Umeå Center for functional brain imaging - UFBI

Annual Report 2021

UFBI
Umeå center for
Functional Brain Imaging

UFBI 2021 Annual Report

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Welcome to the Annual Report for 2021

No longer a teenager!
UFBI turned 20 years as a center during 2021. The small note on this anniversary on page 22 is consistent with the minimal attention this landmark event could be given in the midst of the global pandemic. Hopefully, this will soon change so we can celebrate our 20-year-old during the UFBI annual day in June. Congratulations UFBI!

Brain research has taught us that the developmental phase continues well into the 20's, and in a similar vein we see no signs that UFBI activities are beginning to slow down. Rather, the scientific output is higher than ever and UFBI researchers continue to secure grants, appear in the media, and showcase UFBI activities at international meetings. You can read about some of these activities in this report.

We have put a special focus in the report on the hard and successful work by post-doctoral fellows and PhD-students. To continue the brain-development metaphor, by generating new ideas, trimming away old and no-longer-relevant information and methods, and establishing new local and distal connections ('neurogenesis, pruning, synaptogenesis'), the fellows and students are absolutely vital for the growing UFBI activities.

At the end of 2021 and continuing in the first half of the 2022, we started the process of installing new MRI hardware. In this report, our former MRI physicist Greger Orädd reflects on the past decade of activities. I like to thank Greger and the old scanner for excellent collaboration; I hope the new system will generate as much new knowledge in the future.

Today, in early March 2022, the society and universities are beginning to open up. I ended last year's report by expressing the wish that we soon would meet on campus. "Soon" turned out to be quite a bit longer than what most of us had hoped, but now I am optimistic that the restrictions are finally over. Regrettably, this does not mean that the world situation is calm and peaceful. On the contrary, a war against Ukraine is ongoing, with numerous personal losses and tragedies as a consequence. For many of us it is therefore very hard to focus on work currently, and this is of course manyfold much more difficult for our colleagues who have family, friends, and loved ones in Ukraine. Times like these remind us of the values of academic freedom and freedom of speech. Our thoughts are with you!

Photo: Mattias Petterson (Umeå Universitet)

Lars Nyberg
UFBI Director (2001 - Present)

In short

In 2021 the members of UFBI produced:

234
fMRI-scans

16 clinical fMRI-scans

52
articles

2 dissertations

1589
clinical MRI scans

34 PET-MR
UFBI research scans

20 PET-CT
UFBI research scans

Dopamine D2-receptor decline in the aging brain: insights from COBRA

The dopamine (DA) system is described as one of the most age-sensitive systems of the brain. This statement finds support from nearly 100 independent imaging studies, that collectively demonstrate reduced numbers of DA markers in older, as compared to younger, adults. Several lines of research have demonstrated that dopaminergic disturbances are accompanied by cognitive deficits. Therefore, one principal theory in cognitive neuroscience is that the age-sensitivity of the dopamine system underlies cognitive decline in aging. Past in vivo dopamine studies have typically been conducted in cross-sectional settings, with limited sample sizes. The lack of longitudinal dopamine studies has obscured investigations of true rates and patterns of DA decline, and whether within-person dopamine reductions are associated with cognitive decline.

The Cognition, Brain, and Aging (COBRA) study is a collaboration between researchers at UFBI, Karolinska Institutet, University of Gothenburg, and Max Planck Institute for Human Development; with the primary aim of to cover these gaps in knowledge. At baseline, 181 healthy, older adults (ages: 64-48 years) underwent PET with 11C-raclopride for D2-like receptor assessment, MRI for evaluation of brain structure and function, and also, cognitive, lifestyle and genetic mapping. The 5-years follow-up took place during 2017-2019, during which approximately 70% of the original sample repeated all tests once more. We found significant 5-year D2-receptor reductions in the striatum and in a few extrastriatal regions, and also, large individual differences in the magnitude of D2 change. Striatal D2-receptor decline was ~50% of past cross-sectional estimates, suggesting overestimated decline rates in past research, and once again, underscoring the necessity of longitudinal measurements. Among the structural 5-year changes, perfusion reductions and white-matter lesion progression were particularly sizeable. Importantly, change-change associations were found for these cerebrovascular markers in relation to D2-receptor losses across several associative and limbic regions. Furthermore, we have found support for that within-person dopaminergic decline is associated with reduced cognitive performance.

COBRA has provided several new insights about neurocognitive aging, endeavors that have resulted in about 20 research articles. The third wave of data collection will be initiated during 2022.

Nina Karalija

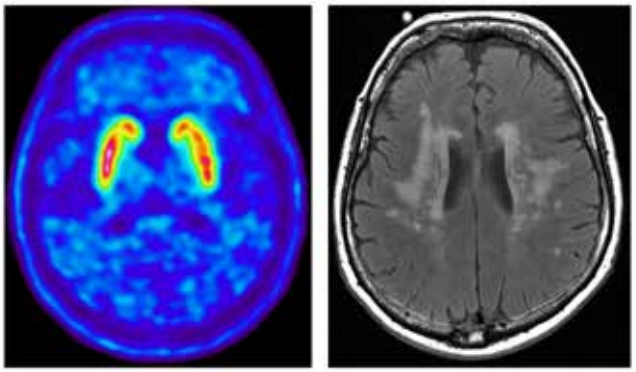


Illustration: Nina Karalija

Dopamine D2-receptor availability is highest in the striatum (red and yellow areas in left image). D2 decline was faster in individuals with elevated white-matter lesion progression (white areas in right image).

Post-doc projects

At the heart of brain aging

We are all - whether we want to or not - getting older. Thanks largely to improvements in healthcare, sanitation, and general living standards, global demographics are shifting to an increasingly elderly population. This is positive news, yet it also presents new challenges. More resources are typically needed to ensure that elderly people can live happy and healthy lives. Typically, but not always - what is it about those people that age better than others? Can we disentangle the factors that improve our chances of aging successfully? These are the questions I have largely focussed on during my postdoc at UFBI.

Recent research has highlighted how the links between the heart and brain can be critical to our health and the aging process. For our first study, we expanded upon this, examining how long-term heart health can predict brain-based outcomes. We used data from the Betula study, collected over 20-25 years, to follow the longitudinal trajectory of participants' cardiovascular risk. We found that, while most participants had similar heart-health starting points, those who exhibited an accelerating cardiovascular risk were more likely to develop either Alzheimer's disease or vascular dementia, compared to those with normal or stable trajectories. Controlling heart health appears to be an important investment to improve the chances of avoiding dementia later in life. This indicates that long-term heart health can be important for maintaining brain health, but is there something that can be done on a more short-term basis to slow the negative effects of aging in the brain? Our second study examined the effects of a 6-month physical exercise intervention with elderly participants, with data from the PHIBRA study. There are various hallmarks of decline in aging, including a decline of working memory, and a stable reduction of striatal dopamine. We know from previous research that while physical fitness is linked to improved working memory, and an attenuation of dopamine decline, interventions don't appear to robustly improve either of these components. In other words - it appears that being fit is linked to better brain health, but getting fit doesn't necessarily improve brain health - how can this be? We explored the possibility that there might be individual differences that restrict the potential for plasticity - specifically that participants with a large degree of brain lesions might be limited in their capacity to improve their brain health, even if they improve their physical fitness. We split participants into two groups (high and low) based on their lesion severity. By using PET and MRI scans alongside cognitive and physiological testing, we found that while all participants were able to improve their physiological fitness, only participants with a minimal amount of brain lesions showed improvements to their working memory and dopamine levels. This suggests that brain lesions may be limiting the possibility for plasticity following an intervention, underscoring the importance of controlling brain health throughout life.

These two manuscripts are now submitted, with further work ongoing. In particular, we are exploring the links between cardiovascular risk, brain outcomes, and cognitive performance. While we might not yet know the direct determinants of successful aging yet, it's our hope that this research points us a little closer to an answer.

Bryn Farnsworth von Cederwald

Telomere length and DNA methylation as prediction markers of Alzheimer's disease

In February 2020 I left Porto Alegre's summer to arrive in Umeå's winter, at the beginning of a rumour that turned out to be a global pandemic. After a month of novelties and warm welcomes, social isolation and work-from-home took place. But with the support of a bright research group and Zoom meetings full of excitement, we were able to put together two studies on blood markers of Alzheimer's disease (AD). These studies, under the scope of the Betula project, were designed to evaluate whether the aging markers telomere length and DNAm patterns in blood can be use as AD predictors, and may capture etiological roles of DNAm in AD pathology.

While I was trying to compensate fika side effects by walking to Nydalasjön, we first evaluated leukocyte telomere length as a marker using a time-to-event study design (n=1306, 149 AD cases). Two complementary time-to-event models that account for competing risks were used to estimate the association between the rLTL tertiles and the cumulative incidence and the cause-specific risk of AD. Vascular dementia and death were considered competing risk events. Models' results indicate that short telomere length can improve AD prediction in non-APOE ε4-carriers, on average 8 years before onset (find more details in https://doi.org/10.1186/s13195-021-00871-y).

I was already proficient in hunting mushrooms, berries and the aurora when we started the DNAm study. We used a longitudinal follow-up of AD cases (n=49) and age- and sex-matched controls (n=49) to study leukocyte DNAm patterns as potential prediction markers of AD, long before (16 to 10 years before), close before (9 to 3 years before) and after (0 to 8 years after) AD onset. The epigenetic clocks Hannum, Horvath, PhenoAge and DunedinPoAm are markers of biological aging, and were estimated to evaluate whether AD cases age faster than controls. In our study, these clocks did not differ between AD cases and controls, so they may not be suitable markers of AD. Further, univariate and multivariate approaches were used to identify sets of DNAm sites potentially associated with AD pathology and that may be used as early AD predictors. In the univariate approach, we identified DNAm sites that discriminate AD cases from controls longitudinally. A score was obtained from β-values of 73 identified DNAm sites, which was able to predict AD on average 8 years before onset. The multivariate analysis used a machine learning approach for variable selection. Two selected sets of DNAm sites, identified from the long-before and after AD time-points were also used to estimate scores as predictors of AD, which were both able to predict AD on average 8 years before onset.

Together, our studies improve the understanding on AD time-course, and contribute to the early identification of individuals at risk for AD. Although unfortunately it will not be possible to work with UFBI for the next year, I look forward to keep collaborating with you, hopefully in non-pandemic times.

Fernanda Schäfer Hackenhaar

A 2-year post-doc review

When reviewing my post-doc experience at UFBI between 2019 and 2021, I can only describe it as 'blessed'. Some might argue given the locality of my stay, that descriptions in line with 'darkness' or 'freezing' would be more appropriate experiences. Not to mention the pandemic outbreak (2019- still ongoing), which may add experiences like 'isolation', 'confined', and 'limitations' to the expected list. However, no doom and gloom from the outside was able to stop the machinery that is UFBI to continue strong. The UFBI spirit contributed much to the results and achievements during my post-doc. Most importantly was the sense of unity and availability from all members at UFBI, despite the circumstances. As a result, I managed during the two year post-doc to be involved in an interesting project with Sara Pudas where we tried to better understand episodic memory processing during midlife. I was also privileged to be involved in other side projects and collaborations. Basically, I was given the freedom to be the researcher I wanted here at UFBI, and was met by support around every corner. My main focus was to integrate and be a part of the scientific environment as a post-doc and beyond. Having previously spent time in the UFBI lab finishing my master's thesis, and then later Karolinska Institute during my PhD, I circled back to UFBI for deeper understandings in modern science, and what makes for a successful researcher. Some of the most fulfilling time spent was when sharing the gospel of Christ with colleagues, discussing results and their relations to theories, testing and re-testing ideas, exploring new statistical avenues, and twisting and turning basically everything - together mainly with Sara Pudas, but also with PhD students and other colleagues. All in all, my post-doc time at UFBI served as a good foundation for a continuation within modern science and academia. I am therefore very grateful for all the learning experiences, and mostly for being accepted and included in the UFBI family.

George Samrani

Data collections during 2021

Exploring the limits of unconscious working memory

Working memory (WM) is critical to store and manipulate information and is foundational to the organization of goal-directed behaviour. WM has been traditionally considered as an explicit memory system operating only on consciously perceived information; yet, recent reports of unconscious WM challenge this view. Specifically, several studies have reported short-term maintenance of unconscious information, independent of conscious awareness. However, it is still far from clear whether goal-directed use of task-relevant information can also occur on unconsciously presented stimuli.

