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Conference report: Progress in Biomedicine & Neuromedicine. Workshop with Nobel Prize Winner Professor Erwin Neher, Krakow 21–23.06.2015

The scientific conference: "Progress in Biomedicine & Neuromedicine. Workshop with Nobel Prize Winner Professor Erwin Neher" took place in Krakow, on 21–23.06.2015.The conference was organised by Societas Humboltiana Polonorum, Polish Chemical Society, Chemical Faculty of AGH – University of Science and Technology in Krakow (AGH), under auspices of Alexander von Humboldt Foundation and AGH –University of Science and Technology in Krakow. The Chairman of Organising Committee of the conference was Professor Edeltrauda Helios-Rybicka with Co-Chairman Professor Marian Jaskuła who edited proceedings of the conference as a book. The ceremony of opening was honored by Professor Zbigniew Kąkol, Prorector of University of Science and Technology in Krakow (AGH) and Professor Piotr Leider, Prorector of Jagiellonian University Medical College.

As psychiatrists we have a field of very fundamental basic neurobiological knowledge. This knowledge is so established, certain and known to everyone that it is unlikely to ask ourselves about the primary sources of it. How do we know about the morphology and functions of neurons, synaptic and electrical signaling in axons and dendrites, ion channels, neurotransmitters? In everyday practice we use medications, and action of our drugs is based on elements and functions listed above. But can we link such names as Santiago Ramón y Cajal and Camillo Golgi, Alan L. Hodkin, Andrew F. Huxley, Bernard Katz and Julius Axelrod, Ulf von Euler, Bert Sakmann and Erwin Neher with their discoveries, our own knowledge and day-to-day practice? The unusual occasion to listen to the lecture of the person who discovered some of this fundamental aspect of the brain's function was the conference with Nobel Prize Winner in Physiology and Medicine (1991), Professor Ervin Neher. He was honored with Nobel Prize together with Bert Sakmann for their discoveries concerning "the function of single ion channels in cells". They both have developed a technique (the patch-clamp technique) that allows to record low electrical currents that pass through single ion channels located in cells membranes. Ion channels are pore-forming mem-

brane proteins whose functions include establishing a resting membrane potential, shaping action potentials and other electrical signals by gating the flow of ions across the cell membrane. Prof Ervin Neher (born in 1944) is actually director at Max Planck Institute for Biophysical Chemistry in Göttingen.

The lecture of Professor Ervin Neher "Ion channels: their discovery, their function and their role in disease" started with the review of the history of research on bioelectricity. He recalled such names as Santiago Ramón y Cajal who studied and described the morphology of neurons. In early 1950s Alan L. Hodgkin and Andrew F. Huxley were able to show that the nerve impulse is carried by permeability changes of its membrane and fluxes of cations: sodium (+NA) and potassium (+K). The presentation of Prof. Neher was based on the reflection: "we did not expect that results of our research will be so important for future of science and medicine". According to him when he and Bert Sakmann started to address the question what causes permeability changes, they thought that there is about 5–10 kinds of ion channels and that an answer would resolve not more than an issue related to nerve excitability. They wanted to prove that ion channels in the nerve membrane open and close in order to provide the precisely timed current pulses, that make nerve impulse go. Now there are known about 300 kinds of ion channels and researches revealed that ion channels are present in basically all cell types of body and they fulfil a variety of functions. They are present in our sensory organs, where they transduce smell, taste, sound and temperature as well as in kidney, heart and bones. Ion channels as regulators of cell functions turned out to be prime targets for pharmacological interventions, and by interaction between the drug and ion channels all over the body drugs are able to inhibit or stimulate the functions of organs. Ion channels are also important when considering different pathologies, and for example it is important which kind of ion channel is involved in pathophysiology the arrhythmias of the heart. Professor Neher concluded that the testing of candidate molecules for new drugs using human cell lines may give better clues for their success in clinical trial than current methods.

