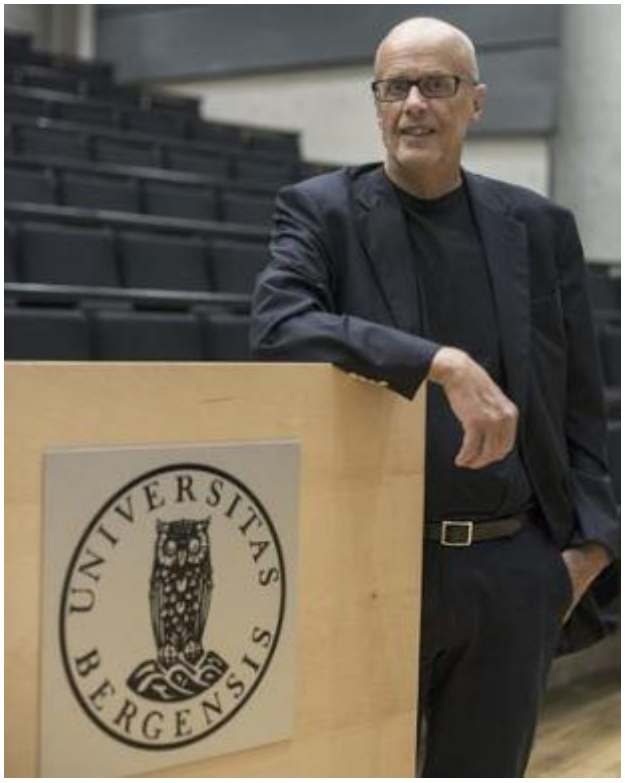
Interview with Professor Kenneth Hugdahl



Professor Kenneth Hugdahl. Photo: Thor Brødreskift

Background

Professor Kenneth Hugdahl from Department of Biological and Medical Psychology, UiB was born in Östersund, Sweden. -How was it to grow up in Östersund?

-You know, Östersund is a small town in the northern part of Sweden. I have a blue collar working class background. I was the only one in our family and among our relatives who went to the gymnasium, Professor Kenneth Hugdahl memorizes.

-Where did you carry out your University education?

-Actually, I started as a law student at University of Uppsala in 1967, but the law topics did not match my intellectual interests, so I was looking for something more challenging. Then we reached 1968 and everything "exploded" in the society, so to say, facing hippies (a liberal counterculture) crowding in the parks in almost all the big cities in USA and western Europe, facing the student riots in Paris where the French workers joined the student protests for the first time with a one-day general strike, and facing new music forms like rock and psychedelic music genres. However, people in the law school were not at the forefront to adapt to these overwhelming new megatrends. As a young student I was strongly influenced by the trends and decided to go on with studies of social science and economic history. I also studied psychology because I was academically interested in the brain, the mind and the function of the body, but did not touch brain and behavior in my lower degree studies, Kenneth says.

-Later, when I did my psychology studies, I did a thesis (similar to Master) under supervision of Arne Öhman (later Professor at the Karolinska Institute, Stockholm), and for the first time I did research in biological psychology, studying brain and behavior. The equipment at that time was however far from what we have available today. We performed crude measures of the galvanic skin response, to monitor sweat glands in the fingers as sensors of mental states. The responses from the sweat glands were indirect measures of the autonomous nervous system, and the funny thing is that we nevertheless got reliable data, measured 1 m away from the brain, Kenneth adds with a smile. We applied this to studies of emotional states and in particular phobic anxiety, which became the topic of my PhD-thesis in 1977, entitled "Conditioning, stimulus relevance, and cognitive factors in phobic fears", Professor Hugdahl tells.

-Then I was lucky when I got the opportunity to go to the USA for a postdoc period in Philadelphia in 1979 -1980. I went there together with my wife Märit and our four years old daughter. It was a rough

city at the time, and we learned to cope with strange situations that challenged our way of living. There was a clear segregation between different social cultures and a lot of crime, which caused latent fear or uncertainty. All in all, it was an experience for life time for the whole family and I became part of an interesting scientific network this way. Märit studied initially English and History and worked as a teacher in Uppsala. Later she became a special educator for individuals with special needs, when we came to Bergen, and gradually she became a speech therapist as an expert in languages. My lovely wife has thus been my language advisor for some of my later studies on brain asymmetry, Kenneth explains.

- In 1980 we went back to Sweden and I continued my work in Uppsala. In the meantime my earlier supervisor Arne Öman had moved to Bergen as Professor in 1976 but he never really settled down here, never accepting the traffic jam to Åsane and the rain(!), so he returned to Uppsala in the early 1980s. He suggested at a lunch we had one day; "Why don't you apply for my professorship in Bergen? At UiB they will eventually take good care of you, whereas in Uppsala the future is more uncertain because the Academia here is probably more competetive, not easy to handle for a 34-year young man." I followed Arne's advice and submitted an application to the University of Bergen, Kenneth memorizes.

