The Danish National Research Foundation's
Center of Functionally Integrative Neuroscience

ANNUAL REPORT 2007

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PET
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CFIN Annual Report 2007, published March 2008
Center of Functionally Integrative Neuroscience (CFIN)
Aarhus University / Aarhus University Hospital
Aarhus Hospital, Building 14A, Nørrebrogade 44, DK-8000 Aarhus C, Denmark

www.cfin.au.dk

Editors: Leif Østergaard and Henriette Blæsild Vuust, CFIN
Design and layout: Henriette Blæsild Vuust
Printed in Denmark by GP-Tryk A/S

ISBN 978-87-992371-0-4

CFIN is growing: Leif Østergaard, CFIN director, inspects the renovation of the Yellow Villa prior to the inaguration of the Interacting Minds project.

Introduction - 2007 in words

by Leif Østergaard

It remains CFINs vision to foster cutting-edge neurocognitive research in an environment where leading scientists work curiously across traditional disciplines to generate new knowledge of the human brain and mind, ultimately improving the quality of life for patients with severe neuropsychiatric diseases.
With a strategy to attract leading international scientists, bright young students and adapt cutting-edge brain imaging methods to pursue this vision, 2007 was a very successful year for CFIN.

The Interacting Minds group, made possible by a Niels Bohr professorship from the Danish National Research Foundation to attract two of the most influential international cognitive neuroscientists, Professor Uta Frith and Professor Chris Frith, started its research. Coordinated by Andreas Roepstorff, the project has hosted a number of symposia and lectures featuring yet more leading international scientists.
Go to: http://www.interacting-minds.net.
With generous help from Århus Sygehus, the Yellow Villa in Peter Sabroes gade is now the home of the Interacting Minds project – and a source of inspiration and intense interaction with national and international scientists converging on CFIN's pioneering frontier.

Morten L. Kringelbach, Senior Research Fellow at the Department of Psychiatry, University of Oxford received 10 M DDK from TrygFonden to establish the TrygFonden Research Group, a transnational research group based both at CFIN and in the Department of Psychiatry, Oxford. Aiming to study neural mechanisms underlying human sensory and social pleasures, and their role in depression, obesity and eating disorders, the group marked a successful start with a publication in *Nature Neuroscience Reviews*. With the participation of Professor Tipu Aziz, Oxford, scientific collaborations are now evolving, including neurosurgeons and basic neuroscientists in Aarhus.

The ludomania group, lead by Arne Møller and Jakob Linnet received 5.8 M DDK, to expand their fundamental work within dopaminergic neurotransmission and pathological gambling.
The Neuroconnectivity group, lead by Peter Vestergaard-Poulsen and their collaborators at InSpin (professor Niels Christian Nielsen) received 3.2 M DDK to further develop a fruitful collaboration with the University of Florida (Professor Steven Blackband). Meanwhile, new research areas expand their activities: The neuroinformatics group, lead by Kim Mouridsen, and the biophysics in neuroscience group, lead by Sune Nørhøj-Jespersen, generated critical breakthroughs and contributed to projects across all research areas at CFIN.
Peter Vuust was appointed professor at The Royal Academy of Music and associate professor at the Clinical Institute, Faculty of Health Sciences, Aarhus University, marking the unique collaboration between these institutions. The Music in the Brain group, lead by Peter Vuust, has now grown to include 5 Ph.D. students with numerous international collaborators.

With the support of the Faculties at Aarhus University and the Danish National Research Foundation, CFIN pursues a strategy to offer neuroscience, neuroimaging and cognition courses to students across institutes and Faculties.
See http://www.cfin.au.dk/neuroviden.
In 2007, a Neuroscience program was added to the Biomedical Engineering program (see http://www.biomedtek.au.dk), featuring well-attended courses in Functional Neuroanatomy and Neurological Diseases (Carsten Bjarkam, Leif Østergaard, Per Borghammer, course organizers) and Neurotransmission and Psychiatric Disease (Arne Møller and Rikke B. Dalby, course organizer).

With the increasing activity, CFIN threatens to outgrow its office space and experimental facilities. While the construction of the Danish Neuroscience Center proceeds according to schedule, CFIN entered a highly competitive bid for funding of a magnetoencephalograph and hyper-scanning 3T MRI equipment under the National Programme for Research Infrastructure. In December, the Danish Agency for Science, Technology and Innovation granted 20 M DDK to place this equipment as a national center at CFIN.

On behalf of the CFIN scientific coordinators

Leif Østergaard

NEUROENERGETICS

by Albert Gjedde

Progress in 2007

Neuroenergetics is the study of the brain's work and how the work is organized, both in terms of the neurochemistry and the functionally integrative neuroanatomy that subserves the work. Three topics therefore are the foci of exploration in the neuroenergetics group: Oxygen homeostasis in human brain, uncoupling of blood flow and metabolism in different regions of the human brain in different physiological and pathological states, and the relation of different coupling ratios and their relation to the measures of functional integrity of neuronal networks in the human forebrain, also known as functionally integrative neuroanatomy. The research of this group is inspired by the observation that it is much more difficult to determine where the changes occur in the brain than to measure the actual magnitudes of the changes. Contrary to convention, brain regions are not anatomically and functionally well-defined and appear to be rather randomly recruited for specific work on the basis of functional relations rather than of rigid anatomical rules. This is an important reason for the uncertainties that face the researcher who wants to know all three aspects of the triangle of location, magnitude and functional role of a changing signal from brain tissue.

Uncoupling of oxygen consumption from ATP turnover

Brain metabolism is predominantly oxidative but the relations between glucose and oxygen consumption rates on one hand, and ATP and heat production rates on the other, are complex. Current calculations and measurements suggest that, on the average, 90% of the glucose consumed by normal human brain is metabolized to carbon dioxide. Of this, 85% (of the total) is coupled to ATP rephosphorylation, while the rest appears to be coupled to heat production rather than to ATP rephosphorylation, in part by the action of so-called uncoupling proteins that reside in the membranes of the mitochondria and allow hydrogen ions to bypass the ATP synthases and maintain electron flux and oxygen consumption without coupling to ATP production. Thus, oxygen consumption is as imperfect a measure of functional activity in the brain as glucose consumption. Measurements of blood flow, glucose metabolism and oxygen consumption reveal major differences among individuals who display no overt differences of brain function, just as individuals differ with respect to body size and weight. The neuroenergetics team is now in the process of testing the hypothesis that the fraction of oxygen consumption related to actual brain work rather than lactate and heat production (on the average 75%) is regulated within much more narrow limits than the total rates of glucose metabolism and blood flow. This test uses novel methods of direct estimation of ATP turnover with magnetic resonance spectroscopy. This test uses novel methods of direct estimation of ATP turnover with magnetic resonance spectroscopy. The relation between brain function and oxidative metabolism is the subject of a current PhD-project (Christopher Bailey, with Fahmeed Hyder at Yale). Uncoupling of oxygen consumption from ATP-turnover may be the reason for the development of hepatic encephalopathy, currently explored in a PhD-project by Peter Iversen (with Susanne Keiding).

Oxygen homeostasis and uncoupling of blood flow and metabolism

Previous convention held that blood flow, glucose metabolism, and oxygen consumption maintain fixed ratios in different functional states but this understanding is not substantiated by more recent evidence of significant uncoupling of these relations. The uncoupling is the key to novel theories of neurodegeneration, based on the regulation of oxygen tensions in brain tissue. Aging is now known to lead to the uncoupling of blood flow from metabolism, with consequences for mitochondrial function and the potential for apoptosis. The 'uncoupling with age' is the topic of a current PhD-project (Joel Astrup). A similar process may be active in Parkinson's disease when insufficient incorporation of dopamine in dopaminergic neurons raises the intracellular dopamine concentration. This accelerates the oxidant action of dopamine, which affects mitochondrial function. This is the topic of a current PhD-project where in the relations between oxygen metabolism and blood flow in different parts of the brain have been reassessed (Per Borghammer). Among other conclusions, the researchers suggest that previous conventional methods of normalization of measures of blood flow and metabolism to a global gray matter average generates artefactual patterns of change and association. Also heat-stress uncouples blood flow from metabolism, increases perceived exertion, and accelerates fatigue. It is feasible that the heat-generated hyperventilation lowers blood flow, carbon dioxide tensions in brain tissue, and possibly raises the affinity of cytochrome oxidase for oxygen, which would tend to lower oxygen tensions to critically low levels at the mitochondria. In a collaborative PhD-project with Rigshospitalet (Peter Rasmussen and Niels H. Secher), we estimated cerebral mitochondrial oxygen tension in exercising males from measures of whole-brain blood flow and arterio-

jugular oxygen differences. During exercise with the little temperature increase, the mitochondrial oxygen tension did not change and the subjects continued to exercise for 1 hour more with normal exertion. Subjects exercising for one hour with significantly increased core temperatures reported maximal exertion, and the corresponding mitochondrial tension declined significantly towards zero. The collaborators conclude that low mitochondrial oxygen tensions may explain fatigue. The methods of calculating mitochondrial oxygen tensions, developed in Aarhus, are also used in collaborative work with Glostrup Hospital (Kirsten Caesar, Kirsten Thomsen, and Martin Lauritzen).

Functionally integrative neuroanatomy

The measures of blood flow and metabolism, as well as of transmitter binding potentials and receptor densities, commonly serve to identify functional networks in the human brain, frequently by reference to a map of the histology of brain regions dating from 1909. This map has been shown, first, to be insufficiently detailed and, second, to indicate that the anatomical overlap of functional regions among individuals is astoundingly poor. Recent work with autoradiography and voxel-based morphometry of MR images focuses on the refinement of these maps. In a current post-doctoral project (Mallar Chakravarthy), the group develops novel maps of the volumetric relations among measures of metabolism and receptor binding in healthy human beingss and patients with Alzheimer's Disease (PhD-student Joel Astrup), Parkinson's Disease (doctoral student Jacob Geday), depression (senior scientist Donald Smith), ludomania (PhD-student Ericka Peterson), and Functionally Somatic Disorders (PhD-student Ruta Kuzminskyte, Associate Professor Per Fink), as well as in pig and rat models of these diseases (post-doctoral fellow Anne Landau, medical student Adjmal Nahimi, Professor Doris Doudet). Monoamines, with special reference to dopamine, are involved in the particularly evolved integration of prefrontal and subcortical activity in human brain. In the group, Professor Hans C. Lou has shown that meaningful perception of exogenous signals is associated with release of dopamine in the striatum, and doctoral student Jacob Geday has shown that part of the effect can be ascribed to the ratio of inhibitory to excitatory monoamine receptors, particularly serotonin 5HT-1A and –2A in the ventromedial prefrontal cortex. This region is part of a network, which is now called "default" by some, because it is said to be the part of the brain that conscious activity "returns" to when the individual appears not to be doing anything in particular, although the concepts of

SELECTED RESEARCH PROJECTS:

Per Borghammer, Joel Astrup Aanerud, Albert Gjedde:
Studies of brain flow and metabolism in humans.

Michael Sørensen, Peter Iversen, Susanne Keiding:
Kan antidiuretisk hormon hindre 18F-FDG udskillelse i blæren.

Anders Nykjær, Dirk Bender: AD-ANA mice.

Mahmoud Ashkanian, Albert Gjedde, Leif Østergaard:
Changes in brain oxygen uptake and blood flow in patients with severe occlusion of the carotid artery compared to healthy controls.

Lise Schlünzen, Georg Cold: Focal cerebral changes in glucose metabolism in the transition from unconscious to conscious state.

Peter Iversen, Albert Gjedde, Susanne Keiding: Brain metabolism in patients with liver cirrosis and acute hepatic ecephalopaty measured with PET.

Dirk Bender: Binding of NS 1209 in pigs.

Jakob Linnet, Arne Møller, Albert Gjedde: Clinical, psychological and neurobiological aspects of gender differences in pathological gambling.

Susanne Lerche, Ole Schmitz, Albert Gjedde: Effect of GLP-1 on glucose uptake in CNS and heart in healthy persons evaluated with PET.

Niels Hjort, Christine Sølling, Leif Østergaard: Focal cerebral changes in glucose metabolism in the transition from conscious to unconscious state.

Mahmoud Ashkanian, Albert Gjedde, Christine Sølling, Leif Østergaard: Changes in brain oxygen uptake and flow during hypoxia caused by breath holding in free divers.

Aage Olsen, Joel astrup Aanerud, Dirk Bender: Beta-amyloid imaging in older Goettingen minipigs.

Per Borghammer, Albert Gjedde: Cerebral perfusion and metabolisme in non-treated Parkinsons Disease.

Albert Gjedde, Søren Laurberg, Arne Møller: Sacral nerve stimulation.

"return" and "not doing anything in particular" remain elusive. Originally, the discoverers of the "default" network defined it as the regions in the brain where normal oxygen extraction percentages of 40% would increase when individuals engaged in goal-directed activity, such as attending to external stimuli. Thus activity in this part of the brain rises (with lowering of oxygen extraction) when individuals appear passive, including being passively overcome by emotions, while it declines (with increase of oxygen extraction) when individuals appear to actively attend to an external stimulus. However, both PhD-student Karen Johanne Pallesen and doctoral student Jacob Geday now show that emotionally salient external stimuli may in fact serve to maintain activity in the "default" network, depending on individual dispositions that may in part be related to regional differences of monoaminergic receptors.

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NEW FACE AT CFIN

Professor Hans C. Lou, was appointed professor by Aarhus University in May 2007. Hans Lou is a neurologist and pediatrist and was earlier employed at Dept. of Neurology, Roskilde Sygehus and at the Kennedy Institute in Glostrup. During his time at the Kennedy Institute he established a close collaboration with professor Albert Gjedde, CFIN and PET Center at Aarhus Hospital, on the causes of the hyperactivity syndrome ADHD. This lead to a research professorship funded by Lundbeckfonden and now to his employment at CFIN funded by The Danish National Research Foundation.

The main focus of Hans Lou's research is to examine the processes in the human brain that enables us to be conscious about ourselves and the surrounding world. Even though this is basic research it is the aim of Hans Los' research to use the knowledge from the research projects to contribute to the understanding of a number of diseases like mental retardation, ADHD, autisme, schizofrenia and also drug abuse.
Hans Lou is employed as professor at CFIN from 2007-2009.

NEUROENERGETICS

Brain Metabolism in Parkinson's Disease

by Per Borghammer

Parkinson's disease is the second most common neurodegenerative disease of old age, affecting 1-2% of the population of above 65 years. In later disease-stages, the patients are in need of a complicated regime of medication to manage the increasingly debilitating motor symptoms. Furthermore, patients often develop depression and dementia. There is therefore a great need to develop novel treatment strategies to Parkinson's disease; treatments focusing not only on improving the motor and cognitive symptoms, but also on rescuing the remaining neurons, thus delaying further disease progression.

It has been proposed that a particular class of pharmaceuticals termed NMDA-antagonists could exhibit such neuroprotective properties in Parkinson's disease. One such drug, memantine, is currently used in Alzheimer's disease, in which it seems to postpone the development of severe cognitive disturbance and memantine could theoretically display similar properties in Parkinson's disease. We therefore undertook an investigation of memantine's neurophysiological properties in Parkinson's disease. Using PET, we mapped the cerebral blood flow and oxygen metabolism in the brain of patients before and during ingestion of memantine. Several small brain structures are known to be overactive in Parkinson's disease and we were able to demonstrate that memantine does indeed tend to normalize the activity of the neurons in these structures (Borghammer et al, Acta Neurol Scand, In press 2007). We did not find a clinical effect on the patients' symptoms and further research is needed to more comprehensively determine whether memantine could have a protective effect on the remaining neurons in Parkinson's disease.

PET studies of brain blood flow and glucose metabolism have been performed for nearly three decades to elucidate the abnormal changes seen in the brains of patients with Parkinson's disease. This has several implications. First, improved understanding of the metabolic perturbations in the parkinsonian brain is necessary for a better understanding of the underlying disease mechanisms, which is essential for the development of new therapies. Second, the metabolic fingerprint in the brain of Parkinson patients can be used for diagnostic purposes. Indeed, it is often difficult for clinical neurologists to differentiate Parkinson's disease from a number of other rare movement disorders, so called atypical Parkinson disorders. Several imaging centres around the world are working towards developing analysis methods with which a differential diagnosis can be made on the basis of a PET image of glucose consumption or brain perfusion.

We compared brain perfusion and oxygen consumption in the brain of Parkinson patients to healthy controls. In the process of this work, we discovered a very important methodological issue, which has never been adressed in the Parkinson literature. We believe that most of the previous PET studies of Parkinson's disease and indeed many other disorders have been analyzed wrongly. We found that conventional analysis of the effects of healthy aging and of patients with liver-coma produced very similar metabolic patterns in the brain compared to the "Parkinson-pattern"(Borghammer et al, 2008, Neuroimage, in press). This common pattern seems difficult to explain, and moreover, is not in accordance with the studies of animal models of Parkinson's disease. We have suggested an alternative analysis strategy, which produces results in agreement with the animal literature (Figure 1).

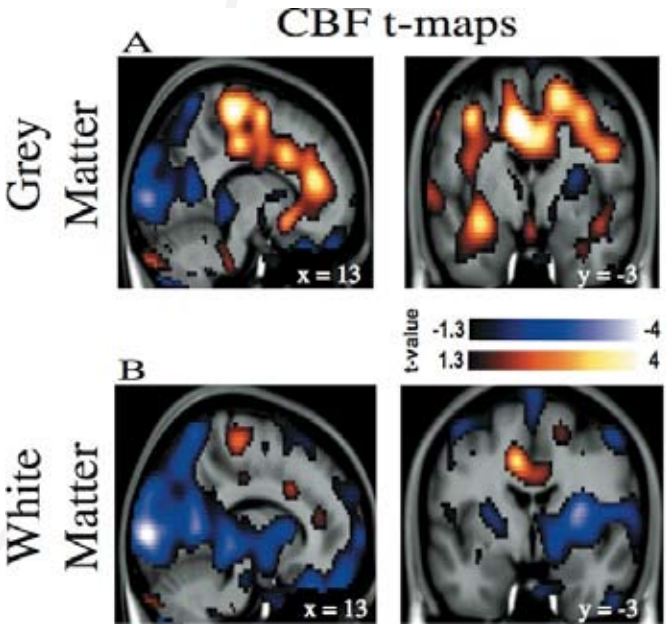


Figure 1
A. When analyzed with the conventional methodology, i.e. grey matter normalization, patients with Parkinson's disease display small clusters of decreased CBF (blue color) and larger clusters of increased CBF in central brain regions (red color).
B. When analyzed with the alternative white matter normalization strategy, a pattern of large CBF decreases and hardly any subcortical increases emerge. This is more in accord with evidence from animal literature and PET studies using alternative analysis strategies.

NEUROENERGETICS

Monoanimergic regulation of activity in the prefrontal cortex

by Jacob Geday

The medial aspect of the frontal lobes is the medial prefrontal cortex (MPFC). It is believed to be critically involved in the attention that we as humans pay to ourselves and to the world around us. People attend as long as necessary for them to react purposefully. Due to the close connections with the rest of the brain, the MPFC anatomically is ideally placed to serve as a switchboard for signals from many different parts of the brain. The dorsomedial part of the MPFC receives projections from motor cortex and dorsolateral prefrontal cortex. This part of the region is most active when attention is directed towards external stimuli that may require action. The lower part of the MPFC receives projections from limbic regions such as the amygdala and the cingulate gyrus; it is most active when attention is directed inwardly towards the emotions of the individual, including assessment of the rewarding or punitive qualities of these emotions. For these reasons, the MPFC is the natural choice for a neuronal network with functions and connections that explain the different personalities of people. On this basis we claim that the most likely neuroanatomical correlate of personality is a network centered on the MPFC.

The functions of the MPFC are modulated by monoaminergic neurotransmitters among which serotonin plays a key role. The neurons that release this neuromodulators arise in the brain stem project their serotonergic fibres to most of the neocortex, including the MPFC where serotonin binds predominantly to two receptor subtypes, $5HT_{1A}$ and $5HT_{2A}$. The subtypes have different properties and actions. The $5HT_{1A}$ receptors bind serotonin with high affinity and serve functions in the MPFC by inhibiting the excitability of target neurons and thus lowering the signal-to-noise ratio of signals from the rest of the brain. The $5HT_{2A}$ receptors bind serotonin with lower affinity but then raise the excitability of target neurons when the serotonin concentration rises. Stimulation of $5HT_{1A}$ receptors lowers the activity in the MPFC while stimulation of $5HT_{2A}$ receptors raises the activity.

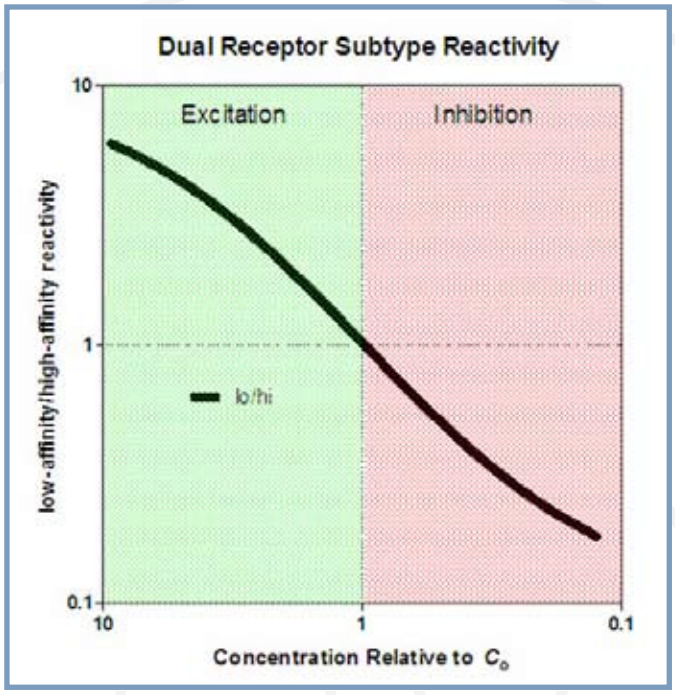


Figure 1
Net effect of a monoaminergic neuromodulator surge as a function of baseline monoamine concentration, relative to threshold concentration (C_o) where net effect goes from excitatory to inhibitory or vice versa.

When a region of the brain enjoys two or more transmitter populations with opposite effects on the excitability and differential binding affinities, a threshold transmitter concentration ("C_o") can then be estimated at which the reactivity of the system switches from on the average being inhibitory to on-the-average being excitatory. The magnitude of this threshold concentration depends on the ratio between affinities and the ratio between densities. The same change of transmitter concentration can have opposite actions, therefore, depending on the baseline concentration to which the change is added.

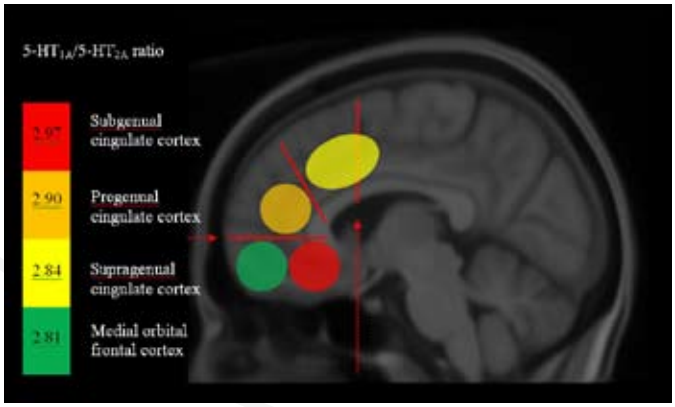
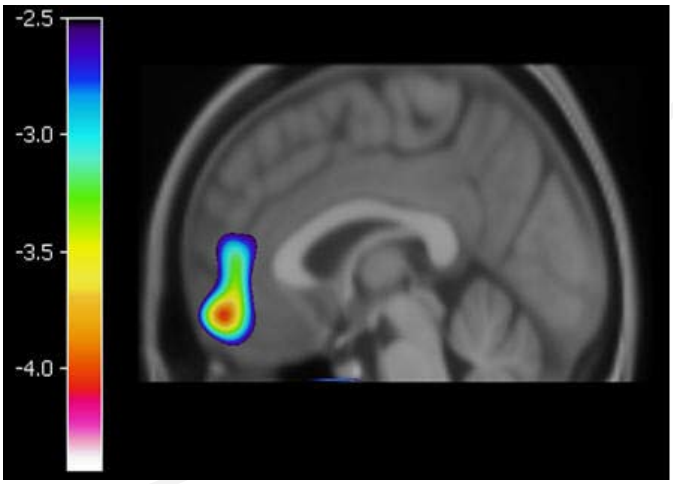


Figure 2
The ratios between 5HTIA and 5HT2A receptors are different in the medial prefrontal, indicating that the threshold concentration (Co) will be different at different sites, and that the same change in concentration of baseline serotonin may in one site lead to an excitation, but in the other may lead to an inhibition. The highest relative amount of the exitatory 5HT2A receptors (compared to the inhibitory receptors) is found in the lower part of the medial prefrontal cortex.

It also means that the same change of transmitter concentration can be inhibitory in one region of the brain and excitatory in another. This is dependent on the receptor density and affinity ratios.

On the average, for serotinin, there are more $5HT_{1A}$ recepts than $5HT_{2A}$ receptors in the lowest and most posterior part of the MPFC (colored red in the figure above). Firstly, when receptor densities are considered individually, the variability among people is comparatively low for the $5HT_{2A}$ while it varies considerably more for the $5HT_{1A}$ receptors, particularly in the ventromedial prefrontal cortex (colored green in the figure above). The spectrum of possible actions of serotonin is therefore wide in the lower portions of the MPFC, in the part that is most important to the manner in which people encode and process emotions. We currently test the hypothesis that serotonin and noradrenaline are the transmitters that dictate the individual reactions of people to emotive stimuli.
To test this hypothesis, we psychologically tested ten individuals who previously in a completely separate session participated in a PET experiment in which we determined the reactivity (measured as blood flow change) to drugs that blocks serotonin and noradrenaline reuptake sites (SNRI) or selectively only serotonin reuptake sites (SSRI) by comparing blood flow measured before and after administration of one or the other drug. These drugs are believed to augment the effects of serotonin and noradrenaline by blocking their reuptake after release. The ten individuals were shown emotive images from the Empathy Picture System that consists of 360 standardized images of people in realistic situations that are pleasant, neutral or unpleasant. We asked each individual to rate every image on a scale from -3 til +3, with 0 as neutral. As a measure of the emotional reactivity of the test subjects, we



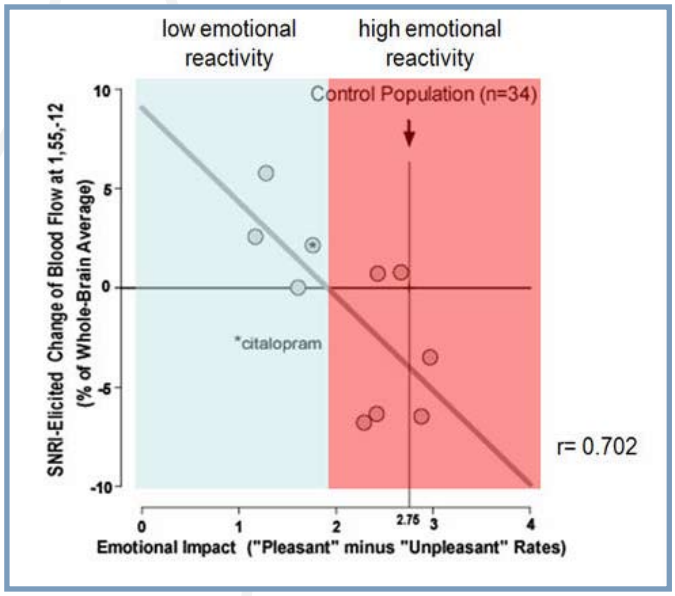


Figure 4
The actual relationship between change in regional cerebral blood flow as a result of a pharmacological challenge with clomipramine and the individual´s emotion impact scores. Note that on average there is little or no change in the area, as the average response to clomipramine varies around zero.

calculated the emotional impact as the average range of rates from the 120 unpleasant to the 120 pleasant images, a kind of "amplitude" of impact. We then used the impact as a regressor for the change of blood flow in the MPFC elicited by the previous, unrelated drug administration.

We found that the previously recorded change and direction-of-change of blood flow in the MPFC accurately predicted the emotional impact of the EPS images on the individuals, as rated by themselves. Thus, the emotional impact was correlated with the ability, on a completely separate occasion, of the drugs that either raise or reduce activity in this part of the brain. We therefore propose that that one explanation of the differential reactivity of different personalities may be the peculiarities of monoaminergic receptors in the MPFC, particularly the ratios between the affinities and densities of the serotonin $5HT_{1A}$ and $5HT_{2A}$ receptors in the lower portions of the frontal lobe.

Figure 3
The site in the medial prefrontal cortex where people's emotional impact and effect of a clomipramine surge interact.

