





## **ESF-FENS The Brain Conference**

# The Neurobiology of Action

20-24 October 2013 Hotel La Palma, Stresa, Italy

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http://www.esf.org/conferences/13426

# **Highlights & Scientific Report**

## **Conference Highlights**

*Please provide a brief summary of the conference and its highlights in non-specialist terms (especially for highly technical subjects) for communication and publicity purposes. (ca. 400-500 words)* 

The output of the nervous system is coordinated movements, "whether whispering or felling a forest" as formulated by C.S. Sherington long ago. The focus of the meeting on Neurobiology of Action was to address the control of action at different levels of organization. We first analyzed the microcircuits responsible for generating different motor patterns like that of walking, breathing and eye and orienting movements. When these circuits are turned on a given type of movement will be generated with appropriate timing between all the different muscles. In the last few years, through a combination of genetics and electrophysiology the operation of these circuits is now to a large degree understood at the cellular, synaptic and network level. This is important also from the perspective of designing novel ways of therapy for movement disorders.

The next level of control deals with the neural mechanism underlying the selection of when a given motor program should be recruited. This is a form of decision-making, in which the basal ganglia, a forebrain structure, play a prominent role. Novel approaches show that the basal ganglia contain circuits that initiate behavior by releasing motor programs from inhibition, while conflicting motor programs are instead suppressed. Moreover, these circuits are critical for the control of behavior and maintain all the different motor circuits under tight control. The basic design of these decision-making circuits has been conserved throughout vertebrate evolution and thus was "invented" already at the dawn of vertebrate evolution. Similarly, the dopamine innervation has been conserved. Recent findings show that different dopamine neurons are engaged in the control of the frontal lobe, the ventral and dorsal striatum respectively. The dopamine neurons play a role in se

tting the responsiveness of striatum, the input level of the basal ganglia, but it also plays a major role for motor learning and the formation of habits. They provide information about whether an action has been successful or if it has led to a negative experience/as aversion. These circuits thus underlie value-based decisions, a critical function in all animals, including man. The entire complex of the basal ganglia, the dopamine system, habenula and amygdala that have been enigmatic, is now understood partially, even at the microcircuit level. These circuits are also central for an understanding of not only Parkinson's but also a number of other neurological and psychiatric diseases, current findings promises to lead to possibilities for targeted therapy in a longer perspective.

Finally, the role of neocortical circuits was discussed and in particular high performancebrain-machine interfaces that can enable a control of robotic appendages represent a rapidlydeveloping technology. It can enable, for instance paraplegic patients (with spinal cord injuryat a very high level) to interact with the environment through a robotic arm manipulatedifferent objects and also eat. This represents a major advance requiring, however, a highlevel of technology with recordings of hundreds of different neurons in the brain.All in all, a fascinating sequence of lectures combined with active contribution of younger*ESF-FENSThe Neurobiology of ActionScientific Report* 

researchers created an atmosphere with creative interaction towards an understanding of how the nervous system controls our actions.

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## **Scientific Report**

#### Executive Summary (2 pages max)

The meeting on The Neurobiology of Action is one of a series of meetings organized jointly by European Science Foundation (ESF) and the Federation of European Neuroscience Societies (FENS). The meeting was held in Stresa, Italy in October 20-24, 2013 and consisted of a series of lectures by established researchers in the field from Europe, the US and Asia. Altogether 32 lectures were given and in addition there were two poster sessions.

The purpose of the meeting was to analyze the mechanism by which the nervous system controls action, in particular the cellular and systems bases of behaviour.

- We first analyzed the microcircuits that are responsible for generating different types of movements like those of breathing, eye and orienting movements, locomotion and voluntary limb movements. A great progress has been made in understanding the spinal circuits in lower vertebrates, like zebrafish, lamprey and amphibian tadpole in terms of the detailed circuitry with synaptic interaction and the importance of cellular properties and even a subdivision in the circuits driving locomotion at different speeds in the zebrafish. The mammalian locomotor network is more complex due to the limb control with a complex motor pattern, but also in this case with a combination of genetic markers and neurophysiological approaches, we are relatively close to an understanding of these circuits. It turns out that the same subtype of interneuron responsible for burst generation in the zebrafish, lamprey and tadpole are also important for the mammalian locomotor generation. The mammalian locomotor network is subdivided in smaller units that can control each synergic muscle group. This part included eight presentations.
- The next sections dealt with spatial navigation. In order to function we need to direct our movements to a particular goal and remember the path we like to take. The neural substrate for this important faculty has been studied in insects that can find their way back to their nests over many kilometers, but the focus in vertebrates has been on neural circuits in hippocampus and the entorhinal cortex. This part included four presentations.
- The next section dealt with 'The Extended Basal ganglia Roles for action selection, habits, value and learning'. The basal ganglia are of critical importance for determining which specific motor behaviour should be initiated in a given moment. The understanding of this circuitry is developing very fast. This includes the microcircuits at the input level, striatum and the input from the cerebral cortex and equally important directly from thalamus. The focus in the literature has recently been on the cortical input, while the thalamic input has been overlooked to some degree. In addition, the dopaminergic innervation sets the sensitivity of the striatal circuits, which

