Krieg Cortical Kudos 2001

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Each year since 1987, the Cajal Club has honored outstanding neuroscientists for their research investigations of the cerebral cortex and/or its connections at its annual meeting. These awards are funded by donations from Dr Wendell J. Krieg, the first president of the Cajal Club, and his wife, Roberta. Wendell was a distinguished neuroanatomist and had a great reverence and respect for the work of Ramón y Cajal on the nervous system. The Kriegs' donation endowed a nonprofit foundation and the proceeds from it were designated to fund the Krieg Cortical Kudos, awards for talented neuroscientists who have made significant and important contributions to understanding the organization, function and development of the cerebral cortex. The awards are presented at the Cajal Club meetings that are held in conjunction with the American Association of Anatomists at the Annual Experimental Biology Meeting. This awards program is unique in that it recognizes research excellence at three levels of achievement. Dr Krieg assigned special names to each of these levels, and by establishing these three tiers he was able to reward researchers throughout their careers for contributions to our understanding of the cerebral cortex.

The Cortical Scholar prize ($1000) is awarded to a predoctoral fellow who is at the endstage of completing their doctoral dissertation.

The Cortical Explorer prize ($3000) is usually awarded to a scientist at an intermediate stage of their career for achievements within 6 years of receiving an advanced professional degree (Ph.D./MD).

The highest level award, the Cortical Discoverer prize ($5000), is given to a senior scientist who has contributed significantly to our understanding of the cerebral cortex. Former recipients of the Cortical Discoverer award, listed alphabetically, include J. DeFelipe, I.T. Diamond, D. Fitzpatrick, T.F. Freund, C. Gilbert, P.S. Goldman-Rakic, E.G. Jones, J. Kaas, H. Killackey, J. Lund, M. Marin-Padilla, M. Merzenich, V. Mountcastle, D. Pandya, A. Peters, P. Rakic, P. Somogyi, L. Ungerleider and E. White.

This year's Cajal Club meeting was held in Orlando, FL on April 1, 2001. The Krieg Cortical Kudos Awards Committee consisted of Charles E. Ribak (President), David G. Whitlock (Secretary/Treasurer), Tamas Freund, Herbert Killackey, Leslie Ungerleider and Enrico Mugnaini.

The Cortical Explorer Award: Zoltan Nusser

This year the award was presented to Dr Zoltan Nusser for his research on the understanding of the subcellular organization and function of neurotransmitter receptors in the neocortex and hippocampal formation using molecular neuroanatomical and electrophysiological techniques. His talk was entitled 'Organizational Principles of the Subcellular Distribution of Amino Acid Neurotransmitter Receptors'.

Zoltan Nusser was born on October 17, 1968 in Bonyhád,

Figure 1. Recipients of the 2001 Krieg Cortical Kudos Awards: Zoltan Nusser (left) and Gyorgy Buzsáki (right), with Charles Ribak, President of the Cajal Club (center).

Hungary. He attended the University of Veterinary Medicine in Budapest, Hungary and graduated in 1992 with a D.V.M. degree. He then traveled to England and earned a D.Phil. at Oxford University in Pharmacology with Dr Peter Somogyi, a former Cortical Discoverer Award winner. Zoltan launched his research career in Peter's laboratory by studying the localization of amino acid neurotransmitter receptors in the hippocampus and cerebellum. His initial studies involved the localization of metabotropic and ionotropic glutamate receptors, and they showed a subsynaptic segregation of these two types. He then embarked on studies involving the localization of different subunits of the $GABA_A$ receptor using immunogold methods. This high-resolution method provided a new understanding of GABAergic synapses by allowing for the examination of the dynamics of the receptors at these synapses. As one of his nominees, Tamas Freund, wrote, 'Zoltan was able to identify that the major source of postsynaptic response variability at GABAergic synapses is the variation in the number of postsynaptic receptors between distinct synapses'. Thus, he correlated an increase in the size of synaptic responses with the number of receptors by combining physiological recordings with electron microscopy.