NEUROENERGETICS

Recovery and serotonergic neurotransmission in stroke and aging

by Mette Møller

The overall aims of this PhD project included the study of changes of serotonergic neurotransmission during recovery from stroke, as well as in relation to aging, and the demonstration of a link among serotonergic neurotransmission, pathological crying, and the potentially modulating effect of a Selective Serotonin Reuptake Inhibitor (SSRI).

To weigh the results from the stroke study against the effect of normal aging on serotonin $5HT_{1A}$ receptor availability, 19 healthy controls aged 23-73 years underwent PET-scanning with the selective radioligand [^{11}C]WAY-100635. The quantification of $5HT_{1A}$ receptor binding with [^{11}C]WAY and interpretation of the results have met with difficulties from the start, as illustrated by the conflicting findings in the literature regarding a potential decline of serotonin $5HT_{1A}$ receptors with age. The reasons for these difficulties include the natural intersubject variability of $5HT_{1A}$ receptor availability in the range of 16-24%, the rapid metabolism of the tracer in the circulation, and the absence of a properly defined reference region in brain. With several kinetic models of receptor binding, we resolved the first uncertainty by demonstrating significant age-related global decrease of receptor availability of 3% per decade (Figure 1).

We then focused on the second issue of the metabolism of the tracer in relation to the use of a reference region in brain rather as the input function than a set of arterial samples. The rapid disappearance of the tracer from the circulation and the consequent brief exchange with brain tissue imply that the tracer behaves much like a “chemical” microsphere. Microspheres are designed for deposition in the vasculature in a single brief exposure, but conventional models of tracer uptake assume that uptake normally occurs over a period of time as a function of the magnitude of the arterial input function. The rapid metabolism in the circulation violates the reference-region requirement that regions-of-interest and reference region continue to exchange radioligand with the circulation during the entire uptake period. If instead reference and binding regions are subject to rates of separate washout from their respective volumes of distribution, then the reference region no longer is a proper surrogate for a common input, and the time-activity functions of different regions instead depend upon regional properties of binding, blood flow and blood-brain barrier permeability.

The third potential problem of quantification concerns the adequacy of the reference region. The adult cerebellum was believed to be almost devoid of $5HT_{1A}$ receptors, but recent studies of adult brain have demonstrated specific residual binding in the vermis and the cortex of cerebellum that may

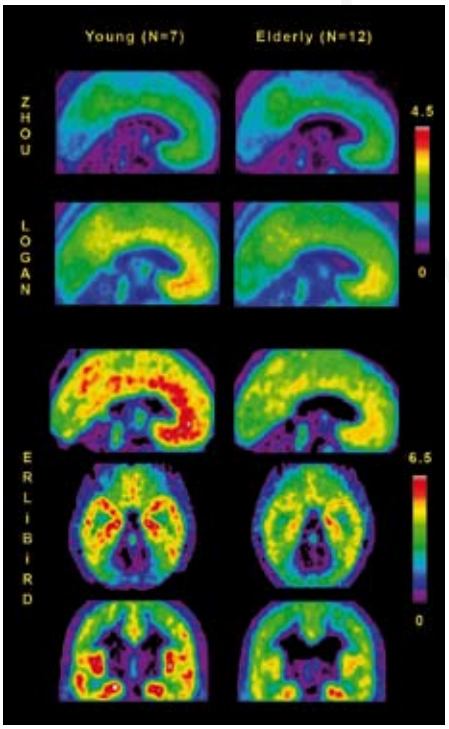


Figure 1
Parametric maps of binding potentials (pB) of radioligand [^{11}C]WAY in selected sections of brain tissue determined by three different methods, multilinear simplified reference tissue regression method LSRTM (Zhou et al. 2003), non-linear regression method ERLIBiRD (Gjedde 2003), and tissue reference version of Logan Plot method (Logan et al. 2000). Top three rows show sagittal views, second-to-last row transaxial view, and bottom row coronal view. Left column shows young adults, right column aged adults. Color bars shown to right of columns show color scale for LSRTM and Logan methods above and color scale for ERLiBiRD method below, respectively.

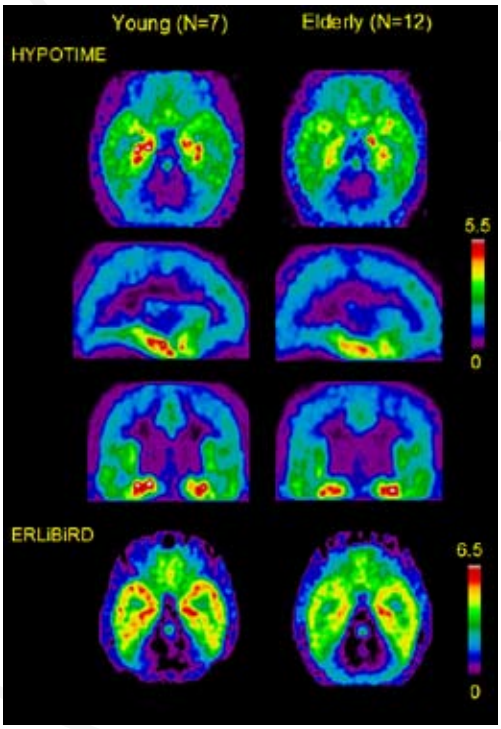


Figure 2
Parametric maps of binding potentials (pB) of radioligand [^{11}C]WAY in selected sections of brain tissue determined by two different methods, HYPOTIME and ERLIBiRD. Left column shows young adults, right column aged adults. Color bars shown for HYPOTIME above and color scale for ERLiBiRD method below.

lead to underestimation of binding in other regions if the vermis and the cortex of cerebellum are included in the reference region.

In order to account for these special properties of the radioligand [^{11}C]WAY-100635 and introduce alternative analyses of the PET data, we developed a new method called Hypotime. The method specifically uses the washout rather than the accumulation of WAY to determine binding potentials, allowing subdivision of brain into specifically and non-specifically binding regions. In comparison with conventional kinetic models, Hypotime is model-independent and uses no regression.
Figure 2 shows the parametric maps generated by the Hypotime and ERLiBiRD methods. The distribution of receptor binding showed the highest values in the hippocampus and the insula, with values of the order 4 to 5 obtained by the Hypotime method, and of the order 5 to 6 obtained by the ERLiBiRD method. In the raphé, binding potentials averaged 2 and 3, respectively. The average values of the binding potentials in the basal ganglia and the cerebellum on the whole were negligible by both methods.

A small group of first-time stroke patients with pathological crying were PET-scanned within one week of onset of stroke and after 30 days (Figure 3).

The patients were randomised to treatment with either SSRI or placebo. Comparisons of follow-up scans with baseline scans of receptor changes after stroke demonstrated a compensatory up-regulation of $5HT_{1A}$ receptors and that these changes can be prevented or reversed by early SSRI treatment. In the study and most pronounced in the chronic phase, the patients on average had lower pre- and postsynaptic $5HT_{1A}$ receptor potentials than control subjects. This shortage may explain the greater vulnerability of some stroke patients to stressors. The changes imply that the availability of $5HT_{1A}$ receptors declined in patients given SSRI, while in patients given placebo, the binding potentials rose. This is first study of the availability of $5HT_{1A}$ receptors after stroke and subsequent chronic SSRI treatment, and also the first demonstration of compensatory changes of binding after stroke and the following SSRI administration.

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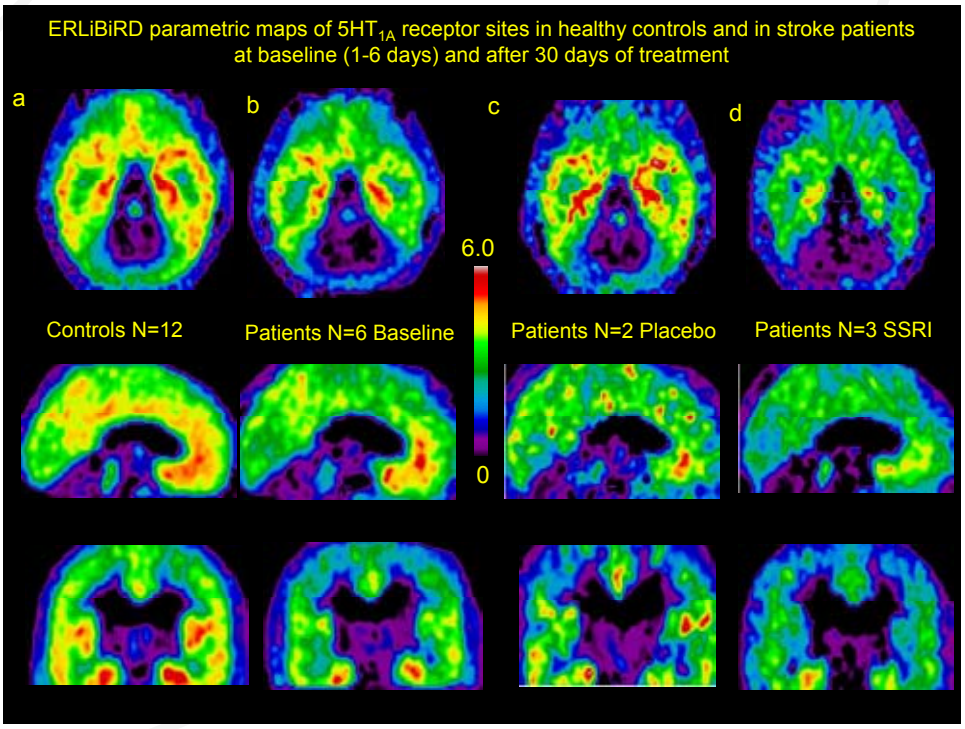

Figure 3
Parametric maps of binding potentials (pB) of radioligand [carbonyl–^{11}C]WAY-100635 determined by the method, ERLiBIiRD.
Column a: axial, sagittal and coronal view of 12 healthy control subjects. Column b: maps of six stroke patients at baseline (day 1-6). Column c: maps of two patients after administration of placebo in 30 days. Column d: maps of three patients after 30 days of treatment with SSRI.

NEUROTRANSMISSION

by Arne Møller

Progress in 2007

2007 was a very exciting and inspiring year in the field of Neurotransmission Research. Luciano Minuzzi and Mette Møller received their PhD degrees. Professor Doris Doudet launched programs in the areas of Vagal Nerve stimulation and electroconvulsive therapy, assisted by Anne M. Landau who joined CFIN after finishing her PhD in Canada (see page 16). Anne also works closely with Adjmal Nahimi (research year student) in his studies of *in vivo* and *in vitro* monoaminergic innervations in a rat model of Parkinson´s Disease.

In the pathological gambling group, Jakob Linnet, PhD, was appointed Associate Professor at University of Aarhus. Trial subjects were included in all three active projects, and we expect to complete the compilation of data for both the project on sensation seeking and dopamine release and the project on the gambling inhibitive slot machine in the spring of 2008. Daniel Campbell-Meiklejohn, who has just completed his PhD in Oxford, joined the group at the end of the year. Daniel is employed in a three-year post-doc position dividing his time between the pathological gambling group and the Interacting Minds project. Line Gebauer Josefsen (psychology student and research assistant) spent five months in Boston at the Division of Addictions, Cambridge Health Alliance, Harvard University. In the beginning of 2008, CFIN and University of Aarhus will sign a partnership agreement with the group in Boston. The group has received a grant from the Danish Research Council. The grant will make it possible for Mette Buhl Callesen and Kristine Rømer Thomsen to begin their PhD studies after completing their psychology degrees in the summer of 2008. Their studies will focus on: Pathological Gambling in relation to dopaminergic neurotransmission. The relation of Gambling to Parkinsons Disease/ Dopamine / Slot Machine / Depression / Parkinson's disease.

Alzheimer's disease

MD, PhD student Joel Astrup Aanerud has started his study in which he is investigating the relationship between changes in amyloid deposits and loss of hippocampal neurons measured using a specific ligand of the serotonergic receptors. In another PhD study, veterinarian Rikke Fast from Copenhagen (LIFE) will use PET scans to look for amyloid plaques in old dogs demonstrating spontaneous dementia-like symptoms.

Minister of Science, Technology and Innovation visits University of Aarhus

On 15 June 2007 Aarhus University had a visit from the Danish Minister of Science, Technology, and Innovation, Helge Sander, and the Danish Parliament's Science Committee.

One of the focuses of this visit was to discuss inter disciplinary research as a key ingredient in the future research envronment in Denmark. As an example of this University of Aarhus had put together a program of short talks by a number of neuroscience researchers from CFIN.

Photo: Søren Kjeldgaard/AU-foto

The program for the visit had talks by:

- Albert Gjedde: *Hjernen, det 21. århundredes store udfordring*
- Leif Østergaard: *Vejen fra Grundforskning til Patientbehandling og Innovation er kort*
- Morten L. Kringelbach: *Hjerneforskning, nydelse og livskvalitet*
- Andreas Roepstorff: *Hjerneforskning på tværs….*
- Dorthe Døjbak Håkonsson, Aarhus Business School, University of Aarhus: *Hjerneforskningens betydning for forståelsen af medarbejderes adfærd - Rationelle følelser og organisatorisk klima*
- Peter Vuust: *Musik på hjernen*

PhD student Ericka Peterson from the Pathological Gambling group and Professor Doris Doudet at CFIN.
Photo: Anne Landau

Parkinson's disease

The group cooperates with MD, PhD student Mette Slot Nielsen (supervisors: Professor Jens Christian Sørensen and Associate Professor Carsten Bjarkam) on a further development of the MTPT minipig model: "A porcine model of progressive Parkinson's disease based on chronic MPTP intoxication".

Music

The protocol to study the effect of musical performance on the reward system in experienced musicians has been approved, and the study will be initiated in early 2008 in collaboration with Associate Professor Peter Vuust.

SELECTED RESEARCH PROJECTS:

Rikke Fast, Aage Olsen, Arne Møller, Mette Berendt: Dementia in Geriatric Canines: A Clinical and Neuroimaging Study Comparing Man and Dog.

Joel Astrup Aanerud, Arne Møller, Hans Brændgaard, Manouchehr Vafaee, Johannes Jakobsen, Leif Østergaard, Albert Gjedde: Relationship between changes in amyloid deposits and loss of hippocampal neurons.

Adjmal Nahimi, Anne M Landau, Doris Doudet, Albert Gjedde: In-vivo and in-vitro evaluation of monoaminergic innervations in a rat model of Parkinson´s Disease.

Arne Møller, Yoshitaka Kumakura , Paul Cumming, Albert Gjedde, Jakob Linnet: Low dopamine receptor availability in brain of high sensation-seeking men.

Anne M Landau, Aage Olsen, Albert Gjedde, Doris Doudet: Effects on electroconvulsive therapy in Parkinsons Disease.

Anne M Landau, Suzan Dyve, Doris Doudet, Albert Gjedde: Effects of Nervus Vagalstimulation on the brain.

Ericka Peterson, Arne Møller, Albert Gjedde, Jakob Linnet: SCR (Skin conduction reaction) and dopamine release.

Ericka Peterson, Kristine Rømer Thomsen, Mette Buhl Callesen, Per Borghammer, Albert Gjedde, Jakob Linnet, Arne Møller: Gender differences in Pathological Gambling.

Mette Buhl Callesen, Kristine Rømer Thomsen, Jakob Linnet, Arne Møller: Pathological Gambling Behavior on Slot Machines.

Jakob Linnet, Line G Josefsen, Howard Shaffer, Kim Mouridsen, Arne Møller: Cognitive bias in poker.

Cognitive biases in gambling

by Jakob Linnet

Cognitive biases are central to decision making, and influence how people gamble and develop gambling-related problems. They refer to a wide variety of perceptions and misperceptions of probability and outcome including: Overestimation or overconfidence of winning; selective attention towards gains; superstitions, rituals or irrational beliefs; and illusion of control.

Cognitive biases are important to our understanding of how the brain processes decisions, and when we make optimal and sub-optimal choices. In particular, cognitive biases are important to the study of pathological gambling because these distortions might help us to understand why pathological gamblers make mistakes when they gamble. Pathological gamblers often take larger risks, continue gambling longer, and continue gambling despite losses ('chasing ones losses').

Altered perception of probability may influence behavior such that individuals are more risk willing when the probability of winning is overestimated and more risk averse when the probability of winning is underestimated. But risk taking may also occur independent of perceived risk. In a series of studies, Goodie and Lakey (Goodie, 2003, 2005; Lakey et al., 2006; Lakey et al., 2007) found that problem- and pathological gamblers were more confident in their decisions on a general knowledge task, even though they had no greater competence or performance level than non-gambling controls. Problem and pathological gamblers were also more likely to accept lower probability gambles, both when gambles were dependent upon their level of confidence, and when gambles were independent of confidence level. Similarly, perception of probability and decision making of accepting or rejecting games may be distinct, but related aspects of cognitive bias.
Other aspects of cognitive biases include task familiarity and competence. The familiarity hypothesis suggests that risk taking increases with task familiarity. Ladouceur et. al. (1986) investigated risk taking behavior in subjects unfamiliar with roulette, as they gained familiarity with the task over three gambling sessions. Subjects significantly increased the level of risk and the amount of money spent gambling from session one to two through session three. The authors found no effect on gambling behavior from gambling in groups vs. gambling alone, and only found a temporary increase in confidence level of performance. The competence hypothesis (Heath & Tversky, 1991) suggests that people prefer to bet on their judgment in areas where they feel competent, but not in areas where they feel incompetent. Individuals also prefer to gamble on their judgment even when offered gambles which exceeds their perceptual level of confidence. Heath and Tversky (1991) suggest that competence has psychological and motivational advantages that incompetence does not. Individuals who feel competent can take credit for successful outcomes, and (sometimes) dismiss failed outcomes as 'upsets'. Novices, in contrast, cannot take credit for successful outcomes (at best claim luck), and face the risk of being confronted with their lack of competence in failed outcomes. These motivational factors may lead to overestimation and overconfidence in experts, and underestimation and lower confidence in novices. Finally, ambiguity of outcome is associated with risk aversion. In the Ellsberg paradox (1961), for instance, people are presented with an urn containing 90 balls, 30 blue and 60 which are either red or yellow. When asked to choose between a gamble on a blue ball being drawn and a gamble on a red ball being drawn, people mostly prefer the blue ball (unambiguous) gamble. Next, before any balls are actually drawn, people are asked to choose between a gamble on a blue or yellow ball being drawn and a gamble on a red or yellow ball being drawn. This time most people prefer the red or yellow ball gamble because the probability is known (60 / 90 = 66.7%), while the blue or yellow ball gamble is ambiguous (x / 90). The Ellsberg paradox has been used to illustrate that people prefer choices of risk over choices of ambiguity, and tend to be more risk averse in choices of ambiguity (Glimcher & Rustichini, 2004).

In a recent study, we wished to investigate the role of cognitive biases in poker (Linnet et al., in review). We compared expert and novice poker players in a 'Texas Hold'em' style gambling task. We hypothesized that poker novices would underestimate winning probabilities while experts would overestimate winning probabilities, in accordance with the familiarity, confidence, and competence hypotheses. We further hypothesized that cognitive bias and decision would be closely associated in poker experts, such that overestimated gambles were accepted and underestimated gambles reject. In contrast, we expected novices to show a poorer association between cognitive biases and decision-making.

The results confirmed the hypotheses (see Figure 1). Poker experts (solid green line) were significantly better at selecting advantageous gambles, and chose no gambles below a 30% winning probability. The differences between expert and novices (solid red line) were highly significant ($p < 0.0001$).

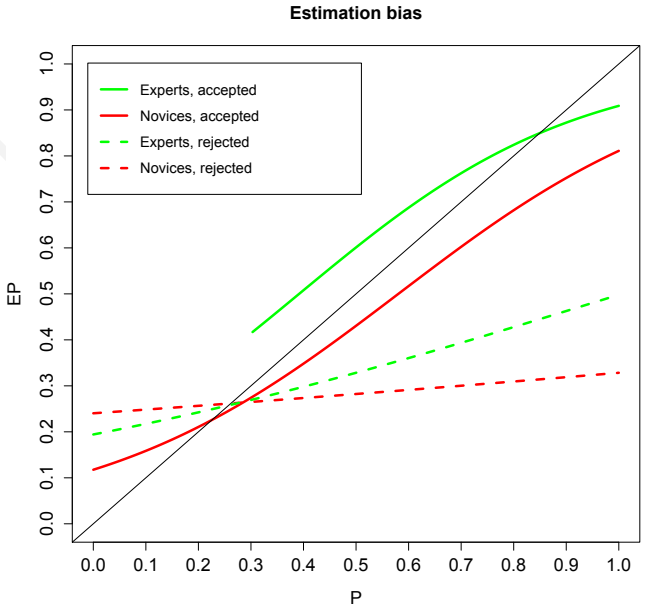

Figure 1
Interaction between probability (P) and estimated probability (EP) of accepted and rejected gambles in experts and novices.
Poker experts overestimate accepted gambles (green solid line) compared with novices (red solid line). Poker experts also show highly significant difference between accepted (solid green line) and rejected gambles (dashed green line), while novices only differ in estimation of accepted (solid red line) and rejected gambles (dashed red line) on probabilities greater than 90%.

Poker experts also showed highly significant differences ($p < 0.0001$) between the overestimation of accepted gambles, and underestimation of rejected gambles (dashed green line). In contrast, novices only differed in estimation of accepted (solid red line) and rejected gambles (dashed red line) on probabilities greater than 90%.

In summary, the data suggest, that cognitive biases in poker change with familiarity from underestimation to overestimation, and that as a player becomes more skillful, the estimation bias is closer associated with choice. In pathological gamblers, we suggest, the cognitive biases may be distorted such that pathological gamblers have the overestimation of experts and the higher acceptance rate of low probability gambles seen in novices. Such cognitive biases, we suggest, may be associated with impaired brain functions in the prefrontal cortex. Currently, we are undertaking studies to confirm these hypotheses.

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Morten Kringelbach and Jakob Linnet at CFIN retreat, Sandbjerg Manor, August 2007.
Photo: Sanne Lodahl

NEUROTRANSMISSION

Effects of electroconvulsive therapy in Parkinson's disease

by Anne Landau and Doris Doudet

Introduction

Parkinson's disease (PD) is a chronic and debilitating movement disorder involving the degeneration of the dopamine-producing neurons in an area of the brain called the substantia nigra. The degeneration of these neurons leads to the symptoms of PD which include bradykinesia (or slowness of movement), rigidity, postural instability and tremor. Depression is one of the most disabling co-morbidities associated with PD and both PD and depression are poorly treated in advanced patients. Various drug treatments exist for PD, but these often elicit debilitating side effects and/or lose their effectiveness after prolonged use. The development of alternative, safe, and effective treatments for both the motor symptoms and depressive features in advanced, elderly PD patients, is an important area of research. Among these treatments, widespread or focal electrical or magnetic stimulation of specific brain regions are gaining recognition as potential alternatives to pharmacological treatments. Electroconvulsive therapy (ECT) leads to both motor improvements and anti-depressive effects, with minimal side effects, although the mechanisms of action are largely unknown.

Specific Aim and Hypothesis

The aim of this study is to explore the neural mechanisms underlying the therapeutic effects of ECT. We believe that ECT can induce changes in the levels of dopamine, serotonin and norepinephrine neurotransmitters in different areas of the brain implicated in motor control and depression. Based on the existing literature and preliminary studies in primates and rodents (Strome et al., 2005, 2007), we hypothesize that ECT will increase serotonin and norepinephrine neurotransmission in the cortex and dopaminergic transmission in the striatum. Furthermore, we propose that ECT can induce regionally specific neurotrophic factor expression (responsible for growth and survival of neurons) in the areas of the brain affected by PD and depression.

Research Plan

Göttingen minipigs, which are large animals with a good brain size for longitudinal imaging studies and use of human ECT devices, will be used in these experiments. The neurotoxin 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) will be administered to minipigs to create a bilateral model of PD with rigidity, bradykinesia, swallowing dysfunction and gait disturbances as previously reported (Mikkelsen et al., 1999). Behavioural rating with a standardized motor scale developed for pig studies will be performed in normal and parkinsonian pigs before and after a clinical course of ECT (3 times per week; 10 treatments; Thymatron stimulator) under thiopental anesthesia. Twelve untreated and 12 MPTP-lesioned pigs (9 active ECT and 3 sham in each condition) will be PET scanned with an HRRT PET scanner before and after the end of the ECT/sham course (48 hrs, 1 week, 4 weeks and 3 months).
At each time point pigs will be sacrificed and the brain taken out. One hemisphere will be used to assess neurotrophic factor expression, the other will be used for autoradiographic binding for neurotransmitter receptors and transporters (see Figure 1). This will provide the rationale and pilot data for the design of studies of the effect of ECT in human subjects.

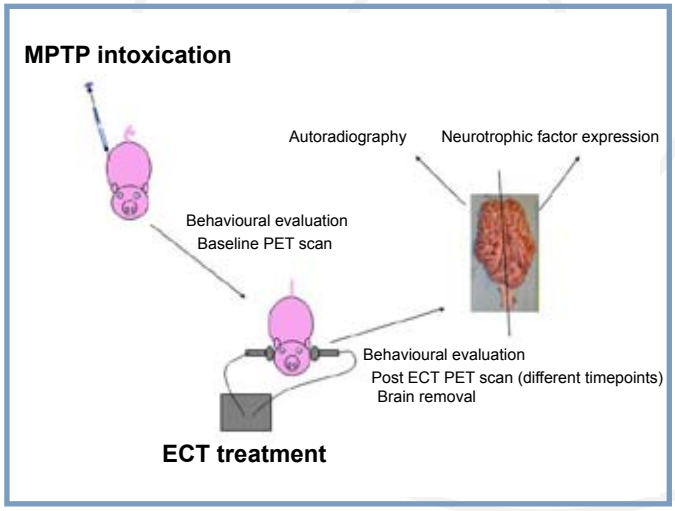

Figure 1
Diagram of research plan. MPTP intoxicated minipigs will undergo ECT treatments. Alterations in behaviour and receptor binding (in vivo by PET) will be observed throughout the study. At designated time points, minipigs will be euthanized and brains removed for post-mortem studies including autoradiography and neurotrophic factor analysis.

To date, two minipigs have undergone ECT treatment. It was possible to induce seizures in both pigs under investigation and a higher current was necessary with each ECT treatment in order to induce the seizure as previously demonstrated to occur in non-human primates (see figure 2) and humans. Brain scans from the pilot ECT pigs are currently being analyzed and post-mortem studies such as autoradiography (receptor binding studies) are currently being conducted.

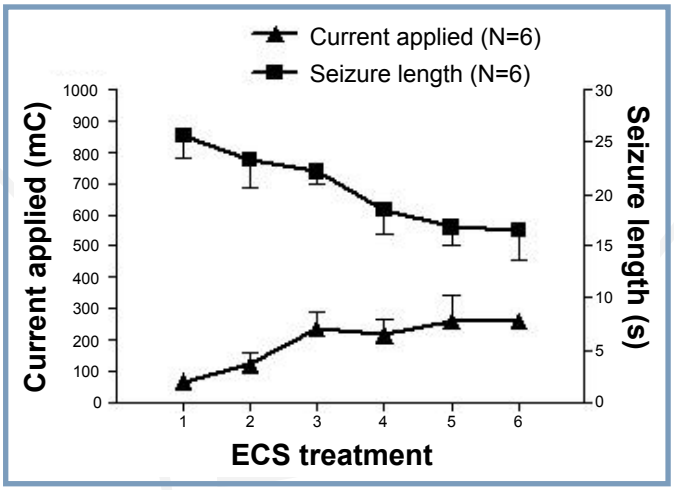

Figure 2
Seizure threshold vs. seizure length. Minipigs demonstrate decreased seizure lengths for the same applied current as more ECT treatments are administered (and therefore the applied current is increased with each ECT treatment), as is shown here in non-human primates.

Relevance

This will be the first comprehensive longitudinal study of the mechanisms of action of a non-pharmacological intervention with known therapeutic effects in both PD and depression. The use of electrical currents to treat various neurological and psychiatric conditions is an active field of research currently lacking well characterized models with which to investigate the mechanism of therapeutic benefits. Validation of the minipig as an animal model will be a valuable contribution to the field. Better understanding of the mechanisms of action of ECT may help in the design of improved therapeutic strategies for depression and/or PD.

Parallel studies

There are some other related projects currently being undertaken by our group and some excellent collaborators from Aarhus University Hospital. One study consists of determining the feasibility of stimulating the vagus nerve of the minipig and the effects of this stimulation on the brain. Vagal nerve stimulation, like ECT, has been found to have antidepressant actions and these two forms of stimulation may share common therapeutic mechanisms. This work is being done in collaboration with Dr. Suzan Dyve. At present, two pigs are being analyzed after vagal nerve stimulator implants.

Furthermore, a new pilot study is being initiated with the goal of validating a new chronic model of depression in minipigs in collaboration with Dr. Carsten Bjarkam and Dr. Jens Christian Sørensen. The first minipig of the pilot study is currently under investigation in a behavioural paradigm. Through validation of this new model, different antidepressant therapies can be tested in an animal model with a large brain suitable for brain imaging.