The purpose of the project ¨Functional neuroimaging of conscious and unconscious working memory¨ is to explore the “silent” side of working memory, characterized by unattended and unconscious working-memory representations. The main question for this project concerns whether it is possible to prioritize task-relevant information over distracting information for tasks that require unconscious WM. Of major interest is whether the brain processes the target stimulus and the distractors differently or not, and whether this differs between consciously and unconsciously presented stimuli.

Data have already been successfully collected and analysed for another experiment where the results indicated a clear prioritization of target for conscious stimuli, in such a way that information about distractor was filtered out and only target was memorized. However, for unconscious stimuli, the same priority was not given - both target and distractor were memorized and used correctly to solve the task. This lack of attentional prioritization for unconscious trials could be consistent with two interpretations. It can reflect either an inability to control selective attention for unconscious stimuli or it could be attributed to the low memory load (at most two locations, including the location of the distractor) that never exceeded the typical working-memory capacity limit (3-4 items). The participants could possibly not fail to remember the distractor! Would a more challenging WM load benefit target selection for the unconscious stimuli?

In order to be able to differentiate between these interpretations, we have now expanded the previous research by carrying out a follow up experiment where we manipulated the memory load by increasing the total number of the task stimuli to five so that not both target and distractors ”fit” in working memory. The participants performed a delayed match-to-sample task. The goal of the task was to remember the spatial location of a relevant stimulus that was always presented simultaneously with one or four irrelevant distractors. The task relevance of the competing stimuli was indicated by a cue, and continuous flash suppression (CFS) was used to manipulate the conscious/unconscious visual experience of the stimuli. CFS refers to an interocular suppression paradigm wherein a static visual stimulus (target) presented to one eye is suppressed from awareness as a result of a dynamically changing high contrast, coloured pattern (called the Mondrian pattern) presented to the other eye.

We have recently completed the data collection and I hope that we will get to share some interesting results in the near future. Providing convincing evidence for the unconscious nature of WM, may lead to reconsideration of several aspects of both working memory and consciousness.

Olympia Karampela

SIMULTAN

The development of biological psychology as a field has always been tightly coupled with the development of new research methods. Neuroimaging in particular has greatly contributed to an emerging understanding of how our brain works because we can literally watch the brain while we think, feel or act. For some years now, we have put special focus on the combination of fMRI and PET to study brain function because we can obtain biochemical information from PET that complements the versatile but indirect nature of the fMRI signal. In several past studies, we have been particularly interested in the combination of fMRI and PET of dopaminergic targets in order to better understand the specific roles of dopamine in cognition and cognitive aging.

In the recently completed SIMULTAN project, we left dopamine behind for a change and used a novel hybrid imaging approach to get at some of the broad, unresolved questions in cognitive neuroscience. For one, we studied common patterns of "deactivations" in the default mode network during cognitive control. Do deactivations reflect a role for this network in the baseline resting state or are deactivation active inhibition of task-irrelevant processes? Since the fMRI signal is always a relative comparison of blood flow patterns, fMRI alone cannot answer this fundamental question regarding our functional brain architecture. Another question that we wanted to tackle was that of greater fMRI activations in older as compared to younger adults, often observed under low task demands. Do overactivations reflect a "harder working" brain in older adults for easy tasks? Again, fMRI alone cannot provide the answer since we do not have a quantifiable measure of neural activity. Faced with these two questions, we designed a novel scan setup in which we combine traditional fMRI imaging with a simultaneous acquisition of PET-based measure of glucose consumption, a quantifiable proxy of synaptic activity. Each scan takes around 60 minutes on the GE PET-MR scanner, located at the hospital CancerCentrum.

Thirty scans for healthy, young adults were swiftly collected during 2018. For our aging project, we started with a data collection of forty older adults in 2018 and then continued to follow them with cognitive testing and a second scan in 2021. In October, we met the final participant for the last time. It was a bitter sweet ending since we know that involvement in our project and regular contact meant a lot to these participants and that many would have gladly continued to meet Vania, especially in times of social isolation and restrictions.

Because SIMULTAN relied on a new imaging technique, there was a high risk of failure to the project. I was excited that the European Commission saw the potential and supported us nonetheless, but it is fair to say that this data collection has also given Lars Stiernman and me many sleepless nights. Will we see enough signal? Did we choose the right task? Did we choose the right timing? In the end, our beautiful data suggests that our efforts paid off. The first results are published (Stiernman et al. 2021, PNAS) and we are excited to continue to analyze data and make exciting discoveries in 2022.

Anna Rieckmann

Photo: Mikael Stiernstedt

The PET/MR-scanner at Norrlands Universitetssjukhus, Umeå.

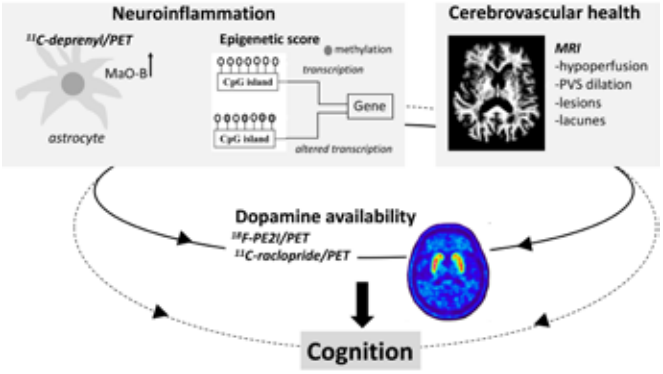
Vascular dysfunction, neuroinflammation, and dopamine loss - a chain of events underlying cognitive decline in aging?

One of the most acknowledged theories in cognitive neuroscience is that the age-sensitivity of the dopamine system underlies cognitive decline in aging. Circumventing dopamine loss may thus constitute one route towards successful cognitive aging. It is therefore motivated to identify the determinants of dopamine loss, which currently remain largely unknown. Low-grade neuroinflammation and cerebrovascular dysfunction are common findings in the aging brain, and coincide with pathological dopamine disturbances in e.g. Parkinson's disease and depression. A new UFBI-based brain imaging study (InflamAge) will test the novel hypothesis that a triad of neuroinflammation, cerebrovascular stress, and dopamine loss are an integral part of one pathological chain of events in the aging brain, leading to concomitant cognitive impairments. InflamAge will be ongoing during 2022-2024, and received funding from the Swedish Research Council for this year's call within humanities and social sciences.