-The application review took almost two years. In January 1984 I received the letter telling that I was ranked as No. 1, which was really a turning point and a highlight of my career. Still, I was in doubt because I had not thought thoroughly through this alternative. Then my wife Märit again said "Why don't we give it a try?" She had seen some brochures from Bryggen exposing fantastic seafood and became inspired. I thought: "It might not hurt to go there and build my career, at least for a few years." Now, I am still here after 32 years with four Norwegian (!) grandchildren. It is funny how life can take new directions. I must add that we really felt us welcome in Bergen from the very first day. Quite early University Director Magne Lerheim arranged a conference at Bellevue and said hello(!) in an informal way, I was positively surprised that the University Director knew my name as a new young professor. I was also positively surprised by the non-authoritarian style in UiB Academia. Later the same year I also got to know Professor Johan H. Aarli from Department of Neurology at Haukeland University Hospital (HUH) when he gave a presentation about an author who had epileptic experience. Professor Aarli also said hello (!) and welcomed me to Bergen, and I immediately felt part of the Academic community here. In fact, I don't like people who behave with ignorance or arrogance, but here I was met with the opposite and with positive attitudes, which indeed was inspiring. Later I was invited to apply for new positions at both Lund University and at Karolinska Institute in Stockholm, and also in the US, but we felt so welcome here and additionally I got all the opportunities to develop my research in brain and behavior that we decided to stay in Bergen. I started also with EEG (electroencephalogram) and what is called ERPs (some minor changes in the EEG signal related to presentation of sensory stimuli), here and I received a research grant from UiB. The grant was entitled "*Event related signals tied to a specific cognitive stimulus"*. Together with Helge Nordby from the Department of Somatic Psychology, we established the Laboratory in the *Fellesbygget* at Årstad, and it actually became the first ERP research-lab in Norway. In this context, it is interesting to note that UiB and HUH now are making huge plans for establishing *«Helsecampus Årstadvollen»* in this area, Professor Hugdahl says.

Bergen fMRI Group

-You are the Research Group Leader of Bergen fMRI Group. What is the short version history behind the origin of the fMRI-group?

-Before I answer that question I have to tell you about a very inspiring paper from 1991 in Science (Bellevieau *et al.*, 1991) that showed an area of the brain that was lit-up when the subject had been exposed to intermittent flickering light stimuli, and which reflected increased blood supply and oxygen consumption by this part of the brain. This confirmed that certain neurons in the occipital cortex showed functional specificity that was tuned to visual stimulation. Due to my already established network in USA, I had become member of a mind-body MacArthur Foundation network and I was monthly or bi-monthly travelling to USA in that period. One of the authors of the 1991 paper came to one of the network meetings and he showed a video of how this part of the brain reacted when the light was turned on and shut-down when the light was turned off, i.e. this part of the brain was evidently processing information and we could see it when it happened, Professor Hugdahl explains. -I remember that we all sat there astounded by what we had just seen.

-On this background, Håkan Sundberg, Lars Ersland, Alf Inge Smievold, Arvid Lundervold, Kjell Inge Gjesdal and Terje Tillung, also including myself, got the bright idea to join forces and establish the Bergen fMRI Group in 1993. Lars Ersland got permission for us to use the 1.0 Tesla MR scanner at Haukeland University Hospital one night a week for research, but the magnetic field strength was actually not high enough for the EPI (echo planar imaging) pulse sequence that we needed to acquire fMRI data, but Arvid and Lars wanted to try it anyway, and they worked it out with another sequence (Figure 1).

Figure to the left shows interior of the very first BOLD-fMRI acquisitions in Norway, at Haukeland University Hospital, autumn 1993. Kenneth Hugdahl is himself the «guinea pig» in the Figure.

Figure to the right shows the resulting brain activation from the first experiment in the visual cortex after repeated periods of flickering light, alternated with periods of darkness, published in Lundervold, Ersland, Gjesdal et al., 1994

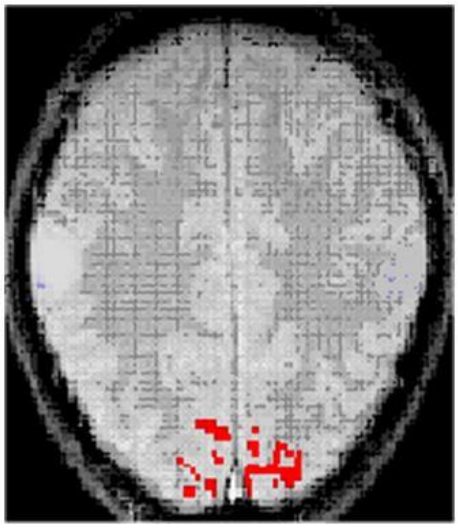


Figure 1. Professor Kenneth Hugdahl became the first volunteer subject for the first fMRI investigation of the brain in Norway in 1993.