This work was quite astonishing. Prior studies suggested that some GABAergic synapses would have a more powerful inhibitory effect because their location was close to the axon hillock where spikes are generated. Thus, the axosomatic and axon initial segment synapses were considered to have a stronger effect than the GABAergic axodendritic synapses. Zoltan provided the first demonstration that GABAergic synapses can have different receptor numbers using postembedding immunogold labeling of different subunits and electron microscopy.

Dr Nusser also conducted postdoctoral work with Dr Somogyi, and this period of time allowed him to continue his studies on the localization of amino acid neurotransmitter receptors. These studies revealed the exclusive extrasynaptic presence of certain ionotropic receptors, the differential expression of postsynaptic AMPA receptors at functionally distinct synapses and the demonstration that certain hippocampal synapses contain few, if any, AMPA-type glutamate receptors. This latter observation provided evidence for the 'silent synapse' hypothesis. While completing his postdoctoral work at Oxford, Zoltan visited the laboratory of Dr Cull-Candy at University College London, where he learned cellular physiology. During this time, he mastered both the technical and theoretical aspects of patch-clamp recordings.

In 1998, Dr Nusser went on to advance his knowledge and expertise in cellular electrophysiology by moving to Dr Istvan Mody's laboratory at UCLA in Los Angeles, CA. Zoltan again made remarkable progress in the field of GABAergic synapses. In this case, he examined the modulation of synaptic $GABA_A$ receptors by phosphorylation and by several clinically important drugs. Furthermore, he showed that the increased postsynaptic response size at GABAergic synapses following temporal lobe epilepsy using the kindling model was the consequence of the insertion of new $GABA_A$ receptors into the postsynaptic membrane of dentate gyrus granule cells in the hippocampus.

More recently, Dr Nusser was appointed a Group Leader Research Scientist at the Institute of Experimental Medicine at the Hungarian Academy of Sciences in Budapest, Hungary. In his new independent position, Zoltan will be continuing his pioneering studies on neurotransmitter receptors. He has also been awarded the Glaxo-Welcome Prize in 1996 for the best D.Phil. thesis in the UK and the Chancellor's Award for Postdoctoral Research in 2000 for the best research at UCLA performed by a postdoctoral fellow. His future looks bright because he has already garnered many grants for his research laboratory, including ones from the Wellcome Trust, Human Frontiers in Science, James McDonnell Foundation, Boehringer Ingelheim Fond's Award and the Hungarian Science Foundation.

The Krieg Explorer Award honors the extraordinary talent and originality of Zoltan Nusser. In only a few years, he has become a leading authority on the localization of amino acid neurotransmitter receptors. We shall look forward to the contributions that he will make in his very promising career, and anticipate that his studies will continue to add to our understanding of the structure and function of the cerebral cortex.

The Cortical Discoverer Award: Gyorgy Buzsáki

This year's award was presented to Dr Gyorgy Buzsáki for his outstanding research in understanding the morphology and electrophysiology of hippocampal pyramidal cells and interneurons. His talk was entitled 'Functional Anatomy of the Hippocampus'.

Gyorgy Buzsáki, MD, Ph.D. is currently a Professor at the Center for Molecular and Behavioral Neuroscience at Rutgers University in Newark, New Jersey. He was born in 1950 in Hungary where he also spent his youth growing up. Earning his medical degree at the University of Pécs in Hungary, he chose to enter the neuroscience field under the direction of the Chairman of the Physiology Department, Dr. Endre Grastyan, a member of the Hungarian Academy of Sciences and a leader in the field of learning and memory. Joining the faculty of this department in 1975, Gyuri started working on research that would ultimately form a major part of his Ph.D. thesis that was entitled 'The Cellular Basis of Hippocampal EEG Activity in the Behaving Rat'.

Dr Buzsáki's early studies involved an analysis of the commissural projection to the dentate gyrus. Using physiological data, he suggested that this projection provided feedforward inhibition to granule cells. Subsequent anatomical studies demonstrated the circuitry underlying this proposed functional pathway. This discovery of feedforward inhibition in the hippocampus led to the reinterpretation of the generation of a long-studied hippocampal activity pattern, the theta oscillation. Gyorgy spent many years following this discovery to systematically analyze this phenomenon down to the single identified neuronal level through *in vivo* intracellular recordings. In so doing, he discovered a novel neuronal pattern, termed hippocampal sharp wave bursts involving infrequently firing pyramidal cells.

