

Torsten Wiesel: twenty nine years after his Nobel Prize



Torsten Wiesel after his lecture at IISc, 15 November 2010 (Courtesy: Mukha Wiesel)

Neuroplasticity is the ability of the brain to change as a result of one's experience, by forming new neural connections. Does the age at the time of experience matter in the efficient manifestation of this capability? Do we 'learn' to use our senses and do they adapt or change with external experiences?

'Do we learn to see?' was the topic of the Indian Institute of Science (IISc) centenary lecture by Torsten Wiesel on 15 November 2010 in Bangalore (Box 1). Wiesel received the Nobel Prize in Physiology or Medicine in 1981, together with David H. Hubel and Roger W. Sperry. The press release by the Nobel Assembly at the Karolinska Institute on 9 October 1981 emphasized the importance of their discoveries, 'For a long time it was thought that the retinal image was transmitted point by point to visual centers in the brain; the cerebral cortex was a movie screen, so to speak, upon which the image in the eye was projected. Through the discoveries of Hubel and Wiesel we now know that behind the origin of the visual perception in the brain there is a considerably more complicated course of events. By following the visual impulses along their path to the various cell layers of the optical cortex, Hubel and Wiesel have been able to demonstrate that the *message about the image falling on the retina undergoes a step-wise analysis in a system of nerve cells stored in columns. In this system each cell has its specific function and is responsible for a specific detail in the pattern of the retinal image*¹'. An account of the impact of their work, by S. P. Arun, is given in Box 2.

From being a faculty member at the Johns Hopkins Medical School, the Harvard Medical School and The Rockefeller

University to becoming President of The Rockefeller University to serving as an advisor in creating research opportunities for young scientists, Wiesel's contributions encompass many spheres. He has also served as the Chair of the Committee of Human Rights of the National Academies of Science, USA and the International Human Rights Network of Academies and Scholarly Societies for 10 years (1994–2004).

Wiesel has won many awards, including the Dr Jules C. Stein Award (1971) from the Trustees for Research to Prevent Blindness and the Hellen Keller Prize for Vision Research (1996) from the Hellen Keller Foundation for Research and Education. The World Eye Organization has set up the Torsten Wiesel Research Institute in China (2007) to focus on research, particularly on the most common Asian eye diseases. Wiesel is, at present, the Director of the Shelby White and Leon Levy Center for Mind, Brain and Behavior at The Rockefeller University and also serves on many advisory boards.

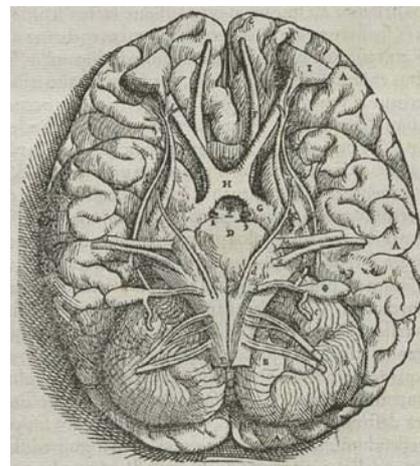
A short interaction with Wiesel is presented here.

*In your autobiography at the time of the Nobel Prize, you said 'I was a rather lazy, mischievous student, interested mainly in sports*²*'. What triggered your sudden interest in academics?*

I was about 18 years old when I began to take my studies more seriously; at the same time I had made up my mind to become a doctor. With my father being the Head of the largest mental hospital in Scandinavia at the time, I was raised along with my four siblings in this environment. This early exposure to patients and the fragility of the human mind, along with my own brother later developing schizophrenia, perhaps more than I was aware of, inspired me to pursue a medical and then scientific career.

Can we better illustrate the brain now as compared to Andreas Vesalius' depiction in the 1500s?

With modern technology, one can have more informative illustrations; but this remains perfectly adequate, besides being a very beautiful drawing of the brain, in my opinion.



Andreas Vesalius' illustration of the brain³.

What benefits accrue in understanding brain functions?

