Anatomy and neurosciences: Understanding the neural circuitry of function or behavior in health and disease.

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Introduction

Astrocytes are now emerging as key participants in many aspects of brain development, function and disease. In particular, new evidence shows that astrocytes powerfully control the formation, maturation, function and elimination of synapses through various secreted and contact-mediated signals. Astrocytes are also increasingly being implicated in the pathophysiology of many psychiatric and neurological disorders that result from synaptic defects. A better understanding of how astrocytes regulate neural circuit development and function in the healthy and diseased brain might lead to the development of therapeutic agents to treat these diseases [1].

The memory of fear extinction is context dependent: fear that is suppressed in one context readily renews in another. Understanding of the underlying neuronal circuits is, therefore, of considerable clinical relevance for anxiety disorders. Prefrontal cortical and hippocampal inputs to the amygdala have recently been shown to regulate the retrieval of fear memories, but the cellular organization of these projections remains unclear. By using anterograde tracing in a transgenic rat in which neurons express a dendritically-targeted PSD-95: Venus fusion protein under the control of a c-fos promoter, we found that, during the retrieval of extinction memory, the dominant input to active neurons in the lateral amygdala was from the infralimbic cortex, whereas the retrieval of fear memory was associated with greater hippocampal and prelimbic inputs. This pattern of retrieval-related afferent input was absent in the central nucleus of the amygdala. Our data show functional anatomy of neural circuits regulating fear and extinction, providing a framework for therapeutic manipulations of these circuits [2].

Spanning functions from the simplest reflex arc to complex cognitive processes, neural circuits have diverse functional roles. In the cerebral cortex, functional domains such as visual processing, attention, memory, and cognitive control rely on the development of distinct yet interconnected sets of anatomically distributed cortical and subcortical regions. The developmental organization of these circuits is a remarkably complex process that is influenced by genetic predispositions, environmental events, and neuroplastic responses to experiential demand that modulates connectivity and communication among neurons, within individual brain regions and circuits, and across neural pathways. Recent advances in neuroimaging and computational neurobiology, together with traditional investigational approaches such as histological studies and cellular and molecular biology, have been invaluable in improving our understanding of these developmental processes in humans in both health and illness. To contextualize the developmental origins of a wide array of neuropsychiatric illnesses, this review describes the development and maturation of neural circuits from the first synapse through critical periods of vulnerability and opportunity to the emergent capacity for cognitive and behavioral regulation, and finally the dynamic interplay across levels of circuit organization and developmental epochs [3, 4].

Research during the last decade has significantly advanced our understanding of the molecular mechanisms at the interface between the nervous system and the immune system. Insight into bidirectional neuro-immune communication has characterized the nervous system as an important partner of the immune system in the regulation of inflammation. Neuronal pathways, including the vagus nerve-based inflammatory reflex, are physiological regulators of immune function and inflammation. In parallel, neuronal function is altered in conditions characterized by immune dysregulation and inflammation. Here, we review these regulatory mechanisms and describe the neural circuitry modulating immunity. Understanding these mechanisms reveals possibilities to use targeted neuromodulation as a therapeutic approach for inflammatory and autoimmune disorders. These findings and current clinical exploration of neuromodulation in the treatment of inflammatory diseases define the emerging field of Bioelectronic Medicine [5].

Conclusion

The maintenance of a mental image in memory over a time scale of seconds is mediated by the persistent discharges of neurons in a distributed brain network. The representation of the spatial location of a remembered visual stimulus has been studied most extensively and provides the best-understood model of how mnemonic information is encoded in the brain. Neural correlates of spatial working memory are manifested in multiple brain areas, including the prefrontal and parietal association cortices. Spatial working memory

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ability is severely compromised in schizophrenia, a condition that has been linked to prefrontal cortical malfunction. Recent computational modeling work, in interplay with physiological studies of behaving monkeys, has begun to identify microcircuit properties and neural dynamics that are sufficient to generate memory-related persistent activity in a recurrent network of excitatory and inhibitory neurons during spatial working memory. This review summarizes recent results and discusses issues of current debate. It is argued that understanding collective neural dynamics in a recurrent microcircuit provides a key step in bridging the gap between network memory function and its underlying cellular mechanisms. Progress in this direction will shed fundamental insights into the neural basis of spatial working memory impairment associated with mental disorders.

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