The project is made in collaboration with:
Adjmal Nahimi[1,2], Aage Kristian Olsen[1,2], Mallar Chakravarty[1,2], Gregers Wegener[3], Poul Videbech[3], Arne Møller[1,2], Albert Gjedde[1,2]

1: PET-Center, Aarhus University Hospital, Aarhus, Denmark
2: Center of Functionally Integrative Neuroscience, University of Aarhus, Denmark
3: Center for Psychiatric Research, University of Aarhus, Risskov, Denmark

and is funded by Danish Medical Research Council and Parkinson Society Canada salary awards to Anne Landau.

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Doris Doudet and Anne Landau at CFIN
Photo: Mallar Chakravarty

NEUROTRANSMISSION

PET Neuroimaging of Antidepressant Binding Sites in Humans

by Donald F. Smith
(Visiting Senior Scientist, Center for Psychiatric Research, Psychiatric Hospital, Aarhus University)

Depression is an extremely disabling and costly disease, with an increasing burden on society. Depression can have prolonged, adverse consequences, because 25 - 30% of patients never get well, despite judicious use of available therapies. We believe that solving the riddle of treating depression effectively will require a detailed knowledge of the effects of antidepressant therapies on neuronal processes in the living human brain.

Positron emission tomography (PET) has become an increasingly popular method for exploring neuronal mechanisms in the living human brain. Numerous PET studies have, for example, assessed the role of monoamine transporters and receptors in depressed patients, but consistent findings are lacking. As a result, the neurobiologic basis of depression and of a positive response to antidepressant therapy remains unknown.

Working with radiochemists at the Aarhus PET Center, we have discovered that a popular antidepressant drug named mirtazapine (Remeron®), radiolabeled with C-11, is particularly well-suited for use in PET. Our recent studies have shown that this radioligand can determine the degree to which receptors in the living brain are functional for therapeutic actions of an antidepressant drug.

The next step in these studies will be to determine by PET whether the binding of [^{11}C]mirtazapine at antidepressant sites differs between healthy subjects and people suffering from treatment-resistant depression. Eventually, these and other studies may provide evidence-based procedures for properly distinguishing between depressive disorders and for selecting the most appropriate antidepressant therapy for each patient.

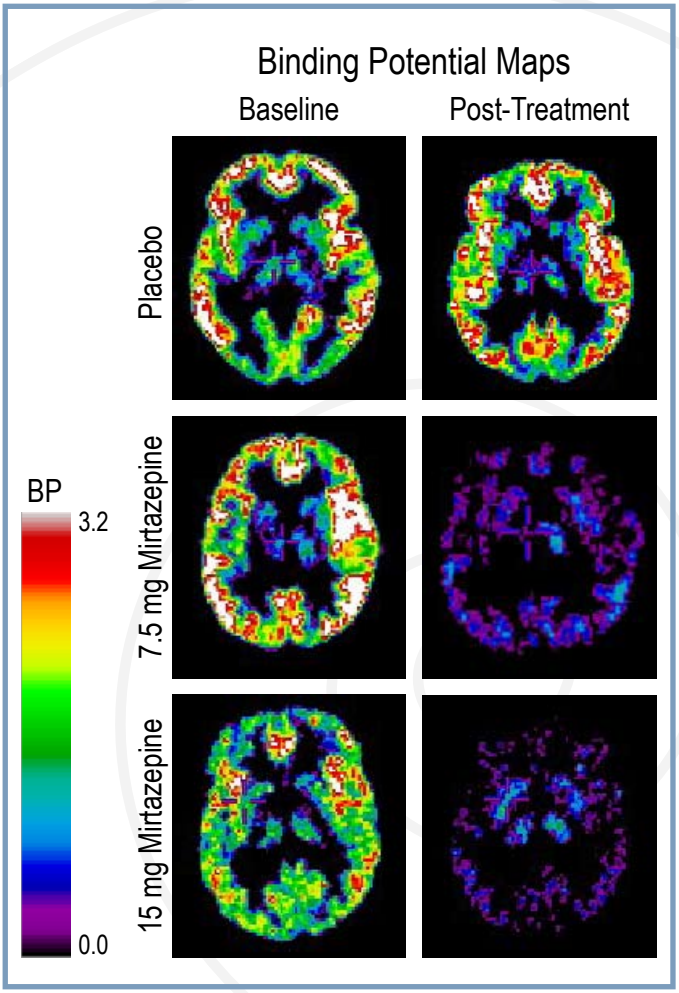

Figure 1
Parametric maps of the binding potential of [11C]mirtazapine in the brain of healthy subjects under baseline condition and after receiving either placebo, 7.5 mg mirtazapine or 15 mg mirtazapine for five days. Note that the binding potential of [11C]mirtazapine is generally greater in cortical regions of the brain than in midbrain regions, and that both doses of mirtazapine produced marked occupancy of the antidepressant binding sites.

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Danish Neuroscience Center (DNC)

by Albert Gjedde

The Danish Neuroscience Center is a joint effort of Aarhus University and Aarhus University Hospitals. Situated between the wings of the brain section of Aarhus Hospital, the DNC will house a number of laboratories and research centers engaged in translational neuroscience. The concept is modeled on the successful cohabitation of hospital and research departments in the Montreal Neurological Institute of McGill University.

The idea of creating such a center was first conceived in 1998, and the construction will be finished almost to the date of the 10th anniversary of the project, in late 2008. The building has progressed rapidly in the last quarter of 2007 and the first quarter of 2008 and the structure now towers several floors above ground on its way to the top. The total square footage of new space, including a new and expanded PET scanning and radiochemistry floor in the basement, is about 75,000, distributed in a basement, a ground floor with conference center and 5 additional floors of laboratory and office space above that.

A grand opening is planned for spring of 2009 in the shape of a scientific conference with the tentative name BrainStorm 2009. It is the intention to invite a number of highly accomplished international speakers to help the local clinician-scientists introduce the topic of "Translational Neuroscience", the effort to focus on scientific explanations and solutions to the most devastating brain disorders of the present and the future.

An international advisory board has been named for this event, consisting of Professor Andres Lozano, neurosurgeon at the University of Toronto, Professor Bruce Rosen, radiologist at Harvard University, Professor Chris Cooper, neurobiologist at Essex University, Professor David Eidelberg, neurologist at New York University, Professor Gerhard Gründer, psychiatrist at University of Aachen, Professor Irene Tracey, neurologist at Oxford University, Professor Kirk Frey, nuclear medicine physician at Ann Arbor University, Professor Peter van Zijl, brain imaging scientist at Johns Hopkins University, and Professor Pierre Magistretti, neurobiologist at the universities of Lausanne and Geneva.

The Danish Neuroscience Center will also house the Graduate Neuroscience Program of the Health Sciences faculty of Aarhus University. This program now has 104 enrolled graduate students from many countries, associated with clinical departments and research groups such as CFIN, the Danish Pain Research Center, the PET center, Departments of Neurology, Neurosurgery, and Neuroradiology, the MIND center, the CCC Consortium (Culture, Cognition & Communication), and the MINDLab equipment facility.

Photos: Sanne Lodahl

NEUROCONNECTIVITY

by Peter Vestergaard-Poulsen

Progress in 2007

Our research focuses on how brain connectivity, integrity, and plasticity are regulated by changes in neurotransmission. Previously, neuronal homeostatasis and structural connectvity in stroke have been the main target of our research. We are focusing our efforts more on applying these methodological techniques to explore the microstructural effects of neuroplastic changes, developing methods to a more direct MR-based detection of neuronal activity than fMRI, as well as using these methods to study the neuroplasticity of long term attentional states.

Our approach mainly involves magnetic resonance imaging (MRI) methods, measuring water self-diffusion which has proven to be extremely sensitive to microstructural changes on a micrometer scale. Using a combination of modeling and experimental studies of brain tissue *in vivo* and *in vitro*, we study basic cellular mechanisms underlying, for example, neuroplaticvity (cell fraction, water exchange, dendrite density and intermolecular interaction). High resolution 3D-MRI and voxel based morphometry and statistical mapping methods using whole-brain voxel-wise statistics are used to find significant regional differences between groups or in a longitudinal setting.

We use state-of-the-art whole-body magnets (3T), high-resolution micro-imaging magnets (16,4T) as well as other high-field magnets at CFIN and with our primary collaborators at inSPIN (Danish National Reserach Foundation Center at Dept. Chemistry, Aarhus University) and McKnight Brain Institute / US National High Field Laboratory (University of Florida). Histological and stereological methods are used in validating the results (in collaboration with Inst. Anatomy, University of Aarhus).

Neuronal Homeostatis

Peter Vestergaard-Poulsen and Brian Hansen completed a cellular multi-compartment model that allows for diffusional and transverse relaxation effects in compartmental heterogeneity. The model is promising in terms of accounting for qualitative and quantitative findings in normal and ischemic cell homeostasis (Vestergaard-Poulsen P et al. 2007)

A novel approach of simulating the neuron as a specific fractal model (reflecting the actual growth and structure of neurons) has been developed. This new model developed by Brian Hansen strongly supports the general assumption that the clinically observed changes in the diffusion weighted signal in e.g. stroke are mainly due to changes in the size of the extracellular space (Hansen, B. et al. *in review*)

To explore a more direct detection of neuronal activtivity than BOLD fMRI, we are currently investigating how neuronal discharge can change the cellular water self diffusion detectable by diffusion weigthed MRi. This is the focus of Brian Hansens work at UFL (see Micro-imaging: Magnetic Resonance Microscopy at very high fields, page 24-25 by Brian Hansen)

Brian Hansen has successfully defended his PhD thesis “Diffusion MRI in neuroscience” at CFIN/Institute of Physics and Astronomy in September 2007.

Neuronal Connectivity

CFIN researchers are studying the structural connectivity in the brain by diffusion tensor measurements and computer based 3D axonal fiber tracking algorithms. This has been used in investigating the relations between plastic changes of the fiber bundles in white matter following ischemic stroke and motor recovery (Mette Møller et al., 2007). The study showed that the developed methods can map the Wallerian degeneration process that follows an infarct. The results reveal an association between the temporal evolution of diffusion related indices, describing how water diffusion is altered in injured fibers, and motor function. These changes may reveal early degeneration of axons compared with higher sensitivity than more conventional MR imaging. Mette Møller successfully defended her PhD thesis : “Recovery and serotonergic neurotransmission in the wake of stroke and recovery” in March 2007.

Efforts to develop functional connectivity acquisitions methods and refine the fiber-tracking acquisition and postprocessing methods have generated important scientific and methodological progress (Jesper Frandsen et al. 2007), now used routinely in presurgical planning. As a fascinating spin-off these methods are valuable in investigations of cardiac anatomy and function. (Smerup et al. 2007, *submitted*) in collaboration with Department of Cardiothoracic & Vascular Surgery, Aarhus University Hospital, Skejby, Center for Functionally Integrative Neuroscience, Aarhus University Hospital, Aarhus Sygehus, Stereology and EM Laboratory and MIND Center, Aarhus University, MR Research Center, Aarhus University Hospital, Aarhus, Klinik und Poliklinik für Thorax-, Herz- und Gefäss-

chirurgie, University Münster, Münster, Germany, Cardiac Unit, Institute of Child Health, University College, London, UK (see further details in this report: Diffusion Tensor Imaging of the heart by Jesper Frandsen, page 23).

Mental Stress

Mental stress has long been known to affect the biology and neurobiology of animals and humans. A number of rat studies have also shown profound changes in neurogenesis and structure in the dendritic tree of the hippocampus upon induction of stress. In rats, restraint stress for only three hours daily causes significant atrophy of apical dendrites of hippocampal CA3 pyramidal neurons in only 21 days (number and length of apical dendritic branches reduced by 18 and 32%, respectively). Studies aim to correlate the symptoms with dependency of neurobiology, structural connectivity changes in WM, especially in the hippocampus, the prefrontral medial cortex and the amygdala.

Our goal is to develop MRI based in-vivo markers to study the structural changes induced by mental stress. This could have considerable impact on the understanding of the stress phenomenon, monitoring development and interventional strategies such as psychotherapy and pscyho pharmaceuticals.

To do this, CFIN researchers utilize biophysical models (to estimate i.e. dendrite density, which is a major feature of cortical plasticity) which is now being applied to high-quality experimental data. The current step towards this goal, validation of the dendrite density models by histology and stereology, is described in the Neurophysics section (page 26-27). Recently we have collected data using a restraint stress rat model and are currently analyzing hippocampal changes. The extreme sensitivity of diffusion imaging combined with high performance MR imaging techniques using 16.4 Tesla MRI microscopy is crucial for these studies. The collaboration includes CFIN, inSPIN, Center for Psychiatric Research, Aarhus University Hospital in Risskov and the Institute of Anatomy, University of Aarhus.

Meditation

Extensive practice involving sustained attention can lead to changes in brain structure. We have now provided evidence of structural changes in the brains of subjects engaged in the long-term practice of meditation. Using magnetic resonance imaging, we observed increased gray matter density in lower brain stem regions of experienced meditators compared with

SELECTED RESEARCH PROJECTS:

Astrid From Frøhlich, Sune Nørhøj Jespersen, Leif Østergaard, Valerij Kiselev (Freiburg University, Germany): The theory behind fiber tracking: diffusion in biological tissue.

Peter Vestergaard-Poulsen, Gregers Wegener, Niels Chr. Nielsen, Thomas Vosegaard, Brian Hansen, Sune Jespersen: The neurobiology of the brain due to mental stress - an MRI approach to detect the structural correlates of induced stress.

Peter Vestergaard-Poulsen, Brian Hansen, Martijn van Beek, Jes Bertelsen, Michael Stubberup, Joshua Skewes, Andreas Roepstorff: The structural correlates of the brain after long term meditation praxis.

Sune Nørhøj Jespersen, Carsten Bjarkam, Brian Hansen, Thomas Vosegaard, Jens R. Nyengaard, Niels Christian Nielsen, Mallar Chakravarty, Daniel Otykier, Peter Vestergaard-Poulsen: Dendrite density from magnetic resonance diffusion measurements: Comparison with histology.

Niels Buhl, Sune Nørhøj Jespersen: A Simulation Framework for Diffusion Weighted MRI in Digitalized Neurons: Extracting Cytoarchitectural Parameters Using a New Theoretical Model for Diffusion.

Brian Hansen, Jeremy Flint and Steve Blackband: Direct detection of neuronal activity in hippocampal slices in-vivo by diffusion microscopy at high fields.

High-field MR Studies of Alzheimer's disease in Transgenic Mice. Collaborators: Louise Munk Rydtoft , Thomas Nielsen, CFIN, inSPIN and Lundbeck A/S)

Mads Sloth Vinding, Thomas Vosegaard, Niels Chr. Nielsen, Sune N. Jespersen, Ryan Sangill and Peter Vestergaard-Poulsen: Optimal Control MRI of the Chronic Stress Induced Neuroplasticity of the Human Hippocampus- a feasibility study.

age-matched non-meditating people. Our findings suggest that the long-term practice of meditation can induce structural changes in brain regions (brain stem) concerned with cardio-respiratory control.

If the practice of meditation does indeed produce structural changes in brain structures concerned with autonomic control, this might provide a mechanism explaining the claim that the regular practice of meditation can induce a lasting sense of calmness and increase resistance to stressful stimuli. The study may provide additional insight into the mechanisms underlying reduced breathing and heart rate that have been shown to be affected by meditation.

Industry

The inSPIN-CFIN collaboration is now sharing research equipment and teaching resources (Biomedical Engineering MRI courses), initiating collaborations with industry (High-field MR Studies of Alzheimer's disease in Transgenic Mice. Collaborators: Louise Munk Rydtoft, Thomas Nielsen, CFIN, inSPIN and Lundbeck A/S).

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Peter Vestergaard-Poulsen, Martijn van Beek, Joshua Skewes, Carsten R. Bjarkam, Michael Stubberup, Jes Bertelsen and Andreas Roepstorff Long-term meditation is associated with increased gray matter density in the brain stem. (Submitted to Neuron)

Morten Smerup, Eva A. Nielsen, Jesper R. Frandsen, Peter Vestergaard, Johnnie Andersen, Jens R. Nyengaard, Michael Pedersen, Steffen Ringgaard, Vibeke Hjortdal, Paul P. Lunkenheimer, Robert H. Anderson. Evidence of the Three-Dimensional Arrangement of the Aggregated Myocytes making up the Mammalian Ventricular Myocardium. (submitted to Circulation)

Eva A. Nielsen, Morten Smerup, Peter Agger, Jesper Frandsen, Steffen Ringgard, Michael Pedersen, Peter Vestergaard, Jens R. Nyengaard, Johnnie B. Andersen, Robert H. Anderson, Vibeke Hjortdal. Right Ventricular Three-dimensional Architecture is Preserved During Experimentally Induced Right Ventricular Hypertrophy - Assessment with Diffusion Tensor Magnetic Resonance Imaging. (submitted to Circulation)

Claus J. Eskerod, A model of water diffusion in white matter investigated with high resolution MRI (Masters thesis, Biomedical Engineering, 2007)

Mette Møller. Recovery and serotonergic neurotransmission in the wake of stroke and recovery. (PhD thesis, CFIN, 2007)

Brian Hansen. Diffusion MRI in neuroscience. (PhD thesis, CFIN/ Instituite of Physics and Astronomy, Aarhus University, 2007)

ISMRM conference in Berlin, May 2007
Photos: Jesper Frandsen

NEUROCONNECTIVITY

Diffusion Tensor Imaging of the heart

by Jesper Frandsen

A report on the collaboration with Department of Cardiothoracic & Vascular Surgery, Aarhus University Hospital, Skejby

Diffusion Tensor Imaging (DTI) has proven to be a powerful tool for probing brain microstructure and studying e.g. brain white matter changes. Applying diffusion gradients along multiple directions, the directional restriction of water diffusion by meso-scopic structures such as white matter axons can be measured. Following the preferred water diffusion at each location of brain is often used to visualize the major fiberbundles in the brain (so-called Fibertracking). A number of projects at CFIN use DTI to elucidate characteristics of the in-vivo brain, be it human or animal brain.

This study represents a different way of utilizing DTI to map the myocardial fiber organization.

The heart is a structurally complex muscular organ of unique endurance and has been the subject of many histological examinations. It has been shown that the myocardium making up the ventricular wall of mammals is composed of elongated contractile cells, the myocytes, which are embedded in a stroma of connective tissue. Furthermore these myocytes in the subepicardial layers of the wall demonstrate a left-handed helix, where as the myocytes in the subendocardial layers trace a right-handed helix. Within the last decade researchers have postulated some degree of secondary and tertiary arrangement within the myocardial mesh, such as the concept of a unique myocardial band or hypothesis that the myocytes are confined in radial laminar sheets. These suggestions have not been validated by anatomical or histological examinations upon exploring the entirety of the left ventricular mass.

The technique of DTI now provides the means to examine the orientation of aggregated myocytes. However, it is extremely difficult to estimate these directly in-vivo with current imaging technique. Instead, DTI was performed on a number of ex-vivo healthy pig hearts.
Each heart was arrested in a diastole or a systole state, fixated and scanned for approx. 14 hours in a 1.5 T MRI scanner. We assessed helical angles at the anterior, lateral, and posterior free walls of the left ventricle, relative to the equatorial plane midway between the apex and the base of the ventricle. Fibertracking was performed using the custom-made software. In all cases, it was possible to track virtual pathways from all chosen voxels of interest, with practically identical patterns being generated in the different hearts. We can summarize our findings to state that endocardial tracks are oriented according to a right hand helix pattern, epicardial tracks in a left hand helix pattern. This is entirely compatible with the detailed dissections carried out by Pettigrew more than 150 years ago. We will perform further invistigations of the pathways amongst the aggregated myocytes making up the walls of the mammalian ventricles.

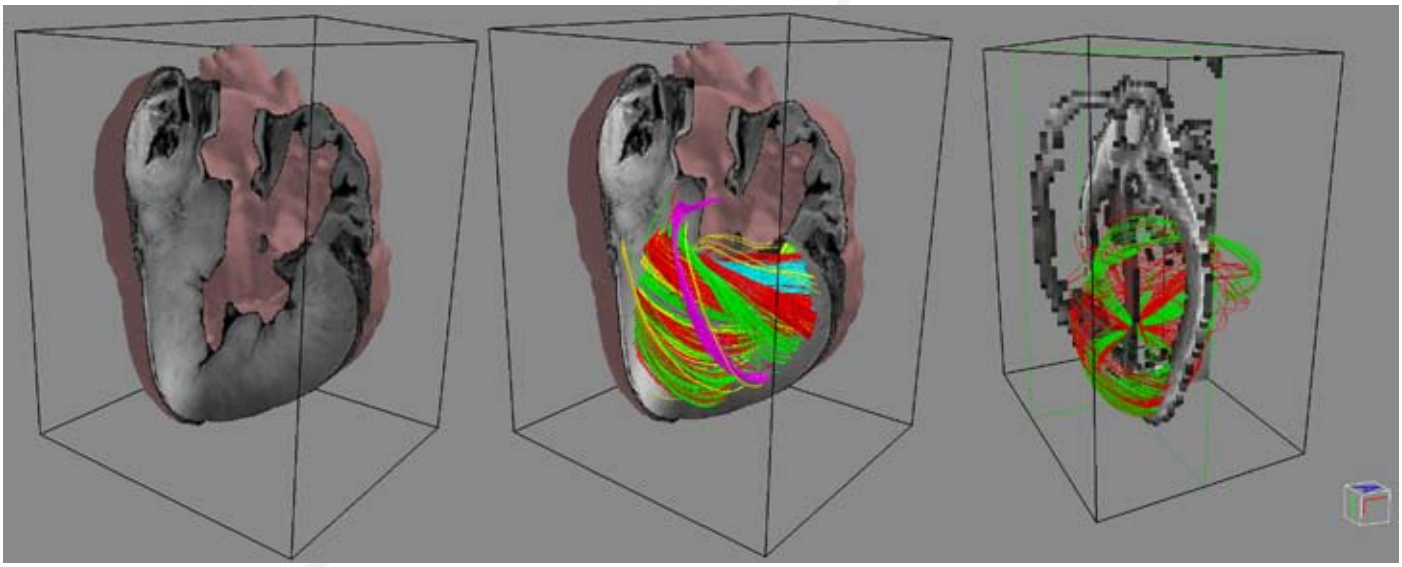

Figure 1
Left and middle image: The heart was arrested in systole state. The anatomical image shows the contraction of the myocardium. A selection of muscle fiber tracts are shown. Right image: Another heart, arrested in diastole state. The helix shape of the selected muscle fiber tracts is easily detected.

NEUROCONNECTIVITY

Micro-imaging: Magnetic Resonance Microscopy at very high fields

by Brian Hansen

Report on the collaboration with McKnight Brain Institute, Florida, USA.

Today most pathologies relating to the human central nervous system are understood in very high detail down to the cellular or molecular level. Modern brain diagnostics rely heavily on magnetic resonance imaging which has brought a vast array of new techniques into the field. In order to improve MR-based diagnostics even further we need to improve our understanding of how pathology at the cellular level is reflected in the MR-signal. In this article, we present studies that use high magnetic field MRI to study tissue structure as well as biological and biophysical processes at the cellular level. It is worth noting that structure and processes belonging to the normal brain may also be studied using the same methods and therefore, the methods presented here may also allow us to investigate the normal brain in greater detail through the "lens" of the magnetic resonance microscope.

The investigation of tissue microstructure and its response to pathology is typically done using diffusion sensitive MR-imaging. CFIN researchers have developed theoretical models for understanding the influence of tissue biophysics on MR-signal, especially in the pathological state known as ischemia which is of special interest in the study of stroke [1,2]. In an effort to experimentally investigate MR-signal formation in brain tissue and the biophysical information contained in the diffusion weighted MR-signal, CFIN researchers have established MR microimaging of high field strength (17 T) in collaboration with University of Aarhus, the Chemistry Institute. To further strengthen this effort collaboration has been established with Prof. Blackband's MR-lab at the McKnight Brain Institute in Gainesville, Florida. Part of this collaboration is a research stay from September 2007 to April 2008. The following describes some of the experiments we are currently working on.

High resolution MR microscopy of rat central nervous system

In an attempt to investigate the MR properties of tissue at the cellular level prototype microcoils with a diameter of 50 μm have been used to produce high resolution images (pixelsize ~15 μm). This allows a very detailed quantitative investigation of the MR properties of tissues with different cellular compositions. The rodent hippocampus is a structure containing many well characterized regions and was therefore chosen for this study. Figure 1 shows an example image of the CA1 cell layer which is a 25 μm wide banded structure containing mainly cell bodies.

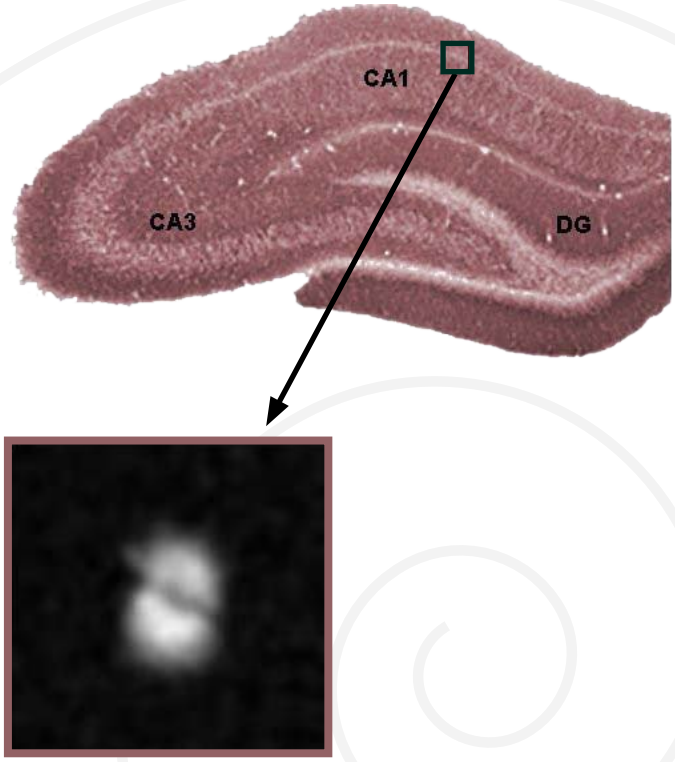

Figure 1
The CA1 cell layer in rodent hippocampus is shown. The area marked by the black box corresponds to the section imaged using the 50 um microcoil. An example of an MR image obtained with the microcoils at a field strength of approximately 13T is inserted in the upper right corner. The CA1 cell layer is clearly seen cutting through the image. The coil's very limited field of view is also evident.

The MR image shown in Figure 1 was obtained in fixed tissue. Preliminary results are presented in Flint et al., Proceedings of the 49th ENC. A perfusion chamber allowing imaging of living tissue has been developed for the microcoils in the Blackband lab. This will allow the investigation of tissue response to varying states of tonicity mimicking the pathological state. Such studies of tissues undergoing controlled perturbations may help us understand the ischemic state in stroke patients and help decision making in the clinical setting.

Living Brain Slices

Studying the working brain is crucial for the progress of neuroscience. MR-based methods (fMRI) for measuring brain activity typically rely on the hemodynamic response to the presented stimuli. However, methods based on diffusion weighted

MR have been demonstrated to hold certain advantages over the blood based fMRI method. In order to gain the most from such a technique the physiology involved must be understood. In an attempt to investigate the physiological basis of the diffusion based fMRI method we have designed a study using live hippocampal slices from rodent brain. These measurements will hopefully reveal the nature of the diffusion-based method's ability to detect neuronal activity.

MR microimaging at very high fields allows us to investigate brain tissue in very high detail beyond what is currently possible in clinical scanners. This is the forefront of imaging research and may well mark the path for conventional MRI to follow as well as allowing in-depth investigation of the human nervous system, its structure, physiology and pathology.

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Brian Hansen in front of McKnight Brain Institute in Florida, USA

Project facts

The National High Magnetic Field Laboratory (NHMFL) is distributed over three sites in the US: Florida State University (Tallahassee), Los Alamos National Labs (New Mexico) and University of Florida in Gainesville. The latter is home to the Advanced Magnetic Resonance Imaging and Spectroscopy (AMRIS) facility which is part of UF's McKnight Brain Institute. AMRIS houses a variety of state-of-the-art instruments for studies, including biological solid-state Nuclear Magnetic Resonance (NMR), solution NMR, micro-imaging, animal imaging and human imaging. These facilities allow researchers to take very high resolution images and do single cell imaging.
The McKnight Brain Institute is one of the world's largest research institutions within brain and nervous system disorders.

