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Kasia Maria Bieszczad, Ph.D.

Neurobiology

University of California, Irvine

Born in 1983 in Kraków, Poland

Studied Biology at McGill University and Neurobiology and Behavior at the University of California, Irvine

FELLOWSHIP
College for Life Sciences

PROJECT

Cortical Mechanisms Underlying the Neurobiological Substrates of Life-Long Learning and Enduring Memory

The overall goal of my research program is to understand the neurobiological processes that underlie memory specificity and strength. Indeed, that memory can be characterized in terms of specificity (being "about" something) and strength (i.e., some experiences are better remembered, while others are easily forgotten) is fundamental and universal to all memory. However, the neural mechanisms responsible for these memory processes are largely unknown.

I use the term specificity to refer to the particular multi-dimensional contents of memory, such as specific details of places, events, and sensations. I refer to strength as the relative effectiveness of any such detail to direct behavior. My research permits a comprehensive understanding of memory strength and specificity by combining investigations of stimulus-specific neuroplasticity in the cortex with corresponding stimulus-specific behavior as animals learn and remember. Furthermore, application beyond immediate interpretation for basic science includes an account of the potential mechanisms liable for specific memory failure (e.g., aging or dementia) or when a specific memory becomes abnormally strong in a variety of psychological disorders (e.g., post-traumatic stress disorder or addiction).

Behaviors are dictated by the functional organization of the brain. Moreover, this organization can change as a function of experience in order to adapt behaviors to new circumstances. Changing associations between objects or events and their meaning induces neural change (called neuroplasticity) and is governed by psychological rules. For example, learning alters neuronal function on the circuit, molecular and even genetic levels through biological mechanisms that can regulate the expression of genes, alter the connectivity and activity of the brain and, ultimately, produce adapted behavior. My project is to write a review paper that will organize my past research into a comprehensive framework and identify the key open questions for future research.

Recommended Reading

Bieszczad, K. M. and N. M. Weinberger (2010a). "Representational gain in cortical area underlies increase of memory strength." Proceedings of the National Academy of Sciences of the United States of America 107, 8: 3793-3798.

Bieszczad, K. M. and N. M. Weinberger (2010b). "Remodeling the cortex in memory: Increased use of a learning strategy increases the representational area of relevant acoustic cues." Neurobiology of Learning and Memory 94, 2: 127-144.

Bieszczad, K. M., A. A. Miasnikov and N. M. Weinberger (in press). "Remodeling sensory cortical maps implants specific behavioral memory." Neuroscience April 29; 246C: 40-51. doi: 10.1016/j.neuroscience.2013.04.038. [Epub ahead of print]

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Does this ring a bell? Here's to making memories - with genes, brain and behavior

Animals (like humans) have a fundamental capacity to promote behaviors that are adaptive. Adaptive behaviors can be appetitive so that animals approach stimuli for obtaining food, finding shelter and having sex; and behaviors can also be aversive so that animals avoid the stimuli that produce discomfort and threaten death. How are such adaptive behaviors made possible? Simply put - animals can remember.

Learning from experiences and recollecting significant information from the memory of those experiences is absolutely essential for adaptive behavior, especially when environments change throughout a lifetime. Luckily, the brain is plastic and is constantly updating the organization of neurons and their connectivity to allow for the formation of an incredible network of memory. Thus, stimuli in our world can become linked (associated) to aversive or appetitive outcomes: neural plasticity endows us all with this capability for associative memory. Yet, there is an additional requirement for associative memory to be useful for adaptive behavior: Memory must have specificity. It is of no use if a honeybee approaches a red flower if it was actually the yellow flower it visited in the past that has the nectar. Nor is it useful if you get up to answer the door when the ring was actually your telephone! What this means is that there must be a brain mechanism, in the plasticity of the brain that allows for associative memories to be specific. Indeed, memory is "about something". It has content.

The foundation of the neurobiology for making memory with specific content is in the plasticity of the sensory cortex, the highest level of information processing in the brain. A remarkable achievement in research about how specific memories can form is the discovery over the past several decades that these "sensory" parts of the cortex that enable perception (e.g., to see, to hear, to taste) are the same parts that help us to remember (e.g., what we watch, what we listen to, what we crave). Importantly, plasticity of the sensory cortex is driven by learning and associative memory. This talk will describe my contribution to a modern extension of the study of associative memory formally starting behavioral psychology in the 1920s by Ivan Pavlov. Pavlov noticed that after ringing a bell consistently before mealtimes, his dogs would one day begin to salivate just when they heard the bell. This was interpreted to show that the sound of the bell "brought to mind" the forthcoming meal - even before food was seen (Now does that ring a bell?). The bell becomes associated with food. Later neurobiological studies using electrophysiology to record from brain cells before and after associative learning show that the neural representation of sound in the auditory cortex completely reorganizes: More neurons represent the significant sound.

My current research asks the question: What happens to neurons, and inside neurons at the level of genes, to make plasticity possible? Any one who has ever taught a class of students will know that the same learning experiences often result in different memories formed - some students perform better than others at test time. Why? I will present research using a rodent model of auditory memory that suggests mechanisms for how plasticity can account (at least in part) for individual differences that make us who we are by changing what, and how, we remember; and even how experience might interact with genetics to induce the plasticity that enables the formation of memory. Indeed, memory can be defined as a collection of what is retained from past experiences that enables our desires, our motivations, our pleasures, and our beliefs. In essence, our memory (at least in part) enables "self". So it is devastating when injury or disease deprives individuals of these channels of personal history. The goal of this work is to gain enough understanding of the neural bases of behavior and plasticity - as animals (like humans) learn and remember - which will permit the development of clinical strategies that can correct learning and memory impairments, when these abilities fail, as people age or suffer from brain dysfunction, learning disorders, dementias and disease.

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Histone deacetylase inhibition via RGFP966 releases the brakes on sensory cortical plasticity and the specificity of memory formation

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