., Birgander, R., Eklund, A., & Malm, J. (2019). Blood Flow Lateralization and Collateral Compensatory Mechanisms in Patients With Carotid Artery Stenosis. Stroke, 50(5), 1081–1088.

Zuo, N., Salami, A., Liu, H., Yang, Z., & Jiang, T. (2019). Functional maintenance in the multiple demand network characterizes superior fluid intelligence in aging. Neurobiology of Aging.

Review articles / Book chapters

Nyberg, L., & Pudas, S. (2019). Successful Memory Aging. Annual Review of Psychology, 70(1), 219–243.

Dissertations

Avelar Pereira, B. (2019). Multimodal imaging: Functional, structural, and molecular brain correlates of cognitive aging. Doctoral dissertation, Karolinska Institutet [contains data from UFBI].

de Boer, L. (2019). Dopamine, decision-making, and aging. Doctoral dissertation, Karolinska Institutet [contains data from UFBI].

Zarrinkoob, L. (2019). Cerebral blood flow distribution, collateral function and pulsatility in healthy and in patients with symptomatic carotid stenosis. Doctoral dissertation, Umeå University [contains data from UFBI].

Holmlund, P. (2019). Fluid dynamic principles for analysis of intracranial pressure control. Doctoral dissertation, Umeå University [contains data from UFBI].

Stillesjö, S. (2019). Similarity-based processes in human multiple-cue judgment: evidence from brain imaging and cognitive modelling. Doctoral dissertation, Umeå University

Nordmark, P. (2019). Structural and functional changes in the brain after surgically repaired median nerve injury. Doctoral dissertation, Umeå University

Gorbach, T. (2019). Methods for longitudinal brain imaging studies with dropout. Doctoral dissertation, Umeå University [contains data from UFBI].

Bäckström, D. (2019). The biology of cognitive decline and reduced survival in Parkinson disease: prognostic factors in a population-based cohort. Doctoral dissertation, Umeå University [contains data from UFBI].

Berginström, N. (2019). Fatigue after traumatic brain injury: exploring novel methods for diagnosis and treatment. Doctoral dissertation, Umeå University [contains data from UFBI].

Malmberg Gavelin, H. (2019). Rehabilitation for improved cognition in stress-related exhaustion: cognitive, neural and clinical perspectives. Doctoral dissertation, Umeå University [contains data from UFBI].

Select conference presentations

Karlsson Wirebing, L. (November 8, 2019). Active compared to passive mathematical learning: durable effects on brain activity one week after constructing your own solutions. Presentation held at the 15th Swedish Cognitive Science Society Conference, Umeå, Sweden.

Stillesjö, S., (November 7, 2019). Retrieval Practice promotes superior memory retention via higher brain activity in Hippocampus and Caudate independent of Cognitive Ability. Presentation held at the 15th Swedish Cognitive Science Society Conference, Umeå, Sweden.

Grill, F. (November 7, 2019). Neural correlates of incentive processing: a two-component response involving hippocampus. Poster presented at the 15th Swedish Cognitive Science Society Conference, Umeå, Sweden.

Fontan, A., Lindgren, L., Pedale, T., Bergström, F., Brorsson, C., & Eriksson, J. (October 23, 2019). Changes in the global state of consciousness affect brain activity related to conscious and non-conscious visual perception differently. Poster presented at Society for Neuroscience, Chicago, USA.

Pedale, T., Fontan, A., Grill, F., Bergström, F., Eriksson, J. (October 23, 2019). Leftward bias in visuospatial attention during a non-conscious working memory task. Poster presented at Society for Neuroscience, Chicago, USA.

Nyberg, L. (September 9, 2019). Talk presented at the Workshop on research definitions for reserve and resilience in cognitive aging and dementia, Bethesda, USA.

Eriksson, J., Pedale, T., Fontan, A., Grill, F., & Bergström, F. (June 27, 2019). An attentional asymmetry in a spatial non-conscious working-memory task. Talk presented at the 23^rd annual meeting of the Association for the Scientific Study of Consciousness, London, Canada.

Grill, F. (June, 2019). Incentive processing modulates activity in a ventral striatum-hippocampus network: data from the human connectome project. Poster presented at 25th Annual Meeting of the Organization for Human Brain Mapping, Rome, Italy.

Johansson, J. (June, 2019). Longitudinal Evidence for Reduced Hemispheric Encoding/Retrieval Asymmetry in Aging. Poster presented at 25th Annual Meeting of the Organization for Human Brain Mapping, Rome, Italy.

Jonasson, L. (June, 2019). BOLD deactivations are not the metabolic opposite of activations: Evidence from hybrid PET/fMRI. Oral presentation (held by Rieckmann, A.) as well as Poster presented at 25th Annual Meeting of the Organization for Human Brain Mapping, Rome, Italy.

Nyberg, L. (May, 2019). Neuroimaging Biomarkers in Brain Ageing, National E-infrastructure on Aging Research in Sweden. Talk presented at International Association of Gerontology and Geriatrics European Region Congress 2019, Gothenburg, Sweden.

Nyberg, L. (May, 2019). Hjärnans plasticitet- hur påverkas våra minnessystem efter traumatisk hjärnskada? Vikten av balans mellan hjärnans aktivets- och vilosystem efter skada. Talk presented at Rehabveckan 2019, Umeå, Sweden.

Berginström, N. (May, 2019) Funktionell och strukturell hjärnavbildning för trötthet efter skallskada. Talk presented at Rehabveckan 2019, Umeå, Sweden.

Malmberg-Gavelin, H. (May, 2019) Utmattningssyndrom, kognition och hjärna – hur kan kognitiva nedsättningar behandlas inom ramen för stressrehabilitering? Talk presented at Rehabveckan 2019, Umeå, Sweden.

Stigsdotter Neely, A. (May, 2019). En fronto-striatal workout för att stärka kognition hos patienter med Parkinsons sjukdom. Talk presented at Rehabveckan 2019, Umeå, Sweden.

Naesström, M. (April, 2019). Fmri evaluation of deep brain stimulation in obsessive-compulsive disorder. Talk presented at European Psychiatry Associations congress, Warsaw, Poland.

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and read previous years' reports as well as summaries of current projects.