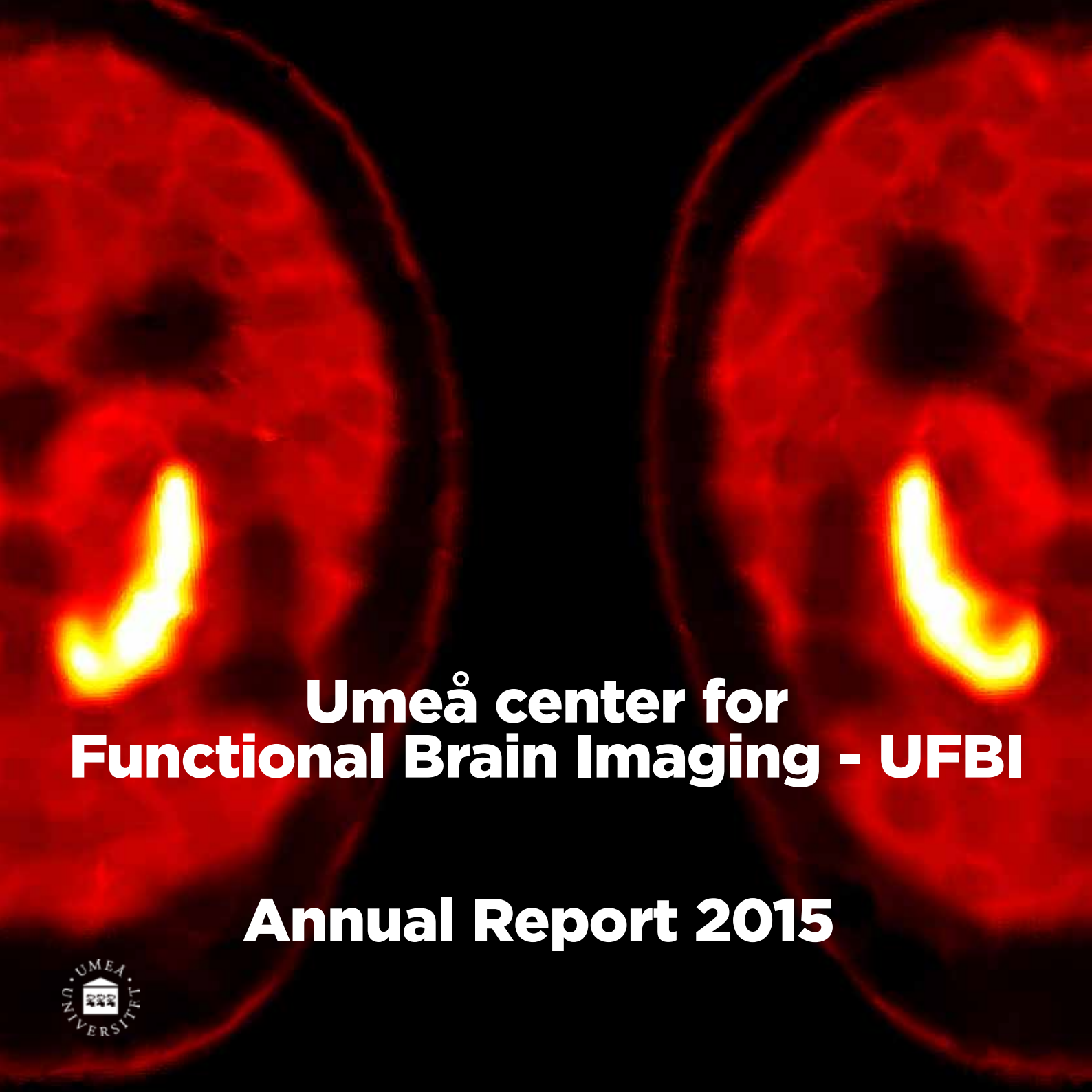

Umeå center for Functional Brain Imaging - UFBI

Annual Report 2015

UFBI
Umeå center for
Functional Brain Imaging

UFBI 2015 Annual Report

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Lars Nyberg's Editorial

Welcome to UFBI's Annual Report for 2015!

This report on UFBI activities strives to convey the wide scope of activities at our center, including both clinical and pre-clinical projects.

During 2015, a record high number of clinical examinations was accomplished. To this we can add the use of fMRI to map sensorimotor and cognitive functions in patients with brain tumors. A novel use of fMRI is as a "window" into the brains of patients who suffer from unresponsive wakefulness syndrome. UFBI's scientific coordinator, Johan Eriksson, presents a snapshot of these and related activities on page 8-9. Relatedly, on page 16, Nils Berginström discusses the use of fMRI in the study of fatigue following traumatic brain injury.

A strong focus of UFBI's research activities is on the aging brain. Here, the Betula project is a rich source of scientific study. A very valuable aspect of Betula is the existence of longitudinal data. On page 18, C-J Boraxbekk zooms in on a study in which current and past data on physical activity were related to brain integrity. Also, on page 10, Sara Pudas describes an exciting new project which will relate cognition and brain status in older age to childhood cognitive ability.

We have previously reported on the COBRA project in which a multimodal imaging approach is used, with scanning of the same individuals with both PET-CT and MRI. A similar approach is used in the PHIBRA project that examines physical influences on the brain in aging. Lars Jonasson and C-J Boraxbekk presents PHIBRA on pages 6-7. On page 11, multimodal imaging is taken to yet another level by Anna Rieckmann in her discussion of hybrid PET-MR. This is the latest methodological development in the field of brain imaging – internationally and within UFBI. Another exciting clinical and research line within UFBI is cerebral hemodynamics. Anders Eklund provides an overview of this field on page 15 – including a discussion of the brain in outer space!

In parallel with expansion of methods for data acquisition is development of analytic approaches. Brain imaging data are rich and possible to analyze in a variety of ways. For fMRI data the focus in the past was on univariate analyzes of how the response of a region changes as a function of a variable or intervention. A strong trend today is to also consider changes in the interactions among the many areas of the brain; so-called functional connectomics. On page 14, Micael Andersson and Anders Wåhlin give a brief overview of this approach. Analytical methods development has also been pursued for structural brain data, in particular images of white-matter hyperintensities. Greger Orädd walks us through recent efforts at implementing analytic procedures to quantify such hyperintensities and examine how they change in aging.

As for our past annual reports, Mikael Stiernstedt is the mastermind behind the layout and composition of the report. I hope we will succeed in sharing some of the excitement of brain research on the pages to follow.

February 29, 2016
Lars Nyberg, UFBI Director (2001 - Present)

In short

In 2015 the members of UFBI produced:

14 published articles

1077 clinical MR sessions

5 clinical fMRI sessions

657 hours of fMRI scanning

16 conference presentations

Research

PHIBRA – Physical influences on brain in aging

PHIBRA is the acronym of an exercise intervention examining how improved cardiovascular fitness is related to brain health in aging. In PHIBRA we have a multimodal imaging approach with a considerable MRI-protocol, including resting state fMRI, structural T1 and T2 images, diffusion tensor imaging, cerebral perfusion and blood flow. In addition, we also have an extensive cognitive test-battery of various memory functions. This battery comprises at least 3 tests of each cognitive domain including episodic memory, working memory updating and shifting, reasoning/visuospatial ability, executive attention and processing speed. A thorough testing of the participant's physical status is also performed.

One could think that this would be enough for a study of exercise-induced improvements of brain functions? But what really stands out in PHIBRA scientifically is that, as the first physical exercise intervention in the world, imaging of the dopamine system is included. This is made possible by having access to the PET/CT facility and the D2 tracer [11C]-raclopride at the University hospital of Northern Sweden. Thus, the goal with PHIBRA is to provide unique insights into the underlying neural mechanisms of exercise-induced improvements in cognitive functions with a particular focus on the dopamine system. Dopaminergic neurotransmission is related to many higher order cognitive abilities, it has a negative relationship with aging, and it has been shown, from another UFBI-study, that dopamine is related to transfer following working memory training. Thus, by including imaging of dopamine we believe that there is a potential for this project to provide novel insights into what underlies successful transfer of cognitive functions, which is the primary goal of most interventions.

