Alzheimer’s disease is a devastating neurodegenerative disease that affects more than 35 million people worldwide. Alzheimer’s disease is a brain disorder. Our brain is a very complex organ which consists of many different cell types. Cells playing a major role in processing of the information and making memories in the brain are called neurons. To perform these functions, neurons form contacts with other neurons called synapses. Via these contacts, neurons in the brain are interconnected into elaborated networks. Neurons not only physically attach to other neurons in the network, but are also able to quickly and reliably signal to other neurons by releasing at synapses special chemicals called neurotransmitters. This process is vital for the ability of our brain to collect and process information. In Alzheimer’s disease, some of the neurons in the brain die, and the integrity of neuronal networks is irreversibly damaged resulting in the impaired brain function.

The causes of the death of neurons in brains of people with Alzheimer’s disease remain incompletely understood. Alzheimer’s disease primarily affects old people, i.e. the risk to attract the disease increases with age. Research of the molecular mechanisms of Alzheimer’s disease over the recent years showed that brains of people affected by this disease accumulate between neurons fragments of a protein called amyloid precursor protein (APP). This protein is normally located at the surface of neurons. In Alzheimer’s disease, however, this protein is cleaved and the fragments, which are released, are toxic, because they can attach to the cell surface of neurons and kill them. Over time, brains of people with Alzheimer’s disease accumulate so much APP fragments, that these fragments aggregate and form plaques, which can be seen under the microscope. Another protein, called tau, aggregates within neurons. These aggregates, appearing as tangles under the microscope, block movement of other proteins and organelles inside of neurons. Because movement of proteins and organelles is required for neuronal survival, tau tangles can also cause neuronal death. It remains however unknown what causes accumulation of APP fragments and formation of tau aggregates in Alzheimer’s disease.

Presently, there is no cure for Alzheimer’s disease. The current approaches to treatment of Alzheimer’s disease provide only temporary symptomatic relief and do not inhibit and/or reverse the underlying disease mechanisms. This highlights the urgent need for disease-modifying drugs. Further research of the mechanisms of neuronal death in Alzheimer’s disease can help to design treatments preventing neuronal loss in the brain. However, another important direction of research is investigation of the causes and initial stages of the disease preceding the neuronal death. Discoveries in this area of research will help us not only to stop the disease, but also prevent the disease or reverse the disease progression.

Importantly, studies in animals indicate that first symptoms of Alzheimer’s disease, such as problems with memory, most probably appear before neurons in the brain die and are
caused by malfunctioning of neurons, which is then followed by neuronal death. This observation is important because it means that if we understand the mechanisms of this malfunction we can develop tools to diagnose and treat the disease before irreversible changes such as neuronal death occur in the brain.

The integrity of neuronal networks and efficient neurotransmission, which are required for brain function, can be affected not only by the death of neurons within the network, but also by the disruption of the synaptic contacts between neurons in the network. Excitingly, research in this area showed that synapse loss is the major cause of the cognitive impairment in Alzheimer’s disease indicating that disruption of synaptic contacts between neurons is one of the earliest changes occurring in the brain suffering from the Alzheimer’s disease (1). Moreover, synaptic contacts between neurons provide particularly strong binding sites for the fragments of APP accumulating in brains of Alzheimer’s disease patients (2) indicating that synaptic contacts play a key role at the initial stages of the disease.

While these findings may be a key to our understanding of the initial stages of neuronal network disintegration in the Alzheimer’s disease, many questions remain unanswered. Synaptic contacts are very stable structures which can exist for many years since the molecules inside of these contacts form a scaffold highly resistant to any form degradation. How this scaffold is affected in Alzheimer’s disease and whether we can prevent its degradation in remaining intact synapses or even repair and restore affected synaptic connections are important questions for further research, which can help us to find a cure for this devastating disorder.

References: