Thirty thousand years ago one of our distant ancestors crept inside a cave in south-eastern France carrying a flaming torch and some paint. Deep inside the cave she found a smooth vertical wall, placed her right hand against the rock and blew paint over it to leave an outline (Fig. 1). These stenciled hands are amongst the earliest painted images in Europe and they heralded a creative stream of 'art' objects, including realistic carvings and paintings, jewelry and even musical instruments, such as bone flutes. When we now look around us, the art and tools we have created are ubiquitous and uncountable, yet the extraordinary thing is, our brain is in shape and size no different from that of our ancestors of 100'000 years ago: we still have the brain of a Paleolithic human.

How is it then that by the age of three, we have...
already acquired competences that would be quite unknown to the adult Paleolithic man or woman? What really has changed in our brain since the Stone Age? In this short time we can effectively rule out any mutations in genes between Upper Paleolithic humans and ourselves so it seems that the major change is in the way we use our brains. Probably the principal component of this 'plasticity' is the neocortex and its connections, which form 85% of volume of the human brain. The principal aim of NCCR Project 5 on Cortical Plasticity is to discover how the networks of the adult neocortex reorganize functionally and structurally during the acquisition or improvement of skills. Remarkably, with just 5 subprojects, all the major lobes of the primate’s neocortex are being explored. This breadth is highly unusual, but it provides us with a multilevel approach that combines structure and function, perceptual and motor learning, and cognitive processing in human and non-human primates.

It has been common amongst philosophers and psychologists to use the image of a Swiss Army knife to describe the functional organization of the neocortex. In this metaphor, the neocortex is viewed as a number of modules, each of which has a specialist task. Thus, the cortical modules are packed together in the same unit, like the components of the Swiss Army knife, but they are not designed to work in concert, as in a ma-

Peter Thier
Professor of Cognitive Neurology*

*Hertie-Institute for Clinical Brain Research, University of Tübingen, Germany, and member of the NCCR Neuro International Review Panel
cerebral regions.' His hypothesis is easily stated, but after a century of work we still are far from understanding even how the cortex reorganizes itself as it learns. Project 5 is an ambitious research program that will certainly require a great deal of mental exercise on the part of the scientists involved, but such exercise will take us another step toward understanding how we can best use this great gift we have inherited - a primate neocortex.

Kevan Martin
Leader of Project 5
Institute of Neuroinformatics,
University and ETH Zurich

In contrast, in the intraparietal sulcus, modulation by visual similarity was found such that new items that were visually different evoked less activation than new items that resembled the prototypes. Adapted from Yago & Ishai, Neuroimage, 2006.

already the results of Project 5 suggest a different view - one in which the neocortical sheet is seen as a highly connected, dynamic network with many more cross-modal interactions than the modular hypothesis envisages. This new view develops from our quest to identify how the networks of cortical areas interact with each other for a given task. For example, what happens in neocortex when we learn ‘prototypes’ for classifying complex images, such as paintings (Fig. 2)?

The gestures we make are also learned. From an early age we learn about the properties of objects: we come to shape our hands appropriately as we reach to pick things up; we anticipate their weight, their temperature and their texture; we decide whether to use a precision or a power grip (see Fig. 3). These actions, which we perform with effortless ease as adults, require an enormously detailed interaction between a number of senses to arrive at a coherent perception of the object and very sophisticated motor planning and control. It is clear from the tools they made and the art objects they created that the people who made the earliest cave paintings had these hand-eye competences coupled to a vivid imagination of the animals they painted. One of the major goals of Project 5 is to understand how the neocortex learns these perceptual and motor skills.

Over a century ago, the great Spanish anatomist Ramon y Cajal speculated that ‘Cerebral gymnastics are not capable of improving the organization of the brain by increasing the number of cells….but it can be admitted as very probable that mental exercise leads to a greater development of the dendritic apparatus and of the system of axonal collaterals in the most utilized cerebral regions.’ His hypothesis is easily stated, but after a century of work we still are far from understanding even how the cortex reorganizes itself as it learns. Project 5 is an ambitious research program that will certainly require a great deal of mental exercise on the part of the scientists involved, but such exercise will take us another step toward understanding how we can best use this great gift we have inherited - a primate neocortex.

Kevan Martin
Leader of Project 5
Institute of Neuroinformatics,
University and ETH Zurich
AWARDS

Sönke Boy, member of Project 7, was awarded the Best Poster Prize by the European Association of Urology at the EAU 2006 on 8 April 2006.

Volker Dietz, Co-Leader of Project 7, was awarded the prestigious Sobek Research Award for his achievements in understanding the locomotion control in health and disease, in particular in spasticity, on 10 November 2006.

Volker Dietz was awarded the distinguished Heiner Sall Lectureship in recognition of outstanding service and leadership by the American Spinal Injury Association in June 2006.

Rudolf Glockshuber, member of Project 2, received the Max-Bergmann Medal 2006 from the Max-Bergmann Kreis zur Förderung peptidchemischer Arbeiten for his contributions to the area of protein folding on 11 October 2006.

Mathias Heikenwälder, member of Project 6, received the Empiris Award for Research on Brain Diseases for his research on prions on 7 November 2006.

Christoph Hock, member of Project 2, received the Dorian Prize 2006 in recognition of his outstanding achievements in Alzheimer research on 6 November 2006.

Alumit Ishai, member of Project 5, was awarded the Young Investigator Award in Cognitive Neuroscience 2006 given by the American Cognitive Neuroscience Society for her fMRI studies on the representation of objects and faces in the human brain.

Thierry Keller, member of Project 7 and 8, and Klaus Schönberger received a Diploma CTI member of Project 8, received the Student Prize of the German, Austrian and Swiss Society for Experimental Biology on 24 February 2006.

Robert Riener, member of Project 1, won the GS K Neural Stem Cell FENS Research Award 2006 in recognition of his outstanding and innovative scientific work in neural stem cell research on 12 July 2006.

Joachim von Zitzewitz, member of Project 8, was awarded the Förderpreis for the Best Diploma Thesis on control strategies for robot-aided gait therapy by the Alumni Association at Graz University of Technology on 18 October 2006.

Björn Zörner, member of Project 7, won the Best Poster Award at the Combined Scientific Meeting ASIA / ISCOG on 28 June 2006.

PUBLICATION HIGHLIGHTS

Multiple Sclerosis


A novel therapeutic strategy for the treatment of multiple sclerosis (MS) is proposed. This inflammatory demyelinating disease of the CNS involves loss of axonal integrity leading to progressive neurological deficit. Although the precise aetiology of the disease is unclear, it is widely held that an autoimmune attack against neuroantigen is the underlying cause. In the animal model of MS, the immune cells responsible for causing damage to the CNS are a subtype of T cells known as CD4+ T cells. However this pathogenic cell type must initially be instructed by antigen presenting cells (APCs) to perform the attack; thus our goal was to understand the communication between CD4+ T cells and such APCs during autoimmunity. We discovered that the expression of IL-18 receptors on APCs is absolutely vital for driving disease-inducing T cell yet independent of its known ligand, IL-18. By blocking this communication pathway, we were able to prevent CNS destruction without disturbing the normal defense mechanisms of the immune system.

Molecular Imaging

Basic Principles and Applications in Biomedical Research

Markus Rudin, Imperial College Press

Markus Rudin, leader of the Center for Animal Imaging, introduces in this book basic aspects of molecular imaging technology and probe design and presents numerous examples from current research. Molecular imaging is a rapidly emerging field that translates concepts developed for molecular biology and cellular imaging to in vivo imaging of animals including, ultimately, humans. Molecular imaging approaches will therefore become indispensable tools for biomedical research including drug discovery and development.