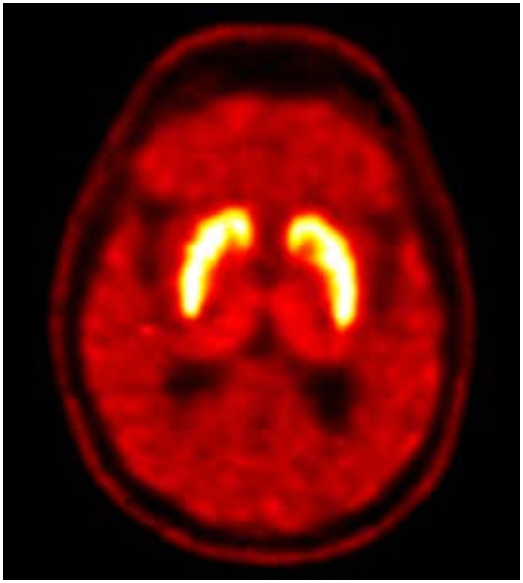
In PHIBRA, 60 participants (64-78 years of age) were randomized either into an aerobic exercise group or an active control group. The aerobic exercise included

Photo: Angelica Sandström

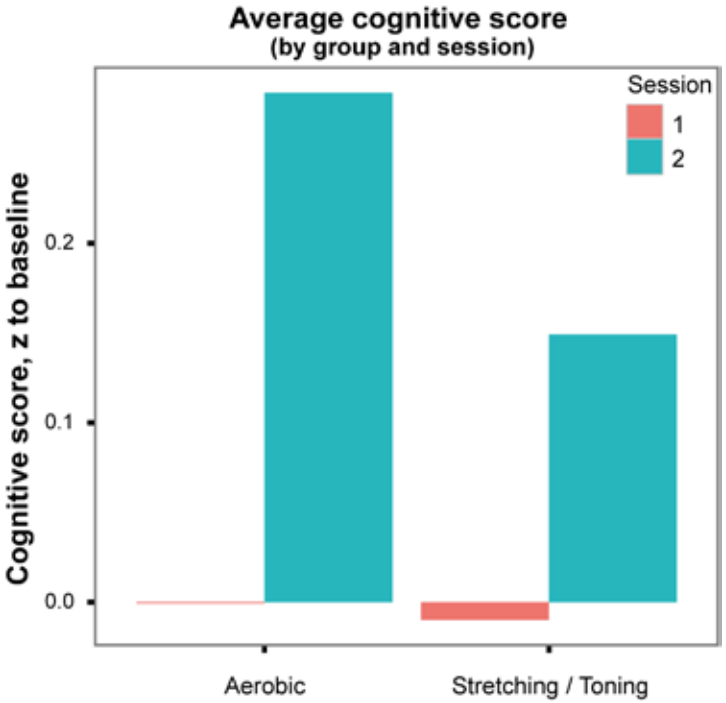
Participants in the aerobic training group during one of their training sessions.

power walking, cross training, or cycling at individualized training intensities based on the results from the physical status at pre-test. Training took place with a dedicated trainer 3 times per week, approximately 1 hour each time. The control group also met 3 times per week for balance, stretching and core stability training. 59 (!) of the included 60 participants completed the intervention. In total we have close to 1000 hours of testing on 763 separate testing occasions, providing us with a multitude of important brain and cognitive outcome variables.

We can already now say that the intervention was a success. The physical fitness data show that we have a clear difference in improved oxygen uptake in favor of the aerobic training group. This may sound trivial and easily accomplished, but it is actually essential and not at all something one can take for granted will occur when doing intervention studies. So, the first step in order to further understand exercise effects on brain function and the role of dopamine is taken. We can also see an initial effect favoring the aerobic training group on a broad measure of cognitive functioning. We are now currently analyzing



Dopamine D2 binding potential. Due to its' high density of D2 receptors, striatum appears brighter than other brain areas.



Illustrations: Lars Jonasson

The cognitive score is derived from the average of episodic memory, processing speed, working memory updating and shifting, and executive attention. The graph shows that aerobic exercisers had improved cognitive score compared to our control group.

more of the imaging data, which of course is very exciting.

To complete a study like PHIBRA it requires a team from many different disciplines, including sports medicine, radiology, radiochemistry, physics, and cognitive neuroscience. We believe PHIBRA should be seen as a good example of how people from different disciplines can join together within UFBI to complete studies targeting important questions such as brain health in aging. Without the infrastructure and variety of competencies this study would not have taken place.

We would also like to highlight that PHIBRA is making a nice link into another UFBI dopamine project, the longitudinal study COBRA. This should also be seen as a strength. Having similar types of data collected in different groups within UFBI gives us more power and possibilities when mapping and understanding the functions of the human brain.

Lars Jonasson
Carl-Johan Boraxbekk

Studying patients with fMRI

Since 2008, we at UFBI have performed functional brain imaging on patients at Norrland's University Hospital (NUS). Some examinations have been driven purely by clinical questions and others have been more research oriented. On the clinical side, we have in collaboration with neurosurgeons at NUS performed pre-operative mapping of a number of sensorimotor and cognitive functions in patients with brain tumors, and also mapping of topological representations to improve placement of electrodes implanted to alleviate chronic pain (see UFBI Annual Report 2011). More than 40 patients have been mapped over the years, and pre-operative mapping is now almost done by routine.

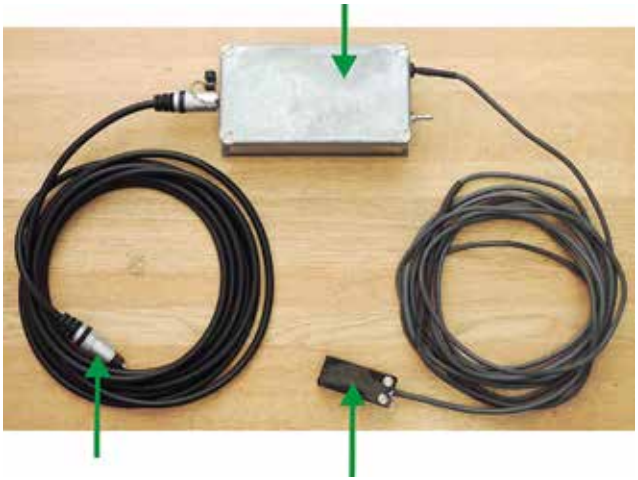
A tragic but intriguing group is patients with so-called "unresponsive wakefulness syndrome", including states of coma, "vegetative state", and minimally conscious states. Given that they are unresponsive to verbal commands and sensory stimulation as part of their condition, these patients are very difficult to characterize by standard clinical means. Recent research has demonstrated that some such patients can show signs of complex mental activity when examined with fMRI, and we are currently helping the neurorehabilitation center at NUS with such examinations.

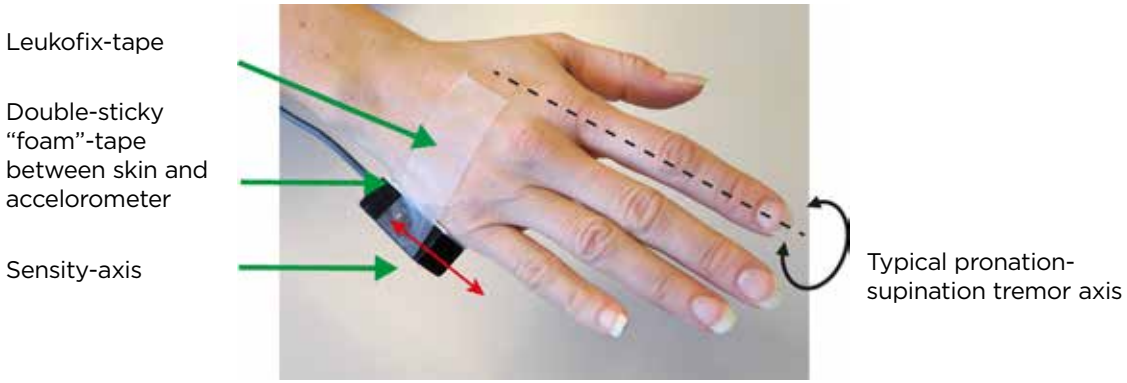
On the more research-oriented side, we are currently investigating spared brain-body connectivity in spinal cord injury patients (see UFBI Annual Report 2014), and are collaborating with the Deep Brain Stimulation (DBS) unit at NUS to better understand the neuropathological mechanisms of essential tremor and obsessive-compulsive disorder. The effects of DBS stimulation are characterized with fMRI, a combination that poses several methodological challenges.

A highly valued person that works with us at UFBI is the research engineer Göran Westling. Göran can build almost anything that is required for performing fMRI experiments even though the high-field magnets severely limits the use of regular equipment, and his gadgets have been indispensable in many research projects. This is nicely exemplified by the accelerometer that he built for characterizing the tremor-alleviating effects of DBS, that can be attached to the patients hand even during fMRI examination without distorting the MR signal (see figures). The DBS effects on tremor can thereby be precisely quantified and related to how brain activity changes as a function of the DBS stimulation.