People

From CFIN: Brian Hansen, Sune Nørhøj Jespersen and Peter Vestergaard-Poulsen
From McKnight Brain Institute: Jeremy Flint, Choong-Heon Lee and Steve Blackband

This project has obtained funding from the following sources:
- The Danish National Research Foundation (CFIN)
- The Denmark-America Foundation
- Dagmar Marshall's Foundation
- Julie von Müllen's Foundation (The Royal Academy of Science)
- The Oticon Foundation

NEUROPHYSICS

by Sune Nørhøj Jespersen

Introduction

Neurophysics research at CFIN is concerned with the application and development of methods from theoretical physics to problems in neuroscience. It is our opinion that this approach, used in collaborations with other research groups at CFIN, will not only lead to the development of new methods, but also deepen our understanding of some of the fundamental questions in neuroscience. The underlying basic hypothesis is that developing and analyzing physical models of tissue structure and function will open new windows into the state and working of the living brain. These new properties will be measured in collaboration with advanced imaging and used as input to e.g. statistical models of disease progression with the Neuroinformatics Group. The main focus in 2007 has been within diffusion modeling and modeling of blood flow heterogeneity. First of all, we have developed and are now validating a method to allow us to potentially use diffusion MRI as a veritable microscope, offering a noninvasive view into the microstructure of the living brain. The perspectives for such a method are numerous, allowing researchers to study cytoarchitectural changes occurring during normal development and learning, or as a result of e.g. mental stress and disease. Second, based on MRI perfusion measurements and models of capillary oxygen extraction, we have devised a framework to measure microvascular flow heterogeneity and obtain cerebral oxygen extraction maps. During stroke for example, oxygen metabolism becomes compromised, and the ability to evaluate oxygen extraction using MR scanners may aid the prediction of infarct evolution, and may be helpful for diagnosis and treatment. In the following, we will describe our efforts in these two areas in more detail.

Diffusion modeling

"Can one hear the shape of a drum?" is the title of a famous paper by Kac in 1966 and it captures metaphorically the promises of MRI diffusion modeling. Diffusion refers to the ceaseless tumbling that all molecules are engaged in, and MRI experiments can be made particularly sensitive to the thermal motion of water molecules. During a typical diffusion experiment, water molecules will travel distances on the order of micrometers, so despite the fact that the physical dimensions of the pixels are on the order of millimeters, the signal carries information about the structure of the tissue on a much smaller scale. Given an appropriate model and mathematical framework, this information can be disentangled from the signal, in essence facilitating MR microscopy of the living brain. In a previous work, we devised a new model of water diffusion in neural tissue in collaboration with researchers at Washington University, St. Louis. Using this model to interpret high-field MRI diffusion data, enabled us to measure the intracellular diffusion constant, neurite (i.e. dendrites and axons) radii, neurite architecture, and neurite density. The intracellular diffusion constant is a sensitive probe of the intracellular milieu and an indicator of cellular viability, and the quantification of neurite architecture, density and radii is important for example for studying cerebral plasticity as occurring during learning, stress and disease. Much of our work in 2007 has been concerned with expanding and validating this framework.

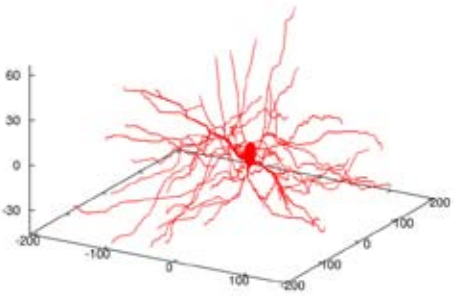

Figure 1
Digital neuron (Computational Neurobiology and Imaging Center at the Mount Sinai School of Medicine) used in numerical simulations.

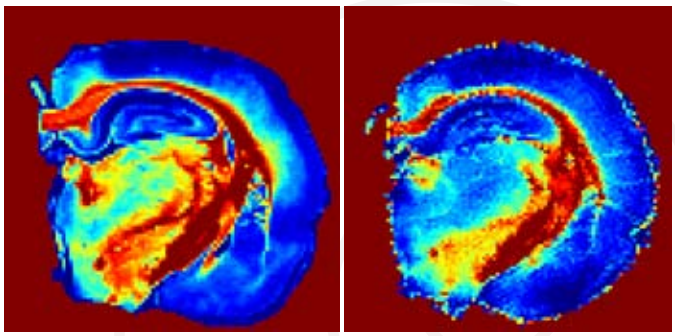

Figure 2
Comparison of histological image (left) to MR-parameter map (right).

In one study, Ph.D. student Niels Buhl has constructed a comprehensive numerical framework for simulating diffusion in digitalized neurons obtained from fluorescence microscopy. This approach has allowed us to selectively validate individual aspects of the model, and resulted in a set of guidelines regarding the choices of optimal experimental protocols. In another project, Masters student Claus J. Eskerod has used simulations and experiments to examine the conditions necessary for measurement of axonal radius. Finally, we have collected data from healthy rats, and compared model parameter maps with information obtained from conventional histology. The results are very promising and provide support for the ability of the model to measure neurite density. The same

rats are currently being analyzed using stereological methods for further validation of the model. In a separate study, Peter Vestergaard-Poulsen has initiated an investigation of the effects of mental stress, applying the model to detect subtle cytoarchitectural changes in the rat hippocampus.

In a parallel line of research, Ph.D student Astrid F. Staanum is investigating the behavior of the diffusion signal in the vicinity of impermeable membranes, allowing us to better understand the effect of different pulse sequences, and helping us to interpret experimental data in terms of microstructure.

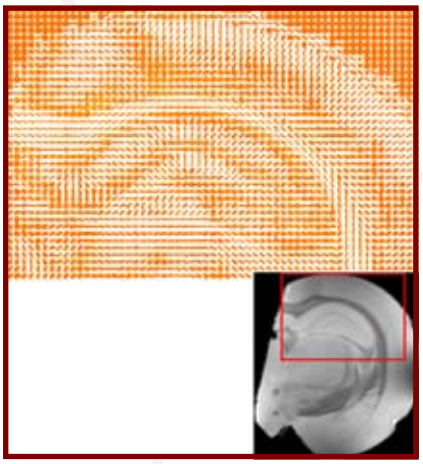

Figure 3
Illustration of neurite orientation distribution.

Oxygen extraction fraction and flow heterogeneity

Flow heterogeneity refers to the observation of a wide distribution of flow velocities in the capillaries of the brain. This phenomenon has been hypothesized to play a role in the regulation of oxygen extraction during ischemia or functional activation. Leif Østergaard has previously introduced a non-invasive method to measure micro vascular flow distributions based on dynamic contrast susceptibility weighted perfusion MRI, and the method has been further improved by Kim Mouridsen using a physiologically informed Bayesian estimation framework. We have combined these methods with a model relating capillary flow to oxygen extraction, enabling us to compute local oxygen extraction from MRI perfusion data. In 2007 we have continued our work with the analysis and validation of this method by comparing its performance to oxygen extraction as measured by PET on a number of patients suffering from carotid occlusion. There is a high degree of agreement between the two modalities, despite relying on completely different measurement techniques and assumptions. Simultaneously, Kim Mouridsen and colleagues are investigating the sensitivity of the MR based oxygen extraction maps for use in tissue survival prediction schemes, and preliminary results indicate a superior performance in this respect.

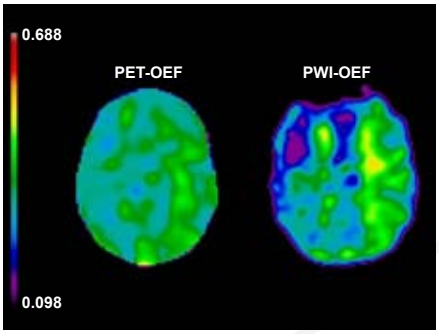

Figure 4
Comparison of oxygen extraction fraction (OEF) as obtained from PET (left) to OEF derived from MR-perfusion images.

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FUNCTIONAL HEMODYNAMICS

by Leif Østergaard

Progress in 2007

Functional haemodynamics research has made exciting progress in 2007:
Extending CFIN's efforts to model the dependency of oxygen delivery to brain tissue on the heterogeneity of microscopic flows, Sune Nørhøj Jespersen combined modeling with robust estimates of the tissue residue function developed by Kim Mouridsen to determine oxygen extraction fraction. These results lend hope to better characterizing the haemodynamic and metabolic derangement after ischemia – and better predict tissue outcome in acute stroke patients. The data was first presented at the International Society for Magnetic Resonance in Medicines workshop on Cerebral Perfusion and Brain Function in Salvador da Bahía (see page 27).

Mahmoud Ashkanian has developed a thorough framework for studying the effects of physiological gases on cerebral blood flow and metabolism, with an aim to develop strategies to enhance neuronal survival in ischemia. In collaboration with Dr. Grethe Andersen, head of the Department of Neurology Stroke Unit, this study is now pursuing the validation of the perfusion MRI based estimates of cerebral oxygen extraction fraction described above by positron-emission-tomography values
The preliminary studies are indeed encouraging and will be extended to studies of acute stroke patients in collaboration with at University of Cambridge (Prof. Jean-Claude Baron) in conjunction with the I-Know study lead by CFIN.
See http://www.i-know-stroke.eu

In an effort to transform progress in basic neuroscience into better patient management, CFIN scientists have made software for advanced clinical perfusion analysis available on the CFIN website (see page 31).
This form of disseminating our scientific results remain an important source of interaction with treating physicians as well as clinical neuroscientists.

In a longstanding collaboration between CFIN and the department of Physics at Freiburg University (Valerij Kiselev), Birgitte Fuglsang Kjølby finalized advanced modeling of the arterial input functions used with dynamic susceptibility contrast MRI, discovering surprising effects of the underlying susceptibility physics on the measurements of cerebral blood flow, blood volume and tissue mean transit time used in our research. This insight will be exploited in future improvements of these methodologies.

Niels Hjort finalized his Ph.D. thesis in 2007, with a number of studies published in leading international Journals. A remarkable discovery was the finding that ischemia and subsequent reperfusion seemingly disrupts the blood-brain-barrier in a process that ultimately leads to haemorrhage. While this is potentially of paramount importance in future prevention of symptomatic haemorrhage after thrombolytic therapy, this provides us with a first tool to study the delicate dynamics of blood-brain-barrier permeability in response to various levels of ischemia.

NEW FACE AT CFIN

Photo: Isak Hoffmeyer

Professor Morten L. Kringelbach, D.Phil., is the director of the TrygFonden Research Group. He is a Senior Research Fellow at Department of Psychiatry, University of Oxford and a Professor at Aarhus University, as well as Extraordinary JRF and College Lecturer in Neuroscience at The Queen's College, University of Oxford.
Morten Kringelbach's research focuses on understanding the functional neuroanatomy of human conscious and unconscious processing, and in particular those aspects related to pleasure, desire, emotion, learning, reward and hedonic processing.
He is the author and co-author of a large number of scientific articles on neuroscience, among these an article published in *Nature Neuroscience Review* in 2007.
The TrygFonden Research Group was established in 2007 and is initially funded for a period of five years. The overall goal is to understand the fundamental neural mechanisms underlying human sensory and social pleasures, in order to increase our understanding and potential treatment of depression, obesity and eating disorders as well as with problems of parent-child attachment. This is accomplished through the study of normal, neuropsychiatric and clinical populations using converging neuroimaging methods such as magnetoencephalography (MEG) and deep brain stimulation (DBS) combined with functional MRI, PET and DTI.

Photo: Hasse Ferrold

Leif Østergaard receives the Ministry of Science, Technology and Innovation's 2007 EliteForsk Award, presented by the Her Royal Highness, Crown Princess Mary at the EliteForsk Conference in Copenhagen, 24 January 2008.

The EliteForsk Prize is instituted by the Danish Minister of Science, Technology and Innovation, recognizing 'young, internationally outstanding scientists who made extraordinary contributions to promote Danish Research', based on the recommendations of the Danish Agencies for Independent Research.

Leif Østergaard was awarded for his work within the theoretical and clinical application of magnetic resonance imaging (MRI) techniques to measure cerebral blood flow. Using basic physics and mathematical modeling, he developed techniques that are now used world-wide, especially in the diagnosis and individualized treatment of stroke patients. The Award Committee emphasized Leif Østergaard and CFIN as driving forces behind a close integration of basic research and cutting-edge patient management.
http://www.eliteforsk.dk

SELECTED RESEARCH PROJECTS:

Birgitte Fuglsang Kjølby, Leif Østergaard, Valerij Kiselev (Freiburg University, Germany): Relationship between relaxation and contrast concentration in DSC MRI.

Peter Johannsen, Elisabeth Petersen, Kim Mouridsen, Leif Østergaard: Perfusion and Predictive Models in Hereditary Frontal Dementia.

Birgitte Fuglsang Kjølby, Leif Østergaard, Valerij Kiselev (Freiburg University, Germany): Theoretical analysis and modelling of arterial input functions in DSC MRI.

Christine Sølling, Grethe Andersen, Leif Østergaard: Impact of MRI-based thrombolysis in acute stroke.

Kim Mouridsen, Sune Jespersen, Mahmoud Ashkanian, Leif Østergaard: Modelling of flow heterogenuity.

Kim Mouridsen, Kristjana Yr Jonsdóttir, Leif Østergaard: Inferential models in acute stroke.

Rikke Beese Dalby, Leif Østergaard, Raben Rosenberg, Poul Videbech: Perfusion and connectivity in late-onset dementia.

Kim Mouridsen, Thórdís Linda Thórarinsdóttir, Kristjana Yr Jonsdóttir, Eva Vedel Jensen, Leif Østergaard: Functional Connectivity.

Louise Gyldensted, Hans Brændgaard, Dementia Clinic (Neurological Department, Århus Sygehus), Jamila Ahdidan, Kim Mouridsen, Anders Rodell, Søren Christensen, Peter Vestergaard Poulsen, Leif Østergaard, Carsten Gyldensted: Magnetic Resonance Imaging (MRI) and Alzheimer's Disease.

Mahmoud Ashkanian, Grethe Andersen, Leif Østergaard, Manouchehr Vafaee: Examination of oxygen metabolisme and cerebral blood flow in the ischemic penumbra compared to healthy brain tissue, a PET study.

Mahmoud Ashkanian, Kim Mouridsen, Sune Jespersen, Grethe Andersen, Jean-Claude Baron, Leif Østergaard: Oxygen delivery in acute stroke.

Niels Hjort, Mahmoud Ashkanian, Christine Sølling: MRI selection and monitoring of acute stroke patients for treatment with intraveneus thrombolysis.

Niels Hjort, Kristjana Ýr Jonsdottir, Kim Mouridsen, Lars Ribe, Leif Østergaard: I-Know: Integrating Information from Molecule to Man: Knowledge Discovery Accelerates Drug Development and Personalized Treatment in Acute Stroke" (I-Know project under EU's 6th framework program).

Ona Wu, Kim Mouridsen, Kristjane Yr Jonsdottir, Niels Hjort, Leif Østergaard: Predictive models in acute stroke.

NEUROINFORMATICS

Predicting disease progression and outcome

by Kim Mouridsen

Integrating information – see the big picture

CFIN, across columns, generates a wealth of image information. Modalities include metabolic indices by PET, micro structural indices by diffusion tensor imaging (DTI), haemodynamic indices by perfusion weighted imaging (PWI) and dynamic measures of oxygen metabolism related to regional brain function (fMRI). The list continues to expand with fx the forthcoming acquisition of an MEG scanner. Integrating this information is immensely challenging – yet may be a crucial prerequisite for our ongoing quest to understand the brain at a number of organizational levels.

A similarly dramatic increase in data generation was seen when geneticists began sequencing the human genome in 1990. Powerful mathematical techniques were required to solve the needle-in-a-haystack problem of identifying biologically functional fragments in the 3 billion nucleotide long human DNA sequence. This spurred a new branch of research, coined bioinformatics. In a similar fashion, advanced mathematical techniques are needed to identify the complex relations between heterogenous imaging biomarkers acquired in modern neuroscience. This has generated a new line of research within neuroscience, dubbed Neuroinformatics.

The principal aim of Neuroinformatics research at CFIN is to build models of disease and disease progression by integrating diverse imaging modalities using elements from mathematics, statistics, computer science and enginering.The integrative models are hypothesized to substantially increase sensitivity to subtle, pre-symptomatic pathological variations, thereby promoting early disease detection and accurate prediction of disease progression (Mouridsen, Østergaard 2007).

Predicting tissue outcome in acute stroke

The main focus of Neuroinformatics at CFIN so far has been prediction of final lesion in acute stroke patients at the level of single voxels (image elements). When a major artery to the brain is partially or completely occluded, ischemia in downstream tissue ensues leading to loss of motor, sensory or cognitive function. If blood flow is not re-established within minutes or hours, neuronal damage evolves and spreads, making the initial neurological deficits irreversible. A range of MRI modalities are routinely acquired in the clinic, but isolated modalities do not correlate well with outcome due to the complex physiological processes involved in stroke progression.

Datamining tools are ideal for integrating measures of regional blood flow with markers of cytostructural integrity to calculate actual infarction risk. In particular, statistical techniques can be used to assign quantitative importance to individual predictors (Jonsdottir et al, 2007) and assess the robustness of prognostic models to different training scenarios (Ribe et al, 2008). Moreover, we have demonstrated that multimodal models can be used to predict subacute outcome (Jonsdottir et al, 2008). Modeling infarction risk at progressive stages after symptom onset allows us to study the effect of late recanalization (restoring of normal blood supply). This has implications for subsequent treatment, which includes thrombolytic therapy and administration of neuroprotective agents.

Modeling capillary flow

Accurate assessment of the distribution of capillary flow is important because disturbance of tissue perfusion is a key predictor of subsequent cell death. In collaboration with Professor Karl Friston at University College London, a Bayesian framework has been developed which produces

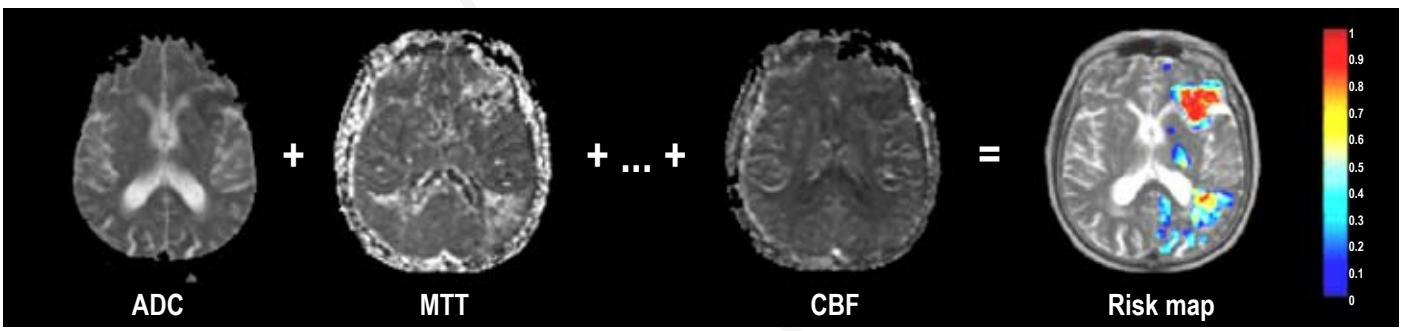

Figure 1
Using statistical techniques such as MARS (Mouridsen et al, 2004) the risk of infarction can be calculated using images of diffusion and perfusion.

regularized estimates of the entire microvascular flow distribution (Mouridsen et al, 2006a). Recently, we have shown this leads to better estimates of final tissue outcome compared to previous methods (Mouridsen et al, 2007b).

These estimates are now used in an oxygen delivery model developed by Sune Jespersen, which allows computation of oxygen extraction fraction (Jespersen et al, 2007). This is speculated to be a highly sensitive marker of ischemia and we will investigate this in a combined PET and MRI study of stroke patients in collaboration with Professor Jean-Claude Baron, Cambridge. With Mahmoud Ashkanian, this new methodology is also used in a study of patients with chronic stenosis of the carotid arteries (Jespersen et al, 2007, 2008). We also investigate the hemodynamic response to intracerebral hemorrhage in collaboration with Dr. Ken Butcher, Dept. of Neurology, University of Alberta, Canada.

Neurodegenerative disease

It is our aim to extend these statistical techniques to neurodegenerative diseases such as dementia and sclerosis. General strategies for integrating voxel-wise, multimodal information have been presented in (Mouridsen, Østergaard 2007). Elisabeth Pedersen is currently applying these techniques to imaging data from patients with a genetic mutation, causing fronto-temporal dementia at an early age. The aim is to identify imaging biomarkers sensitive to pre-symptomatic changes in brain physiology involved in development of dementia. Elisabeth Pedersen has just been enrolled in a PhD program jointly funded by CFIN, the Thiele Center for Applied Mathematics in Natural Science and the Faculty of Science. This extends our ongoing collaboration with Professor Eva Vedel Jensen on resting state networks and intersubject synchronization during natural stimulus in fMRI.

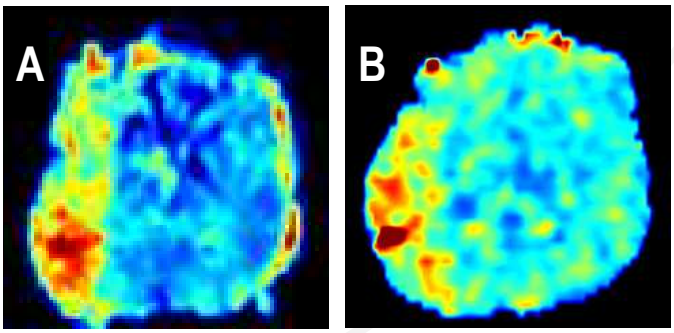

Figure 2
Oxygen extraction fraction in a stroke patient. The image obtained with MR shows the same pattern of ischemia as the PET image, which is considered gold standard. A: MR stroke OEF map - B: PET stroke OEF map

Ensuring general access. Software development

It is a key priority to ensure availability of new analytical tools to clinicians and neuroscientists. This practical focus serves to keep Neuroinformatics research in line with clinical demands and demonstrate face value of new techniques, which is best done in large patient populations. Both the automatic arterial input search algorithm developed earlier (Mouridsen 2006b), the deconvolution technique and the OEF model have been implemented jointly with Søren Christensen in our perfusion analysis software PENGUIN, which now has about 50 registered users at international stroke clinics and research centers (see http://www.cfin.au.dk/software). Lars Ribe is currently adapting our perfusion software into medical image processing environment as part of the I-Know project. As more robust and general techniques are developed for analyzing neuroimaging data, we aim to embed them in a software environment where entire analyses can be planned and executed via a simple graphical user interface.

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TrygFonden Research Group

Pleasure and the brain

by Morten L. Kringelbach

A generous donation from TrygFonden has enabled the creation of the TrygFonden Research Group, which is a transnational research group based at CFIN, Aarhus University and University of Oxford, UK. The main purpose of this research is to further our understanding of the functional neuroanatomy of depression and eating disorders, including obesity. The research is being carried out using a combination of neuroimaging methods in normal, neuropsychiatric and clinical populations. This may help develop new clinical and psychiatric interventions.

The central hypothesis for the research is that in order to effectively deal with these disorders, we need to develop a better understanding of hedonic processing - that is the affective component of sensory processing - in the human brain (Kringelbach, 2005). Importantly, malignant disorders such as unipolar depression, chronic pain and eating disorders are characterised by the lowered or missing ability to experience pleasure, anhedonia (Kringelbach, 2004). Thus, in order to understand and to effectively treat these disorders, we will have to further our understanding of the cortical and subcortical mechanisms involved in sensory and social pleasures (Kringelbach and Berridge, 2008).

In Oxford, TrygFonden Research Group is pursuing the research questions in close collaboration with two world-leading scientists: Professor Alan Stein and Professor Tipu Aziz, whose expertises are crucial for the success of the project. These collaborations will uniquely allow us to investigate fundamental questions regarding brain function in normal and neuropsychiatric populations, as well as investigating the brain mechanisms involved in novel treatments in clinical populations.

Professor Stein is leading the extensive and unique Wellcome Trust Oxford Parent Project which has been following a large group of parents and infants since before birth. Through this close collaboration, we have direct access to a psychologically well-characterized group of parents and infants, some of whom are suffering from clinical post-natal depression and eating disorders. Through the use of primary and secondary reinforcers such as taste, smell and face expressions, we can use magnetoencephalograpy (MEG) to characterize the spatiotemporal brain responses of the healthy adults and in the adults with neuropsychiatric disorders.

Professor Aziz is a neurosurgeon who has pioneered the use of DBS for treatment-resistant affective disorders including depression, Parkinson's Disease (PD) and chronic pain; an approach which has shown remarkable promise in alleviating the symptoms of these debilitating disorders and bettering the lives of the sufferers (Kringelbach et al., 2007b). We will use similar neuroimaging paradigms as those used in the healthy and neuropsychiatric populations mentioned above to characterize the brain responses to primary and secondary reinforcers, but crucially with the added benefit of being able to switch the causal DBS effective treatment on and off (Kringelbach et al., 2007a).

In Aarhus, the planned research into affective and hedonic brain processing will complement existing CFIN activities, and we are already setting up collaborations with Interacting Minds, Pathological Gambling, PET Centre and Music in the Brain, to name a few. Now that we have acquired the funds for the first Danish MEG scanner, we are planning to help transfer MEG expertise from Oxford to Aarhus.

In the following we have included two recent projects as examples of the research in the group.

Merton Playing Fields, Oxford University

Queen's College / High Street, Oxford

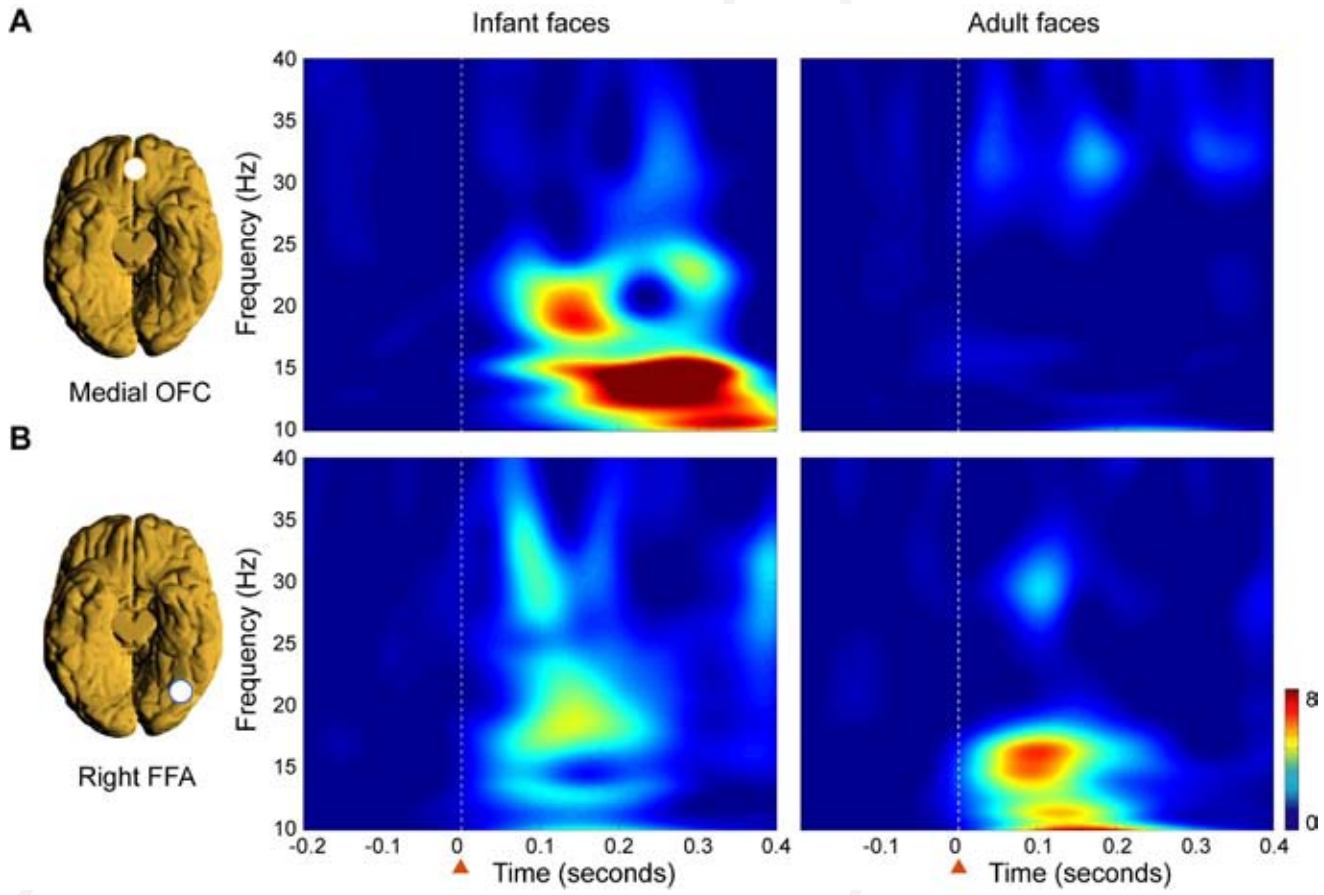

Figure 1
Time-frequency analysis of neural activity in medial orbitofrontal cortex (OFC) and the right fusiform face area (FFA). Significantly different responses were found in the medial OFC but not in the right FFA between viewing infant compared to adult faces. A) Time-frequency representations of the normalised evoked average group responses to infant and adult faces from the virtual electrodes in the medial OFC reveal that the initial response to infant faces is present in the 12-20 Hz band from around 130 ms - and not present to adult faces. B) The responses in right FFA occurred earlier in time but were not significantly different before 165 ms when viewing infant compared to adult faces. This can be seen from the time-frequency representations of the normalised evoked average group from the virtual electrodes, where initial activity was present from around 100 ms in the 10-20Hz and in the 25-35Hz bands. The white stippled line and the orange arrow indicates when the faces were presented in time. (Kringelbach et al., 2008).