The next speaker Professor Jerzy Vetulani reported the results and history of discoveries of the 2104 in the field of physiology and medicine. First he described how important it is to compose the scientific results to make discovery and the importance of scientific intuition and un-conscious processing of information that is a basis of discoveries made by sudden deep insight into the nature of observed phenomena. The Nobel prize in 2014 went to John O'Keefe and Edvard Moser and May-Britt Moser for their discoveries in answering the question: how we know where we are and how we navigate in space. There is deep philosophical problem hidden in that question, that is contradictory opinion of Locke and Hume on the one side and Kant on the other (do mind know about the position of the organism on the basis of sensory perceptions or inborn categories). Experimental research on space perception was initiated by Edward C. Tolman's studies on animal navigation in 1930's and 1940's.

He suggested that animal formed a cognitive map of surroundings. The knowledge about the nature of those maps started with studies of John O'Keefe on single cells activities in rat hippocampus. He discovered "place cells", that firm a system in which particular neurons are active when the animal approaches a given place, Head direction cell were discovered by J.B. Rank in 1984. These cells fire when the head is directed toward one of chosen environmental markers in space. The third type of cells, grid cells were discovered by Edvard and May-Britt Moser. Grid cells are activated when an animal enters a particular place in space, regardless the presence or absence of objects. They for a hexagonal grid projected by the animal on space, like cartographic grid of meridians on a map. The border cell fire when the animal is close to the borders of proximal environment. The far-reaching significance of those results transcendent the realm of physiology and medicine and answers some philosophical questions about our understanding of the word.

Lecture of Professor Dominika Dudek, entitled "Brain and mind – duality or unity" was devoted to the very fundamental in our way of thinking problem of unity/duality between mind and brain. In the first part of her presentation she described the history of attitudes toward people with mental disorders in western societies over the last centuries, including the problem of stigmatisation of them. In the next part of presentation Prof. Dudek raised the topic of "the titanic human struggle to understand abnormal behaviours" in the context of the unity or duality of mind and brain in the evolution of psychiatry. René Descartes view of the mind and body as separated influenced the human thinking in western societies and medicine, and it has been widely influential over centuries in psychiatry. Antonio Damscio in his famous book "Descartes' error" argues that this error was Descartes dualist separation of mind and body, rationality and emotion. A clear distinction between neurology and psychiatry existed for long decades. Neurologists treated organic illnesses (like stroke, brain tumour), the field of psychiatry were restricted to such disease, in which structural brain abnormalities were unknown. The belief in the distinction between "neurological" and "psychiatric" disease is still often held by the significant number of general public as well by medical community. But, as pointed by Prof. Dudek "Nowadays the dichotomy of 'neurological' and 'psychiatric' cannot be further valid". Neurological disorders cause behavioural and emotional disturbances, and on the other hand modern neurobiology finds more and more data on structural changes in the brains of patients with "purely" psychiatric disorders like schizophrenia, bipolar disorder and major depression. Thanks to neuroimaging methods there is strong evidence for existing changes in gray and white matters as well as in subcortical structures in individuals with those disorders. Psychotherapy considered as pure psychological treatment was proved to influence structures and functions of the brain in example by altering synaptic plasticity. At the end Professor Dudek cited the opinion of Joseph B. Martin "the separation of two categories is arbitrary, often influenced by beliefs

rather than proven scientific observations. And the fact that the brain and mind are one makes the separation artificial anyway".

Professor Tadeusz Marek gave a very interesting presentation about functions of the sleep in the context of brain functions. According to Cirelli and Tononi sleep can regroup the brain by giving the synapses a chance to return back to baseline levels following a whole day of learning. Some studies indicated that REM sleep is necessary for turning off the release of neurotransmitters and allow their receptors to recover from desensitisation and regain sensitivity. Ribeiro argue that sleep promotes global synaptic downscaling, leading to reset of synaptic weight that is necessary for the acquisition of new memories and on the other hand also promotes synaptic upscaling able to consolidate recently acquired memories. The result of Lulu Xie research are very exciting as they show that sleep changes the cellular structure of the brain and is associated with a 60% increase in the interstitial space, resulting in a striking increase in convective exchange of cerebrospinal fluid with interstitial fluid and removal of neurotoxic waste products. He ended with the newest (2015, published in "Nature") discovery of potential great importance, made by Antoine Louveau et al., of functional lymphatic vessels in the dural sinuses.