The study will encompass 60 healthy, older adults between the ages of 60-80 years. Participants will undergo MRI to assess brain structure and function, and cerebrovascular status via e.g. perfusion, dilation of perivascular spaces, and manifestation of lesions and lacunes. Furthermore, the participants will be scanned twice with PET and ligands binding to markers of astrocytosis (11C-Deprenyl) and dopamine integrity (18F-PE2I). The battery further includes cognitive testing (episodic memory, working memory, perceptual speed), blood sampling for assessment of peripheral inflammatory markers, and health/lifestyle assessment via questionnaires. With these data at hand, we will firstly assess whether some indicators of cerebrovascular dysfunction are associated with an inflammatory response. Then, we will assess whether elevated levels of inflammation and cerebrovascular dysfunction are associated with reduced dopamine integrity. Thirdly, we will investigate whether reduced cognitive performance is found in groups characterized by low dopamine integrity and elevated levels of neuroinflammation and vascular dysfunction. In order to study whether changes in these neurocognitive variables correlate in aging, longitudinal analyses will be conducted in the Cognition, Brain, and Aging (COBRA) study. COBRA and InflamAge are comparable in terms of the cognitive battery and MRI paradigm. In COBRA, an epigenetic score (via DNA methylation) will be used as a proxy for inflammation.

Taken together, this project allows for assessment of several detrimental processes in the aging brain, ranging from neurochemistry to brain structure. Hence, it holds potential to generate new knowledge for the interrelations of key brain processes at the path of compromised brain maintenance.

Nina Karalija



Imaging molecular leakage across the blood-brain barrier and subsequent brain clearance

Leakage of toxic molecules across the blood-brain barrier as well as dysfunction of the brain ability to clear such molecules and metabolic waste from tissue are two potential causes of neural dysfunction and cognitive decline in aging. To characterize and quantify these two processes in the human brain, we developed a “two-birds in one strike” imaging protocol optimized to track how intravenously injected molecules first enter brain tissue across the blood-brain barrier and then gets cleared via-draining pathways to extracranial locations. The methodological work leading up to the final MRI sequences of the project represents a team effort from researchers at UFBI, the department of radiation sciences as well as the department of applied physics and electronics. The unique protocol involved both dynamic and high-resolution quantitative imaging of contrast agent concentration and required research persons to stay at the MRI facility for more than 4 hours!

During the autumn of 2021, after important vaccine rollouts and before the emergence of new alarming escape-variants of the coronavirus, we could perform the entire data collection. The research persons (older individuals from the population) showed a tremendous commitment to the study, and all enrolled participants endured the lengthy protocol. In addition, an excellent ability of the MRI staff to gracefully orchestrate the data collection made it feasible to execute the project alongside clinical investigations. Data collection in 60 research persons could be completed in just three months.

We think that our approach of studying molecular uptake and clearance with MRI can provide many important insights into brain physiology and we also think that there is a great potential for clinical translation, e.g. in dementia were the mechanism leading to the buildup of toxic proteins is of central interest. Due to additional MRI sequences, intertwined in the imaging protocol, the project will also answer important questions regarding the relationship between vascular health, brain clearance function, and brain function, as well as enable the identification of regions of high vulnerability to dysfunction in the investigated mechanisms.

Anders Wåhlin

Zooming in

Active math and grammar learning engages overlapping brain networks

Active learning has received a lot of interest during the past decade, both among scientists and educators, as it improves learning and learning outcome in a variety of situations (Freeman et al., 2014). By using fMRI, we recently provided novel evidence for that active learning leads to superior memory via overlapping learning processes for Grammar learning and Mathematics in brain networks related to deeper information processing (Stillesjö et al., 2021, PNAS).

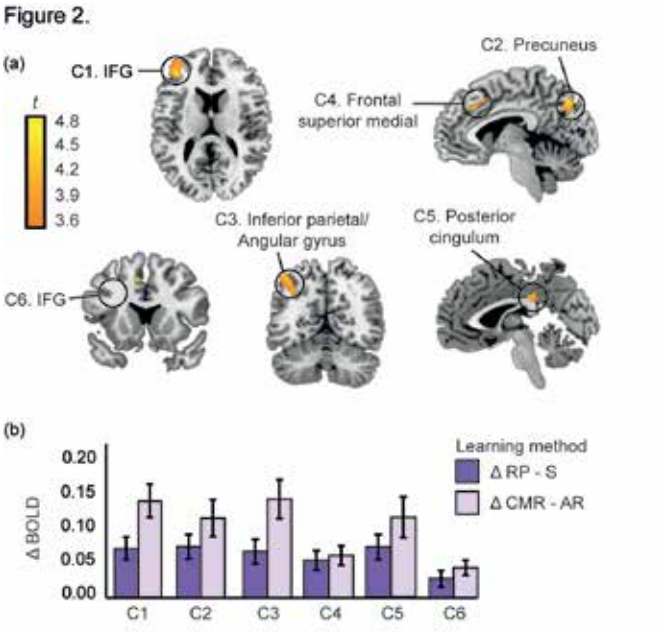
As part of the research project "Learning to engage the brain" we studied the learning effects one week after active learning in Grammar learning and Mathematics with fMRI. Using a within-subject design, upper-secondary school students (N=86) learned a foreign language vocabulary, half by means of active retrieval practice and half by means of passive study. The same students (n=72) learned to solve mathematical problems via active creative mathematical reasoning and passive imitative algorithmic reasoning. All students returned to take a retention test in the MR-scanner one week later.

As expected, behavioral performance was significantly higher after active learning at the one-week retention test compared to passive learning. Moreover, using a conjunction analysis on fMRI data revealed shared higher brain activity for the active learning conditions in a number of cortical brain regions, including the inferior frontal gyrus, the precuneus, the angular gyrus, the posterior cingulum and the middle prefrontal gyrus. The overlapping brain activity likely reflect reactivation of common active learning processes. Such processes are known to be related to reactivation of semantic representations by the IFG, fact retrieval and attention processes for the angular gyrus, and reactivation of contextually linked information in the precuneus. There was no shared brain activity for the passive learning conditions.