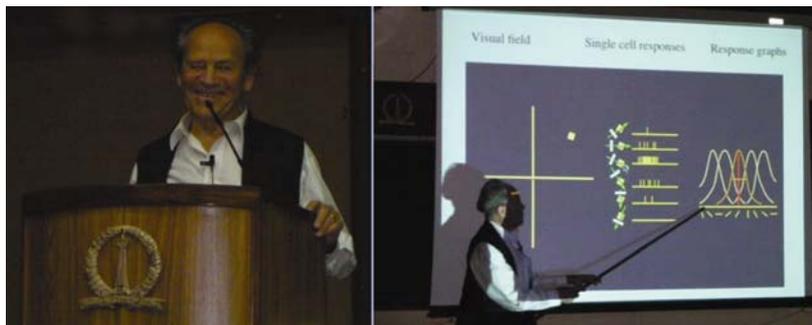
By understanding the malfunctions of the brain, we can rationally treat illnesses such as schizophrenia, depression or Alzheimer's disease. Personally, the excitement of studying the neurobasis of perception that David Hubel and I started 50 years ago and continued with Charles Gilbert, has been the joy of discovering the beauty and elegance of nature's secrets.

Are there any dangers in a better understanding?

We must always keep in mind that our minds can be impressed in many ways and my concern has been that once we understand how the brain works, then we may have the means to control the brain not only by individuals, but also by special interest groups such as governments, propaganda machines or media. During the Nobel festivities in 1981 when I received the Prize, I recall someone asking me, 'Torsten, do you think we will ever be able to control the brain?' My reply is the same I would give today, 'Never, I hope.'

What is the link between perception and consciousness?

I have always kept a distance between visual perception and consciousness, in

Box 1. IISc centenary lecture by Wiesel.

In the lecture on 15 November 2010, Torsten Wiesel explained the research areas that David Hubel and he had worked on and ‘why’ they got the Nobel Prize in 1981. He said that although many of these discoveries were made 50 years ago, the work is still relevant today and ‘maybe it is fun to hear the story from the beginning’.

Wiesel described their efforts related to orientation selectivity, binocular interactions, columnar organization, innate connections, effects of visual deprivation and critical periods. The basic technical change that enabled these discoveries was that it was possible to record electrical activity of single neurons. Wiesel showed how each receptive field of single neurons has a specific topographical localization in different parts of the brain. This work was based on the studies on retinal ganglion cells in cats by Stephen Kuffler. Wiesel showed a schematic diagram, which Hubel and he came up with, on how to create orientation-selective cortical cells – this diagram caused a controversy in the field for 40–50 years, but people finally agreed that it was a good model.

Vernon B. Mountcastle had previously reported that cortical neurons with common response properties are grouped into columns. The work of Wiesel and Hubel (through penetration studies) on the monkey striate cortex revealed ocular dominance patches in the cross-section of the cortex, which supported the columnar concept. These ocular dominance columns are 1/2 mm wide in monkeys and 1 mm wide in humans.

To find out which connections are innate and which are formed due to experience, Wiesel and Hubel experimented on newborn monkeys. They established that orientation selectivity and organization columns were innate, and the basic cortical architecture and selectivity of cells is provided through genetics. Hubel and Wiesel studied the effect of monocular lid closure from birth on dominance columns – the monkey was blind in the sutured eye when it was one year old. Competition was observed in both eyes; the active eye takes over the brain territory that, by birth, belonged to the closed eye. Wiesel said that a manipulation such as closing one eye can change the circuitry that the animal was born with.

In short, even if the cortical architecture is laid down by genetic mechanism, it was shown that ocular dominance balance and columnar organization are strongly influenced by the environment.

In a macaque monkey, the first 4–6 weeks is ‘critical’. During this period, if one eye is closed for a week, the above phenomenon is observed. If after a week, the other eye is closed while opening the previously closed eye, a reversal of effects is observed. Wiesel observed that the eye is sensitive early in life and as age increases, the effects are less striking.

Wiesel finally summarized the ‘why’ for their Nobel Prize: specificity of neural connection, cortical architecture and the balance between nature and nurture. He added, ‘I was very fortunate in my life to have good mentors’, unlike some other young scientists under a professor who do not have the freedom to develop their own ideas and do their own science. Hubel and he were lucky in this regard.

part because it is outside my field of interest and secondly, because in my view it is a question that we as experimentalists are not ready to approach. My simplistic answer to your question is that if we close our eyes, we have no visual perception and therefore, we are not conscious about our visual environment.

What was Stephen Kuffler’s contribution to the field?

Not only was Steve Kuffler a great mentor to me, but he was also regarded as the authority on the synapse, which was the main focus of his work. His first major accomplishment was the localization of the endplate, the region where the nerve connects with the muscle, otherwise known as the synapse. His studies of ganglion cells in the cat retina demonstrating the on/off centre of the receptive fields laid the groundwork for the work by Hubel and me in the central visual pathways. He also created the first Neurobiology Department, not only in the United States (at Harvard) but also in the world.

It is now 29 years since you won the Nobel Prize. What developments have taken place since then in our understanding of the neural basis of perception?