We borrowed a flicker-lamp from the Neurology Dept. at HUH that we used as our first stimulus source. We were allowed to use the MR- scanner every Thursday night (1700 - 0700) after the dayshift at the Radiology Dept. at HUH and did pioneering research during the nighttime. We replicated within a few weeks what they had accomplished at Harvard University two years before. The subjects had their head in a headcoil (looks like a helmet) inside the MR scanner. The coil had opening for the eyes, where we taped a mirror so that the subjects would receive the light flickers at 30 or 40 sec. intervals, and I became the first volunteer subject for the first fMRI investigation of the brain in Norway, which was in September or October 1993, if I remember correctly. As you see, the experimental set-up was a bit primitive, however, it worked and we collected loads of experimental data. Today the protocols are of course much more advanced and computer automated down to millisecond synchronizations. We were quite euphoric the night we managed to show the first brain activations to light in the visual cortex, and published a conference abstract (Lundervold *et al.* 1994) and a paper the year after (Lundervold *et al.* 1995) on fMRI of primary visual cortex. This represented a kind of a breakthrough for the Bergen fMRI Group, Professor Kenneth Hugdahl explains. See also http://www.uib.no/en/rg/fmri . The history of the Bergen fMRI Group was filmed some years ago, and the video can be seen on YouTube; https://www.youtube.com/watch?v=6UhfAX3RusE

-Based on this enthusiasm we tested the one complex cognitive phenomenon after the other: e.g. monitoring phantom pains in the arm and the fingers in a patient that had lost his arm. We asked him to move his fingers by imagination and noticed that the brain responded during these movements as if the fingers were still there. We even tested subjects who meditated in the scanner, and when subjects had to perform arithmetic calculations, or to decide if a string of letters made up a real word or not, but the results and conclusions were not always clear and easy interpretable. Anyway, all the enthusiasm from this pioneering period strengthened the research cooperation between colleagues both in Norway and internationally, and we slowly became part of the international functional imaging community. Based on the wave of constructive interactions, the fMRI Group was also involved in the startup of MedViz around 2006, and of the NordicNeuroLab a/s company in 2001, he adds.

-fMRI has now spread all over the world, and it is today perhaps more important to focus on what fMRI *cannot* do than what it actually can do. We have to be critical. Today we have several imaging modalities available, and fMRI is only one modality. We also need brain structure information and to map neural tracts between different parts of the brain as well. Presently we talk more about cortical networks and interactions between networks, than isolated activated areas, which we relate to e.g. psychiatric disorders, like schizophrenia. A hot topic today is to move beyond the classic functional imaging level, and look into how neurotransmitters modulate the activation observed at the fMRI imaging level, like glutamate and GABA, by using MR spectroscopy. We have thus recently established an informal subgroup, led by Dr. Renate Grüner, who is looking into the opportunities of MR spectroscopy. We have a PhD student, Gerard Dwyer, and a research technician Alex Craven hired to specifically work on MR spectroscopy, Kenneth tells.

European Research Council (ERC) Advanced Grant

Professor Kenneth Hugdahl has now received his 2nd prestigious ERC Advanced Grant. This has only happened once before in Norway by Nobel Laurate Edvard Moser from NTNU. Both grants are for the study of brain markers of auditory hallucinations in schizophrenia.

-What are the conclusions from your first grant period (2011-2015) and the main aims for the 2nd grant period (2016 – 2020)?

-In the 1st grant period we concluded that there were areas in the speech perception region in the temporal lobe (Figure 2) that were spontaneously activated in the schizophrenia patients who heard hallucinated voices, in the absence of an external speaking person. When a speaking person's voice was presented simultaneously with the inner voices, it looked like the inner voice blocked the outer voice, and the activation to the outer voice disappeared. It may be important in this context to point out that any mental phenomenon, also auditory hallucinations, can be explained at what I have called "levels of explanation". Hallucinations can be explained from cultural, religious, social and all the way down to "wet" physiological and molecular levels. As researchers, we have a tendency to stay at our "favorite" level, and expand horizontally by adding ever more sophisticated methods and analysis tools, but all the time at the same level. The challenge is, however, that we need to move vertically through these levels and test our hypotheses at different levels, only then can we move our science forwards, Hugdahl explains. -We then had the idea at the end of the first grant period that in order to understand what caused these spontaneous fMRI activations in the temporal, and other lobe areas, we had to get down to the transmitter and receptor level of explanation, and we hypothesized that the transmitters glutamate and GABA may play a critical role in this respect.