Infant and infantile faces as a tool for understanding social attachment

The scientific interest in the cuteness of infant faces started with Charles Darwin who pointed out that in order for infants to survive and to perpetuate the human species, adults need to respond and care for their young (Darwin, 1872). The Nobel Prize-winner Konrad Lorenz proposed that it is the specific structure of the infant face that serves to elicit these parental responses, but the biological basis for this has remained elusive (Lorenz, 1943). Using MEG in adults, Professor Stein and I recently found that highly specific brain activity occurred within a seventh of a second in response to (unfamiliar) infant faces but not to adult faces (Kringelbach et al., 2008). This activity occurred in the medial OFC, an area implicated in reward-related behaviour (Kringelbach, 2005), identifying for the first time a neural basis for this vital evolutionary process.

Lorenz argued that infantile features serve as “innate releasing mechanisms” for affection and nurturing in adult humans and that most of these features are evident in the face including a relatively large head, predominance of the brain capsule, large and low lying eyes and bulging cheek region. Thus it is argued that these “babyish” features of infants increase the infant’s chance of survival by evoking parental responses, and the parents’ ability to respond is important for the survival of the species.

While a considerable body of research has focused on how the human brain processes adult faces, much less research has investigated the processing of infant faces. We used MEG to investigate the temporal and spatial distribution of the underlying neural systems for these facial responses in 12 adult human participants. Consistent with previous findings, we found that face processing of both adult and infant faces elicits a wave of activity starting in the striate cortices and spreading along ventral and dorsal pathways.

In addition, however, we found that at around 130 ms after presentation of the infant faces, activity occurred in the medial OFC. This was not evident in response to the adult faces. These specific responses to unfamiliar infant faces occurred so fast that they are almost certainly quicker than anything under conscious control suggesting that they are automatised.

These findings provide evidence in humans of a potential brain basis for the "innate releasing mechanisms" described by Lorenz for affection and nurturing of young infants. This has potentially important clinical applications in relation to postnatal depression, and could provide opportunities for early identification of families at risk.

Deep brain stimulation and chronic pain mapped with MEG

Recent developments in deep brain stimulation (DBS) of specific targets in the human brain have been successful in alleviating the symptoms of otherwise treatment-resistant disorders; mainly chronic neuropathic pain, phantom pain and Parkinson's disease and other motor disorders such as dystonia with some success also reported for unipolar depression (Kringelbach et al., 2007b). However, while treatment and associated neurosurgical methods have shown remarkable promise, the underlying neural mechanisms for DBS are not fully understood and in particular, it is not at all clear how DBS of specific brain targets changes the neural activity in wider cortical and subcortical regions.

Remarkably, patients with chronic pain who have had DBS of the PVG/PAG report experiencing much less pain. Similar subjective changes are found in patient with DBS in the subgenual cingulate (Mayberg et al., 2005).
In some select patients, this chronic pain can be significantly changed over a short period of time with the DBS stimulation. This subjective change can be measured with MEG when switching the DBS stimulation on and off, and acquiring repeated subjective measurements on a visual scale. This can then be used in the data analysis to reveal the brain regions which mediate the change in subjective hedonic experience.

We were the first group in the world to use magnetoencephalography (MEG) to make direct measurements of the whole-brain elicited by DBS. When DBS was turned off, the participant reported significant increases in subjective pain.

This direct non-invasive procedure allows us to explore the whole-brain activity related to DBS, and this was successfully carried out in a 58-year right-handed male patient with a 4-year history of severe left leg phantom limb pain. Pre-operative interventions included sympathectomy, a spinal nerve stimulator, hypnosis and a variety of medications with little apparent benefit. The patient was then implanted with a DBS in the right PVG/PAG, which subsequently had to be replaced due to a fall. Effective settings for stimulation in this patient are 1.5 volts and a frequency of 7 Hz. DBS has significantly decreased the level of chronic pain in the patient to a manageable level.

During the pain relief we found corresponding significant changes in brain activity in a network that comprises the regions of the emotional brain and includes the mid-anterior orbitofrontal and subgenual cingulate cortices (Kringelbach et al., 2007a). We also found similar changes in a patient with depression and in a patient with intractable cluster headache.

These findings open up the possibility not only for a better understanding of the underlying neural mechanisms of DBS, but also of the pathological brain states that it helps treat. The results could potentially lead to the introduction of more novel efficacious targets for DBS, which in turn could help treat affective disorders such as depression and chronic pain.

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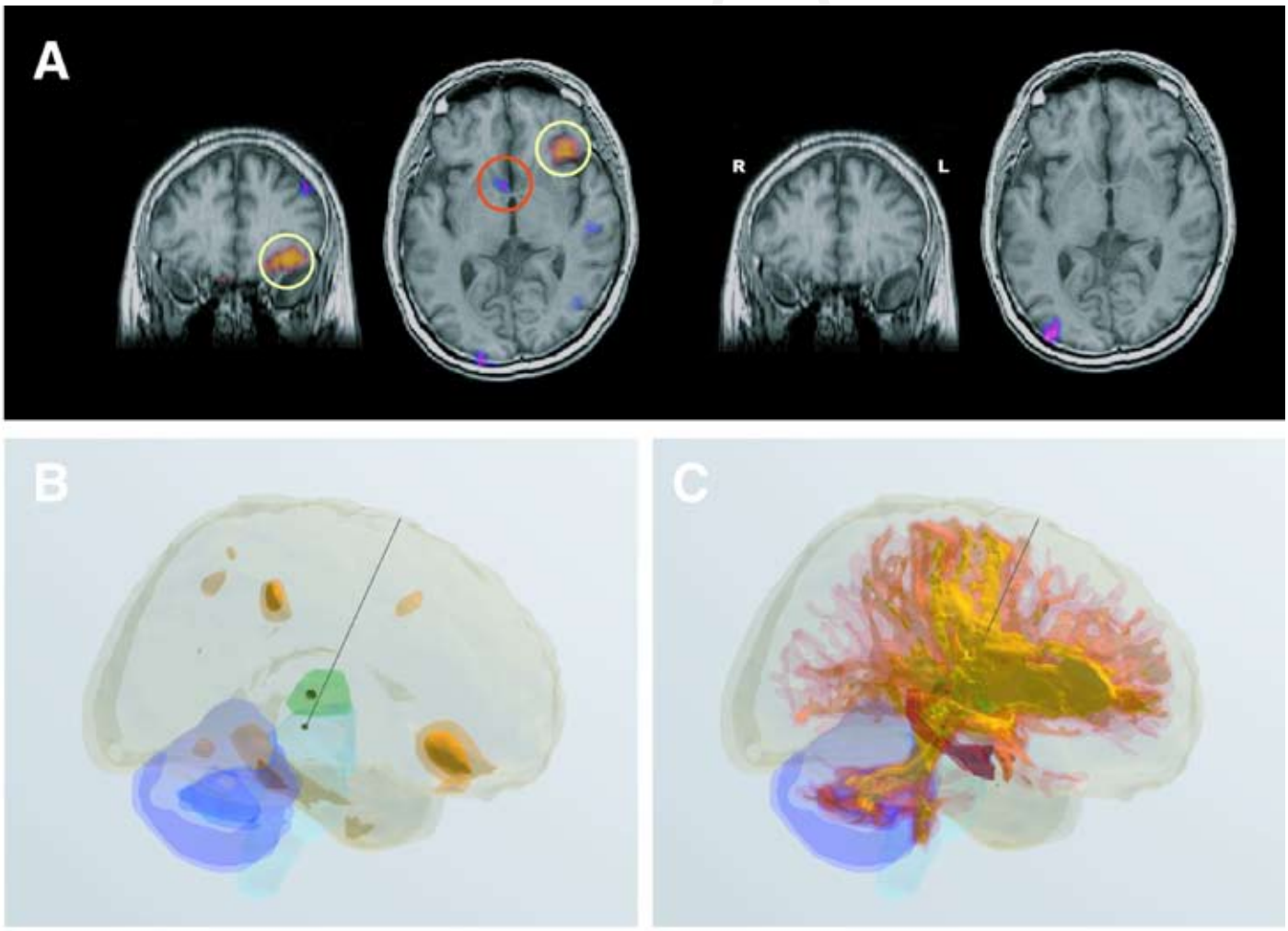

Figure 2
Pain relief induced DBS. A) Data from our MEG experiment of DBS stimulation in the periventricular/periaquaeductal grey area (PVG/PAG) for the treatment of phantom limb pain. When subjective pain relief was obtained with DBS, there were significant activity increases in the left mid-anterior orbitofrontal cortex and right subgenual cingulate cortex (left coronal and axial brain slices). Activity in these brain regions was not found when DBS was turned off, resulting in significant more pain (right coronal and axial brain slices) (Kringelbach et al., 2007a). The significant changes in event-related synchronous and desynchronous power in specific frequency bands are shown on scales from light yellow to red and from purple to dark blue, respectively. B) Three-dimensional rendering of activity measured with MEG on the human brain with a DBS electrode implanted in the PVG/PAG for the treatment of chronic pain. The significant increases in activity are shown in shades of orange, while the other colours represent landmark brain structures: thalamus (green), cerebellum (blue) and brainstem (light blue). C) Three-dimensional rendering of the anatomical connectivity from the four DBS electrode contact sites in the PVG/PAG as assessed with DTI, with the probabilistic tractography presented in different colours from more (yellow) to less significant (dark red). Note the extensive connections with the prefrontal cortex and in particular the orbitofrontal cortex.

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TrygFonden

COGNITION RESEARCH

by Andreas Roepstorff

Progress in 2007
Research

The group has seen a significant increase in published, accepted and submitted publications across most research fields. Most notably in how language interacts with the brain (Christensen *in press*, Christensen *submitted*, Christensen et al. *submitted*, Wallentin, Roepstorff, and Burgess 2008, Wallentin et al. 2007). These conceptual and experimental approaches have increasingly been extended to include also other symbol systems, as in the use of music, numbers and objects (Christensen, Roepstorff, and Saddy *submitted*, Green et al. *accepted*, Roepstorff Accepted, Tylén, Wallentin, and Roepstorff *submitted*, Vuust et al. *under review*). In an exemplary move, Mikkel Wallentin has extended his previous findings on spatial processing of language in being applicable to memory research both in processing of visual scenes and of expert chess competence (Wallentin, Roepstorff, and Burgess 2008, Wallentin et al. *submitted*, Wallentin et al. 2007).
The use, and potential misuse, of brain scanning techniques for detecting deception has recently been a scientifically and publically 'hot issue', and our review article on the topic made it to the front cover of Trends in Cognitive Sciences (Sip et al. 2008) where it sparked a subsequent debate (Sip et al. *in press*).

During 2007, it became obvious to most researchers in the field that understanding "the social" would become a major new focus for neuroscientific research. We have predicted this turn a while ago (Roepstorff 2001), and CFIN is very well prepared for this development. On one hand, the assocation of Chris and Uta Frith with CFIN through the Niels Bohr professorship, *Interacting Minds - a biological basis*, means that we are part in spearheading this development (Frith *in press*, Frith and Frith 2007a, Frith and Frith 2007b, Frith and Frith 2008). On the other hand, our strong institutional and intellectual links with humanities, the social sciences, and theology at University of Aarhus means that we have a unique interdisciplinary basis for research. Work in the field has been ongoing for a while, and we are starting to see the first publications (Petersen, Roepstorff, and Serritzlew *in press*, Schjødt et al. *submitted-a*, Schjødt et al. *submitted-b*). We expect this to increase in the future.

Along more theoretical lines, we have further continued our work to examine how a 'predictive coding' framework may explain cognitive processes in basic perception (Hohwy, Roepstorff, and Friston *under review*, Vuust et al. *under review*).

2007 has seen a number of very productive collaborations between the research groups at CFIN. With the gambling group, we have completed an fMRI study on expertise in chess (Wallentin et al. submitted), with the dopamine group, we have completed a combined PET study/psychopharmacological experiment on conscious perception (Lou et al. *submitted*) with the structural connectivity group we have completed a study on brain morphology in people with long-term meditation experience (Vestergaard-Poulsen et al. *submitted*), and we have continued collaboration with the Music in the Brain group (Green et al. *accepted*, Vuust et al. *under review*). Over time, our expertise is also being used by research groups outside of CFIN, who are interested in studying the interplay between perception, cognition and brain activity across different experimental paradigms e.g. hypnotic modulation of pain (Abrahamsen et al. *submitted abstract*) or functional electrical stimulation.

It is a stated ambition of the group to contribute to a meta-discussion on how to understand and frame current developments in cognitive neuroscience and biology in a larger perspective. We have done that through publications (Petersen, Roepstorff, and Serritzlew *in press*, Roepstorff 2007a, Roepstorff 2007b, Roepstorff 2007c, Sip et al. 2008, Sip et al. *in press*, Wallentin 2007b, Wallentin 2007c), the research stay of Andreas Roepstorff with Nik Rose at BIOS, LSE in the first quarter of 2007, a number of scientific and public talks, appearance in elecronic and printed media in Denmark (Wallentin 2007a) and abroad, and through new research collaborations. The tight integration between actual research and a reflexive discussion of the research process and – outcome is a quite unique property of the cognitive group at CFIN, also in an international perspective.

Professor Chris Frith at the opening reception of the Interacting Minds project.
Photo: Sanne Lodahl

Formal research networks and -collaborations

Together with Dan Zahavi, Danish National Research Foundation's Centre for Subjectivity Research, University of Copenhagen, Andreas Roepstorff has established the collaborative research project *Agency, Self and Other, an Interdisciplinary Investigation*, which formally began in 2007. The project is funded by Research Council for Communication and Culture for three years with a grant of 2.6 million DKK, (1 million to AU). The grant is affiliated with the EUROCORES project BASIC (brain, agency, self, intersubjectiviy, and consciousness) headed by Andreas Roepstorff, 2007-10. This project is part of European Science Foundation's CNCC initiative, which studies consciousness in a natural and a cultural context. Andreas Roepsorff is on the scientific board of the program, further can be found on: http://www.esf.org/cncc. Andreas Roepstorff has become member of the steering committee of the European Neuroscience and Society Network, which is sponsored by ESF 2007-12, http://www.neurosocieties.eu/. The research group has become part of the research network ATACD (a topological approach to cultural dynamics, http://www.atacd.net), supported by funding under the sixth framework program of the European Union.

Scientific exchange

The group has had extended research visits from Cristina Becchio, PhD University of Torino (October – December) and Kristian Tylen, PhD student, University of Southern Denmark (January-December). Andreas Roepstorff has been academic visitor at Functional Imaging Laboratory, UCL, London and BIOS, LSE, London January – April. Kamila Sip has been research student at Functional Imaging Laboratory, UCL, London, January – July.

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SELECTED RESEARCH PROJECTS:

Andreas Roepstorff, Peter Vestergaard-Poulsen, Martijn van Beek: Attention control: brain activity during meditation.

Chris Frith, Uta Frith, Andreas Roepstorff: Interacting minds - a biological basis.

Jakob Geday, Albert Gjedde, Ron Kupers: Effect of emotional valense on social perception.

Joshua Skewes, Andreas Roepstorff og Dan Zahavi: Agency, Self and Other, and Interdisciplinary investigation.

Kamila Ewa Sip, Andreas Roepstorff, Bill McGregor, Chris Frith: Neuropragmatics of deception.

Mikkel Wallentin, Andreas Roepstorff, Svend Østergaard: Cognition, communication and context.

Mikkel Wallentin, Andreas Roepstorff, Leif Østergaard, Arne Møller, Jakob Linnet: Chess.

Morten Overgaard, Andreas Roepstorff, Sanne Lodahl: Introspective conditions.

Randi Abrahamsen, Sanne Lodahl, Andreas Roepstorff, Leif Østergaard, Bobby Zachariae, Peter Svensson: Imaging pain.

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NEW FACE AT CFIN

Post.doc. Torben Ellegaard Lund, was appointed assistant professor in May 2007.
Torben E. Lund has a masters degree in applied physics from DTU and a PhD in medicine from University of Copenhagen. Torben was earlier employed on the Danish Research Centre for MR, in Hvidovre, where he has been doing methodological development of fMRI acquisition and data-analysis, and supervised MSc and PhD students. The main focus of Torbens work has been on noise modelling in fMRI, but he also have 9 year-long experience with simultaneous acquisition of EEG and fMRI. His work was awarded with the NeuroImage Editors Choice Award in 2006. His employment at CFIN is funded by The Danish National Research Foundation.

Torben will, in collaboration with CFIN researchers, continue his research within the field of fMRI methods and modelling. In 2008 he starts teaching a course on statistical analysis of neuroimaging data.

Peter Vuust appointed professor at the Royal Academy of Music

Photo: Lars Kruse, AU-foto

In November 2007, The Royal Academy of Music (DJM) appointed Peter Vuust as research professor with special responsibility for research. Peter Vuust is going to develop and implement DJM's research strategy and ensure international collaborations and networking.

Peter Vuust has an academic background in Mathematics, French, and Music from Aarhus University, and he has been employed as associate professor at DJM since 1996, teaching music theory, ear training, ensemble playing, and bass. Since 2002 he has also been employed at CFIN in a joint position funded by DJM and Aarhus University. Peter Vuust's research has explored the links between music and the brain in a number of different studies, and he obtained his PhD degree at the Faculty of Health Sciences, University of Aarhus in February 2006 with the thesis *Neural Processing of Polyrhythmic Structures in Music*.

The research professorship marks DJM's with extended focus on research in perception, cognition, and learning. The goal is research of high international standard relevant to the academy's general aim to provide research based education in music and music pedagogy at the highest level. With the collaboration between DJM and University of Aarhus, the academy is able to offer PhD education for students in co-sponsored positions.

Apart from his research career Peter Vuust is a composer and performing artist, and has as bass player performed with a number of Danish and foreign artists - mostly within modern jazz music. He has recorded 4 CD's with his own jazz orchestra Peter Vuust Quartet with musicians Lars Janson (p), Ove Ingemarsson (s), and Alex Riel (dr).

Peter Vuust's position as research professor provides unique knowledge of music, and music cognition and learning to the inter disciplinary research environment at CFIN.

Life in the Yellow Villa - home of the Interacting Minds project / From opening reception and Tuesday morning breakfast meetings (visit from Giacomo Rizzolatti).
Photos: Sanne Lodahl

COGNITION RESEARCH

Neuroimaging Deception

by Kamila Ewa Sip

The question of how people lie and how to detect lies has been widely discussed in the literature of psychology. Within the last few years, the examination of deception has entered a field of neuroimaging. However, there is much more to processing deception than brain activity. First, we must recognise that deception involves a social dimension and needs to be studied as such (Sip et al. *in press a*). Secondly, we must develop paradigms in which subjects have a real choice as to whether and when to lie (Sip et al. *in press a*).

To investigate real-life deceptive behavior, we need to be aware that deception draws on a number of cognitive processes that are not in themselves deceptive. Deception involves risk-taking and information manipulation, as well as appreciating the perspective of others; comprehending their intentions and goals, and assessing and adjusting performance on the basis of their reactions. Also, we should be aware that in complicated deceptive acts like bluffing (e.g. in Poker games; political and criminal negotiations), telling the truth may have as much deceptive intent as telling a lie. Consequently, the goal of our studies was to identify neural correlates of realistic deceptive interactions that would elucidate deception in all its complexity.

In collaboration between CFIN at University of Aarhus and Wellcome Trust Center for Neuroimaging at University College London, we have conducted three interaction-based deception studies to investigate human brain activity during deceptive behaviour.

1st study: deceptive game Mejer

Here, we conducted an fMRI study of a competitive, deceptive game. The subjects played a computerized version of a turn-taking dice game, Mejer, with a real opponent while being examined in a 3Tesla scanner. The game alternated between two aspects of deception: (1) expressive – where the subject in the scanner tried to deceive the opponent outside the scanner, and (2) receptive – where the subject in the scanner tried to detect whether they were being deceived. The subjects repeatedly decide whether to lie or not depending on their own judgements and account of the game progression.
When comparing "deciding that the opponent is deceiving" with "deciding that the opponent is telling the truth", we found activity in a network of midbrain, dopaminergic and insular structures including nucleus accumbens that have previously been implicated in processing reward and revenge, during trust and reciprocity games (Figure 1).

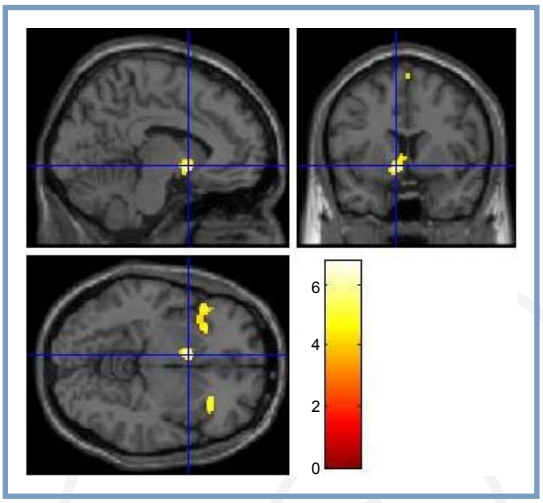

Figure 1
The direct contrast between disbelieving and believing suggests that dopaminergic systems are activated in conjunction with insular structures as a result of very risky decision. This activation is connected to choices and immediate consequences (p>0.001 uncorrected).

Deciding to tell the truth in the context of the potential to lie is processed very differently from deciding to tell the truth when there is no other option. Lying increases the cognitive load even further than telling the truth in the same context (Figure 2 and 3; Sip et al. (*in prep.*)).

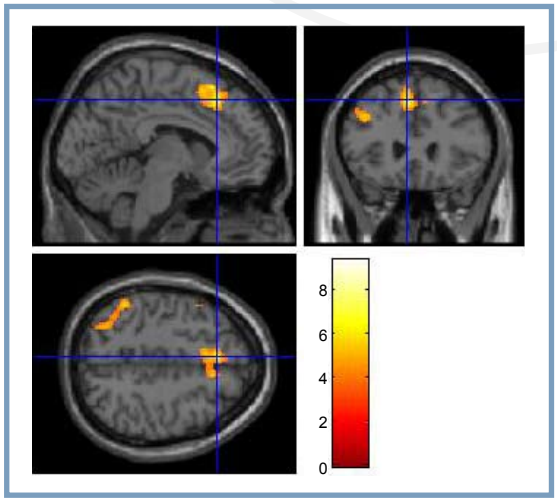

Figure 2
In the direct contrast between false and truth in the game we can see activation in an area that has been implicated in management of uncertainty in decision-making processes.

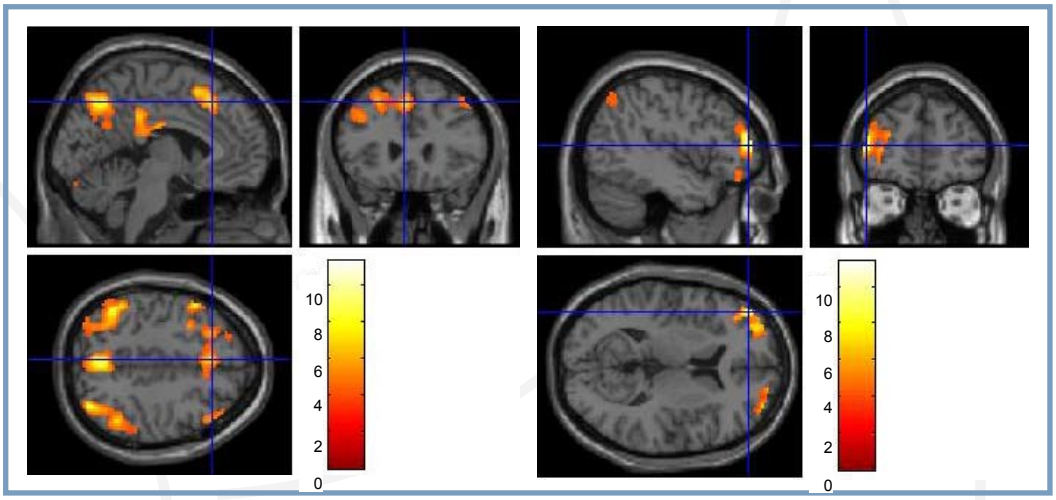

Figure 3
In the contrast against control, both the decision to lie and tell the truth has very strong activation in areas responsible for planning, reasoning and decision-making. This suggests strong context-dependence on processing both decisions to lie and tell the truth if there is a potential to deceive ($p > 0.05$ FDR corrected).

2nd study: Secrets and lies

The aim of this study was to investigate the neural correlates of deceptive behaviour in a social interaction based on different access to knowledge. The paradigm was based on a simple game where the subjects were questioned about their knowledge/information presented on an interface consisted of a representation of a 3D box with 16 compartments (4x4x1) that contain 7 different objects visible either to both the subject and the researcher or only to the subject (see Box 1/Figure 4). While being scanned the subjects were asked about their knowledge of the content of the shelves. The subjects played either against human or a computer, and they could sometimes be checked whether they lied or not. Behavioural results show that subjects lied less if there is a chance to be checked ($p < 0.004$), also they lied more to a computer ($p < 0.042$). In terms of reaction times, telling the truth took longer if there was an option to lie in the check conditions ($p < 0.016$), subjects were significantly faster to lie than to tell the truth ($p < 0.024$). Analysis of the neural activity associated with this behavior is currently in progress.

3rd study: Mock-crime scenario

The aim of this study was to investigate the effect of pre-scanning induced beliefs about neural activity in deceptive scenarios, again giving subjects a relatively free-choice on whether or not to be deceptive. Based on a common, lay-man's belief in the power of the polygraph as a lie-detector, we decided to test whether the presence of the lie-detector would influence the neural correlates of deception. The subjects committed a mock-crime in the laboratory and then went through an interrogation while being scanned with fMRI. The analysis of this study is currently in progress.

Together these results, demonstrate that deception and detection of deception are highly context dependent processes, which relate truth and lies in terms of consequences, risk taking, and reward processing. This is reflected both in the neuroimaging and behavioral results that show that the brain processes the same action differently depending on the context.

The projects are made in collaboration with William McGregor, Andreas Roepstorff, Chris D. Frith, and Jennifer Marchant and is funded by Danish Research Council for Cognition, Communication and Culture (SFN); The Danish National Research Foundation, and the Wellcome Trust.

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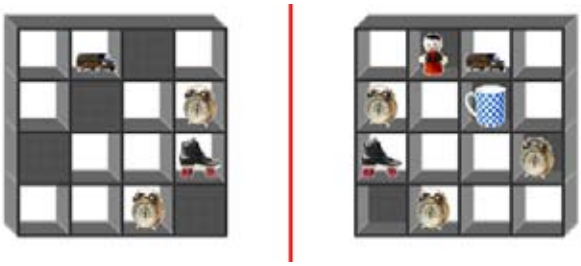


Figure 4
Box 1. The left side of the interface is seen by the researcher, the right is the subject's view while answering researchers' questions: e.g. 'Do you see ... a rollerskate/more than two clocks/a giraffe?

COGNITION RESEARCH

Chess skills in the brain

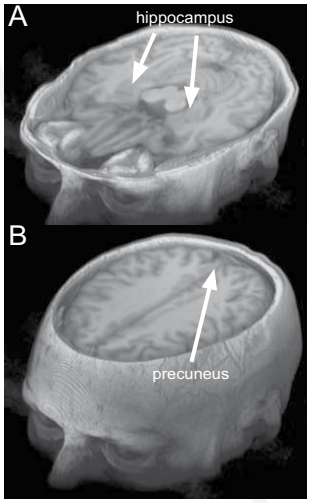
by Mikkel Wallentin

Chess-players use their long-term memory and working memory differently depending on the type of chess position and level of expertise

Exercise transforms talent into expertise. But what happens to our brains during this process?

Chess has been a key model in the study of expertise in cognitive research, due to the high level of regularity of the game, coupled with a large degree of unpredictability, yielding room for human creativity (Gobet & Charness, 2006). Much is therefore known about the game and its participants. Chess has been thoroughly modelled using the world's most powerful computers, such as "Deep blue" which, in 1997, was the first machine to beat a human chess world champion, Gary Kasparov. Further, human expertise is precisely measured using the Elo chess-rating system in which players are rated according to how often they win and loose against opponents of different strength, e.g. a beginner will start at a rating around 1000, while Kasparov in 1999 had a rating of 2852, the highest rating ever achieved. But while chess has been intensely studied for more than 100 years, very little brain imaging research has been conducted on chess-players and chess playing strategies.