Dr Sławomir Murawiec presented a lecture about neuropsychoanalysis – research on combining discoveries and techniques of psychoanalysis with contemporary neurobiological knowledge and tools used within this field, such as functional magnetic resonance imaging (fMRI). According to its founding Fathers Jaak Panksepp and Mark Solms neuropsychoanalysis is a domain that explores understanding of the human mind, especially as it relates to first-person experience. Neuropsychoanalysis recognises the essential role of neuroscience in such quests and what is central for this stance that it places mind and brain on an equal footing. Philosophical framework formulated by Kant is helpful here – the existence of "things-in-themselves" that can be tested with both perspectives and use their research tools. In this context Solms writes that according to his way of thinking mind is a subjective aspect of the brain, a way of being the brain. Neurobiological research can contribute to the understanding of psychoanalytic concepts such as libido (understood more broadly than the sex drive) by linking them to research on SEEKING system (curiosity and motivation of exploratory) by Panksepp (or mesolimbic dopamine system). This allows the comparison of operating principles formulated at metapsychological level and specific rules of operation described on the basis of neurochemical and neuroanatomical studies. Similarly, psychological studies on defence mechanism of repression using fMRI (AC Schmidt), psychodynamic conflict (P. Siegel), a technique of free association (R. Viviani) are being conducted. This leads to the formation of "first-person neuroscience", such neurobiological studies that – to objective functioning of the brain – remain in its range of perspective and a richness of personal experiencing.

In the second day of the conference Professor Włodzisław Duch presented the lecture "Grand challenge: neurophenomics for understanding people, from genes to behaviour". He started from the statement that "the complexity of the brain is unmatched in the known universe". Phenomic is concerned with detailed description of all aspects of organism, from their physical foundations at genetic, epigenetic, molecular and cellular level, through tissues, structures and organs, to the whole organism up to the behavioural and psychological traits –. According to him creating full phenotypes will be extremely difficult, but it is the only way to complete understanding of relations between mind and brain, mental states, behaviours including medical aspects of all those topics. He proposed more general approach, neurocognitive phenomics, treating the brain as a substrate for mental processes shaped by genetic, epigenetic, cellular and environmental factors. According to Prof. Duch "understanding mental processes in a conceptual way at the social or psychological level, without taking into account underlying neurodynamics, will always be limited". In this context he described some examples of behaviour explanation based on neurocognitive phenomics: autism and ADHD, neurobiological foundations for learning styles and formation of beliefs and conspiracy theories, based on distorted memories due to the interplay between learning and emotions. Neurodynamics simulated by computational models of neural structures can be used to understand cognitive and affective aspects of mental states and to understand the influence of biophysical parameters that describe neural activity. The grand challenge of understanding behaviour has computational modelling as its centre, pointing down to molecular and genetic level, and up to behavioural level".

Lecture of Adrian Andrzej Chrobak and Professor Dominika Dudek concerned the role of the cerebellum in cognitive and emotional processes in mental disorders. The cerebellum has traditionally been described as a part of the brain responsible for controlling motor functions. It turned out, however, that the cerebellum is not connected only to the motor areas, but also to areas related to cognition and emotion control such as the prefrontal cortex, the parietal cortex, temporal cortex or amygdala. Schmahmann and Sherman showed in their works that patients with lesions of the cerebellum represent complex cognitive-emotional symptoms, beyond the motor dysfunction. The set of these symptoms was categorised as the Cerebellar Cognitive-Affective Syndrome. During the lecture clinical cases illustrating the effects of damage to the left and right hemispheres of the cerebellum were presented. The rest of the presentation was dedicated to the role of the cerebellum in psychiatric disorders. Authors discussed neuroimaging, clinical and neuropathological abnormalities indicating the structure and function of the cerebellum in autism spectrum disorders, schizophrenia, bipolar disorder, depression and PTSD.

Lectures summarised above were ones the most connected to the field of psychiatry, but many other fascinating topics in the field of biomedicine and neuromedicine

were presented during the conference. Among them such interesting papers as those dealing with, biomedical engineering, stem cells in neurology, endovascular treatment of acute brain ischemic stroke and topics connected with stress response and stress induced plasticity, electrophysiological studies and effect of prenatal stress on synaptic transmission.

Sławomir Murawiec, Adrian Andrzej Chrobak