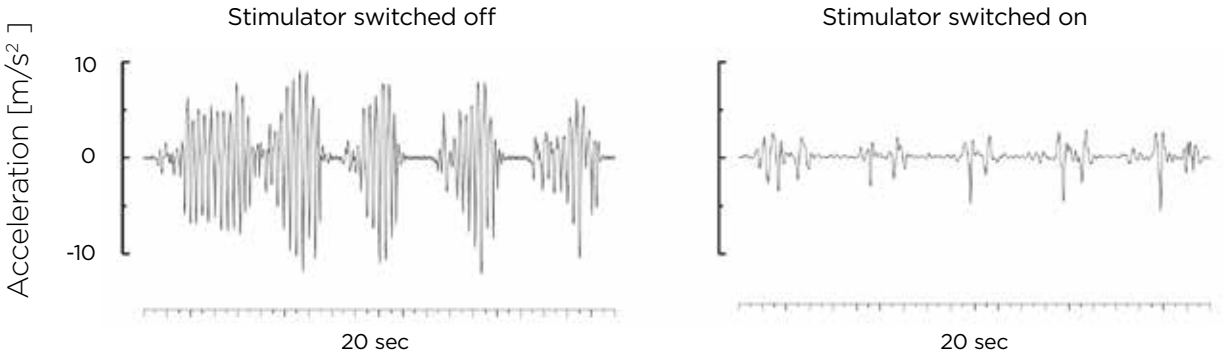
Many other patient groups have been studied with fMRI here at UFBI over the years, including patients with Parkinson's disease, stroke, depression and stress-related conditions, peripheral nerve damage, and social anxiety. In addition to the new scientific knowledge that has been generated, it is rewarding to put our knowledge of fMRI and brain function to use in helping others.

Johan Eriksson





Photos and illustration: Göran Westling



Acceleration during five reaching movement in a Philips 1.5 Tesla MR-scanner by a patient with a deep brain stimulator.

The determinants and neural correlates of lifespan changes in cognition

In June 2015 the Royal Swedish Academy of Sciences awarded 1.5 million SEK to a project that will investigate how childhood cognitive ability is associated with cognition and brain status in old age, and how lifestyle factors may relate to cognitive changes across the lifespan. The funds come from the Lennart "Aktiestinsen" Israelsson Foundation.

The project will involve supplementing the existing Betula database with school grades as a proxy measure for cognitive ability in childhood. As the Betula database already contains longitudinal cognitive, health, and questionnaire data for up to 25 years for a large number of individuals, in addition to two neuroimaging sessions, this will constitute a truly unique setting to investigate the questions at hand.

We hope that the upcoming project will replicate and extend previous findings of relationships between childhood IQ test scores and cognitive and neural outcomes in older age, as well as studies from the Karolinska Institute that have found school grades to predict the occurrence of dementia. In the current project we intend to investigate, for instance, whether school grades predict age-related cognitive and neural changes in the absence of dementia, and whether we can identify lifestyle factors such as educational and occupational attainment, or health behaviors, which may mediate or moderate the association between childhood and old age cognitive ability.

The project is currently in the start-up phase, with collection of school grades from the city archive (Stadsarkivet) in Umeå expected to commence early in the spring of 2016. Two project assistants will be hired to perform this data collection, in which we hope to retrieve grades for up to 1000 Betula participants.

Sara Pudas

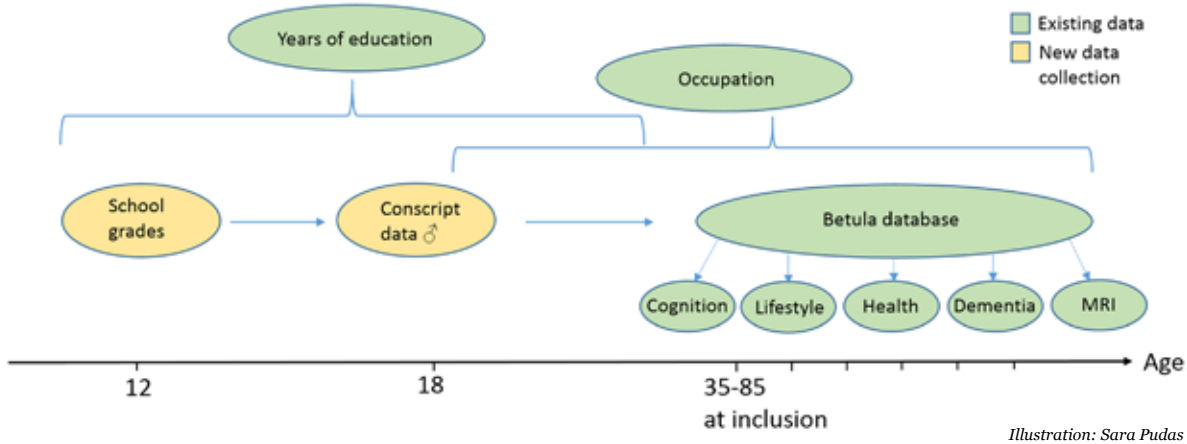


Illustration: Sara Pudas

Hybrid PET-MR: A new era for functional brain imaging?

There is no doubt that fMRI led to a breakthrough in our ability to measure how the complexities of the mind are rooted in biology. However, while fMRI measurements are sensitive to transient changes in mental and behavioral states, they are not quantifiable relative to an absolute zero point and reflect complex interplay between hemodynamic and metabolic demands that cannot be resolved by fMRI alone.

The recent development of a hybrid positron emission tomography (PET)-MR scanner allows simultaneous assessment of fMRI signals and measurements of synaptic activity and neurotransmitter densities. In November 2014, one of two hybrid PET/MR scanners in Sweden was installed at Umeå University hospital and in the fall of 2015, researchers at UFBI started to explore the usefulness of PET/MR in functional brain imaging. A first pilot study explore whether it is possible to concurrently track fMRI signal changes and dopamine release in motor areas of the basal ganglia during a simple finger movement task. The dopamine system has long been of interest to Lars Nyberg's lab at UFBI because of its involvement in cognitive decline in aging as well as neurodegenerative and psychiatric disease.

Early results are suggesting that, as an individual begins to move their left hand, fMRI activation in the corresponding motor area of the basal ganglia is accompanied by PET-based measures of dopamine release that correlate both in space and time (see Figure). Although the experimental design and analyses are still under development, and the results require further validation, these preliminary efforts encourage the application of this method to more complex cognitive tasks and different patient populations. The research is conducted in Lars Nyberg's group by Anna Rieckmann, together with Jan Axelsson and Patrik Brynolfsson, and in close collaboration with Katrine Åhlström Riklund.

Anna Rieckmann

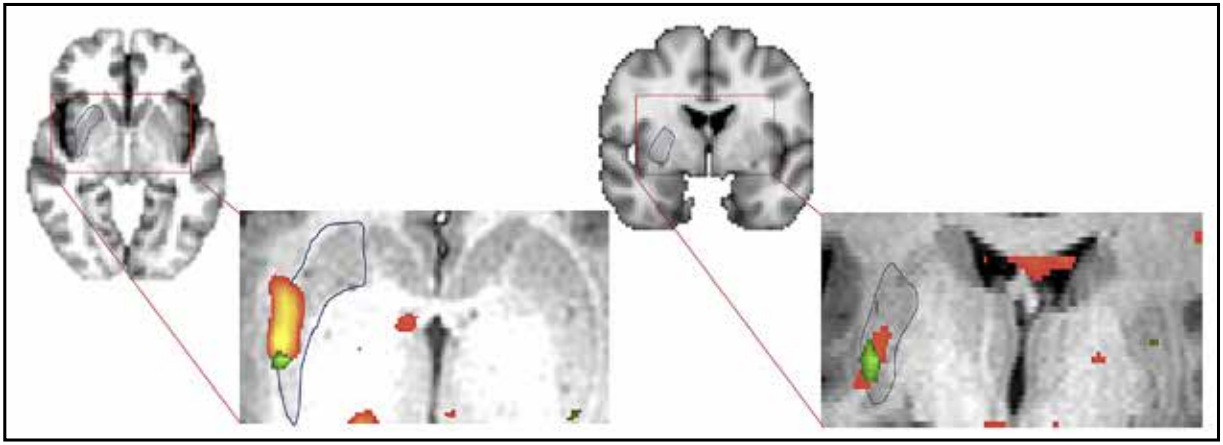


Illustration: Anna Rieckmann

A close up of the motor region of the basal ganglia (highlighted in blue) shows concurrent fMRI activation in red-yellow and dopamine release in green (measured simultaneously with PET) as an individual starts to move their left hand.

White matter hyperintensities

White matter hyperintensities (WMH) is the name of lesions observed in MR and CT-scans of the brain. They are more common in elderly people and reflect demyelination and axonal loss of the white matter (WM). The cause of WMH is believed to be chronic ischemia caused by cerebral small vessel disease. In MR they are seen as hyperintense regions in proton density, T2-weighted, and flair images. WMH is known to contribute to cognitive decline in aging, although the coupling between WMH burden and cognition is rather weak. This might be a consequence of the difficulty in quantifying the WMH burden.

There are several different methods of quantifying WMH, ranging from visual rating to semi-automatic and automatic methods. In the large datasets presented in e.g. the Betula project, visual rating will be very time-consuming and we have therefore investigated methods for automated WMH quantification. The method described here is based on simple thresholding in flair images.

Figure 1 shows schematically the procedure used. First, the T1-weighted image is used for WM segmentation. Two different software packages are used, FreeSurfer and SPM12, and the results are combined to one WM mask in order to be as inclusive as possible. This mask is applied to the flair image to extract the WM data. The intensities are fit to a normal distribution from which the mean, μ, and standard deviation, σ, are extracted. A threshold is calculated as $\mu + 3.5^{*} \sigma$ and all intensities above that value is regarded as WMH.