In sum, the results extend behavioral evidence as they provide mechanistic insights to why active learning methods in grammar learning and mathematics improves performance. The findings have implications for how we plan and execute learning activities for students as well as for educators.

Sara Stillesjö

Figure 2.



(A) Brain regions showing higher activity following active learning vs. passive learning (RP > S ∩ CMR > AR). (B) The bar graph shows the difference (indicated by Δ) in blood-oxygen-level–dependent (BOLD) activity when contrasting active > passive learning for each brain region (C1–C6) and course subject (dark purple bars = Δ RP-S; light purple bars = Δ CMR-AR). S is study (passive); RP is retrieval practice (active); AR is algorithmic reasoning (passive); CMR is creative mathematical reasoning (active). Error bars display ±1 SE mean.

Stillesjö, S., Karlsson Wirebring, L., Andersson, M., Granberg, C., Lithner, J., Jonsson, B., Nyberg, L., & Wiklund-Hörnqvist, C. (2021). Active math and grammar learning engages overlapping brain networks. Proceedings of the National Academy of Sciences, 118(46), e2106520118. https://doi.org/10.1073/pnas.2106520118

Grants

The Medical faculty's strategic research funds at Umeå Unversity, 700 000 SEK/year for three years

Karolina Kauppi was awarded the medical faculty's strategic research funds for identifying unique and shared genetic networks of normal neurocognitive aging and Alzheimer's disease (AD). How well we preserve our cognitive abilities and brain structure in aging is to some extent genetic, and partly overlaps with genetic factors linked to AD. The project aims to untangle the genetic complexity of those traits by mapping genetic variations in genes coding for proteins involved in the same biological network or pathway to specific behavioral and clinical phenotypes of aging and AD, such as brain volume and biomarkers of neurodegeneration. The work will be carried out primarily using data from the Betula project, as the long follow-up time in this sample importantly enables distinguishing preclinical AD from normal aging, but data from the Swedish twin registry at KI and the UK biobank will also be included.

Sara Pudas was awarded the strategic grant that will allow a continuation of her existing VR funded project about biomarkers for neurocognitive aging and dementia. The plan is to conduct an additional study investigating whether leukocyte telomere length interacts with other established biomarkers in prediction of neurocognitive aging outcomes. They will also analyze additional blood samples for biomarkers to increase sample size for upcoming studies, focusing particularly on participants from the Betula study's neuroimaging subsample.

Carl-Johan Boraxbekk and Erik Rosendahl was awarded the strategic grant for the HIT-project (a description of that project can be read on page 18).

Vetenskapsrådet
- Nina Karalija, for a project on vascular dysfunction, neuroinflammation, and dopamine loss (described on page 12) (4.8 million SEK).
- Alireza Salami, for the DYNAMIC-project (described in UFBI Annual Report 2018)(4.7 million SEK).

Hjärt-lung Fonden
- Anders Wåhlin, for a project using 4D flow MRI to understand the link between the health of the heart and the brain (1.8 million sek).

JPND (Joint Programme - Neurodegenerative Disease research)
- Anders Eklund, for a project on human brain clearance imaging (2.5 million SEK).

Spjutspets-ALF (Region Västerbotten)
- Anders Eklund, for a project to analyze the brain's arterial system and how it redistributes the blood between the different parts of the brain before and after surgery to identify risks in patient that are going to undergo cardiovascular-surgery (3 million SEK).

Dissertations & Mid-term seminars

Dissertation: 4D flow MRI and modelling to assess cerebral arterial hemodynamics

Like many at UFBI, I am interested in the blood flow of the brain and how we can model this. In my thesis, I investigated methods for analysing the hemodynamics of the larger arteries of the brain. One focus was on using a velocity-sensitive technique called 4D flow MRI, a research sequence that we in our group use in research on healthy aging and cerebrovascular diseases. In the first part of the thesis, we developed and evaluated methods for flow measurements with 4D flow MRI and found that it was accurate compared to the reference 2D PC-MRI method.

In the second part of the thesis, we combined 4D flow MRI with computational fluid dynamics (CFD), with implementation in a group of patients with symptomatic carotid stenosis. CFD can be used to simulate and analyse hemodynamic properties that are otherwise difficult to measure or assess. The patient group is interesting because the stenosis may disturb the blood flow supply and decrease the perfusion pressure to the brain. A way to better understand the disease is to analyse these blood flow and pressure disturbances.

While not entirely true, I have to friends and family said I spend the first half of 2021 in my living room, writing my thesis. It was a good winter for cross country skiing, with much-needed lunch breaks at Mariehemsängarna. When I try to remember the thesis writing, I think, “Well, it was quite a good time!”, repressing the sometimes stressful hours inside the house. I defended my thesis in May, with Professor Ronnie Wirestem at Lund university as my opponent. I couldn’t have a party, but I spent my evening with my family, during one of the sunniest summer days this year. Today, I’m doing a postdoc at the Department of Clinical Science (Neurosciences), using the 4D flow MRI technique for studying blood flow rates on a cohort of patients with carotid stenosis.

I’m so grateful to have had the possibility to work at the Department of Radiation sciences, and especially at Biomedical engineering. You caught my interest already during the master’s courses. I am also grateful for the chance of working in collaboration with UFBI, which gave me the possibility to recruit study participants and work with the MR-scanner. Now I’m curious about the future and hope that more people realize that the place of the heart is in the brain.

Madelene Holmgren

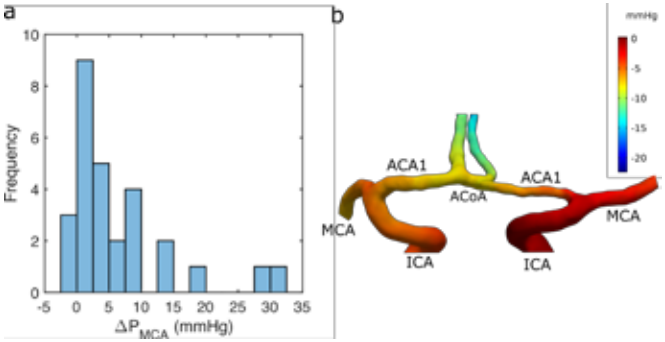


Illustration from Holmgren et al. (2021) Middle cerebral artery pressure laterality in patients with symptomatic ICA stenosis. PLoS ONE 16(1): e0245337.

