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Symposium at the Annual SFN Meeting San Diego, Ca.

New Techniques in Electro- and Optophysiology

Sunday, Nov. 4, 2018, 6:30-8:30pm, San Diego Convention Center Room 4

Modern neuroscience is concerned with how individual neurons coordinate their activity to create coherent spatiotemporal patterns. Methods for high resolution electrical/optical recording, focal delivery of compounds down to the synaptic level, and new in vivo recording techniques, all for studying the brain and its associated diseases at high functional levels using microelectrodes and optical setups in reduced preparations and in freely moving animals, will be presented.

Talks and Speakers:

The neuroscience of perceptual categorization in pigeons – an *in vivo* study

Roland Pusch

Biopsychology, Institute of Cognitive Neuroscience, Faculty of Psychology, Ruhr-University Bochum, 44801 Bochum, Germany

Summary

Perceptual categorization of objects is a vital process for humans as well as for all other vertebrates. In humans, higher order visual and prefrontal cortical areas play a key role in categorization. Birds lack these cortical brain structures and have evolved nuclear aggregations instead. Birds are capable of an astonishing variety of cognitive behaviors including categorization - despite the absence of a layered cortex. Thus, the neural fundaments of these behaviors are quite invariant to the differences in the anatomical organization of the respective brains.
Pigeons (Columba livia) were the first non-human animal in which the ability to categorize was shown and a large body of literature has emerged investigating behavioral aspects of categorization in these animals. Despite the detailed knowledge of the behavioral processes, their neuronal fundaments remain poorly understood. We combine behavioral experiments and extracellular recordings in freely moving pigeons to investigate the neural basis of the categorization behavior. We recorded single neurons in two visual areas in the avian forebrain: the entopallium, the first telencephalic recipient area and the mesopallium ventrolaterale (MVL), an associative visual area of the bird brain.
In our task the birds were confronted with visual stimuli belonging to different categories (e.g. animate vs. inanimate). Importantly, the pigeons do not have to categorize these stimuli during our experiments but merely had to peck on each stimulus, irrespective of its content. Thus, instead of training pigeons on predefined categories, we simply presented the stimuli and analyzed the neural output.
Using a linear classifier, we found that population activity in the visual associative area MVL distinguishes between animate and inanimate objects, although this distinction is not required by the task. By contrast, a population of cells in the entopallium, a region lower in the hierarchy of visual areas, lacked this information. A model that pools responses of simple cells can account for the animate vs. inanimate categorization in the MVL, but the model performance is based on different features. Therefore, processing in MVL cells is very likely more abstract than simple computations on the output of edge detectors.

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Güntürkün, O., Koenen, C., Iovine, F., Garland, A. and Pusch, R. (2018): “The neuroscience of perceptual categorization in pigeons: A mechanistic hypothesis”, Learning & Behavior, DOI 10.3758/s13420-018-0321-6.

Layer 4 barrel cortex neurons retain their response properties during whisker replacement

Eduard Maier

Bernstein Center for Computational Neuroscience Berlin, Humboldt-Universität zu Berlin, 10115 Berlin, Germany

Summary:

Bodies change continuously, but we do not know if and how these changes affect somatosensory cortex. We address this issue in the whisker-barrel-cortex-pathway. We ask how outgrowing whiskers are mapped onto layer 4 barrel neuron responses. Half of whisker follicles contained dual whiskers, a shorter presumably outgrowing whisker (referred to as young whisker) and a longer one (referred to as old whisker). Young whiskers were much thinner than old ones but were inserted more deeply into the whisker follicle. Both whiskers were embedded in one outer root sheath surrounded by a common set of afferent nerve fibers. We juxtacellularly identified layer 4 barrel neurons representing dual whiskers with variable whisker length differences in anesthetized rats. Strength and latency of neuronal responses were strongly correlated for deflections of young and old whiskers but were not correlated with whisker length. The direction preferences of young and old whiskers were more similar than expected by chance. Old whiskers evoked marginally stronger and slightly shorter latency spike and local field potential responses than young whiskers. Our data suggest a conservative rewiring mechanism, which connects young whiskers to existing peripheral sensors. The fact that layer 4 barrel neurons retain their response properties is remarkable given the different length, thickness, and insertion depth of young and old whiskers. Retention of cortical response properties might be related to the placement of young and old whisker in one common outer root sheath and may contribute to perceptual stability across whisker replacement.

References:

Maier E, Brecht M. Layer 4 barrel cortex neurons retain their responseproperties during whisker replacement. J Neurophysiol. 2018, doi:10.1152/jn.00333.2018.