Using the method outlined above, the WMH volume can be automatically extracted for all subjects and the results are shown in Figure 2, showing that WMH tend to increase with age, in line with previous studies. We also have indications that the rate of change increases with age. We are presently investigating if cognitive changes can be coupled to WMH progression.

Greger Orädd

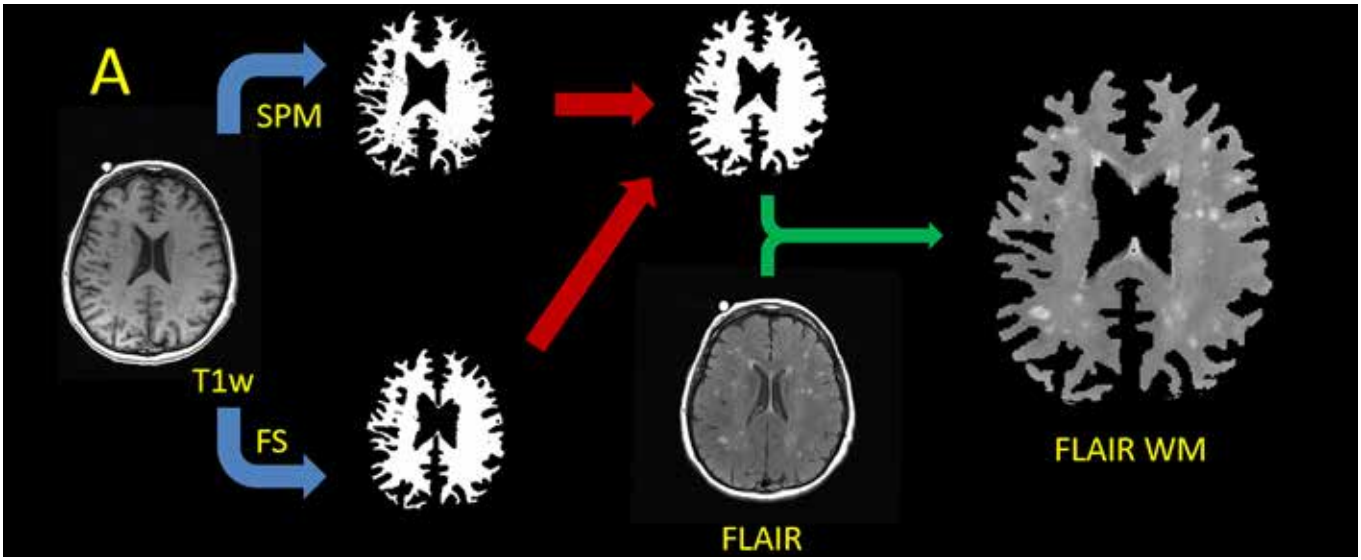


Figure 1. Schematic illustration of the method. A) Selection of flair WM. Blue arrows: creation of WM masks, Red arrows: Combination of the two masks into the WM mask, Green arrow: masking the flair image to extract WM voxels. B) Histogram of the intensities of the WM voxels with fit to normal distribution. The threshold is indicated by the blue vertical line, with normal WM to the left of it and WMH to the right. C) Resulting WMH in red, superimposed on the flair image.

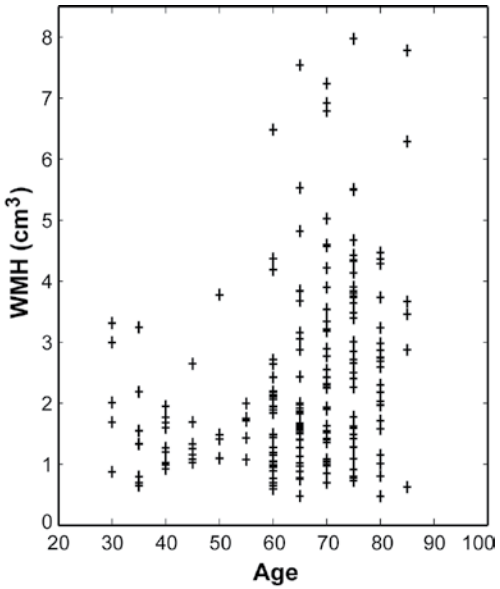
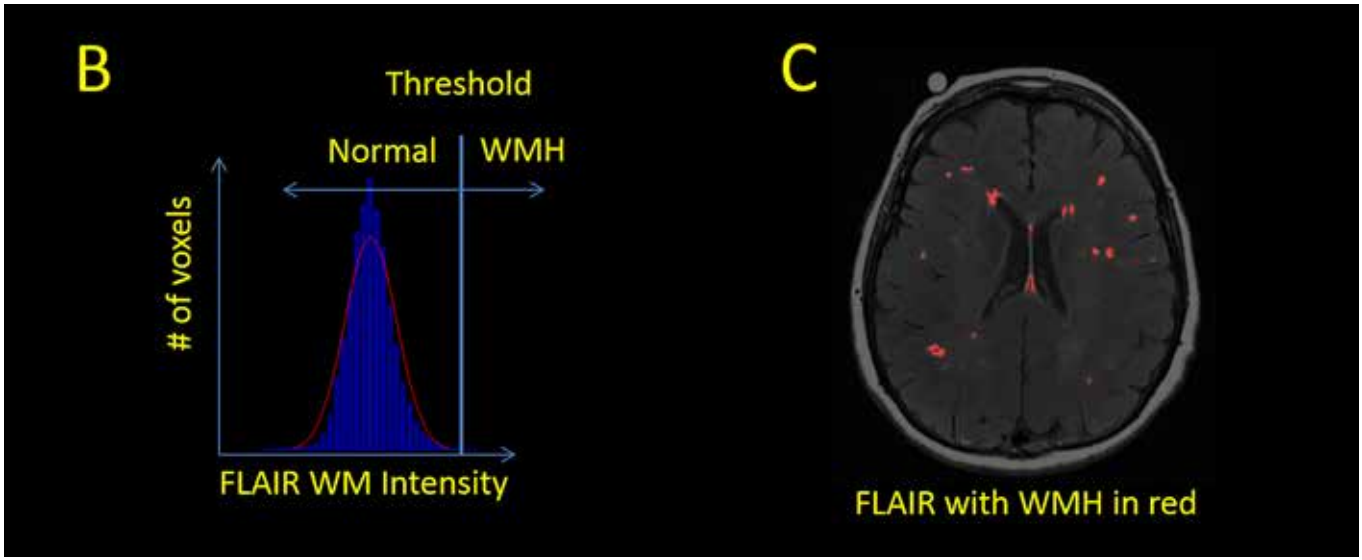


Figure 2. WMHs from 213 subjects in the Betula study.



Illustrations: Greger Orädd

Functional connectome research

Coherent brain activity defines neural networks and network interactions that ultimately determine our individual behavior. The macro-scale (>1 mm) architecture of such coherent brain activity can be mapped using functional MRI by assessing the temporal correlation between all possible combinations of brain regions, i.e. the functional connectome. Even at this macro-scale level, the functional connectome display vast unique individual features that sub-serve our behavior.

At UFBI, we are currently implementing such connectome analyses for discovering cohesive brain systems accounting for important cognitive domains. Specifically we are examining the functional connectome at rest and at task (and the difference between those two states) and their relation to cognition. This approach will allow us to reveal if spontaneous neural communication or neural communication recruited by a specific task is correlated to level of performance.

Using longitudinal data from the Betula project, we will examine sensitivity to aging and characterize the neurodegenerative alteration with respect to models of neural signaling. Here, an important step will be integration of cerebral blood flow measurements into the analyses in order to better make distinctions regarding the underlying neurodegenerative mechanism.

Alongside our research we perform technical development aimed at improving both the sensitivity and robustness of our connectome analysis. A key ambition in this work is to finding optimal ways of reducing the size of the data in the final statistical tests while preserving as much of the individual richness in the data as possible. Our algorithms for detecting connectome-cognition associations are also being integrated in the local software DataZ to provide an accessible framework for collaborators to participate in the endeavour of tying functions to the functional connectome.

Micael Andersson & Anders Wåhlin

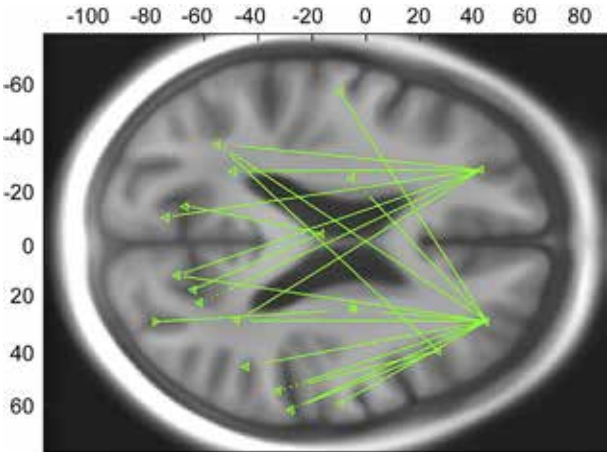


Illustration: Micael Andersson

Connectome at Z=-20. Frontal lobe GM-areas have a widespread longitudinal difference in temporal correlations that are related with the longitudinal difference in episodic memory performance. Temporal correlations were calculated during a resting state fMRI-series.