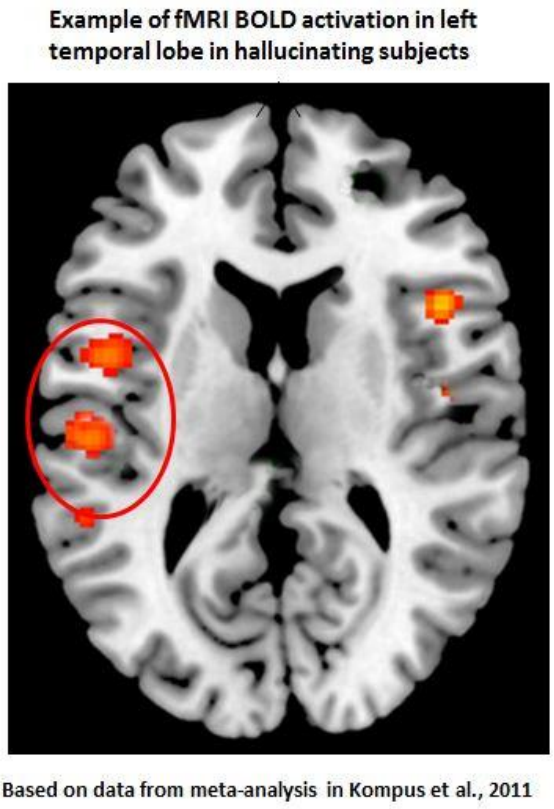


Figure 2. Figure from the 1st ERC Advanced Grant period.

-In the 2nd grant proposal, we continued the discussion that schizophrenia patients are preoccupied by the voice, but no one has this inner voice turned on continuously. So there must be a turn-off signal. We also asked questions how about the fluctuation of the voices over time? This must have something to do with brain chemistry. The balance between excitatory and inhibitory transmitter signals could be of interest for pharmacy industry. If we could re-open the 60 years old so called dopamine-hypothesis for schizophrenia, and complement with suggestions for drugs tailor-made for a specific symptom rather than the diagnosis itself, pharmacy could perhaps further develop this. Earlier I did not focus too much on the applications of our science, but today I realize that a first priority is always to help the patients, based on our scientific knowledge and approach, Professor Hugdahl states.

-When it comes to funding of science, Professor Edvard Moser from NTNU once said that ERC is “God’s gift to mankind”. I have in other contexts said that there is a clear distinction between

"science" and "research", although we tend to treat these words as synonymous. Science does only need an idea, whereas research needs time, resources and money to test the idea. Research funding today has put too much focus on research, collaborations and networks, and organization, to the expense of science. Horizon2020 is extreme in this context because they first decide what you should do research on, like a 5-years communistic plan, then you get caught in a bureaucratic reporting system. FRIPRO and ERC are honorable exceptions. ERC has established an algorithm for the evaluation of proposals based on the ratio of high gain/ high risk: High-risk applications have high gain if they are successful, Kenneth adds.

-The grant review of our 2nd ERC Advanced Grant was performed by 10 Reviewers who used a 6-graded scale on five criteria and weighted the final scores in one overall grade. Out of the 50, we got 30 outstanding scores (best), 18 excellent (second best) and 2 very good (third best) scores. I believe that the key to success in ERC, is an extremely focused hypothesis, with simplicity and common sense as important aspects of every ERC application. In order to test the hypothesis, or view, of balancing transmitters, I wrote that I only needed a small expert group of four persons that already had the necessary skills, else we would have to spend too much time to train them. ERC does not have so much training function, so here we will focus on science, Kenneth says.

-My scientific career is a long story and within two years I will turn 70 and eventually retire, so we will see how this story ends. As every other scientist I have also had my disappointments and down-periods, and it has certainly not been only up-hills strolling. For example, I was Principal Investigator for a SFF initiative in 2006 and *Bergens Tidende* wrote that this proposal was expected to win, but two days before Christmas I received a message on my computer screen in the office that "Oslo took the grand slam", and that our proposal was not among the funded ones, not the best Christmas I have had, Hugdahl remembers. I have had many grant proposals turned down, but one should strive at having at least 51 % of them accepted to survive. My final advices to young researchers are therefore: Never, ever give up! When you apply for funding, stick to your ideas even if they seem crazy, do not back out just because others have turned down your ideas. It is the science that matters (!), Professor Kenneth Hugdahl concludes.

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