(a) Hemispheric pressure lateralities between the ipsi- and contralateral middle cerebral artery (ΔP_{MCA}), for the whole carotid stenosis cohort. (b) CFD simulated pressure distribution in the cerebral arteries for one patient.

Dissertation: Deep brain stimulation in obsessive compulsive disorder

I started my clinical training in psychiatry in the spring of 2014. The local team's research on deep brain stimulation (DBS) for psychiatry welcomed me. I was initially hesitant over my choice: snow stays in Umeå until early May. However, until my thesis defense in October 2020, I have spent many winters and summers here working with psychiatric patients and researching DBS for severe obsessive-compulsive disorder (OCD). I've investigated the effect of DBS on severe OCD, which anatomical areas were being affected by the stimulation and the potential mechanism of action of the treatment.

Additionally, I explored the knowledge and concerns regarding DBS in OCD among psychiatrists, psychotherapists, and patients suffering from the disorder. During the defense, I got the opportunity to discuss the thesis studies and results with my excellent opponent, professor Keith Matthews, from the University of Dundee, Scotland. In the studies for my thesis, we investigate clinical outcomes and safety of DBS in a series of 11 participants with severe therapy-refractory OCD using data from clinical scales. Furthermore, using image and stimulation parameters from the same patients, we investigated through participant-specific simulation of the electric field, which anatomical areas were affected by the electric field, and if this could be related to the clinical results. In addition, some of the participants were evaluated with symptom-provoking fMRI pre-operatively. Finally, a web-based survey estimated psychiatrists, patients, and cognitive-behavioral therapists' previous understanding of DBS, source of knowledge, attitudes, and concerns towards the therapy.

Results from our study showed promising results. After one year of treatment, the participant's symptoms subsided on average from extremely severe to a lower range of moderate OCD. Concurrent depressive symptoms also reduced significantly. No severe complications occurred: the most common side-effect was transient insomnia. Our results were in line with previous publications regarding the effect and safety profile of DBS as a treatment in OCD. The individual electric stimulation fields by stimulation were similar at the 12, and 24-months follow-up, involving mainly other areas targeted for DBS near the anterior limb of the internal capsule. Our fMRI study found a significant decrease in anxiety-related brain activity in the pre-supplementary motor area (pre-SMA) and the anterior insula—two brain regions that play an essential role in the pathophysiology of OCD. Our survey found that psychiatrists and psychotherapists learn about DBS primarily from scientific sources. The patients' primary source of information was the media. Common concerns among all groups included complications from surgery, anaesthesia, stimulation side effects, and the novelty of the treatment. Specific concerns for the groups included; personality changes mentioned by patients and psychotherapists and ethical concerns among psychiatrists. I am very grateful for my doctoral study on an exciting topic, leveraging different study methods. UFBI and my advisor there, Johan Eriksson, supported my work with fMRI greatly. I have met many colleagues at the center and learned from their projects. The brain is a fascinating organ; I am looking forward to more clinical work and research in psychiatry and neuroscience.

Matilda Alexandra Naesström

Photo: Johan Eriksson

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Mid-term seminar: Increasing physical exercise intensity for older people: A HIT for body and brain?

I'm a PhD-student in sports medicine at the department of community medicine and rehabilitation, connected to UFBI and "Boraxbekk Brain Buddies". My mid-term seminar (October, 2021) was a great opportunity to evaluate my work so far, but also to discuss and reflect upon how to best proceed with the time that's left. My work is focused on physical exercise for healthy ageing among older adults. More specifically, examining motivation to exercise (PHIBRA Study and Umeå HIT Study), and effects of exercise, its duration and intensity on factors related to healthy ageing (Umeå HIT Study). The first study is based on data from the PHIBRA-study, and explores the link between dopamine D2R availability and exercise-related motivation, where it seems that frontal D2R availability play a role in intrinsic regulation of autonomous motivation to exercise.

The second study is based on data from the Umeå HIT Study, and what I'm currently working on. Here we examine the effects of regulated supramaximal high-intensity interval training (10 x 6-second intervals), as compared to 40 minutes of moderate-intensity training, on aerobic capacity and global cognition among older adults. Next, I will explore within-person change throughout the Umeå HIT Study exercise intervention with the aim to pinpoint important characteristics of our exercise protocols, that might be governing and add some explanation to the outcomes of study 2. These findings will hopefully also help shape the final study, which aim to further explore the effects of exercise on age-sensitive aspects of hippocampal structure and function, and a UFBI in-house episodic memory paradigm of pattern separation and pattern completion. Hopefully, this will add new insights of how different exercise modalities contribute to maintained health, and provide this population with new and effective exercise regimes that help promote healthy ageing throughout the lifespan.

Emma Simonsson

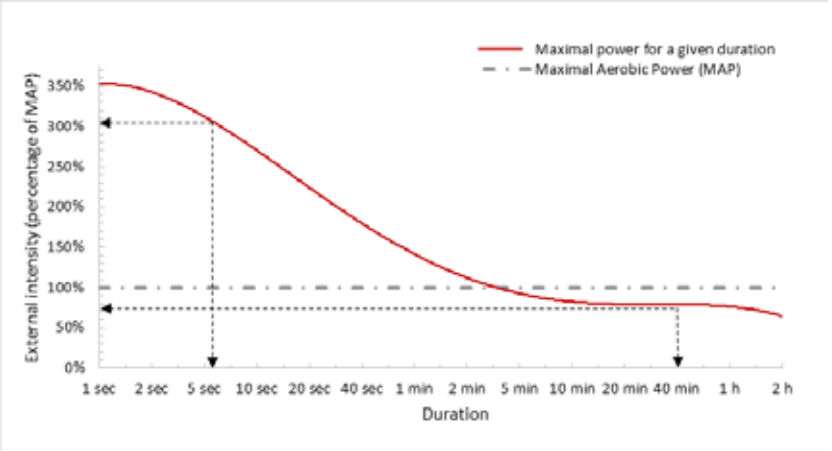

Illustration: André Nyberg

Figure of the relationship between external power output (as % of MAP) and work duration, highlighting the difference of mean maximal power that can be produced during 6 seconds compared to prolonged work of 40 minutes.