Cerebral hemodynamics

In collaboration with PIs Jan Malm and Anders Eklund at the Departments of Clinical Neuroscience and Biomedical Engineering, respectively, we are investigating cerebral blood flow in aging and stroke. We are also investigating stroke related functional deficits and potential benefits from innovative rehabilitation strategies by mapping brain function in task and rest conditions.

Stroke is one of the leading causes of death and chronic disability in the world. Moreover, vascular risk factors are frequently associated with cerebral aging and dementia. We aim to improve the stroke diagnosis by adding valuable information concerning the capacity of the secondary, emergency blood vessels that the brain possesses in order to withstand deviations in blood flow of the large cerebral arteries. Ultimately, this information will be used to predict disease development. Another direction of our research in cerebral hemodynamics tries to relate deviations in blood flow, such as decreased perfusion and increased pulsatility, to structural damage and cognitive decline among elderly subjects.

We are also studying the physiology of the cerebral venous drainage and its relationship to hydrostatic effects from gravity. The background is a syndrome identified in astronauts who have had long duration mission on the space station. They get visual symptoms that can cause permanent problems for the astronauts and jeopardizes future planned space activities such as long duration stays at the Space Station or missions towards Mars. For the diseased astronauts the visual symptoms are often associated with an increased intracranial pressure and a possible disturbance in venous drainage. Understanding this physiology can potentially be of importance in diseases like glaucoma, hydrocephalus and intracranial hypertension.

To assess the cerebral vessel hemodynamics we apply high-resolution phase contrast flow measurements with whole brain coverage (4D flow). Additionally we apply 3D arterial spin labeling to quantify brain tissue perfusion. The complementary nature of these techniques allows a comprehensive analysis of deviations in blood flow. The 4D flow measurements have been developed at the University of Wisconsin and within a productive collaboration we are applying this technique to extract vital and previously unknown properties of the cerebral circulation. A technical development is paralleling our clinical studies. Here, we strive to improve 4D post-processing strategies and to develop rational tools that ultimately can be used by clinicians.

Illustration: Anders Wåhlin

4D based flow tracking, showing cerebral arterial branches supplied by the main artery of the neck, the Internal Carotid Artery.

In order to understand the neuronal mechanisms underlying stroke related symptoms and effects from symptom rehabilitation we are applying conventional fMRI as well as functional connectivity analyses. Such connectivity analyses maps correlated patterns of intrinsic and/or evoked activity across surface of the brain and adds a further dimension to the MR-based characterization of the neural integrity. This rich information will generate new insights regarding the brain's functional organization and potential functional reorganization following a stroke.

Anders Eklund

Traumatic brain injury and fatigue

Traumatic brain injury (TBI) has been reported to annually affect more than 10 million people globally. A majority of survivors of TBI recover well within the first weeks or months, but some will experience persisting and disabling symptoms for years to come. One of the most common sequelae for patients with persisting symptoms after TBI is fatigue, which has been reported to be found in up to 75% of TBI patients with persisting symptoms. Fatigue is a truly disabling symptom which affects both activities in daily life and occupational ability as well as physical and social functioning.

Despite the incidence of post TBI fatigue, understandings of what it is and its etiology are lacking. Today there are no empirically supported medical or behavioral treatments for fatigue in patients with TBI. Furthermore, due to vague operationalization of the term, the measurement of fatigue is difficult and no "gold standard" for measuring post TBI fatigue exists.

We aimed at studying post TBI fatigue using fMRI. We recruited patients with TBI suffering from fatigue (n = 57) from the clinical trial of OSU6162 set at the Neurorehabilitation clinic at the Northern University Hospital in Umeå. Healthy controls (n = 27) with no previous history of TBI or any other neurological disorders were also included.

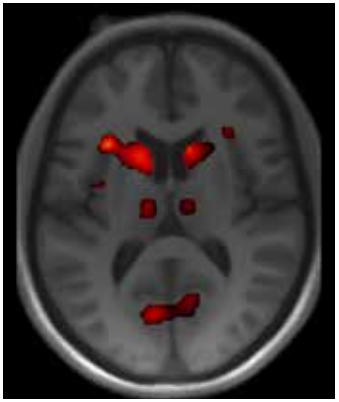


Illustration: Nils Berginström

Differences in task activation between patients with TBI and controls. The figure shows regions (Bilateral caudate, thalamus, anterior insula and calcarine) where controls activated higher than patients with TBI.

All participants performed a fatiguing sustained attention task (the modified Symbol Digit Modalities Test) while in the fMRI scanner. Immediately before and after the task, participants were asked to rate their fatigue. There were no differences between groups in accuracy when performing the task, but the TBI group had slower reaction times. Furthermore, the TBI group showed a greater increase in fatigue from before to after performance of the task.

The fMRI data revealed major differences between patients with TBI and controls in recruitment of regions within the basal ganglia (caudate and putamen), thalamus and other subcortical areas. Within these areas, patients had markedly reduced activation. When controlling for differences in reaction time, education and depression, the differences were attenuated but remained within the caudate, left insula, and some other subcortical areas. These results lend support to the hypothesis that central fatigue in TBI and other neurological disorders to some extent is dependent on striato-thalamic-cortical loops.

Furthermore, the data showed that controls deactivated to a larger extent within these regions over time, while patients with TBI remained on a more constant level of activation. This was seen despite no group showing neither decline nor improvement in performance. This indicates that studying only level of performance on neuropsychological tasks with the aim of measuring fatigue, may not be enough.

This being the first larger study to show differences in brain activation that could be related to fatigue in patients with TBI, more research is needed to replicate and further elaborate on these results.

Nils Berginström

The Human Brain Project

In October 2013 the "Human Brain Project" (HBP) was inaugurated, involving as many as 135 institutions across Europe, including UFBI. The general goal of the HBP is to integrate as much knowledge of the human brain as possible, in order to further our understanding of "the most complex structure in the universe", but also to develop new informatics and computer tools. To achieve this, efforts are made at multiple fronts, from detailed anatomical mapping of mouse and human brains, to neurorobotics, computer simulations, and hardware development. The UFBI contribution to this colossal project has been to describe the "cognitive architecture" of working memory, which will serve as a high-level description that can be implemented in, and constrain, computational models.

Work on cognitive architectures has been the lead topic for "sub-project 3" (SP3; the HBP consists of 13 SPs in total) and recently resulted in a special issue in Neuron. In addition to the UFBI contribution on working memory, the issue also included descriptions of sequence representations, memory consolidation, spatial navigation, confidence, infant brains, attention, visual perception, body representations, action processing, the social brain, large-scale brain networks, and brain oscillations – topics that together represent the work of SP3 during the first 2.5 years of the HBP, the so-called "ramp-up phase". By March 2016, the next phase of the HBP will start, where the SP3 is completely reorganized and will not contain any of the current research groups, including UFBI.

The work of describing the cognitive architecture of working memory has included exploring the possibility of non-conscious working memory (as has been described in previous Annual Reports). This and other explorations of working memory will continue at UFBI, but outside the regimen of the HBP.

Johan Eriksson

Zooming in

Very few people, if any, question that a good way of maintaining our bodily health is to engage in physical exercise. What many may not realize is that staying physically active may also positively affect our brain health. In the last decade there has been a substantial increase in studies investigating the relationship between physical exercise and brain function. The important question we are asking us in this research field is whether we, by staying physically active, can reduce some of the negative effects age has on brain function, structure and memory performance?

Evidently this is a multifaceted question. Many previous studies, however, have addressed this question by using a single imaging modality. Although important, these studies have only given us answers about how one particular brain measure is related to physical activity. The downside with this tactic is that it makes it a bit difficult to get a clear picture of the overall, combined effect, of physical activity on brain health. To overcome this issue we decided to have a different approach. Instead, we used the rich material offered from the Betula cohort, which includes health data related to physical activity, a comprehensive cognitive test battery, and imaging data on functional connectivity, gray matter volumes, cerebral perfusion and white matter integrity. By combining these different modalities into the same analysis we believe that we can gain a deeper understanding regarding the association of physical activity and brain health in aging.

We started the analysis by focusing on whether physical activity was positively affecting the functional connectivity within age-sensitive resting state networks. We then further quantified the gray matter volume, the cerebral perfusion and the white matter integrity in any physical activity sensitive resting state regions. This way, we were able to gain a combined idea regarding how various brain regions are affected by physical activity based on multiple brain imaging measures.