This obviously is not the place to outline the major advances during the last 50 years in vision research. I will only mention that great interest and much research has been focused on the discovery by Charles Gross in USA and Tanaka in Japan that neurons in the infra temporal lobe of the monkey respond to specific stimuli such as faces, otherwise known as face recognition. There is recent evidence that there are such cells in corresponding regions in the human. The new methods of brain imaging have technically become a major advancement, important both in research and in the clinic.

What progress do you expect in the future?

I prefer not to speculate about the future.

During the IISc centenary lecture, you said that you would like to work on the auditory system, if you were to start your research anew. Do you

Box 2. On the impact of the work by Wiesel and Hubel.

We see and recognize objects with such ease – so vision must be an extremely simple process. This is what everyone thought for a long time, until evidence began to emerge that vision is not as simple as it seems. At first, Stephen Kuffler and others discovered neurons in the retina with ‘centre-surround’ properties – these neurons respond vigorously to small spots of light, but decrease their responses to light in the surrounding regions. Even these computations were considered rather simple until David Hubel and Torsten Wiesel discovered that neurons in the primary visual cortex respond to oriented bars. It was the first demonstration that the brain performs sophisticated computations with the visual input coming from the retina and has had a profound influence on the field. In fact, computer vision algorithms even today use oriented edge detectors inspired by the work of Hubel and Wiesel for many vision applications. The studies by Hubel and Wiesel regarding the development of the visual system (in particular, orientation selectivity) have shown that these properties are genetically pre-determined and that orientation selectivity, in contrast to eye preference, is not affected by visual deprivation. These were among the first demonstrations of the ‘critical period’ during which neuronal circuitry is profoundly influenced by the environment.

Since the studies by Hubel and Wiesel, many others have furthered this work in various ways. Today we know that visual information gets heavily processed in the brain, culminating in an area called the inferior temporal cortex, where neurons are selective for faces and other complex natural objects. We also know that the adult brain retains some of its neuroplasticity, whereas the visual system loses its plasticity early in life. We know the functional contributions of different brain areas. However, understanding the principles governing visual information processing remains a significant challenge. We all know what it feels like to see, but we are far from understanding why we see the way we do.

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expect results similar to the visual system?

The reason for my answer, in contrast to the other neuro-sensory fields, is that our understanding of the central processing of auditory information is still limited. When Hubel and I began to work in the visual cortex, this was also unknown territory and we were excited to explore it. Therefore, the auditory system is an excellent opportunity for young and creative scientists to embark on. In reference to expecting results, my advice would be to enter such a study with an open mind and use your imagination.

Why is timing so important in cataract surgery in the case of an infant compared to an adult?

Hubel and I showed that in the monkey, there is a critical period during which connections present at birth could be made dysfunctional by occluding the eye. We could also show in the monkey that the sensitivity to eye closure was high during the first four to six weeks, and then declined, so that when the monkey was a year old the neural connections were resistant to effects of eye

deprivation. In contrast, we are all familiar with cataracts developed later in life, which can be present for many years and still when the lenses are removed, the vision is fully restored with glasses or proper optical correction.

Why does neuroplasticity vary with age?

We have no full understanding of the basis of neuroplasticity, but there are hopeful signs from animal experiments that specific nerve growth factors can induce plasticity in the adult nervous system. This is obviously a very important research topic with direct clinical implications that might be realized in the future.

How important is interdisciplinary research and cross-country collaboration?

To quote the Nobel Laureate Sydney Brenner, ‘All natural sciences are now converging onto biological sciences’. I have shared this view for many years. For example, as President of The Rockefeller University, I had initiated a Center for Studies in Physics and Biology and as

Secretary General of the Human Frontier Science Program, I had the opportunity to reinforce the cooperation among scientists from different disciplines and countries. If you examine the history of major developments in biology, many breakthroughs have been possible because of the introduction of new physical and chemical methods. My belief is that in the future these cross-disciplinary interactions will continue to be important for major advances.

1. Physiology or Medicine 1981 – Press Release; http://nobelprize.org/nobel_prizes/medicine/laureates/1981/press.html
2. Torsten N. Wiesel Autobiography; http://nobelprize.org/nobel_prizes/medicine/laureates/1981/wiesel-autobio.html
3. Scanned image from Andreas Vesalius’ book *De humani corporis fabrica libri septem* available at the National Library of Medicine website: http://www.nlm.nih.gov/exhibition/historicalanatomies/Images/1200_pixels/Vesalius_Pg_418.jpg

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