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High-precision behavioral neuroscience: combined two-photon imaging and cell-attached recording in the auditory cortex of behaving mice

Hongbo Jia[1,2,3,4]

[1] Brain Research Instrument Innovation Center, Suzhou Institute of Biomedical Engineering and Technology, Chinese Academy of Sciences, Suzhou 215163, China, [2] Brain Research Center and State Key Laboratory of Trauma, Burns, and Combined Injury, Third Military Medical University, Chongqing 400038, China, [3] Institute of Neuroscience, Technical University Munich, Biedersteinerstrasse 29, 80802 Munich, Germany, [4] Institute of Neurointelligence, School of Medicine, Chongqing University, Chongqing 401331, China

Summary

It has been more than two decades since the first in-vivo neuroscience application of two-photon microscopy (Svoboda et al, Nature 1997) for investigating physiological signals of neurons at very high spatial and temporal precision in intact brains of anesthetized animals. Those pioneering studies involved highly challenging experiments by performing electrophysiological recordings simultaneously with two-photon imaging. However, there has not been many reports of such combined recordings thereafter. In contrast, the two-photon imaging and the electrophysiology had been largely used as two separate methods for neuroscience studies.

Since the two methods' advantages very well covered each other's caveats, using them in real-time combination may yield a whole effect that is '1+1>2'. We show here, that by integration of customized instrumentation and adequately trained experimenting skills, it is feasible to perform the same kind of highly challenging 'imaging-ephys-combo' experiments in awake behaving animals.

We trained head-fixed mice for a simple sound-licking association task. By using a synthetic fluorescent Ca2+ indicator Cal-520, we recorded sound-evoked as well as spontaneous Ca2+ transients at multiple scales, including neuronal populations, single neurons, dendrites and single spines, in the primary auditory cortex during active behavior. Furthermore, by using a genetically encoded Ca2+ indicator GCaMP6f, we monitored the neuronal dynamics over days throughout the process of associative learning. Importantly, the cell-attached recordings could be performed on functionally identified neurons based on two-photon Ca2+ imaging, to accurately characterize the spike firing pattern underneath the Ca2+ signals under the same behaving conditions, which otherwise could have been unlikely inferred from knowledge a priori based on other recordings under in-vitro or anesthetized conditions.

Keywords: two-photon Ca2+ imaging, auditory cortex, behaving mouse, dendritic spines, cell-attached recording

References:

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In vivo electrophysiological analyses of genetically dissected cerebellar circuits in mouse

Roy V. Sillitoe[1,2,3,4]

[1]Department of Pathology and Immunology, Baylor College of Medicine, [2]Department of Neuroscience, Baylor College of Medicine, [3]Program in Developmental Biology, Baylor College of Medicine, [4]Jan and Dan Duncan Neurological Research Institute of Texas Children's Hospital, Houston, TX 77030

Summary:

Only five types of neurons form the core of all cerebellar circuits. By controlling these few cell types, the brain is able to coordinate a variety of motor behaviors including locomotion, learning, balance, and posture. What is very striking is that cerebellar dysfunction causes a wide range of movement disorders. Among these disorders are ataxia, dystonia, and tremor. Recent work has expanded the role of the cerebellum to non-motor behaviors such as cognition and emotion. Accordingly, there is evidence that the cerebellum is involved in autism spectrum disorders, attention deficit hyperactivity disorder (ADHD), and schizophrenia. This is intriguing from a cellular standpoint because it raises a critical question; how does the repeated circuitry of the cerebellum control so many behaviors and contribute to a diverse array of motor and non-motor disorders? To begin to address this problem, we have proposed to use a genetic approach to delineate the cellular mechanisms that initiate different cerebellar motor diseases. Understanding how different disease are controlled by the same circuitry is important because there are many examples in clinical treatment where one region of the brain can be the therapeutic target for two different diseases–for instance, deep brain stimulation of the basal ganglia is an effective remedy for dystonia and Parkinson's disease. Therefore, by delineating how defective cerebellar circuitry triggers different diseases we hope to provide new and perhaps more effective targets for treating the circuits to restore movement. The reason that cerebellar circuit function is so diverse could be due to the roles of its individual synapses. Our preliminary data support this hypothesis, as we have found synaptic neurotransmission, the process that brain cells use to communicate signals between one another, to be a strong factor influencing cerebellar disease. To address these problems, we argue that in each motor disease, circuit behavior is determined by how neuronal communication is altered. We therefore devised a genetic toolkit to manipulate cerebellar activity and then record the resulting neural signals in behaving mice. Extracellular single unit recordings performed in awake behaving mice has revealed the possibility of specific abnormal firing signatures in each cerebellar driven mouse mutant. Single neurons with abnormal spike patterns were identified post-recording using an *in vivo* loose-patch juxtacellular recording-labeling approach. The identification of defective cerebellar output signals led us to postulate that eliminating these signals might recover normal mobility. Our efforts are now aimed at using our *in vivo* tools to test how cerebellar-directed deep brain stimulation (DBS) corrects altered signals and rescues behavior in different models.

Keywords: cerebellum, *in vivo* electrophysiology, ataxia, tremor, dystonia, genetics, DBS, neuromodulation

References:

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