Expertise includes having both a large inventory of remembered task material and having the ability to manipulate this material online during the solving of a particular task. In cognitive research the inventory store is usually called "long-term memory", whereas the online manipulations are conducted in "working memory".



This fMRI-study (Wallentin et al., submitted) is the first to investigate expert chess-players' move selection with chess positions, known as "tactical" and "strategic" positions (see Figure 1). To novices these positions are undistinguishable, but experts instantly recognize them. In tactical positions the right move immediately leads to a reward or determination

Figure 1. Stimuli
Subjects were shown tactical and strategic chess positions and asked to choose between two predetermined moves. Top: A typical tactical position where the game can be determined by finding the right series of moves. The right move is Qh6. Bg7 is then forced and white plays Qg6 which forces a mate on h7 by the white knight. Bottom: A typical position with strategic considerations only. The best move in this position is c4, which fixates the black pawn on c5 as a target for the white bishop, and at the same time restricts the manoeuvring possibilities of the black bishop. These are long-term considerations and do not imply an immediate reward.

of the game, whereas "strategic" considerations concerns dominance and long-term planning without immediate gains. We therefore hypothesised that finding the right move in a strategic position would profile long-term memory processes to a higher degree than working memory processes, whereas tactical positions would profile working memory processes. Subject reports confirmed this prediction (Figure 2).

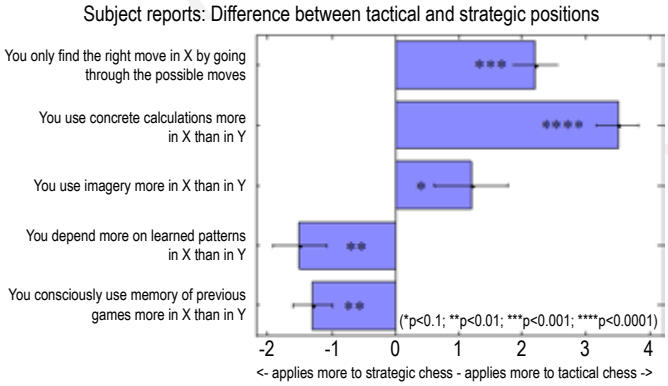


Figure 2. Questionaire responses
Subjects filled in a questionnaire about differences between strategic and tactical positions. They were asked to indicate whether or not they agreed with a given statement, e.g. "In tactical positions you depend more on learned patterns than in strategic positions?" In order not to bias responses they were given each question twice, the first stated that tactical positions required more of some cognitive process, and the second said that strategic positions required more of the same process. Bar plots show differences in subject agreement for the two opposite questions. Negative numbers mean that subjects thought that the utterance applied more to strategic positions, whereas positive numbers reflects that the utterance applied more to tactical positions.

A long tradition for studying memory has found that hippocampus plays a key role in long-term storage (e.g. Squire, Stark, & Clark, 2004). On the other hand, visuospatial working memory is known to rely on parietal structures of the brain, especially precuneus (Wallentin, Roepstorff, Glover, & Burgess, 2006; Wallentin, Weed, Østergaard, Mouridsen, & Roepstorff, in press).

fMRI-scanning during chess move selection showed that tactical positions evoked higher activation in precuneus compared to strategic positions, whereas strategic positions evoked greater responses in hippocampus (figure 3). An analysis that took level of expertise into account found that the precuneus and hippocampus findings were complicated by significant effects of subjects' chess rating. High-ranking players had more activity during tactical positions in both regions. This highlights the importance of obtaining performance measures to inform scanning data in neuroimaging experiments and clearly demonstrates how acquired expertise modulates both task-solving strategy and the underlying brain activity.

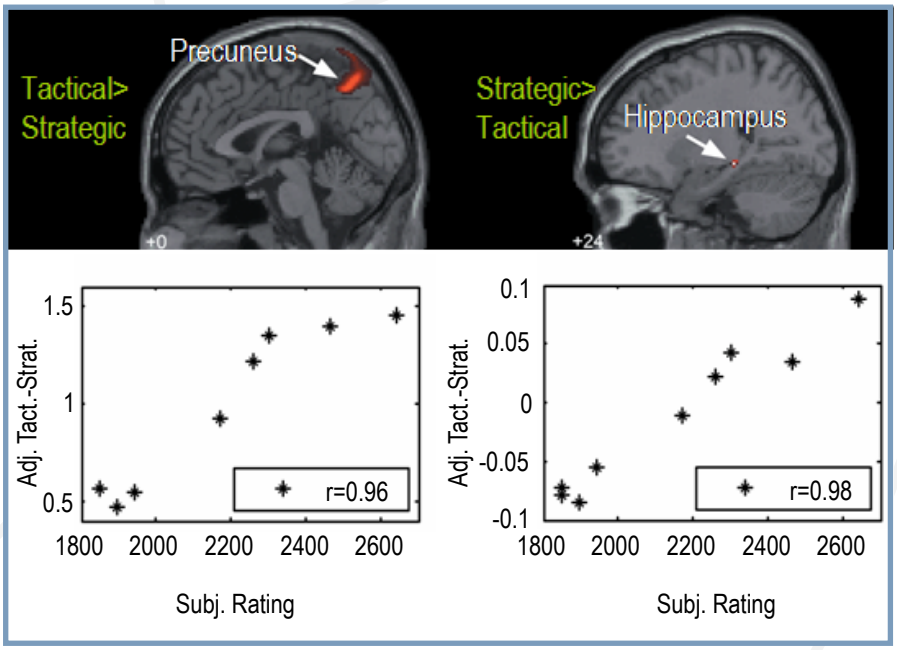


Figure 3. Brain imaging results
Top: Tactical positions yielded a greater fMRI response in precuneus compared to strategic positions. This corresponds to an overall profiling of working memory for this task. Strategic positions gave a greater response in hippocampus compared to tactical positions. This corresponds to an overall profiling of long-term memory for this task.
Bottom: There was a strong linear relationship between subject rating and difference of responses in precuneus and hippocampus. Subjects with a higher chess rating had a greater response during tactical positions in both precuneus and hippocampus. This shows how training changes the way we process information.

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Mikkel Wallentin and Torben Lund. CFIN Retreat at Sandbjerg Manor, August 2007.
Photo: Sanne Lodahl

MUSIC IN THE BRAIN

by Peter Vuust

In recent years it has become apparent that music theory can gain tremendously in validity and interest when accompanied by research on the influences of music on people, particularly music perception and cognition. At the forefront of this development is the study of how music affects the human brain. This line of research, propagated by the development of novel brain recording and imaging methods, offers musicologists new opportunities to address questions regarding music of a much more fundamental nature than previously possible. Basic questions such as why humans have the ability to communicate through music and what influence culture has on this ability can now be pursued experimentally. On the other hand, neurobiological studies of human cognition benefits greatly from the collaboration with musical scholars, who can provide knowledge about musical practice on the highest artistic level and music teaching on all levels.

Such research questions involving experimental brain scanning studies, conceptual studies of cognitive semiotics, linguistics, psychology, and theoretical neurobiology are of fundamental multidisciplinary nature. Therefore, multi-institutional co-operations using resources and specialist knowledge from various fields are prerequisites. This is the background for the current collaboration between the Center of Functionally Integrative Neuroscience (CFIN) and the Royal Academy of Music (DJM), and it is the main aim of DJM's focus area: Musical perception, cognition and learning, in which the relationship between music and subject is brought into focus.

This collaboration is now formalized by the formation of the Music in the Brain group headed by Peter Vuust, who holds a joint position as professor at DJM and associate professor at CFIN, Aarhus University. The group furthermore consists of PhD-students Karen Johanne Pallesen (CFIN), Anders Christian Green (Dep. of Psychology), Bjørn Petersen (DJM/CFIN), Eduardo Garza (DJM/CFIN), Anders Dohn and masters student Morten Friis (Dep. of Biology, University of Copenhagen). Furthermore, PhD-student Ivana Konvalinka, masters student Niels Christian Hansen (DJM) and masters student Line Gebauer (Dept. of Psychology) are associated with the group. As of 2008, EEG/MEG-specialist Risto Näätänen will join the group as visiting professor.

The Music in the Brain group collaborates with well-established research institutions in Denmark and abroad. As main collaborators should be mentioned prof. Mari Tervaniemi, and post doc. Elvira Brattico, (Cognitive Brain Research Unit, Department of Psychology, University of Helsinki-CBRU), Eckart Altenmüller Institut für Musikphysiologie und Musikermedizin, Hannover, Prof. Niels Tommerup, Wilhelm Johannsen Centre for Functional Genome Research, ICMM, University of Copenhagen and prof. Therese Ovesen, dept. of Oto-, Rhino-, Laryngology, Aarhus University Hospital. Music in the Brain also benefits greatly from collaboration with other groups within CFIN in particular the gambling group and the Interacting Minds group.

The Music in the Brain group aims at providing neuroscientific research in music that can change the way we play, teach and listen to music.

Current research projects within the group:

Musical communication, improvisation and creativity

Morten Friis, Mikkel Wallentin, Andreas Roepstorff and Peter Vuust.

Music is an important means of human communication. In contemporary improvisational music such as jazz, musicians exchange non-verbal signs as messages, and from this interaction, the music emerges as a concrete form. Imitation and 'call/response' are two of the main ways in which jazz musicians interact during performances. By using fMRI, we study brain activation when jazz/rock musicians imitate and respond to rhythms. We expect to find activation of brain areas related to language, especially in the inferior frontal gyrus.

Neural processing of hierarchical structures in music

Eduardo Garza, Elvira Braticco, Sakari Leino, Mari Tervaniemi and Peter Vuust.

The aim of this project is to study to what extent brain mechanisms involved in music and language processing overlap. In Western tonal music, the rules of harmony determine the order and hierarchical importance of events in a musical piece. For example, the tonic chord, built on the first note of the diatonic scale, is usually placed at the end of chord sequences. We recently conducted a study to test whether the early right anterior negativity (ERAN: a brain response elicited when a harmonically incongruous chord is inserted within or at the end of a musical sequence) reflects the processing of harmony rather than the building of a tonal context and whether the ERAN is also elicited by violations of the tuning of the sounds upon which harmony is based (Leino et al., 2007). This study indicates that language and music processing in the brain may

involve similar brain resources: Currently we are studying the question of localization, timing and the influence of expertise on the ERAN compared to the mismatch negativity (MMN). Knowledge about the relationship between the neural processing of music and language is important to a range of different issues including the ongoing political debate about the potential transfer effect of music training to other cognitive domains. Clinically, this research may have far reaching consequences for rehabilitation in relation to language disorders, neurosurgery, and cochlear implantees.

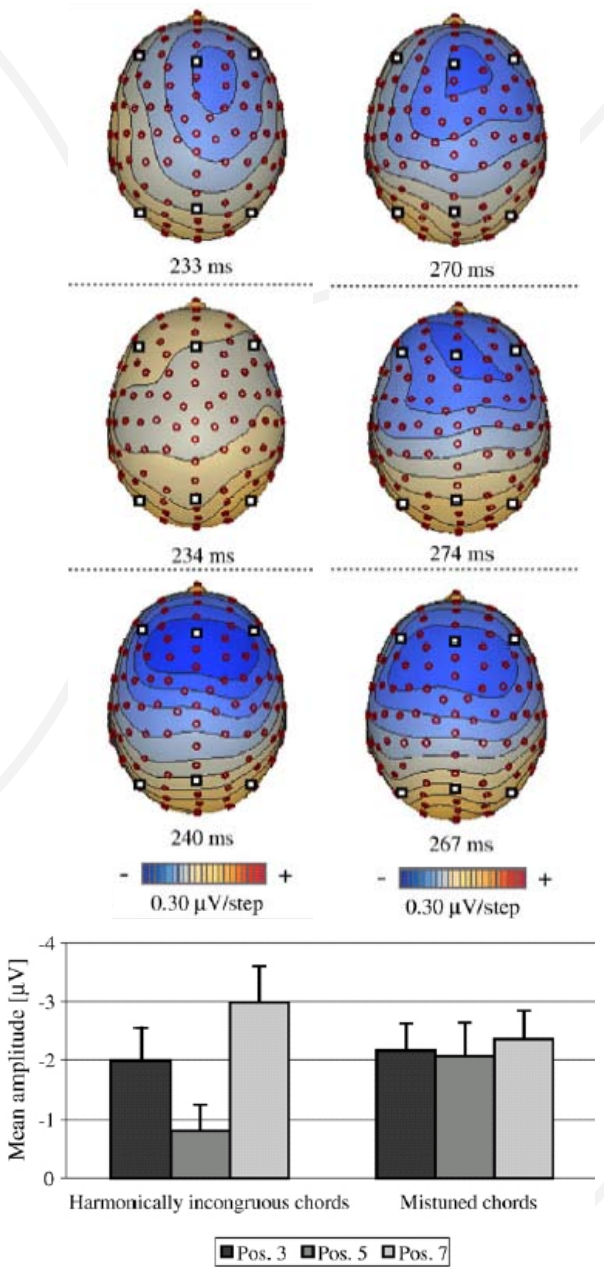


Figure 1
Top: EEG voltage isopotential maps of the difference between responses to Neapolitan subdominants (left) and mistuned chords (right) in different cadence positions at average peak latency. Bottom: Average mean amplitudes (in µV) of the ERP responses to harmonically incongruous (left) and mistuned chords (right) placed in different cadence positions. The plot clearly shows that the ERP-component (the ERAN) caused by the Neapolitan violation is dependent on cadence position. Leino et al. Brain Res. 2007.

Reestablishing speech understanding through musical ear training after Cochlear Implantation - a study of the potential of cortical plasticity in the brain

Bjørn Petersen, Malene Vejby Mortensen, Therese Ovesen, Albert Gjedde and Peter Vuust.

Cochlear implantation (CI) is a surgical treatment, helping deaf people to regain hearing abilities. A successful rehabilitation though is highly dependant on the ability of the brain to adjust to the electrical signal from the implant, which significantly differs from the natural signal of the ear. Through musical training it is expected that CI-implantees will increase their ability to perceive and appreciate music and thereby also their speech perception. The experiment is a case-control study that involves newly operated adults, who for a period of 6 months agree to take part in a weekly lesson of music plus ½ hour of daily homework. To observe how different regions of the brain develop concurrently with the training, participants will be PET -scanned three times during the experiment. This research may be of great importance to the quality of life of CI-users and to the understanding of the neural basis of speech and music perception.

Assessing musical potential

Peter Vuust, Elvira Brattico, Mia Sepänen, Risto Näätänen and Mari Tervaniemi.

Early exposure to musical training is a necessary but unfortunately not sufficient condition for achieving musical expertise. A reliable assessment of musical potential in infants could spare many fruitless music lessons in some and inspire others with a real potential for a musical career. Behavioural measures of musical potential in general are not very well validated in a wider population and may not apply to infants, in so far that these tests are built on verbal communication. Therefore, it would be of great value to have an objective measure of musical talent. The mismatch negativity (the MMNm) as measured by magnetic encephalography (MEG) (or electro encephalography - EEG) has proven to be a strong indicator of musical expertise in adults. Superiority in the auditory

processing of different musical parameters such as pitch, rhythm, intensity, sound source localization, and timbre have been found in musicians as compared to non-musicians. Using a novel multi-feature paradigm the ensuing project proposes: 1) to develop adequate behavioural measures for measuring musical abilities and potential, and
2) to test whether this measure correlates with psychophysical measures (MMNm) of musical abilities.

Music and Emotion - Processing of musical chords in the human brain

Karen Johanne Pallesen, Christopher Bailey, Irina Anourova, Elvira Brattico, Olga Varyagina, Synnøve Carlson.

This project aims to investigate the neural correlates of emotions and aestetic experience elicited by music and the influence of competence on the neural processing patterns. The series of studies investigate the neural processing of major, minor and dissonant musical chords. Functional magnetic resonance imaging (fMRI) is used to localize neural populations involved in cognitive and emotional processing of major, minor and dissonant chords, and magnetoencephalography (MEG) is used to study the time course of early neural representations of these chords in the auditory cortex. Professional musicians are compared with musically untrained subjects to study the effects of stimulus competence on the brain responses.

In a behavioural study (Study 1) the emotional salience of major and minor chords is tested by having musically untrained subjects rating the chords on graded scales. Subsequently, the neural coding of the emotional chord qualities is investigated with fMRI in a study where BOLD responses to major, minor and dissonant chords are contrasted (Study 2). The influence of cognitive processes on responses in emotion coding brain structures is specifically studied by contrasting the brain responses to the musical chords during passive listening and working memory (Study 3). By recruiting both musician and nonmusician subjects the influence of musical competence on the above-mentioned processes is explored. A separate study focuses on the effect of musical competence on the cognitive processing of the chords (Study 4). The experimental paradigm is additionally used in an investigation of cerebellar involvement in non-verbal cognitive processes (Study 5). The MEG data are analyzed to investigate the temporal aspects of neural representation formation of major minor and dissonant chords, based on synchronization in the gamma frequency band (Study 6).

Musical Learning and Liking

Anders Green, Peter Vuust, Andreas Roepstorff and Klaus Bærentsen.

This project examines the neuronal substrate and dynamics as the brain learns and recognizes music and melodies. Empirical behavioral studies have shown that learning – i.e. how well one knows a given piece of music - to a certain extent

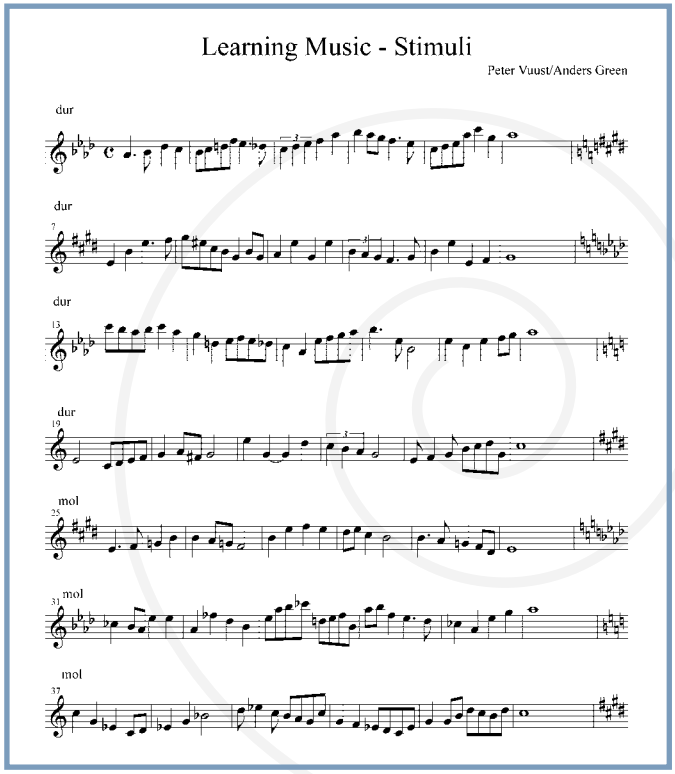


Figure 2
Music examples displaying examples of music exerpts in major and minor mode, used in the learning and liking study.

determines how well one likes the music. The so-called Wundt inverted-U curve effect between knowing and liking predicts that few as well as multiple exposures to a piece of music is associated with a low score for 'liking' the piece. The neural correlates to this psychological effect are, however, unknown. Using fMRI we study the effect of repetition of major and minor melodies on brain activity.


Photos: Martin Dam Kristensen

Absolute Pitch

Anders Dohn, Mikkel Wallentin, Andreas Roepstorff, Leif Østergaard and Peter Vuust.

Absolute Pitch (AP), the ability to name a tone, is a known musical ability that some musicians and composers possess. The development of AP is thought to have a genetic component, but musical training during a critical period of the human development is a prerequisite. The aim of the current project is to study the anatomical basis of AP using fiber-tracking and, using fMRI, to compare the ability to identify tones with the ability to produce them as well as to study the dysfunctional aspects of the AP ability.

Peter Vuust
Photo: Lars Kruse/AU-foto

MUSIC IN THE BRAIN

http://www.musicinthebrain.dk

Why do we play music? Examining the role of dopamine

Peter Vuust, Jakob Linnet, Doris Doudet, Arne Møller, Line Gebauer and Albert Gjedde.

The ability to experience and perform music is a fundamental human ability and music is an integral part of all human cultures, yet its purpose in an evolutionary perspective remains unknown. A possible explanation could be found in the euphoria that many people experiences during musical performances. Similar euphoric conditions of a less desirable nature is know from different types of addiction e.g. drug addiction and pathological gambling. The neurotransmitter, dopamine, play an important role the anticipation and receipt of reward and has been implicated in studies of addiction. In the present study we intend to study the possible dopamine release in musicians self-reporting to experience euphoria when playing.

Photo: Martin Dam Kristensen

The genetic component of musicality

Iben Bache, Peter Vuust and Niels Tommerup (with Wilhelm Johannsen Centre for Functional Genome Research).

One of the most intriguing question regarding human musical abilities concerns the role of heritability of music skills. Monozygotic twins are more concordant for the ability to discriminate pitch than dizygotic twins. Thus, the heritability of pitch discrimination has been estimated to be 70-80%. It is also estimated that around 4% of the population cannot discriminate pitch. They are tone-deaf (have amusia). At the other extreme, people with perfect pitch can accurately name and remember a tone. We have identified a total of 120 translocation carriers that may serve as a starting point for identification of candidate genes for perfect pitch and amusia once genome scans implicate the presence of musicality loci in overlapping regions of the genome. Furthermore, we will map those breakpoints, where the phenotype segregate with the translocation within families and the overlapping independent breakpoints in order to identify candidate genes that can be used for mutation studies. The end goal of this investigation is to determine to what extent musicality runs in the genes.

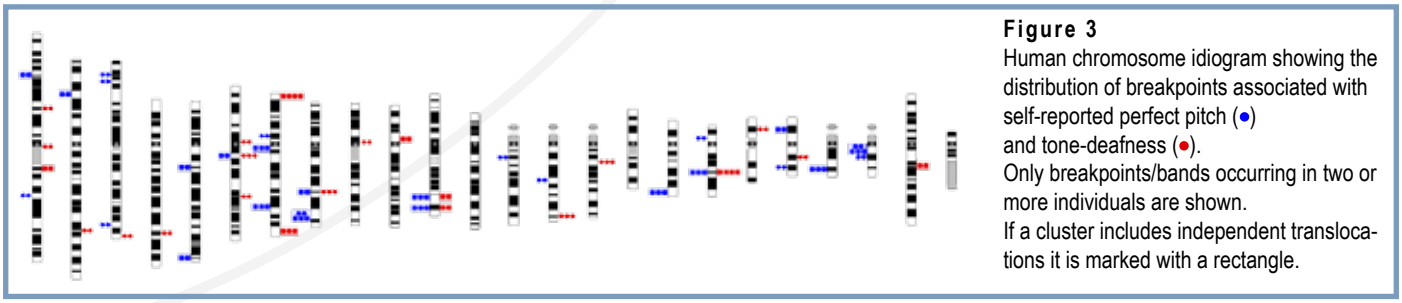


Figure 3
Human chromosome idiogram showing the distribution of breakpoints associated with self-reported perfect pitch (●) and tone-deafness (●).
Only breakpoints/bands occurring in two or more individuals are shown.
If a cluster includes independent translocations it is marked with a rectangle.

CFIN staff

Head of CFIN - Professor Leif Østergaard

Professors:
Hans C. Lou
Doris Doudet
Chris Frith
Uta Frith
Albert Gjedde
Morten L. Kringelbach
Leif Østergaard

Associate professors:
Sune Nørhøj Jespersen
Jakob Linnet
Arne Møller
Andreas Roepstorff
Peter Vestergaard-Poulsen
Peter Vuust
Ona Wu

Senior scientists / Post.docs:
Bhador Bahrami
Daniel Campbell-Meiklejohn
Mallar Chakravarty
Ken Ramshøj Christensen
Pernille Jansen
Kristjana Yr Jonsdottir
Anne M. Landau
Torben Ellegaard Lund
Irene Klærke Mikkelsen
Malene Vejby Mortensen
Kim Mouridsen
Yoshiyuki Nomura
Anders Bertil Rodell
Donald F. Smith
Manouchehr Seyedi Vafaee
Mikkel Wallentin

PhD students:
Joel Fredrik Astrup Aanerud
Mahmoud Ashkanian
Christopher Bailey
Per Borghammer
Niels Buhl
Søren Christensen (Melbourne)
Anders Dohn
Jesper Frandsen
Jacob Geday
Anders Christian Green
Louise Gyldensted
Brian Hansen (PhD degree 14.09.07.)
Niels Hjort (PhD degree 22.03.07.)
Yi Ching Lynn Ho (Singapore)
Birgitte Fuglsang Kjølby
Luciano Minuzzi (PhD degree 11.01.07.)
Mette Møller (PhD degree 09.03.07.)
Thomas Nielsen (PhD degree 21.06.07.)
Karen Johanne Pallesen
Esben Thade Pedersen (Singapore)
Bjørn Petersen
Ericka Peterson
Lars Riisgaard Ribe
Uffe Schjødt
Kamila Ewa Sip
Joshua Charles Skewes
Astrid Frøhlich Staanum

CFIN staff at Sandbjerg Manor, August 2007.
Photo: Sanne Lodahl

Christine Sølling
Kristian Tylén, Guest Researcher
Eduardo Adrián Garza Villarreal

Research year students:
Adjhmal Nahimi
Erik Søndergaard Poulsen

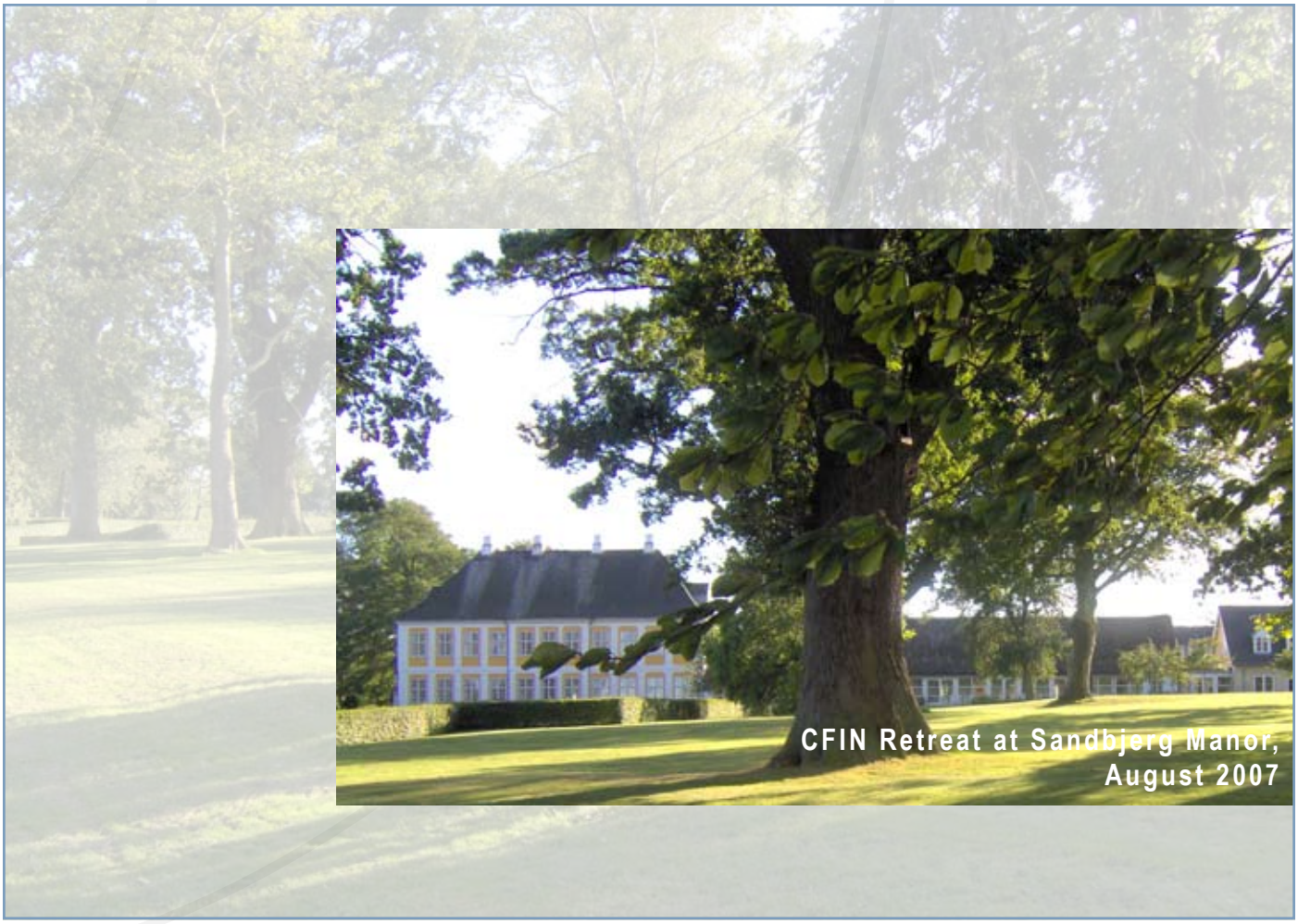
Thesis students:
Morten Friis-Olivarius
Rune Vingborg

Research Assistants:
Mette Buhl Callesen
Martin Carlsen
Line Gebauer Josefsen
Ivana Konvalinka
Sita Ramchandra Kotnis
Sanne Lodahl

Anders Bay Neumann
Elisabeth Pedersen
Kristine Rømer Thomsen
Ethan Weed

Technical Staff:
Michael Geneser, Radiographer
Kim Vang Hansen, Imaging Analyst
Jørgen Kold, Imaging Analyst
Poul Erik Nielsen, System Administrator
Ryan Sangill, MR Physicist
Dora Zeidler, Research Radiographer

Administrative Staff:
Mai Drustrup, Secretary
Michele Gammeltoft, Secretary
Palle Monefeldt, Logistics Coordinator
Lea Skewes, Projects coordinator, Interacting Minds
Henriette Blæsild Vuust, Communications Coordinator



CFIN Retreat at Sandbjerg Manor, August 2007

Photos: Henriette Blæsild Vuust

Facts about CFIN

Teaching

In 2005 CFIN started coordination of courses across all five faculties at the University of Aarhus in a course catalogue called NEUROVIDEN 2005/2006. This catalog offered an overview of courses in neuroimaging, cognition, brain research and similar topics. In 2006/2007 the course catalogue became web-based. Read more at: http://www.cfin.au.dk/neuroviden

CFIN researchers have developed a curriculum of courses within neuroimaging, neurotransmission, functional neuroanatomy, clinical neurology and psychiatry with collaborators across University of Aarhus. These are offered as masters degree courses as part of the Biomedical Engineering program and as PhD courses within CFIN. Read more at: http://www.cfin.au.dk/SFINX

In the spring 2007 CFIN hosted a course in *Functional Neuroanatomy and Neurological Diseases* coordinated by Carsten Bjarkam, Leif Østergaard, and Per Borghammer.
In the fall 2007 CFIN hosted a course in *Neurotransmission, psychiatry and neuropharmacology*. Associate professor Arne Møller and M.D. Rikke B. Dalby coordinated this course.
Read more at : http://www.cfin.au.dk//neurotransmission

Leif Østergaard:
- MR in Acute Stroke: A-course in Neuroradiology, Special medical education in diagnostic radiology, 22-24 October 2007.