Boraxbekk, C.-J., Salami, A., Wåhlin, A., & Nyberg, L. (2015). Physical activity over a decade modifies age-related decline in perfusion, gray matter volume, and functional connectivity of the posterior default mode network - a multimodal approach. NeuroImage.

What we discovered was that one particular region of the brain, the posterior cingulate cortex (PCC), which is part of the default mode network, was related to physical activity in all imaging modalities except fractional anisotropy, our white matter integrity measure. We found this result very exciting, because for the first time we were able to show how various brain measures point in the same direction, making a stronger case regarding what effects one can expect from physical activity on brain health.

One reason why this finding was so exciting is because this particular brain region (PCC) appears to be a central region to keep in good shape in order to maintain good brain health throughout the lifespan. It has been shown that this part of the posterior default mode network may be a region affected by atrophy, accumulation of beta-amyloid, and reduced connectivity in the early stages of dementia. Thus, our observation that this particular region is maintaining its integrity if you are staying physically active gives us further evidence regarding how important physical activity may be to reduce cognitive decline and possibly postpone dementia onset.

In this study, we concluded that the multimodal imaging approach undertaken here shows that physical activity exerts an influence on brain-behavior relationship in a brain region important for good brain health in aging. The next step will be to use multimodal imaging to further understand how the brain reacts when older people's exercise levels are changed.

Carl-Johan Boraxbekk

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, and results are discussed in an informal setting to benefit from the whole brain trust of UFBI.

Besides these in-house meetings, members of UFBI usually attend several meetings and conferences held in and outside Sweden. A list of attended conferences is shown on page 25-26. In addition to visiting conferences, members of UFBI are often invited to give talks and presentations to the public at different events. To the right is a list of some of the presentations that were given during 2015.

UFBI lag day, June 18, 2015.

Public science presentations

Eriksson, J. (2015, November 24). Medvetandet och hjärnan. Research talk given in relation to the exhibit "The world was flat" at Bildmuseet, Umeå, Sweden.

Nyberg, L. (2015, November 13). Myten om åldersglömskan. Presentation at Sopplunch och föredrag: Ersboda folkets hus, Umeå, Sweden.

Boraxbekk, CJ. (2015, April 23). Challenging the views of aging. Talk presented at TEDx, Sliperiet, Umeå, Sweden.

Jonasson, L. (2015, March 19). Prospective reward: effects on dopamine release and cognitive control. Presentation at Sympoisa on Mechanisms of reward and associative learning. Stockholm, Sweden.

Karlsson Wirebring, L. (2015, March 19). A reinforcement learning approach to testing hypotheses about causal structure. Presentation at Sympoisa on Mechanisms of reward and associative learning. Stockholm, Sweden.

Wiklund-Hörnqvist, C. (2015, March 19). Key factors that influence the Testing Effect: Repeated Retrieval & Feedback. Presentation at Sympoisa on Mechanisms of reward and associative learning. Stockholm, Sweden.

Nyberg, L. (2015, March 18). Minnet och glömska. Talk presented at Hjärnans Dag, theme day by Hjärnfonden, Stockholm, Sweden.

In late November (24-25), there was a workshop on longitudinal imaging studies, which UFBI co-organized together with the Karolinska Institute (KI) and the StratNeuro research program. It was held at KI, and featured speakers from UFBI, KI, Leiden University and the University of Illinois. The workshop started in the afternoon of the 24th with a methodological introduction, primarily focused on statistical methods for analyzing longitudinal studies in general and imaging studies in particular. It was given by the workshop organizers, Rita Almeida from KI and Anders Lundquist from UFBI. Following the introduction, the remainder of the workshop featured 11 contributed talks on a variety of topics. Four talks were given by UFBI members (Amar Awad, Anna Rieckmann, Lars Jonasson, Sara Pudas). The experiences from this workshop were all positive, we feel encouraged to proceed with further co-organized UFBI/KI workshops.

Organizers Anders Lundquist (UFBI)
Rita Almeida (KI)

Members

Group Boraxbekk

Photo: Angelica Sandström

Name: Carl-Johan Boraxbekk
Discipline: Neuroscience
Research and work: I work as an Associate Professor (Docent) of Neuroscience at the Ageing and Living Conditions Programme (ALC). In my work I am examining how life style factors such as diet and physical exercise may help to preserve brain structure and function across the lifespan.

Name: Frida Bergman
Discipline: Medicine
Research and work: I am a physiotherapist and PhD student who is currently working within a project where we will investigate the effects on cognition, functional brain response and brain structure when decreasing sedentary time and increasing NEAT - that is, everyday exercise – at offices.

Name: Lars Jonasson
Discipline: Cognitive neuroscience
Research and work: I am a PhD student part of the PHIBRA project (Physical Influences on Brain in Aging). We use PET to investigate potential plasticity-induced changes to the brain's dopamine system and cognition following physical activity. This is particularly exciting as the system is associated with multiple aspects of cognition.

Name: Hanna Malmberg-Gavelin
Discipline: Cognitive neuroscience
Research and work: I am a PhD student in the RECO-project (Rehabilitation for Improved Cognition). My main focus concerns the impact of stress on cognition and treatment of cognitive impairments in patients with stress-related illness. The aim is to examine the possibilities of using computer-based cognitive training for improving cognitive functions.

Other people affiliated to group Boraxbekk: Andreas Stomby (PhD), Peter Lundström (research assistant), Kristoffer Månsson (PhD student).

Group Eriksson

Name: Johan Eriksson
Discipline: Cognitive Neuroscience
Research and work: I am a researcher and scientific coordinator at UFBI and use fMRI to study the neural correlates of consciousness, several forms of memory and other cognitive functions, and to perform preoperative mapping of brain functions.

Name: Amar Awad
Discipline: Clinical Neuroscience
Research and work: I am a medical doctor and a PhD student. My interests revolve around clinically oriented brain imaging research such as exploring the mechanisms of deep brain stimulation in treatment of essential tremor, residual sensory function following spinal cord injury and the clinical impact of white matter hyperintensities.

Name: Fredrik Bergström
Discipline: Cognitive Neuroscience
Research and work: I am a PhD student that uses fMRI to study the neural correlates of consciousness. I am particularly interested in the role of attention and memory for consciousness, and is currently investigating the possibility of working memory without conscious experience and its potential limitations.

Other people affiliated to group Eriksson: Urban Ekman (PhD), Matilda Naesström (PhD student).

Group Nyberg

Name: Lars Nyberg
Discipline: Cognitive neuroscience
Research and work: I am a professor of Neuroscience and the Director of UFBI. PI for work on cognitive training and imaging within the longitudinal Betula project. I am a member of the Swedish Royal Academy of Sciences. In 2007 I received the Göran Gustafsson award in medicine, and in 2009 I became a Wallenberg scholar.

Name: Nina Karalija
Discipline: Neuroscience
Research and work: I am a postdoc at the Department of Radiation Sciences. The focus of my research is the study of brain structure and function that could be responsible for cognitive decline in the healthy elderly population. My project revolves around investigating changes in the dopamine system by measuring dopamine receptor availability using PET.

Name: Lenita Lindgren
Discipline: Nursing
Research and work: I am a PhD whose main interest is to understand emotional and physiological responses observed during rewarding stimuli such as human touch. In my research I used fMRI to identify brain regions activated by pleasant human touch.

Name: Anders Lundquist
Discipline: Statistics
Research and work: I am Senior Lecturer at the Statistics department, my time is split roughly equal between the Stats department and UFBI. My methodological research mainly deals with longitudinal imaging studies with nonrandom dropout, which applies to e.g. the BETULA and COBRA studies. I also do applied research with UFBI researchers

Name: Sara Pudas
Discipline: Cognitive Neuroscience
Research and work: I am a PhD in psychology, and work on data from the Betula project to investigate how age-related brain changes relate to changes in cognitive functions. I am also initiating a project to investigate lifespan changes in cognition, their determinants, and relation to neuroimaging markers in older age.

Name: Anna Rieckmann
Discipline: Cognitive Neuroscience
Research and work: I am a Marie Curie Postdoctoral Fellow at the Department of Radiation Sciences. I use PET and fMRI to explore how different neurobiological cascades contribute to cognitive decline in human aging. In 2016, I start a VR Young Researchers award to explore the neurobiology of schizophrenia using human brain imaging.

Name: Alireza Salami
Discipline: Computational neuroscience
Research and work: I completed my PhD in computational neuroscience in 2012 at Umeå University where I implemented various multivariate and multimodal techniques for analysis of different imaging modalities. I am now a joint postdoctoral researcher at (UFBI) and at Aging Research Center (ARC).

Name: Carola Wiklund-Hörnqvist
Discipline: Psychology
Research and work: I am a PhD investigating how different learning methods are related to successful learning. My main focus is to identify the cognitive processes, particularly memory processes, related to pedagogical methods including elements of testing. The effects will be examined using brain imaging and behavioral data.

Other people affiliated to group Nyberg: Tetiana Gorbach (PhD student), Karolina Kauppi (Post-doc).