also can be modulated by 5-HT, histamine (diurnally) and oxytocin. The downstream control of the output via the direct pathway can help to initiate a given motor pattern like saccadic eye movements and locomotion, while the indirect pathway can prevent activation of motor patterns that are not compatible with the movement initiated. The dopamine innervation plays a major role also to signal whether an action has been successful or conversely negative. The enhanced reward activity can initiate synaptic plasticity, particularly at the input level, to striatum and thereby create a neural substrate for the formation of new habits. The responsible circuits also involve the thalamic loop back to cortex and not only the direct input to brainstem motor centres. This part included fourteen presentations.

• The following session dealt with the role of pallium/cortex in the control of action. The cerebral cortex and its counterpart in birds and lower vertebrates, the pallium, are important in this context, and in particular the frontal lobe. There are two major outputs from cortical pyramidal neurons, one activating directly brainstem motor centres and the spinal cord, and a second that targets striatum and represents a major input to the basal ganglia, presumably important for decision-making.

One major focus was on different forms of brain machine interactions in terms of both the ability to utilize signals from the primate brain and population of cells to control robotic arms and manipulate objects in a quite successful manner and also bidirectional interaction between the brain and implantable computers as well as the specific types of processing going on in sensory motor modules. The intricate role of cerebellar modules was also discussed. This section contained six presentations.

### Scientific Content of the Conference

(1 page min.)

Summary of the conference sessions focusing on the scientific highlights
Assessment of the results and their potential impact on future research or applications

The conference included the leading researchers in this field of brain science from all parts of the world and included also briefer presentations of younger researchers. The main lectures were 40 minutes long including discussion of the particular topic. We also had rich time for informal discussions after each session to be able to extract generalities as well as identifying remaining questions to be addressed. The meeting had altogether 32 lectures and was divided into the following sessions:

- The Neural Underpinning of Specific Patterns of Behaviour
- Spatial Navigation, role of hippocampal/entorhinal circuits
- The Extended Basal ganglia Roles for action selection, habits, value and learning
- Role of Pallium/Cortex in the control of action
- Role of cerebellum in Action
  - In addition, we had two poster sessions which resulted in a good interaction with

lively discussions between the participants.

#### Forward Look

(1 page min.)

Assessment of the results

Contribution to the future direction of the field – identification of issues in the 5-10 years timeframe
 Identification of emerging topics

The meeting on *The Neurobiology of Action* is one in a series on Brain conferences organized initially in interaction between FENS and ESF, and these meetings will continue as collaboration between FENS and the Grethe Lundbeck's Foundation organizing the Brain Prize. The topic of this meeting is very central to an understanding of integrative brain science and includes the mechanism by which the nervous system makes decisions. In the future, the planning committee for the conferences may return to the central theme of this meeting.

Is there a need for a foresight-type initiative?

I think it would be very useful to have a foresight initiative on integrative neuroscience, particularly directed towards accounting for brain function from the level of microcircuits (like cortical columns or motor programs) and how this information can be integrated to account for function at the systems level. There is a gap in current neuroscience between on one hand the cellular and microcircuit level and on the other global brain function. To bridge this gap represents a major challenge for neuroscience and is of critical importance if we are to understand the brain based on knowledge at the cellular and synaptic level. Such knowledge is also critical for an understanding of the many neurological and psychiatric diseases that represent a burden for the individual, their families and society.

#### **Business Meeting Outcomes**

Election of the Organising Committee of the next conference
Identified Topics
Next Steps

This series of conferences is organized in collaboration between ESF and FENS by a joint committee chaired by Professor Pico Caroni, Friedrich Miescher Institute for Biomedical Research, Basel.

#### Atmosphere and Infrastructure

• The reaction of the participants to the location and the organisation, including networking, and any other relevant comments

The location of the conference at Stresa was in principle a very nice location, although during the few days of the conference it happened to be misty and rainy. The hotel was excellent and the staff very helpful. The arrangements with the lecture hall and for the posters were appropriate. Overall the premises were very stimulating and invited to creative discussions in an informal setting.

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Date & Author: January 31, 2014 Sten Grillner, Professor and Chair of the meeting