In the mid-1980s, Gyorgy worked in a few laboratories in the USA, where he continued his analysis of hippocampal function. Working with Dr Fred H. Gage at UC San Diego, he studied the mechanism of action of neural grafts on the deafferented hippocampus. His need to know the extent of the graft and its connections led to his interest in neuroanatomical analyses of the hippocampus that began in earnest in 1988 with a collaboration with Dr Tamas Freund, a winner of two Krieg Cortical Kudos, the Explorer and Discoverer. In this first collaboration of many to come, they examined excitatory and GABAergic inhibitory connections in hippocampal transplants. Peter Somogyi wrote 'Gyuri realized that in order to relate the activity of different cell classes to the activity of neuronal ensembles and ultimately to the behavior of the animal, it is essential to define accurately the connections of the participating cells in a quantitative manner'.

Subsequent to these studies on hippocampal transplants, Dr Buzsáki went on to record from probably all of the major

classes of neurons in the hippocampus using *in vivo* recordings and visualizing them for identification and synaptic connections. Thus, he combined physiological, morphological and immunocytochemical techniques to discover relationships between the various projection and local circuit neurons of the hippocampus. Combining his results with those of others, Gyorgy and Tamas Freund summarized the data for hippocampal interneurons in a landmark monograph that was published in 1996 in the journal *Hippocampus* (Freund and Buzsáki, 1996). This issue of *Hippocampus* is now the standard reference for hippocampal interneurons. What is surprising is that they have not published a similar monograph on the hippocampal projection cells because they have also studied the CA1 and CA3 pyramidal cells as well as dentate gyrus granule cells.

Another important field of his research involves the mechanism for network cooperation in the thalamocortical system. Dr Rodolfo Llinas, a leader in the field of thalamic oscillations, wrote that 'Gyorgy successfully developed insightful hypotheses and related experiments to examine the ability of *in vitro* observations in the intact nervous system'. In fact, Dr. Buzsáki's laboratory is one of only a few in the world that successfully records from large numbers of individual neurons in the awake animal using state of the art 'high-tech' silicon devices and interpreting the complex interactions in a meaningful way. Furthermore, Dr. Buzsáki's goal is expressed on his web page where he states that his 'hope is that the convergence of the two approaches (single cells and multiple groups) will allow us and the neuroscience community to understand when (i.e. under what behavioral conditions) and where (i.e. what region, what synapse) synaptic modifications take place and how the hippocampus assists the neocortex in the construction and maintenance of long-term memory traces'.

The Krieg Cortical Kudos is not the first award that Gyorgy has received for his exciting research discoveries. His other prizes include a Fogarty International Senior Fellow to study in Paris, France, the First Pierre Gloor Award from the American Clinical Neurophysiology Society, an Excellence in Research Award from Rutgers University, and the J.D. French Foundation Fellowship. It needs to be noted that he has given many named lectures, including the Moruzzi, Travelling Grass, F. Botazzi and Swammerdam.

Not only does he perform stellar research, but Gyorgy is also able to communicate his enthusiasm for his research to students and other scientists. He has hosted over 20 postdoctoral fellows in his laboratory. Furthermore, he co-organized four international meetings and is a co-editor on three books: *Electrical Activity of the Archicortex* (Buzsáki and Vanderwolf, 1985), *Synaptic Plasticity in the Hippocampus* (Haas and Buzsáki, 1987) and *Temporal Coding in the Brain* (Buzsáki *et al.*, 1994). In addition, he co-organizes a hippocampus seminar group at the Rockefeller University with Bruce McEwen, a former Harmon Lecturer (1999) at the Cajal Club Meeting in Washington, DC.

In summary, Dr Buzsáki is an exceptionally creative scientist whose work has provided us with a better understanding of the properties and connections of identified cortical cell types. This information has been placed into the context of global brain activity patterns and behavioral states, which has led to many discoveries and insights into the organization of cortical circuits. These studies provide new insights into the cerebral cortex from the level of synaptic organization to that of the whole organism, truly in the Cajal tradition.

Notes

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