Arne Møller:
- PET scanning in rodents, Aarhus University, advanced course in Laboratory Animal Science, Aarhus, DK, 13 September 2007.

Peter Vestergaard-Poulsen:
- Magnetic Resonance Imaging (course leader). PhD course, Faculuty of Health Sciences, Aarhus University

Andreas Roepstorff:
- Information seeking, Aarhus University, The Faculty of Humanities, Institute of Anthropology, Archaeology and Linguistics. 2007.

Invited lectures

In 2007, CFIN researchers gave invited lectures at the following events.

Leif Østergaard:
- European Congress of Radiology, 12 March 2007. *Diffusion and Perfusion MR imaging of the brain: Imaging techniques, protocols and post-processing.*
- Depressionspatienten i praksis: Symposium for general practicioners, 24 March 2007. *Music and depression.*
- ISMRM/ESMRMB Joint Annual Meeting, Berlin, Germany, 19 May 2007. *MRI in Stroke.*
- ISMRM/ESMRMB Annual Meeting, Berlin, Germany, 24 May 2007. *Gadovist and Acute Stroke.* Keynote speaker.
- Annual Meeting, Nordic Society of Neuroradiology, 1 June 2007. *Introduction to tumor perfusion.*
- Annual Meeting, Nordic Society of Neuroradiology, 1 June 2007. *MR or conventional CT in thrombolysis treatment. Does it make a difference?*
- Annual Meeting, Nordic Society of Neuroradiology, Denmark, 1 June 2007. *Fiber tracking as part of preoperative planning in brain tumors.*
- Annual Meeting, Nordic Society of Neuroradiology, 1 June 2007. *Perfusion and diffusion MR in Stroke: Latest techniques.*
- Visit by the Danish Parliaments Committee on Science and Technology and the Danish Minister of Science, Technology and Innovation (Helge Sander), 15 June 2007. *Vejen fra Grundforskning til Patientbehandling og Innovation er kort (The road from basic research to patient treatment and innovation is short).*
- Workshop on Cerebral Perfusion and Brain Function, ISMRM: Novel Techniques and Applications, 30 Aug 2007. *Latest Advances in DSC-MRI in Acute Stroke.* Keynote speaker.
- Workshop on Cerebral Perfusion and Brain Function, ISMRM: Novel Techniques and Applications, 31 August 2007. *Modeling the regulation of cerebral oxygen extraction by flow heterogeneity.*
- NER Foundation Workshop on Advanced Neuroimaging and Acute Stroke, Washington DC, USA, 7 September 2007. *Perfusion MRI Methodology.* Keynote speaker.
- Nordic Stroke 2007 - 14th Nordic Meeting on Cerebrovascular diseases, 12 September 2007. *Advanced Stroke MRI: Prediction of Outcome.*
- Staff-meeting, Aarhus University Hospital, 12 September 2007. *Avanceret billeddannelse ved akut apopleksi.*
- University of Aarhus Anniversary, 14 September 2007. *Hjerneforskning: Fra Fysik og Musik til Patientbehandling (Brain research: From Physics and music to patient treatment).*
- 25. landsmøde Dansk Medicoteknisk Selskab, 20 September 2007. *About modern scanning methods, brain and music.* Keynote speaker.
- Staff Meeting, Center of Pervasive Computing, 24 September 2007. *I-Know - A Diagnostic Support System in the Treatment of Acute Stroke.*
- nICE Workshop, Bergen, Norge, 2 October 2007. *Stroke MRI.*
- Staff Meeting, Rikshospitalet Oslo, Norway, 3 October 2007. *MR in Acute Stroke.*
- Seminar, Management group of the New University Hospital in Aarhus (DNU), 4 October 2007. *Faglige fællesskaber som Det Nye Universitetshospitals organiseringsprincip: Billeddiagnostik.*
- iNANO Autumn School, Fuglsø, Danmark, 5 October 2007. *Bioimaging and nano-technology.*
- *Introduction to Perfusion and Physiology*. Quantitative Perfusion Imaging, Freiburg, Germany, 10 October 2007.

- *Clinical Importance of Perfusion Imaging.* Quantitative Perfusion Imaging, Freiburg, Germany, 10 October 2007.
- *Dynamic Susceptibility Contrast Perfusion Imaging*. Quantitative Perfusion Imaging, Freiburg, Germany, 12 October 2007.
- Perfusion MRI, Scandinavian MR Physics Course, Lund, Sweden, 24 October 2007.
- Forskningens Dag, Aarhus, Denmark, Aarhus Hospital, Aarhus University Hospital. *Vejen er kort fra Grundforskning til Patientbehandling og Innovation (The road from basic research to patient treatment and innovation is short)*. 31 October 2007.
- Danish Neuroradiology Society: E-course. *New perfusion techniques in acute stroke.* Aarhus, Denmark, 6 November 2007.
- Forskningsledernetværket FL1. *Vilkår for Tværdisciplinær Forskningsledelse*, Copenhagen, 14 November 2007.

Albert Gjedde:
- Ældre Sagen, Galten. 4 January 2007. Talk on Functions of the Brain.
- Bibliotekar i Tværkulturelt Arbejde, Kolding. 1 February 2007. *Sproglige kompetencer som ressource.*
- Krop og Bevidstheds arrangement i forbindelse med HjerneUgen, Copenhagen. 12 March 2007. Talk on Ludomania.
- Opening of HjerneUgen 2007, *Cigaretter, whiskey og hed elskov.* Copenhagen March 2007.
- Johns Hopkins University, USA. *Dopamine release in Schizophrenia*. 6 March 2007.
- Ældredagene `07, LederForum, Social & Sundhedssektoren, Christiansborg. *Ny viden om hjernens henfald.* 12 March 2007.
- Krogerup Højskole. *Hjerner kan spå, især om fremtiden.* 17 March 2007.
- Neurocluster Generalforsamling, 19 April 2007. *Indsigt, indbildning eller ønsketænkning: Hvor vil vi hen med den danske neurovidenskab*?
- Teknologisk Institut, Taastrup. Tidens teenagere: Umodne og modne hjerner: Indsigt I hjernens udvikling. 26 April 2007.
- Visit by the Danish parliaments Committee on Science and Technology and the Danish Minister of Science, Technology and Innnovation (Helge Sander), *Hjernen i den 21år hundredes store udfordring.* 15 June 2007.
- Oxygenation in Brain. How far from the Brink?, 18 July 2007.
- Evolution versus intelligent design. Himmelev Summer School, 19 July 2007.
- Alzheimerforeningen, Skanderborg. *Ny viden om hjernens henfald.* 21 September 2007.
- Vidar Skolen. *Mennesket, en maskine?* 22 September 2007.
- International Neuroinformatics workshop, Karolinska Institute, Sweden, 30 August 2007.
- ISOTT. *Regulation of brain oxygenation: Lessons from PET, MR and NIRS*, Atrium congress Centre, Uppsala, 31 August 2007.
- Støttekredsen for voksne autister, Hinnerup Kollegiet, 7 September 2007.
- University of Aarhus Anniversary, 14 September 2007. *Hvad skal fremtiden bringe? Om hjernens spådomme.*
- Dansk Institut for Ekstern Kvalitetssikring for Laboratorier i Sundhedssektoren. *Doping og dopamin: Målinger på hjernen.* Odense, 19 September 2007.
- Kursuslederinspirationskursus, Bispebjerg Hospital. *Hjernens behandling af sanseindtryk,* 25 September 2007.
- CFIN , 26 September 2007, *Blood-Brain Transfer and Metabolism of Oxygen seminar*.
- Invited speaker at the Advanced Science & Technology Adjudication Resource Centre, Johns Hopkins University School of Medicine, October 2007.

Andreas Roepstorff:
- Department of Social Anthropology, Cognition and Culture research seminar series, GB, 17 January 2007. *The neuroturn: challenging anthropology or anthropological challenge?*
- Albert Newen, Alexandra Zinck, Kai Vogelei, Social Cognition, Emotion and Self Consciousness, Delmenhorst, DE, 8 March 2007. *Symbols, a 'missing link' in social cognition?*
- BIOS, London, GB, 15 March 2007. *Imaging Brains - interacting Minds: from brain research to biopower*
- Goodenough College, London, GB, 21 March 2007. *Seeing me, Seeing You, Seeing Brains*
- First BASIC Workshop: subjectivity, intersubjectivity and self-representation, Snekkersten, DK, 12 May 2007. *Mapping Subjectivity, BASIC*
- Anne Line Dalsgaard, Emotion and Anthropology, Aarhus, DK, 29 May 2007. *Emotion and Embrainment*
- Cognition, Culture and Religion, Symbolization, DK, 1 June 2007. *Transcendental Brain Areas...*
- Mind & Life Institute, Mind & Life Summer institute, US, 7 June 2007. *Mapping Subjectivity a Reflexive Approach*
- Visit by the Danish parliaments Committee on Science and Technology and the Danish Minister of Science, Technology and Innnovation (Helge Sander), Aarhus, DK, 15 June 2007. *Hjerneforskning på tværs.*
- Susan Hurley, CNCC conference: perception action and consciousness, 3 July 2007. *An emergence of persons in cognitive neuroscience?*
- Daniel Hutto & Shaun Gallagher, Narrative alternatives to theory of mind, Hertfordshire, GB, 15 July 2007. *The Person Doctrine*
- Forum for Psykologisk Antropologi, Human Mind - Human Kind, 16 August 2007. *Reciprocity and exchange: a neurosocial contextualisation*
- Colin Renfrew, Lambros Malafouris, Chris Frith, Archaeology and Neuroscience, 16 September 2007. *Thinking Through Things*
- Armin Geertz, Explaining Religion, 17 September 2007. *Response*
- European Neuroscience and Society Network, Neurosocieties. The rise and impact of the new brain sciences, 13 November 2007. *Public Health and the Politics of the Neurosciences.*
- Missing Links. Symbolic Species II, Copenhagen, DK, 23 November 2007. *Symbols: A missing link in social cognition?*

- ATACD: A topological approach to cultural dynamics, Topology for Culture. Metaphors and Tools, Amsterdam, NL, 30 November 2007. *Small world topologies in interdisciplinary research networks.*

Arne Møller:

- Programkomiteen for ikke ioniserende stråling. *PET studium af cerebro-metabolisk effekter af ikke ioniserende stråling.* Copenhagen, DK, 30 May 2007.
- 6th OAK meeting. *Effects of MDMA (esctacy) on dopaminergic radiologand biding in rat striatum - a combined PET/autoradiographic study.* Copenhagen, Danmark, 8 June 2007.
- 6th Annual OAK meeting. *The Gambling Reducing Slot Machine Preliminary results.* Copenhagen, Denmark, 8 June 2007.
- 6th Annual OAK meeting. *Gambling as Self-medication? Preliminary results on Dopamine & Depression in Pathological Gambling.* Copenhagen, 8 June 2007.
- Advanced course in Laboratory Animal Science, Aarhus, Denmark. *PET scanning in rodents.* 13 September 2007.

Peter Vuust:

- Meaning Construction in Aesthetic and Everyday Perception, Center for Semiotics, University of Aarhus, Denmark, 29 January 2007. *Harmony and rhythm: Neural processing of musical "syntax".*
- Gyngen, 20 February 2007. *Music and brain.*
- Bohuslän Museum, 24 February 2007. *Language of music.*
- Opponent/discussant. LO-skolen, Gl. Hellebækvej 70, 23 March 2007. *Hvorfor musik? : Begrundelser for musikundervisning.*
- NUMU-kongres 2007, Vejen, Denmark, 30 March 2007. *Music and brain.* Keynote speaker.
- Dialogue meeting, Ministery of Culture Research Committee, Copenhagen, Denmark, 12 April 2007. *Cognition, Perception and Learning: From praxis to research at DJM.* Keynote speaker.
- Forskningens Døgn, Danmark, 27 April 2007. *Musical development and learning.*
- DeCIbel Ringsted, 28 April 2007. *About learning the language of music.* Keynote speaker.
- Neuroimaging of Human Cognition - XXI Sandbjerg Symposium, Danish Society for Neuroscience , Sønderborg, Denmark, 7 May 2007. *Expecting harmony and rhythm: - Neural processing of musical "syntax".*
- Music and Brain Club, FIL, London, GB, 15 May 2007. *Anticipation of musical structure.*
- Skive musikskole, 8 August 2007. *Musical learning and brain.*
- Sandbjerg Manor, 29 August 2007. *Music in the brain.*
- University of Aarhus, 30 August 2007. *Music and Language.*
- Arkitektskolen, 3 September 2007. *About creating.*
- FOF, Lyngby. *Music and brain.* 25 September 2007.
- Skanderborg konferencen, Denmark, 3 October 2007. *Musical development and learning.*
- Thisted musikskole. *Music and brain.* 4 October 2007.
- Dansk Bibliotekar Forening, Nyborg. *Music and brain.* 5 October 2007.
- University of Aarhus, Denmark. *Music in the brain: Neural processing of polyrhythmic structures in music.* 10 October 2007.
- Nordplus 2007, The Royal Academy of Music, Aarhus, Denmark. *Music Perception, Cognition and Learning.* 22 October 2007. Keynote speaker.
- The Royal Academy of Music, Aarhus. *Research at the Royal Academy of Music.* 24 October 2007.

Chris Frith:

- Workshop with Chris Frith & Uta Frith, Copenhagen, Danmark, Professor Daniel Zahavy. *What is special about social signals used in communication?* Keynote speaker. 13 December 2007.

Morten Kringelbach:

- Røde Kors, Aarhus, Denmark *Kreativitet i den følelsesfulde hjerne.* 15 March, 2007.
- Synscenter Refsnæs, Kalundborg, Denmark, *Hjerne, læring og valg.* 10 April, 2007.
- Rigshospitalet, Copenhagen, Denmark, *Rigshospitalet 250 år: hjernen i farver.* 17 April, 2007.
- Plenary lecture, DaNS congress, Odense, Denmark, *Børns læring og nydelse*. 26 April, 2007.
- CFIN, Aarhus, Denmark, *Hjerneforskning, nydelse og livskvalitet.* 15 June, 2007.
- EU / ISBNPA2007, Oslo, Norway, *Pleasures of the brain: the functional neuroanatomy of food intake.* 22 June, 2007.
- Charles Wolfson Trust, Oxford. *DBS and MEG*. 10 September, 2007
- HOPE conference, Oxford. *Happiness and pleasure.* 19 September, 2007

ISMRM conference in Berlin, May 2007
Photos: Jesper Frandsen

- CFIN, Aarhus, Denmark. *Deep brain stimulation as a neuroscientific tool.* 21 Sept, 2007
- Autumn School 2007, Oxford. *MEG and deep brain stimulation.* 24 September, 2007
- Festsalen, Copenhagen University. *Nydelsens neurobiologi.* 2 October, 2007
- Kulturnatten, Statens Museum for Kunst. *Kunstværker*. 12 October, 2007
- Betty Nansens Teater, Copenhagen. *Nydelse og begær.* 13 October, 2007.
- MBA, *Nydelsesfyldte hjerner.* 1 December, 2007

Hans Lou:
- Guest lecturer at Sapienza University, Rome, Italy, 13-15 March 2007.
- *Dopamin 50* - 50th Anniversary of the discovery of Dopamine, Göteborg, Sweden, May 2007. Invited lecturer: *Dopamine and ADHD.*

Kim Mouridsen:
- ISMRM 15th Scientific Meeting & Exhibition, Berlin, Germany. *Which Arterial Input Function?* Keynote speaker. 20 May 2007.

Jakob Linnet:
- Weekend course at Folkeuniversitetet, Copenhagen. *Ludomani: Biologiske, psykologiske og sociale faktorer ved spilleafhængighed.* 3- 4 March 2007.
- Medford, Harvard University. *Pathological gambling research at CFIN: -Today with special focus on poker.* 3 October 2007.
- CFIN, Aarhus. *Win - Win, Lose - Lose.* 26 October 2007.
- CFIN, Aarhus. *Pathological Gambling: -Today on reward prediction error, its possibilities and challenges to pathological gambling research.* 23 November 2007.

Torben E. Lund:
- *Default vascular connectivity*, CNT Default Mode workshop, Functional Imaging Laboratory, Institute of Neurology, University College London, London, United Kingdom. September 2007.

Mikkel Wallentin:
- Wallentin, M., Roepstorff, A., Vestergaard-Poulsen, P., Østergaard, L., Gebauer, L., Linnet, J., Østergaard, S. 2007, *"Strategic" and "tactical" chess differentiate in their hippocampal and precuneus requirements in expert chess players*, Presented at oral session at Society for Neuroscience Conference, San Diego, 3-7 November 2007.

Other CFIN researchers:
- Jesper Frandsen, *Future Stereology* - In Honour of Hans Jørgen G. Gundersen, 21 September 2007.
- Per Borghammer, Brain and Mind Forum 2007, Helsinge, Denmark, Copenhagen University. *PET/SPECT studies of cerebral blood flow (CBF) and glucose consumption.* 14 September 2007.
- Kristine Rømer Thomsen, Sixth Annual OAK Meeting for Danish Brain Research Laboratories, Copenhagen, Danmark. *Gambling as Self-medication? - Preliminary results on Dopamine and Depression in Pathological Gambling.* 9 June 2007.
- Kristine Rømer Thomsen, Misbrugscenteret Slagelse. *Ludomani og ludomaniforskning.* 17 September 2007.
- Mette Buhl Callesen, Misbrugscenteret Slagelse. *Ludomani og ludomaniforskning.* 17 September 2007.
- Mette Buhl Callesen, Sixth Annual OAK Meeting for Danish Brain Research Laboratories, Copenhagen, Denmark. *The Gambling Reducing Slot Machine.* 9 June 2007.

Conferences

CFIN researchers have organised or participated in the following congresses and conferences during 2007:

Leif Østergaard:
- International Stroke Conference 2007, 7-9 February 2007, San Francisco, US.
- European Congress of Radiology 2007, 9-13 March 2007, Vienna, AT.
- ISMRM/ESMRMB Joint Annual Meeting, 19-25 May 2007, Berlin, DE.
- 16th European Stroke Conference, 29 May - 1 June 2007, Glasgow, GB.
- Nordic Society of Neuroradiology Annual Meeting, 31 May - 1 June 2007, Odense, DK.
- ISMRM Workshop on Cerebral Perfusion and Brain Function: Novel Techniques and Applications, Salvador da Bahia, Brazil. 28 July - 1 August 2007.
- Gordon Conference, Brain Energy Metabolism & Blood Flow, Magdalen College, Oxford. August 2007.
- Nordic Stroke 2007, 13-15 September 2007, Aarhus, DK.

Albert Gjedde:
- 48th Annual Meeting of the Scandinavian College of NeuroPsychopharmacology, April 2007.
- Nordic Centre of Excellence, mid-term meeting, Copenhagen, May 2007.
- Gordon Conference, Brain Energy Metabolism & Blood Flow, Magdalen College, Oxford. August 2007.
- Annual Congress of the European Association of Nuclear Medicine, Copenhagen.

Chris Frith:
- Anthropology and Neuroscience. University of Cambridge.

Arne Møller:
- 6th Annual OAK Meeting, Copenhagen, DK, 8-9 June 2007. Chair on *Imaging and Metabolism* session.
- EANM: Annual Congress of the European Association of Nuclear Medicine, 13-17 October 2007.
- Society for Neuroscience, 3-7 November 2007.
- Annual NCRG Conference on Gambling and Addiction,11-13 November 2007.

Peter Vestergaard-Poulsen:
- Advanced High field MRI, Bruker Systems GMBH. 15-20 April 2007.
- International Society of Magnetic resonance, Annual meeting. 19-25 May 2007. Berlin, Germany.
- Human Brain Mapping. 9-15 June 2007. Chicago, USA.
- High-Field MR, Max-Planck-Institute for Biological Cybernetics headed by Dr. Kamil Ugurbil. Tübingen 11-17 July 2007.

Andreas Roepstorff:
- First BASIC workshop: subjectivity, intersubjectivity and self-representation, 10-12 May 2007, Snekkersten, DK.
- Language in Cognition, Cognition in Language, 11-13 October 2007, Aarhus, DK.
- Interacting minds and their biological basis - pathological perspectives, Aarhus University Hospital, 9 November 2007.
- Bi-monthly Interacting Minds Seminar Series (October- December, Andreas Roepstorff organiser) http://www.interacting-minds.net
- Monthly CCC workshops, (Andreas Roepstorff, organiser) http://www.ccc.au.dk/en/news/events/comingwrkshps

Peter Vuust:
- Hvorfor Musik? (Why music?), 23-24 March 2007, Helsingør, DK.
- Forskning ved DJM (Research at the Royal Academy of Music), 8 May 2007, Århus, DK.
- Kulturministeriets kunstråds Musikudvalgs konference (The Ministery for Culture's Music Committee conference), 25 September 2007, Copenhagen, DK.

Other CFIN researchers:
- Research Day. Aarhus Hospital. 9 February 2007.
- Joint Annual Meeting ISMRM-ESMRMB. 19-25 May 2007.
- Kim Mouridsen, ISMRM Workshop on Cerebral Perfusion and Brain Function:Novel Techniques and Applications, Salvador da Bahia, Brazil. 28 July - 1 August 2007.
- Language and cognition. Linguistic Research Colloquium, The State Library, Aarhus, 29 November 2007. (Ken Ramshøj Christensen, organiser).
- On the interface between pragmatics and the brain. Seminar on Neurolinguistics. Aarhus University, 4-6 December 2007 (Ken Ramshøj Christensen and Mikkel Wallentin, co-organisers)

Radio / TV / newspress

CFIN researchers have participated in the following in 2007:

Andreas Roepstorff
- *Waar de wettenschap niet biej kan*, NRC Handelsblad, Amsterdam, 20 January 2007.
- Interview for Orientering, DR P1, 19 February 2007.
- *Hjernen kommer for retten* (The brain stands trial), Kristeligt Dagblad, 6 July 2007.
- Deadline: *Hjernens hemmeligheder* (Secrets of the brain), DR2, 12 August 2007.
- Deadline 2. sektion: *Den femte revolution* (The 5th revolution), DR2, 9 September 2007.
- *Tilværelsens ulideligt mange valgmulig-heder* (The unbearable many choises of life), Berlingke Tidende, 17 September 2007.
- *Minimalselvet*, Weekendavisen, 21 September 2007.

Peter Vuust
- *Musikken är en form av språk- också för hjärnan*, Bohusläningen, 14 February 2007. (interview for newspaper)
- Middagsnyhederne, TV2, 20 february 2007. (TV program)
- *Sød musik er livsfarlig*, TV2 Nyhederne, TV2, 29 April 2007. (TV program)
- *Modspil skaber udvikling*, Kristeligt Dagblad, 11 May 2007. (interview for newspaper)
- *Musik gør os klogere på hjernen*, JP, 11 August 2007. (interview for newspaper)

Leif Østergaard at ISMRM Workshop on Cerebral Perfusion and Brain Function:Novel Techniques and Applications, Salvador da Bahia, Brazil

- *Musik gør os klogere på hjernen*, Jyllandsposten, 12 August 2007. (interview for newspaper)
- *Jazz: Den danske sangskat*, Politiken, 20 August 2007. (interview for newspaper)
- *Viden Om - Musik og stress*, 25 September 2007. (TV program)
- MUSIK PÅ HJERNEN: Musik er et sprog, man skal kunne som menneske. Dansk Sang, 1 October 2007.

Morten Kringelbach
- *Lystens hjerne*, Program for *Lyst* (Betty Nansen Theater), p.8-9
- DR P1 Eksistens, interview about brain's existens, 7 January 2007.
- *Ansigtet - sjælens spejl?*, Politiken, 7 January 2007
- *Når nydelsen ved livet forsvinder*, Politiken, 11 February 2007
- Kreativehjerner.dk, 1 March 2007, TV spots for Danish Red Cross.
- Berlingske Tidende, *Følelser fremfor fornuft*, 3 March 2007. Newspaper article on emotions in the brain.
- Discovery news, *Brain Study: Why Desire Drives Us Wild,* 9 March 2007. Interview on desire.
- Børsen, *Tid*, 11 March 2007. Five Danes on the meaning of time.
- *Nydelse og begær i menneskehjernen*, Politiken, 18 March 2007
- Børsen, *Hvad foregår der i den kreative hjerne?*, 22 March 2007. Part of ad campaign for Danish Red Cross.
- *Nydelse i smertens univers*, Politiken, 15 April 2007
- Lettre Internationale, *Rationalitetens sammenbrud?*, 1 June 2007. Newspaper article on the brain's rationality.
- Morgenavisen Jyllands-Posten, *Jagten på hjernens hemmelighed*, 3 June 2007. Interview on the brain.
- Weekendavisen, *Hjernens følelsesliv*, 3 June 2007 Interview on new research group.
- *Lykkens anatomi er gådefuld*, Politiken, 3 June 2007
- www.bbc.co.uk, *A rough guide to the inside of your brain*, 21 July 2007.
- Ekstrabladet, *Forelskelse er en slags midlertidig sindssyge*, 1 August 2007, Article about love.
- DR P1 Orientering, 6 August 2007, Interview about DBS for coma patients.
- The Guardian, *A half baked miracle?*, 7 August 2007, Interview about deep brain stimulation and coma patients.
- *Lykkens hjernesmed*, Asterisk, 1 September 2007, p.15-17
- DR2 Deadline 22.30, 14 October 2007, Portrait program about the TrygFonden Research Group (12 min).

Other CFIN researchers
- Mikkel Wallentin. *En sexet historie,* Weekendavisen. 2007, 24 August. s. 12, 4. sektion (Ideer), Kronik.
- Arne Møller. *Ny hjerneforskning skal hjælpe ludomaner.* Nyhederne P4 & P3, 8 January 2007. Radio program
- Arne Møller. *Gamblere hjernescannes.* Urban, 29 January 2007.
- Albert Gjedde. Danmarks Radio P1. *Troen på det alternative.* Krause på tværs. 23 May 2007.
- Mahmoud Ashkanian. Forsker søger på tværs af grænser. AUH, 15 November 2007.
- Mahmoud Ashkanian. På tværs af grænser. Lægen i Midten, 15 November 2007.
- Brian Hansen. *Hjernealderens komme?* Book review of Lone Frank's book *The Fifth Revolution*. In Kvant, no.4, page 25, 2007.