Group Karlsson

Name: Linnea Karlsson Wirebring
Discipline: Psychology/Cognitive Science
Research and work: I'm a senior lecturer in Neuropsychology and my research focuses on i) the cognitive neuroscience of human judgment, where I relate cognitive models to fMRI data and ii) educational neuroscience, where I'm interested in the testing effect and mathematical learning.

Name: Linus Andersson
Discipline: Psychology/Cognitive Science
Research and work: I am currently working as a post-doc in a project on decision making. It seems like we humans only occasionally follow statistical or logical rules when making judgments. Under what conditions, if any, do we actually behave like the rational beings we think we are? I am peering into the brain using fMRI to find out.

Name: Sara Stillesjö
Discipline: Cognitive neuroscience
Research and work: I am a PhD student studying the neural correlates of judgment and decision making. My main focus is to investigate how people make inferences, and the neural processes related to it. The main methods are fMRI and cognitive modeling. I am also interested in research on learning and memory.

Group Johansson

Name: Roland Johansson
Discipline: Sensorimotor control in humans
Research and work: I am a professor of physiology working with analysis of neural mechanisms supporting planning and control of dexterous object manipulation with emphasis on sensory, mnemonic and predictive mechanisms. I am also a member of the Swedish Royal Academy of Sciences.

Name: Per Nordmark
Discipline: Physiology
Research and work: I am a PhD student and hand surgery resident. My research focuses on functional and structural changes in the central nervous system in persons that have suffered peripheral nerve injury to their upper limb.

Name: Andrew Pruszynski
Discipline: Neurophysiology
Research and work: I completed my PhD in 2011 at Queen's University in Canada where I studied the fast feedback mechanisms that underlie successful motor behavior. My current research, funded by the Swedish Research Council and the Human Frontier Science Program, investigates information processing in human tactile afferent neurons.

Other people affiliated to group Johansson:
Carola Hjältén (project assistant), Anders Bäckström (engineer), Per Utsi (research engineer).

Group Åhlström Riklund

Photo: Josefin Åhlström Riklund

Name: Katrine Åhlström Riklund
Discipline: Radiology and nuclear medicine
Research and work: I am a professor/consultant doctor who works with movement disorders (parkinsonian diseases), imaging of dopamine function, dementia, imaging of brain function, and PET/CT - oncologic applications.

Photo: VLL

Name: Jan Axelsson
Position: PET physics and image analysis
Research and work: I am working with the COBRA and the PHIBRA projects as the PET expert. This involves data acquisition, pharmacokinetic modeling, methodological questions and method development. I have been working with PET physics since 2003.

Other people affiliated to group Åhlström Riklund:
Kajsa Burström (research nurse), Mats Eriksson (research nurse), Susanna Jakobson Mo (senior lecturer/consultant physician).

Group Eklund

Photo: Gudrun Furtenback

Name: Anders Eklund
Discipline: Biomedical engineering
Research and work: I am a professor of Biomedical engineering at Umeå University. My main areas of interest are physiological measurement techniques, with a focus on measuring, modeling and signal processing with applications in neuroscience and ophthalmology.

Photo: Gudrun Furtenback

Name: Anders Wåhlin
Discipline: MR-Physicist
Research and work: I completed my PhD in 2012 at Department of Radiation Sciences, Umeå University, where I specialized in MR based measurements of cerebral blood flow and cerebrospinal fluid dynamics. My post-doc research, funded by the Swedish Brain Foundation, investigates cerebral blood flow in stroke and aging.

Other people affiliated to group Eklund:
Khalid Ambarki (PhD), Jan Malm (professor), Tora Dunås (PhD student), Laleh Zarrinkoob (PhD student).

MR staff and other UFBI members

Name: Micael Andersson
Discipline: Research engineer
Research and work: I am a diploma engineer and have been working with fMRI since 2004. I make the in-house program DataZ, which is a Matlab-based add-on for the analysis software SPM and is used for batching the analysis and visualizing results. I am also performing the fMRI-analysis for several of the research projects.

Name: Kerstin Englund
Position: X-ray technician/nurse
Assignments: I have been working with MR since 2000. When the new MR-scanner was installed in November 2009, I got the opportunity to start working part time with fMRI. My other workplace is the Interventional Neuroradiology lab at Norrlands University Hospital.

Name: Peter Hägglund
Position: Master of Science in Engineering
Assignments: I am involved in the service and technical support of the MRI scanners at Umeå University and Norrlands University Hospital.

Name: Hans-Olov Karlsson
Position: X-ray technician/nurse
Assignments: I worked with MR between 1993-98, and since 2003 onwards. I then started working part time with fMRI in the autumn of 2009 when the new MR scanner was installed at Umeå University Hospital. When I am not at MR, I work at the Interventional Neuroradiology lab.

Name: Ann-Kathrine Larsson
Position: X-ray technician/nurse
Assignments: I have been working with MR since 1990, and started working with fMRI in 1999. I am currently a research nurse, running logistics for the different studies including method development, creating protocols and making sure that the contacts between the different parts involved in the project are working.

Name: Helen Ledin
Position: X-ray technician/nurse
Assignments: I have been working with MR since 2000. I started working part time at the new research MR-scanner in January 2010. When I am not at MR, I work at the Interventional Neuroradiology lab at Norrlands University Hospital.

Name: Greger Orädd
Discipline: Physics
Assignments: I have been working as an MR physicist since 2009. On the 3T scanner I take care of quality control and general questions regarding MR physics, including improving protocols and procedures for MRI data collection. I am also involved in the national 7T facility in Lund.

Name: Matthias Schenkel
Position: Master of Science in Engineering
Assignments: I am involved in the service and technical support of the MRI scanners at Umeå University and Norrlands University Hospital.

Name: Mikael Stiernstedt
Position: Research engineer
Assignments: I am the lab coordinator for UFBI which includes collecting data for different projects, producing the annual reports, handling the UFBI webpage, and other general matters in the lab. I am also involved in the Betula project where I, among other things, are working on the database.

Name: Peter Vestergren
Discipline: Educational neuroscience
Research and work: I am a PhD and use fMRI to investigate fundamental learning processes from a neuroscientific perspective. I have investigated brain activity related to direct and indirect effects of testing in two projects. My current project deals with the role of relational processing in comprehension during mathematics learning.

Publications

The list below is focused on journal articles, book chapters, doctoral theses and conference proceedings that were based on structural/ functional MRI data and/or PET data collected within UFBI.

Ambarki, K., Wåhlin, A., Zarrinkoob, L., Wirestam, R., Petr, J., Malm, J. & Eklund, A. (2015). Accuracy of parenchymal cerebral blood flow measurements using pseudocontinuous arterial spin-labeling in healthy volunteers. American Journal of Neuroradiology, 36(10), 1816-1821.

Awad, A., Levi, R., Lindgren, L., Hultling, C., Westling, G., Nyberg, L., & Eriksson, J. (2015). Preserved somatosensory conduction in a patient with complete cervical spinal cord injury. Journal of Rehabilitation Medicine, 47, 426-431.

Bergman, F., Boraxbekk, C.-J., Wennberg, P., Sörlin, P., Olsson, T. (2015). Increasing physical activity in office workers – the Inphact Treadmill study; a study protocol for a 13-month randomized controlled trial of treadmill workstations. BMC Public Health, 15 (632), 1-10.

Bergström, F., & Eriksson, J. (2015). The conjunction of non-consciously perceived object identity and spatial position can be retained during a visual short-term memory task. Frontiers in Psychology, 6 (1470), 1–9.

Boraxbekk, C.-J., Salami, A., Wåhlin, A., & Nyberg, L. (2015). Physical activity over a decade modifies age-related decline in perfusion, gray matter volume, and functional connectivity of the posterior default mode network - a multimodal approach. NeuroImage.

Boraxbekk, C.J., Stomby, A., Ryberg, M., Lindahl, B., Larsson, C., Nyberg, L., & Olsson, T. (2015). Diet-induced weight loss alters functional brain responses during an episodic memory task. Obesity Facts.

Hibar, D. P. et al. (2015). Common genetic variants influence human subcortical brain structures. Nature, 520, 224-229.

Karlsson Wirebring, L., Lithner, J., Jonsson, B., Liljekvist, Y., Norqvist, M. & Nyberg, L. (2015). Learning mathematics without a suggested solution method: Durable effects on performance and brain activity. Trends in Neuroscience and Education, 4 (1-2), 6-14.

Karlsson Wirebring, L., Wiklund-Hörnqvist, C., Eriksson, J., Andersson, M., Jonsson, B., & Nyberg, L. (2015). Lesser neural pattern similarity across repeated tests is associated with better long-term memory retention. Journal of Neuroscience, 35(26), 9595–9602.

Mattsson, P., Forsberg, A., Persson, J., Nyberg, L., Nilsson, L.-G., Halldin, C., & Farde, L. (2015). Beta-Amyloid binding in elderly subjects with declining or stable episodic memory function measured with PET and [(11)C]AZD2184. European Journal of Nuclear Medicine and Molecular Imaging.

