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Sommario/riassunto

The vertebrate brain contains neurons and 3 classical types of glia cells, astrocytes, oligodendrocytes and microglia. Astrocytes and microglia have mainly been studied in gray matter, whereas oligodendrocytes myelinate white matter tracts. Until recently microglial effects were considered mainly during pathological conditions, but is now known that microglia plays important roles also in normal brain function. All these 3 glial cell types and their collaboration with neurons are important for learning. The concept that glia cells are important for cognitive function is not new. A glial-neuronal theory of brain function was proposed by Galambos in 1961. Hyden and Egyhazi demonstrated glial RNA changes in microdissected glia cells during learning in rats in 1963, and astrocytic and oligodendrocytic involvement of K+-mediated effects of learning has been suggested and/or demonstrated from the 1960's and onwards as recently reviewed by Hertz and Chen (Neuroscience and Biobehavioural Reviews, 2016). In 1969 van den Berg et al. showed compartmentation of glutamate in brain and thus of production of the neurotransmitters glutamate and GABA, which are essential for learning. That glutamate is synthesized in astrocytes because they in contrast to neurons express the enzyme pyruvate carboxylase was demonstrated 10-15 years later by Yu et al. in cultured astrocytes and Shank et al. in intact brain tissue. However, the present e-book focuses on more recent developments. Most information is available about astrocytic roles in learning. The

importance of astrocytes in the tripartite synapse and of microglia in the tetrapartite synapse is illustrated in the front-page figure, which emphasizes the role of gliotransmitters and of Ca2+ transport through gap junctions, coupling astrocytes into a functional syncytium. Astrocytes are important for establishments of brain rhythms, which may differ in different cognitive tasks, and although the exact reason why knock-out of the astrocytic water channel AQP4 impairs memory remains to be established, several possibilities are discussed. The importance of the two astrocyte specific processes glutamate and glutamine formation and glycogenolysis is discussed in considerable detail. Glycogenolysis is important not only for astrocytic processes involved in learning, but also for those in neurons because glycolytically derived lactate has signaling functions in the extracellular space and may be accumulated in minute quantities into very specific and small neuronal structures. Some neurotransmitters stimulating glycogenolysis are also involved in psychiatric disease. Noradrenaline, released from locus coeruleus exerts direct effects on both astrocytes and neurons and in addition promotes secretion of corticotropin-releasing hormone and adrenocorticotrophic hormone (ACTH) in brain, and of glucocorticoids from the adrenal cortex, all of which are responsible for stress effects on learning. Lead causes memory impairment by inhibition of glutamine formation due to oxidative stress and reduced effectiveness of the glutathione system. The many adverse effects of fetal alcohol exposure on behaviour and learning are caused by a multitude of effects on all three types of glia cells. Traumatic brain injury also exerts multifactorial effects, including microglia/astrocyte-induced secretion of neuroinflammatory molecules and axonal disruption and oligodendrocytic dysfunction. In normal brain oligodendrocytes respond to the depolarization caused by neuronal activity with accelerated conduction velocity and increased compound action potentials which facilitate learning.

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Autore	JENSEN, Johannes Vilhelm
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