Mid-term seminar: The Functional Architecture of the Aging Brain: Structural and Molecular Mechanisms, & Consequences for Cognitive Decline

Being a PhD student has its benefits. For one, you are expected to put in time to learn about a whole lot of exciting things. Although, when everyday life tends to become a bit of a blur, you often don't realize what you have learned until you zoom out and appreciate the broader perspective of things. Indeed, there was a lot of "Zooming" this year – as a means of online communication.

Just before summer, at my mid-term seminar, I had the opportunity to share what I have learned at an online video conference. It's a funny thing though, presenting online. You naturally feel a bit secluded talking to a large audience from the comfort of your own desk, in an otherwise empty office. Nevertheless, presenting my work was a blast, and I got to talk about a project that ultimately resulted in a publication a few weeks later. In that project, based on a broader perspective of brain function, we found that the integrity of large-scale functional brain systems tends to decline in aging. In other words, brain activity across regions forming specialized functional systems become increasingly "blurred" with advancing age. Interestingly, reduction in the functional integrity was partly explained by concurrent changes in white matter integrity, in addition to being associated with reduced cognitive function. As such, like the appreciation of things I learn in the blurry memories of everyday life, changes in the brain's functional organization can be observed by simply zooming out a bit.

Robin Pedersen

Mid-term seminar: Cognitive function, quality of life and functional network: Before and after glioma surgery

My Phd project has its starting point from my position as a neuropsychologist at the neurosurgical clinic at Norrlands Universitetssjukhus where I work with glioma patients. Glioma is the most prevalent primary malignant tumor in the brain. Cognitive function, mental health, quality of life (QoL), somatic health and overall brain function is often significantly affected by the disease.

The first three of my projects have been investigating cognitive function, QoL, motor function and volition after glioma surgery in two specific brain regions; primary face motor area and supplementary motor area (SMA). Surgery in both these areas are associated with minor or temporary neurological deficits (mild face motor dysfunction and transient motor and speech disturbance respectively). We fortunately haven't found any major longstanding negative effects postoperative in either region.

In the fourth project we (me, my supervisor Rickard Sjöberg and co-supervisor Johan Eriksson) will focus on the process facilitating the recovery of motor, speech, and cognitive control functions after resection of SMA. The mechanism of the dramatic recovery of motor and cognitive function after SMA-surgery is not well understood but earlier studies have suggested that reorganization of the sensorimotor network plays an important role in regaining motor functions. We will investigate whether this kind of reorganization of functional connectivity also might be found in the salience and frontoparietal network.

Mattias Stålnacke

Meetings and seminars

The global Covid-19 pandemic continued during 2021 and physical meetings were still not possible and traveling pretty much non-existing. In spite of this, our monthly UFBI lab meetings where project plans, experimental designs, analysis strategies, results and articles are discussed continued in the same pace as during 2020 via Zoom. These meetings are still very well attended with the same number, or more, participants than before during the physical times. During the year we have had a couple of external guests presenting their research: at the March meeting, we were visited by Johan Lundström (SUBIC) and Moa Peter from Karolinska Institute, and at the meeting in December, Athena Demertzi (University of Liège).

In the fall after some of the restrictions had been lifted, a two-day PET-meeting 'NeuroPET' was organized in Umeå covering areas of cognitive neuroscience, neurodegeneration, methods & development as well as the future prospects of PET-imaging.

A list of presentations and given talks by UFBI members during 2021 is listed on page 23.

Photo: Iris Bosch

Participants at the NeuroPET-meeting in Umeå.

Media

The PNAS-publication by Nyberg et al. "Educational attainment does not influence brain aging" got a lot of attention, to the right is some of the media coverage.

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Selection of UFBI in the media during 2021:

”Hjärnforskaren vill hindra åldrandet av minnet”, news segment with Lars Nyberg on svt.se, 2021-12-13.

”Högre hjärnaktivitet efter aktiva lärandemetoder”, article with Sara Stillesjö and Carola Wiklund-Hörnqvist at Umu.se, 2021-12-02.

9 frågor: ”Jag har tillgång till ett fantastiskt forum”, article with Karolina Kauppi on being elected into the Young Academy of Sweden, in Västerbottens-Kuriren, 2021-10-03.

”9 frågor: Han vill förstå hjärnans roll i idrott” article with Carl-Johan Boraxbekk in Västerbottens-Kuriren, 2021-08-31.

”Går att lära nytt hela livet”, article with Lars Nyberg in Dagens Nyheter, 2021-08-23.

”Personer med diabetes får sämre minne av högt blodsocker”, interview with Olov Rolandsson on the PLOS ONE-paper, 2021-04-22.

”Anthony Hopkins som dement kan hjälpa sjuka”, interview with Lars Nyberg in Vetenskapspodden, Sveriges Radio, 2021-04-16.

”Fysisk aktivitet”, C-J Boraxbekk in the Tv-show ”Fråga doktorn Hälsa”, SVT, 2021-01-19


9 frågor: ”Jag har tillgång till ett fantastiskt forum”

Karolina Kauppi in Västerbottens Kuriren on being elected into the Young Academy of Sweden. Read more about it in her text on page 22.


Högre hjärnaktivitet efter aktiva lärandemetoder

NYHET Vilken typ av lärandemetod som används i skolan påverkar hur elevernas hjärnor aktiveras när de får göra kunskapstest vid ett senare tillfälle. En ny studie från Umeå universitet, publicerad i den vetenskapliga tidskriften PNAS, visar att elever som undervisats med aktiva lärandemetoder hade högre aktivitet i områden i hjärnan som kopplas till återaktivering av väl befästa minnen.

Article with Sara Stillesjö and Carola Wiklund-Hörnqvist at Umu.se.


9 frågor: Han vill förstå hjärnans roll i idrott

Interview with Carl-Johan Boraxbekk in Västerbottens Kuriren.