Månsson, NT.K., Frick, A., Boraxbekk, C.-J., Marquand, A., Williams, S., Carlbring, P., Andersson, G., & Furmark, T. (2015). Predicting long-term outcome of internet-delivered cognitive behavior therapy for social anxiety disorder using fMRI and support vector machine learning. Translational Psychiatry, 5(3).

Månsson, K.N.T., Salami, A., Frick, A., Carlbring, P., Andersson, G., Furmark, T., & Boraxbekk, C.J. (in press). Neuroplasticity in response to cognitive behavior therapy for social anxiety disorder, Translational Psychiatry.

Nevalainen, N., Riklund, K., Andersson, M., Axelsson, J., Ögren, M., Lövdén, M., Lindenberger, U., Bäckman, L., & Nyberg, L. (2015). COBRA: A prospective multimodal imaging study of dopamine, brain structure and function, and cognition. Brain Research, 1612, 83-103.

Zarrinkoob, L., Ambarki, K., Wåhlin, A., Birgander, R., Eklund, A. & Malm, J. (2015). Blood flow distribution in cerebral arteries. Journal of Cerebral Blood Flow & Metabolism, 35(4), 648-654.

Dissertations

Stomby, A. (2015). Brain function and glucocorticoids in obesity and type 2 diabetes including effects of lifestyle interventions. Doctoral dissertation, Umeå University *[contains data from UFBI].*

Review articles / Book chapters

Carelli, M. G. & Olsson, C.J. (2015). Neural correlates of time perspective. In M. Stolarski, N. Fieulain, & W. Van Beek (Eds.), Time perspective theory: Review, research and application. Essays in Honor of Philip Zimbardo. Cham, Switzerland: Springer International Publishing.

Eriksson, J., Vogel, E.K., Lansner, A., Bergström, F., & Nyberg, L. (2015). Neurocognitive architecture of working memory. Neuron, 88, 33-46.

Nyberg, L. & Eriksson, J. (2015). Working memory: Maintenance, updating, and the realization of intentions. In Mayford, M., Dudai, Y., & Kandel, E. (Eds.) Learning and memory. Cold Spring Harbor Press.

Wilkund-Hörnqvist, C & Nyberg, L. (2015). Test bidrar till effektiv inlärning. In Bergstrand, M (Ed.) Vägen ut ur skolkrisen. Eddy.se AB.

Conference proceedings

Nyberg, L. (2015, December 17). Multimodal brain imaging of memory functioning in adulthood and aging. Talk given at Frontiers of Science seminar at University of Turku, Turku, Finland.

Jonasson, L. (2015, November). PHIBRA – An Aerobic Exercise Intervention Examining Dopamine D2 Receptors and Cognition in the Aging Brain. Talk held at the StratNeuro workshop on Analysis of Longitudinal Neuroimaging Data, Karolinska Institutet, Stockholm, Sweden.

Eriksson, J. (2015, October). DBS-fMRI of movement and psychiatric disorders. Invited talk at the Workshop on Deep Brain Stimulation and Cognitive Functions in Frontostriatal Disorders, Budapest, Hungary.

Nyberg, L. (2015, October). Memory and executive deficits in relation to fronto-striatal functioning. Invited presentation at Workshop on deep brain stimulation and cognitive functions in frontostriatal disorders. Research Center for Natural Sciences, Budapest, Hungary.

Nyberg, L. (2015, October). Brain maintenance - a key to preserved memory and cognition in older age. Invited presentation at the 23rd Annual Conference of Croatian Psychologists, Siebnik, Croatia.

Eriksson, J. (2015, July). Maintaining non-consciously presented information over brief periods of time engages the prefrontal cortex. Talk presented at the 19th meeting of the Association for the Scientific Study of Consciousness, Paris, France.

Nyberg, L. (2015, June). Lifespan cortical dynamics in relation to changes in high-order cognition. Invited presentation at 1st Nordic Neuroscience Meeting, Trondheim, Norway.

Wiklund-Hörnqvist, C. (2015, March). Key factors that influence the Testing Effect: Repeated Retrieval & Feedback. Presentation at Sympoisa on Mechanisms of reward and associative learning. Stockholm, Sweden.

Bergström, F., & Eriksson, J. (2015, March). Non-conscious visual short-term memory can retain both spatial and object information. Poster presented at the Cognitive Neuroscience Society Annual Meeting 2015, in San Francisco, USA.

Jonasson, L. (2015, March). Prospective Reward: Effects on Dopamine Release and Cognitive Control. Talk held at the StratNeuro workshop on Mechanisms of Reward and Associative Learning, Karolinska Institutet, Stockholm, Sweden.

Stillesjö, S, Eriksson, J, Juslin, P, Nyberg, L, Karlsson, L. (2015, March). Neural correlates to rule-based and similarity-based mathematical models of judgments. Cognitive neuroscience society annual meeting, San Francisco, USA.

Nyberg, L. (2015, March). Brain maintenance - a key to preserved memory and cognition in older age. Invited presentation at the 25th Rotman research institute conference, Toronto, Canada.

Nyberg, L. (2015, March). Memory Decline. Invited presentation at the 27th European Congress of Radiology, Vienna, Austria.

Eriksson, J. (2015, January). Memory-related brain networks and aging. Talk presented at the 33:rd European Workshop on Cognitive Neuropsychology, Bressanone, Italy.

Nyberg, L. (2015, January). A paradox of neural signals associated with long-term memory in cross-sectional and longitudinal designs. Talk presented at Dallas aging & Cognition conference, Dallas, USA.

Pudas, S., Lundquist, A., Samrani, G., Nymberg, C., Klingberg, T., Nilsson, L-G., & Nyberg, L. (2015, January). Cross-sequential estimation of hippocampal volumes and episodic memory development across the human lifespan. Poster presented at Dallas aging & Cognition conference, Dallas, USA.

Visiting Address

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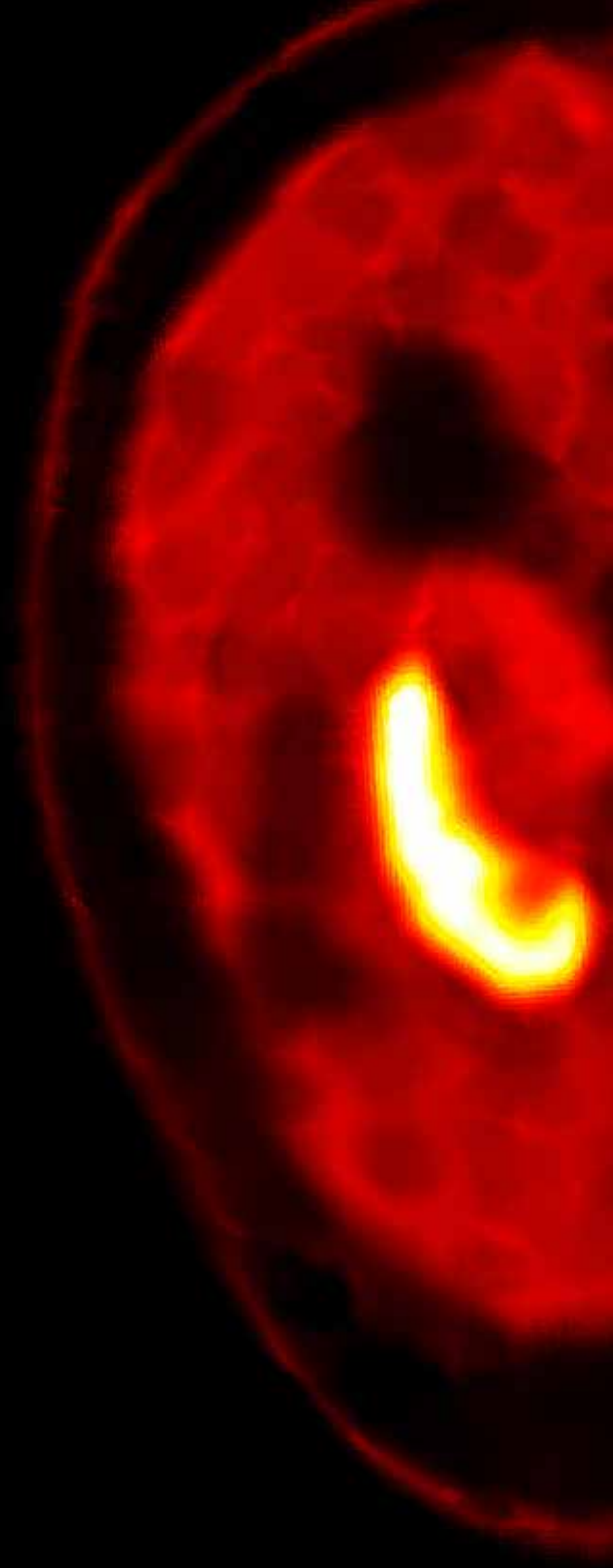

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