Boards / Committees / Editorials

CFIN researchers are involved in the following:

Leif Østergaard:
- Member of work group on organizing image diagnostics in the Masterplan for the reorganization of hospitals in Aarhus.
- Member of Scientific Program Committee, European Society for Magnetic Resonance in Medicine and Biology (ESMRMB)
- Member of Annual Meeting Program Committee (AMPC), International Society for Magnetic Resonance in Medicine (ISMRM)
- Member of Board of Trustees, ISMRM
- Referee, Department of Faculty Affairs, Medical College of Wisconsin. 1 November - 1 December 2007.
- Chairman of editorial board for professorship in biomedical engineering. 15 March - 15 June 2007.
- Referee, Swiss Federal Institute of Technology (ETH), Zürich 1 March - 1 June 2007.
- Referee, ERC Starting Independent Research Grant Programme, European Research Council. 1 April - 1 October 2007.
- Member of research leader network, Forskningsledernetværket FL1.

Albert Gjedde:
- Adjunct Professor, Department of Neurology and Neurosurgery, McGill University, Montreal, Quebec, Canada.
- Member, Royal Society of Canada.
- Member, Centre de recherche en sciences neurologiques, Université de Montréal, Montréal, Québec, Canada.
- Visiting Professorship, Yale University, USA.
- Chairman, Research Advisory Committee, Royal Library of Denmark.
- Member, Medical Research Council, Ministry of Science and Technology, Denmark.
- Member, the Scientific Advisory Board, Arvid Carlsson Institute, University of Gothenburg, Gothenburg, Sweden.
- Member, The Danish Committee on Scientific Dishonesty.
- Member, The European Medical Research Council.
- Member, The Nordic Organisation of Medical Research Councils.

- Vice President 2008 of the Gordon Research Conference on Brain Energy Metabolism and President-Elect of same for 2010
- Adjunct Professor in Radiology, Johns Hopkins Medical Institutions.
- Expert-member of the Program Committee for Health under the 7th European Frame Programe for Research and Technological Development.
- European Research Council Peer Review Evaluation

Additional Peer Review/ Albert Gjedde:
- Academy of Finland.
- Deutsche Forschungsgemeinschaft.

Andreas Roepstorff:
- Project leader, BASIC (Brain, Agency, Self, Intersubjectivity, Consciousness), a ESF EUROCORES CNCC Project, 27 November 2006 - 27 November 2009.
- Member, Scientific Committe, EUROCORES Project CNCC (Consciousness in a Natural and a Cultural Context), 14 November 2006 - 14 November 2009.
- Chairman of Program Committee Understanding and Misunderstanding: Cognition, Mind and Culture, Humanities in the European Research Agenda, 1 May 2006 - 1 January 2007.
- Member, Scientific Committee, 9th Internatinal Conference on Philosophy, Psychiatry and Psychology, 1 January 2006 - 1 July 2006.
- Medlem af "Utvalget for planlegging av nytt forskningsprogram om etiske, juridiske og samfunnmessige aspekter ved bioteknologi, nanoteknologi og kognitiv vitenskap", Forskningsstyrelsen, Norway. (December 2006 - April 2007).
- Member of PhD committee: Niels Nygård, "Arkitektonisk Kvalitet", Arkitektskolen i Aarhus, Denmark.
- Member of board: ELSA program for biotechnology, nanotechnology and cognitive sciences, 1 August 2007– .
- Member, Steering Committee, Neuroscience an Society Network (ENSN), 24 April 2007-31 December 2011.
- Reviewer of research project in Open Competition Research program, 23 October 2007
- Reviewer of research project, 1 October 2007, NL.

Peter Vestergaard-Poulsen:
- Member of Studienævnet for Biomedicinsk Teknik (Board of Studies for Biomedical Engineering), Faculty of Health Sciences, Aarhus University.

Research stays abroad

Andreas Roepstorff: Interacting Minds: from brain research to Biopower, Wellcome Department of Imaging Neuroscience, UCL og BIOS, LSE (1 September 2006 – 1 April 2007)

Kamila Ewa Sip: Research student at Functional Imaging Laboratory, UCL, London, January – July.

Søren Christensen: Royal Melbourne Hospital, Melbourne, Australia (Professor S. Davis) (from 2004 -)

Hans Lou: Research stays at the universities of Düsseldorf, Germany, and Glasgow, Scotland (MEG project), and University of Columbia, New York, USA, (TMS project). 2007.

International scientific partners

- Institut National de la Santé et de Recherche Medicale / Université Claude Bernard, Lyon, France (Professor Norbert Nighoghossian)
- Fundació Privada Institut d'Investigació Biomédica de Girona, Girona, Spain (Professor Salvador Pedraza)
- University of Cambridge , Cambridge, United Kingdom (Professor Jean-Claude Baron)
- Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany (Professor Jens Fiehler)
- Universitätsklinikum Freiburg für die Medizinische Fakultät der Albert-Ludwigs-Universität, Freiburg, Germany (Dr. Valerij Kiselev)
- Royal Melbourne Hospital, Melbourne, Australia (Professor S. Davis)
- MGH Athinoula A. Martinos Center, Massachusetts General Hospital, Boston, USA (Dr. O. Wu)
- Brain Research Institute, Heidelberg West, Victoria, Australia (Dr. F. Calamante)
- McKnight Brain Institute, University of Florida, USA (Professor Steve Blackband)
- Mallinckrodt Institute of Radiology, Washington University, St. Louis, USA (Dr. D. Yablonski and Professor J. Ackerman)
- Dan Zahavi, Center for Subjektivitetsforskning, University of Copenhagen, Denmark
- Morten Overgaard, Neurocenter Hammel, Denmark
- Chris Frith, UCL, London, UK
- Uta Frith, UCL, London, UK
- Patrick Haggard, UCL, London, UK
- Nikolas Rose, LSE, London, UK
- Morten Kringelbach, Oxford University, UK
- Harvey Whitehouse, Oxford University, UK
- Doug Saddy, Reading Universitet, UK
- Simon Cohn, Goldsmith College, London
- Celia Lury, Goldsmith College, London, UK
- Jules Davidoff, Goldsmith College, London, UK
- Evan Thompson, University of Toronto, Canada
- Marc Raichle, Washington University, St. Louis, USA
- Anthony Jack, Washington University, St. Louis, USA
- Alva Noë, University of California, Berkeley, USA

- Kai Vogeley, Köln Universitet, Germany
- Albert Newen, Tübingen University, Germany
- Vittorio Gallese, Parma University, Italy
- Tatjana Nazir, Lyon University, France
- Jakob Hohwy, Monash University, Melbourne, Australia
- Mari Tervaniemi, Cognitive Brain Research Unit, Department of Psychology, University of Helsinki (CBRU) and Helsinki Brain Research Center, Helsinki, Finland
- Elvira Brattico, CBRU and Helsinki Brain Research Center, Helsinki, Finland
- Sakari Leino, CBRU and Helsinki Brain Research Center, Helsinki, Finland
- Eckart Altenmüller, Institut für Musikphysiologie und Musikermedizin, Hannover, Germany
- Karl Friston, Functional Imaging Laboratory (FIL), Wellcome Centre of Cognitive Neuroscience, UCL, UK
- Risto Näätänen Cognitive Brain Research Unit, Department of Psychology, University of Helsinki (CBRU) and Helsinki Brain Research Center, Helsinki, Finland
- Satu Pakarin, CBRU and Helsinki Brain Research Center, Helsinki, Finland
- Professor Roger Dean, Vice-Chancellor and President, University of Canberra, ACT 2601, Australia; Fellow of the Australian Academy of the Humanities (FAHA).
- Antoine Bechara, University of Iowa, USA

Industriel partners

- Systematic Software Engineering A/S , Aarhus, Denmark
- Dimac A/S, Højbjerg, Denmark
- Nordic Neurolab, Bergen, Norway
- GlaxoSmithKline, Cambridge, England
- Schering AG, Berlin, Germany
- GE Medical Systems, Milwaukee, U.S.A.

Completed Ph.D. theses, 2007

- Luciano Minuzzi , M.D. Autoradiographic studies of cerebral monoamine binding sites and animal models of schizophrenia. 11 January 2007.
- Mette Møller, M.D. Recovery and serotonergic neurotransmission in the wake of stroke and aging. 9 March 2007.
- Niels Hjort, M.D. Magnetic Resonance Imaging in Acute Stroke: Monitoring of patients Treated with Intravenous Thrombolysis. 22 March 2007.
- Thomas Nielsen, M.Sc. Tumour Vascularity Assessed by MRI. 21 June 2007.
- Brian Hansen, M.Sc. Diffusion MRI in Neuroscience. 14 September 2007.

CFIN Friday Seminars 2007

CFIN seminar coordinators:
Associate Professor Arne Møller, Communications Coordinator
Henriette Blæsild Vuust, PhD student Birgitte Fuglsang Kjølby.
The CFIN Friday seminars are held every Friday from 10-11.30.
Read more at: http://www.cfin.au.dk//cfinseminars

- Arne Møller: *On the way to the forgetful dog – via stroke and seizures.*
- *The forgetfull dog:*
  Mette Berendt: *Seizure.*
  Rikke Fast: *Geriatric brain.*
  Hanne Gredal: *Stroke.*
- Malene Flensborg Damholdt: *Cognitive impairment in Parkinson's Disease.*
- Per Borghammer: *Normalization of your data - exposing the New York Fraud.*
- Albert Gjedde: *How close are oxygen tensions in the brain to the brink?*
- Joel Aanerud: *Brain metabolism, serotonin receptor binding and amyloid plaque formation in Alzheimer's disease and healthy controls.*
- Albert Gjedde: *On HYPOTIME.*

Niels Hjort's PhD defence 22 March 2007
Opponent: Professor PD Dr.med. Tobias Neumann-Haefelin from Johann Wolfgang Goethe-Universität in Frankfurt, Germany.

- Henrik Rosendahl Kristiansen: *Gut Brain Interactions - Omega-3 and Depression.*
- Anders Rodell & Per Borghammer: *Anders' fantastic mean-brain.*
- Peter Iversen: *The brain as a hepatometer: An acute episode of encephalopathy in cirrhotic patients.*
- Hans Lou & Josh Skewes: *Making Sense: Dopaminergic regulation of conscious experience.*
- Bahador Bahrami: *Low level vision and language comprehension: is it just a matter of bias?*
- Extraordinary CFIN seminar / Guest Talk:
  Daniel Campbell-Meiklejohn: *Knowing When to Quit: The Neural and Pharmacological Substrates of Loss Chasing.*
- Kim Mouridsen: *ISMRM warm up talk.*
- Frederik Jølving: *Temporal patterns in neural activity during working memory - or how the brain works?*
- Conference 'highlights'. Open discussion about ISMRM 07 and BRAIN 07 conference topics.
- Esben Thade Petersen: *Arterial Spin Labeling: Sequence, Quantification, Application and the pitfalls involved.*
- Anne M. Landau: *A novel neuroprotective role for the Fas molecule in models of Parkinson's Disease.*
- Sune Jespersen: *Modeling the influence of flow heterogeneity on cerebral oxygen extraction.*
- Rikke B. Dalby: *Can You See My Depression? MRI Findings in Late-Onset Major Depression.*
- Brian Hansen: *PhD defence lecture warm-up.*
- Stephen J. Blackband: *High field NMR microscopy - beginnings and new directions.*
- Jens Christian Sørensen: *Neuromodulation in neurodegenerative disorders "Do neurosurgeons dream of electric pigs?*
- Irene Klærke Mikkelsen: *Mathematical Modelling of Brain Function.*
- Troels W. Kjær: *Electrophysiology in the study of the Self.*
- Torben E. Lund: *My previous and future fMRI research ... And a proposal for a CFIN course in Neuroimaging.*
- Jakob Linnet: *Win, win, lose, lose.*

CFIN Retreat 2007

The annual CFIN Retreat was held at Sandbjerg Gods 27-29 August 2007. This year's program was:

- Professor Per Roland (Karolinska Institute, Sweden), *Cortical dynamics - a view of brain work from the mesoscopic perspective.*
- Leif Østergaard, *Welcome and presentation of retreat program.*
- Albert Gjedde, *Cerebral Oxygen Metabolism.*
- Torben E. Lund, *Resting State Network.*
- Morten L. Kringelbach, *TrygFonden Research Group.*
- Jakob Linnet, *Double Down in Pathological Gambling.*
- Kim Mouridsen, *So what is neuroinformatics?*
- Sune N. Jespersen, *Biophysical modeling in neuroscience.*
- Andreas Roepstorff et al., *What's up in cognition research?*
- Leif Østergaard et al., *What's up in functional haemodynamics?*
- Peter Vestergaard-Poulsen et al., *What's up in neuroconnectivity?*
- Arne Møller et al., *What's up in neurotransmission?*
- Albert Gjedde et al., *What's up in neuroenergetics?*

Thesis student Morten Friis Olivarius
Photo: Sanne Lodahl

NEW FACE AT CFIN

Post.doc. Irene Klærke Mikkelsen, is an engineer within the field of applied physics. She has ever since her masters studied the possibility to quantify perfusion and related hemodynamic properties with MRI.

Initially, she tested one of the first Danish implementations of the spin-labelling perfusion technique. During her PhD, she focused more on post processing, which lead to an internationally recognized deconvolution technique that improves accuracy of perfusion estimates from contrast enhanced experiments. During her resent post doc at the University of Gothenburg, Sweden, she implemented a new method for perfusion quantification in the brain and developed a pipeline of computer programs for more efficient post-processing.

Irene Klærke Mikkelsen was the first manager of the Data Evaluation Center at the Danish Research Centre for Magnetic Resonance, and has also shortly been a clinical physicist.

At CFIN, Irene will be responsible for the development of mathematical models describing the hemodynamics during brain activation or bolus passage. She will contribute also to the implementation of scanning protocols as well as post processing procedures.

Goodbye SFINX - hello GNP

by Albert Gjedde

CFIN has had an affiliated graduate school, School of Functionally Integrative Neuroscientific Experimentation or SFINX. The Danish National Research Foundation, which funded CFIN as far back as 2001, originally wanted its centers of excellence to have a graduate school or at least to be affiliated with one. Graduate Schools in Denmark was a somewhat confusing concept, created as a consequence of the introduction of PhD-programs in the Anglosaxon tradition in the early nineties. The PhD degree was necessitated by foreign ignorance of traditional Danish degrees, which had three levels, Candidate (for example cand.med. for an MD), Licentiate (lic.med.), and Doctorate (dr.med.). It was difficult for foreign institutions to grasp that the lic.med. degree in practice equaled a PhD, for example in the U.S. Likewise, it was difficult to attract foreign graduate students with the prospect of acquiring a lic.med. degree. As a solution, the Danes scrapped the licentiate and called it a PhD instead and instituted formal training in science as a prerequisite for the degree. One interesting aspect of this revolution meant that anybody in principle could start a graduate school if the Ministry of Science, Technology and Innovation approved. At the start, the schools were associated with a nationwide Research Academy, which the Ministry of Science, Technology and Innovation later subsumed. In 2007, the Minister of Science, Technology and Innovation decided that only proper university faculties can be graduate schools, and the existing schools, including SFINX, became graduate training programs in official faculty graduate schools. SFINX was absorbed by the Faculty of Health Sciences at Aarhus University as its official Graduate Neuroscience Program (GNP). At the same time, GNP was expanded to include all graduate neuroscience students at the faculty. This means that GNP now has 104 PhD-students at Aarhus University and Aarhus University Hospitals. The GNP has a director, a board, and now also a GNP Consultant, who is Manouchehr Vafaee, PhD. He will function as the day-to-day contact person for students and supervisors. The GNP director is Albert Gjedde. In addition to PhD-courses, GNP also plans a summer school and various get-togethers. Also, an Aarhus chapter of the Society for Neuroscience is likely to be formed in 2008, and it is planned that all GNP students be encouraged to join.

2007 Publications

Peer reviewed articles:

Ashkanian M, Hjort N, Sølling C, Gyldensted C, Østergaard L. *Billeddiagnoastik af patofysiologien ved akut apopleksi*. Ugeskrift for Læger. 2007; s. 3369-3372.

Borghammer P. *Normalization of PET Group Comparison Studies - The Importance of a Valid Reference Region.* Neuroimage. 2007.

Borghammer P, Vafaee M, Østergaard K, Rodell A, Bailey C, Cumming P. (2007). *Effect of memantine on CBF and CMRO2 in patients with early Parkinson's disease.* Acta Neurol Scand. 2007 Oct 10; [Epub ahead of print]

Cumming P, Møller M, Benda K, Minuzzi L, Jakobsen S, Jensen SB, Pakkenberg B, Stark AK, Gramsbergen JB, Andreasen MF, Olsen AK. *A PET study of effects of chronic 3,4-methylenedioxymethamphetamine (MDMA, "ecstasy") on serotonin markers in Göttingen minipig brain.* Synapse. 2007 Jul;61(7):478-87.

De Pennington N, Cattrell A, Ray N, Jenkinson N, Aziz TZ, Kringelbach ML. (2007) *Neuroimaging of sensory and affective experience in the human brain.* CoDesign, 3:45-55.

Frandsen JF, Hobolth A, Vedel EB, Vestergaard-Poulsen P, Østergaard L. *Bayesian regularization of diffusion tensor images.* Biostatistics. 2007; årg. 8, nr. 4, s. 784-799

Frith CD, Frith U. *Social Cognition in Humans.* Current Biology 17, R724–R732, August 21, 2007.

Geake J, Kringelbach ML. (2007) *Imaging imagination: brain scanning of the imagined future.* Proceedings of the British Academy, 147: 307-326.

Geday J, Kupers R, Gjedde A. *As Time Goes By: Temporal Constraints on Emotional Activation of Inferior Medial Prefrontal Cortex.* Cereb Cortex. 2007 Dec;17(12):2753-9. 2007 Mar 1; [Epub ahead of print].

Gjedde A, [Peter Ludvig Panum (1820-1885)], Ugeskrift for Læger. 2007 Aug 27;169(35):2862.

Gramsbergen JB, Cumming P. *Serotonin mediates rapid changes of striatal glucose and lactate metabolism after systemic 3,4-methylenedioxymethamphetamine (MDMA, "Ecstasy") administration in awake rats.* Neurochem Int. 2007 Jul;51(1):8-15. Epub 2007 Mar 18.

Hall N, Gjedde A, Kupers R. *Neural mechanisms of voluntary and involuntary recall: A PET study.* Behavioural Brain Research. 2007; 12 s.

Hansen B, Jespersen SN. *Vandets tumlen giver viden om hjernen.* Aktuel Naturvidenskab. 2007 ; årg. 1, s. 10-13

Hjort N, Wu O, Ashkanian M, Sølling C, Mouridsen K, Christensen S, Gyldensted C, Andersen G, Østergaard L. *MRI detection of early blood-brain barrier disruption: Parenchymal Enhancement predicts focal hemorrhagic transformation after thrombolyssis.* Stroke. 2007.

Innis RB, Cunningham VJ, Delforge J, Fujita M, Gjedde A, Gunn RN, Holden J, Houle S, Huang SC, Ichise M, Iida H, Ito H, Kimura Y, Koeppe RA, Knudsen GM, Knuuti J, Lammertsma AA, Laruelle M, Logan J, Maguire RP, Mintun MA, Morris ED, Parsey R, Price JC, Slifstein M, Sossi V, Suhara T, Votaw JR, Wong DF, Carson RE. *Consensus nomenclature for in vivo imaging of reversibly binding radioligands.* J Cereb Blood Flow Metab. 2007 Sep;27(9):1533-9. 2007 May 9; [Epub ahead of print].

Jespersen SN, Kroenke CD, Østergaard L, Ackerman JJ, Yablonskiy DA. *Modeling dendrite density from magnetic resonance diffusion measurements.* NeuroImage. 2007 ; årg. 34, nr. 4, s. 1473-1486.

Johansen ML, Bak LK, Schousboe A, Iversen P, Sørensen M, Keiding S, Vilstrup H, Gjedde A, Ott P, Waagepetersen HS. *The metabolic role of isoleucine in detoxification of ammonia in cultured mouse neurons and astrocytes.* Neurochem Int. 2007 Jun;50(7-8):1042-51.

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CFIN Funding & Bibliometry

by Leif Østergaard

Funding

CFIN depends on the generous support of many funding agencies and institutions to continue its growth. Total personnel and running costs total over € 5 million – See Figure 1.

Funding Source 2001-2011 (DDK)	Total (DDK)	2007 (DDK)
Danish National Research Foundation	83.865.000	9.576.500
Public Grants (Including EU)	47.713.452	11.135.855
Private grants	44.076.414	7.582.768
Major Equipment (MRI, PET, MEG)	57.500.000	
Region Midtjylland		5.268.747
University of Aarhus		5.967.727
Total	**233.154.866**	**39.531.598**

Figure 1
Funding Source 2001-2011 (DKK)

The Danish National Research Foundation (http://www.dg.dk) remains CFINs largest funding source. With the critical mass of scientists and growing scientific impact resulting from this long-term investment, CFINs researchers increasingly attract competitive funding based on their scientific track-records and innovative ideas.

Funding also include important contributions from the Danish Councils for Independent and Strategic Research (http://www.fi.dk), the European Commissions Framework Programmes, and from the Royal Academy of Music and the Danish Ministry of Culture.

Experimental equipment in neuroimaging is expensive, modern scanners ranging from € 2 to €10 million. With the support of donations from The John and Birthe Meyer Foundation, Velux Fonden and in 2007 from the Danish Agency for Science, Technology and Innovation, CFIN has been able to remain competitive in terms of cutting-edge technology.

CFIN has received generous donations from private foundations supporting neuroscience, and extended fruitful collaborations with pharmaceurical industry.

CFIN is grateful to Aarhus University for the continuing support for key researchers and administrative staff, and to facilitate cross-faculty educational activities. Also, the financial support of Region Midtjylland, Aarhus University Hospital, Århus Sygehus and the Department of Neuroradiology (Edith Nielsen and Mona Bundgaard, chairs) and PET Center (Albert Gjedde, Helle Jung Larsen, chairs) remains crucial to maintain infrastructure for equipment and over 80 employees.

CFIN wishes to thank the financial support of the Foundations and Institutions listed below:

The Danish National Research Foundation
University of Aarhus
Region Midtjylland
TrygFonden
University of Aarhus Research Foundation
Århus University Hospital, Århus Sygehus
Department of Neuroradiology
PET-Center
The Danish Medical Research Foundation
Research Council for Communication and Culture
Danish Agency for Science, Technology and Innovation (ludomania)
Cambridge Health Alliance
The European Commissions 6th Framework Programme
Danish Ministry of Culture
Royal Academy of Music
The Lundbeck Foundation
Dansk Parkinsonforening
Novo Nordisk Foundation
Danish Council for Strategic Researchs Programme Commission on Non-ionizing Radiation
Danish Council for Strategic Researchs Programme Commission on Nanoscience, Biotechnology and IT
GlaxoSmithKline
BayerSchering Pharma AG
Toyota Fonden
The Carlsberg Foundation
Danish Cancer Society
The John and Birthe Meyer Foundation
Ulla og Mogens Folmer Andersens Fond
Hørslevfonden
Grosserer L.F.Foghts Fond
Augustinusfonden
The Denmark-America Foundation
Dagmar Marshall's Foundation
Julie von Müllen's Foundation (The Royal Academy of Science)
The Oticon Foundation.

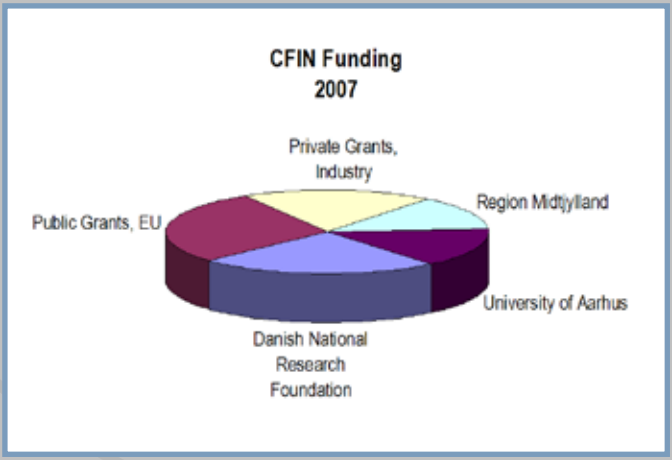

Figure 2
CFIN Funding 2007

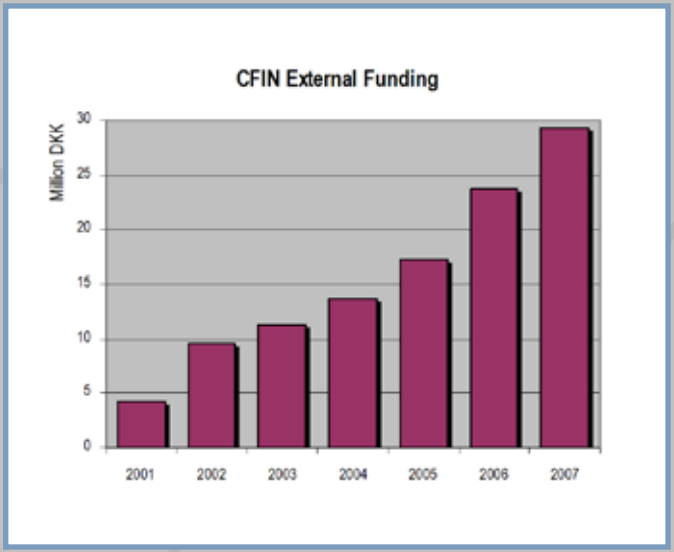

Figure 3
CFIN External Funding

The graph shows the net increase in external, competitive funding since the CFIN was founded by the Danish National Research Foundation's Centre-of- Excellence grant July 1st 2001. Note the steady increase in external funding as emerging ideas and scientific results attract additional grants. With a proportional increase in the number of PhD students and senior researchers, CFIN expects increased productivity in the coming years.

Bibliometry

Scientific and societal impact of CFIN research remains crucial to our mission and continued support.

Impact Factor	2001	2002	2003	2004	2005	2006	2007
Impact Factor 0-1	6	4	12	8	8	3	12
Impact Factor 1-3	8	10	8	9	13	15	12
Impact Factor 3-5	7	6	6	5	8	13	8
Impact Factor 5-7	5	5	7	3	5	7	9
Impact Factor 7-	0	2	2	0	3	2	6
Total	26	27	35	25	37	40	47

Figure 4
Publication Impact Factor *

* As of this year, publication data have been standardized to reflect the year manuscripts appear in print (Electronic publication precede the printed journal by several months). The 2006 CFIN Annual Report bibliometric analysis for 2006 was performed according to date of electronic publication.

The table shows the total number of CFIN publications appearing in journals with peer review since 2001. Publications are subdivided according to Journal Impact Factor. Some publications in the Journal Impact Factor 0-1 are in Danish.

In 2007, total journal publication numbers reached its highest level ever, reflecting the steady increase in CFIN funding and recruitment of researchers over recent years.

We are especially proud that an increasing proportion of CFIN research was published in high-impact journals within our field: One-third of all journal publications in 2007 appeared in Journals with Impact Factor higher than 5.0.

While Journal Impact Factor is low for manuscripts published in Danish peer-reviewed Journals, these publications remain important to increase public awareness of neuroscience and brain diseases in general, and of CFIN research in particular. Publications in Ugeskrift for Læger hence reported important break-throughs in translational neuroscience, originating from basic CFIN research.

Furthermore, CFIN researchers published research and overviews in books that will become future reference within neuroscience and cognition research.

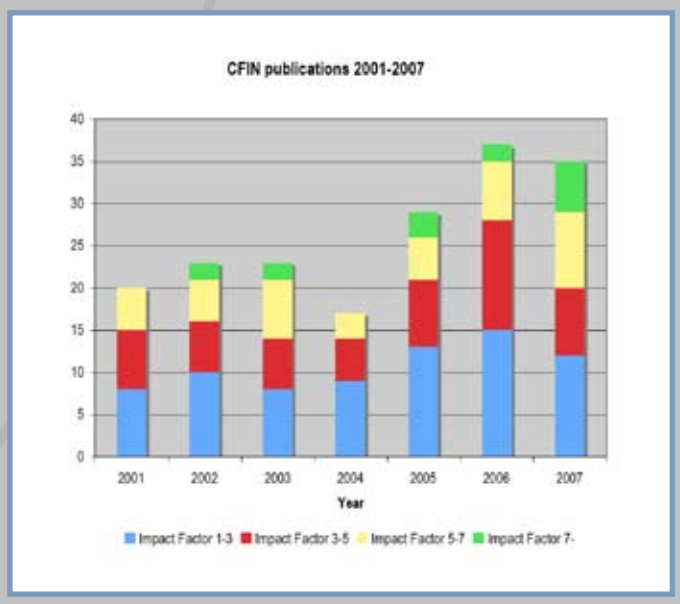

Figure 5
CFIN Publications 2001-2007

neuroinformatics
emotion
functional hemodynamics
neurotransmission
brain
MEG
neuroconnectivity
fMRI
neuroenergetics
subject
stroke

ISBN 978-87-992371-0-4