A decade with a research scanner

The GE scanner was installed in 2009 at the same time as I was employed as an MR physicist at UFBI. It was heavily committed to fMRI research but initially the system was not quite adapted to the vast amount of data that are being produced in such an exam. The system was sluggish and the reconstruction was not fast enough to keep up with the raw data collection, leading to unwanted waiting times in the exams. These problems were eventually overcome by a new reconstruction engine and the scanner has since then been a reliable workhorse for the UFBI researchers.

The projects that has been performed during the years has included many different aspects of brain functions and four out of five senses has been utilized as brain stimulation in the experiments. This has been made possible by a wonderful mix of researchers, doctors, research nurses, engineers and physicists that together have created an exciting and creative environment. Now that the time has come for decommissioning of the scanner I can only hope that the successor will be as useful to the brain research at UFBI as this one has been.

Greger Orädd

Photo: Mikael Stiernstedt

The 3T scanner from GE (General Electric) Discovery MR 750, 2009-2021.

Member of the young academy of science

This year, I was elected for the Swedish young academy of science for five years, that consists of about 35 independent researchers early in their career, from all academic disciplines. The young academy constitutes a strong voice in research politics and also engage in a large variety of outreach activities to increase the interest and trust in research in the society. I truly enjoy engaging in this work together with great young academics from other disciplines and universities.

Karolina Kauppi

UFBI, 20 years as a center

In the spring of 2001 former president of Umeå University (UmU), Inge-Bert Täljedal, invited Lars Nyberg and Roland S Johansson to send in an application to the University Board for some seed money from the strategic funds. Later that year UFBI was officially installed at the medical faculty.

In the midst of the global covid-19 pandemic, UFBI celebrated it's 20th year as a research center during 2021. The actual celebration was postponed due to the pandemic, but our hope is that it will be possible to have the celebration during 2022 if the situation permitts.

Publications

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

Original articles

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Dissertations

Naesström, M. (2021). Deep brain stimulation in obsessive compulsive disorder. Doctoral dissertation, Umeå University [*contains data from UFBI*].

Holmgren, M. (2021). 4D flow MRI and modelling to assess cerebral arterial hemodynamics: method development and evaluation, with implementation in patients with symptomatic carotid stenosis. Doctoral dissertation, Umeå University [*contains data from UFBI*].

Select conference presentations

Karlsson Wirebring, L. (November 3, 2021). Kreativ matematik: Evidens från ögonrörelser och hjärnavbildning. Online workshop presented at Exploratory workshop in cognitive & educational neuroscience, Umeå Universitet, Umeå, Sweden.

Karlsson Wirebring, L. (November 3, 2021). Kreativ matematik: Evidens från ögonrörelser och hjärnavbildning. Online talk presented at Kunskapsveckan Umeå Universitet, Umeå, Sweden.

Nyberg, L. (2021, Oct-Nov). Cross-sectional and Longitudinal Relations between Educational Attainment and Brain Aging. Invited zoom presentation at 3rd Workshop on Research Definitions for Reserve and Resilience in Cognitive Aging & Dementia, Bethesda, USA.

Nyberg, L. (2021, October). In search of transfer effects in cognitive-training studies. Invited zoom presentation at CRC Retreat, University of Magdeburg, Germany.

Nyberg, L. (2021, October). Individual differences in longitudinal memory aging – evidence from Betula. Zoom talk at Cajal course "Ageing Cognition", Bordeaux, France.

Nyberg, L. (2021, October). Educational neuroscience: Examples from studies of learning concepts and mathematics. Keynote presentation at SUBIC Brain Imaging Conference, Stockholm University.

Sandström, S. et al (October 19-20, 2021). Improving cognitive functions with physical exercise – a HIT? Presentation held at SWEAH Milestone Conference, Online.

Nyberg, L. (September 30, 2021). Educational neuroscience: examples from studies of learning concepts and mathematics. Talk presented at Brain Imaging in the Human Sciences, Online and at Stockholm University.

Nyberg, L. (September 28, 2021). Studies of 'brain reserve', 'cognitive reserve', and 'brain maintenance' - and some thoughts on 'resilience'. Keynote speaker at CRCs Neural

Resources of Cognition Annual Retreat 2021, Magdeburg, Germany.

Nyberg, L. (2021, July). Memory aging and brain maintenance. Keynote presentation (virtual) at the 32nd International Congress of Psychology, Prague, Czech Republic.

Nyberg, L. (2021, June). Brain maintenance. Invited zoom lecture for scientists at University of Padova and Geneva.

Pedersen, R., Geerlings, L. & Salami, A. (June 3, 2021). Functional brain networks and their structural underpinnings in the aging brain. Talk presented at Psychologie und Gehirn 2021 (PuG) (Online), Germany.

Björnfot, C. et al, (May 20, 2021). Measuring pulse wave velocity in the cerebral arterial tree using 4D flow MRI. Online talk presented at ISMRM & SMRT Annual Meeting & Exhibition 2021, Online.

Nyberg, L. (March 25, 2021). Individual differences in longitudinal memory aging – evidence from Betula. Talk presented held at Neurobiology of Cognitive Aging (NOCA) Consortium Conference, Online.

Boraxbekk, CJ. (March 24, 2021). Physical fitness and brain aging. Talk presented held at Neurobiology of Cognitive Aging (NOCA) Consortium Conference, Online.

Sandberg, P. (February 5, 2021). Gammal minnesstrategi i ett nytt format - Appbaserad minnesträning för att stärka kognitiv hälsa hos äldre. Talk presented at Riksstämman för Sveriges Neuropsykologers Förening, Sweden.

Eriksson, J. (February 4, 2021). Hur funktionell hjärnavbildning kan användas för att belysa ett ”inre liv” hos icke-responsiva patienter. Talk presented at Riksstämman för Sveriges Neuropsykologers Förening, Sweden.

Select science presentations

Nyberg, L. (Feb 28, 2021). On Memory, Consciousness, and Sorrow. Conversation with director Katarina Pierre in conjunction with Naeem Mohaiemen's new exhibition at Bildmuseet. https://www.bildmuseet.umu.se/en/events/artist-and-researcher-talk2222_10007562/

Nyberg, L. (Jan 21, 2021). Livslångt lärande i en åldrande hjärna. Talk presented at Kunskapsnoden 2021. https://www.umu.se/kalender/kunskapsnoden-2021_9886060/

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