INTRODUCTION

Neurological diseases represent pathological changes that occur in the nervous system. As the main cause of dementia and various motor disorders, neurodegenerative diseases (NDDs) occupy a prominent part in the structure of neurological pathology (Illarioshkin, 2003). This paper will focus on NDDs.

Human NDD research, which is conducted, as a rule, on autopsy material, notes two main pathomorphological signs: the accumulation of multiple (extracellular or intracellular) aggregates of various proteins and the progressive death of neurons in brain structures (Illarioshkin, 2003). At the same time, the increasing number of data clearly demonstrate that synapse dysfunction and degeneration precede the death of neurons and characterize the earliest stages of the disease. Moreover, these data confirm the view that synaptic disorders, which appear as direct consequences of gene mutations or modifications of cellular processes, determine the disease initiation and progress (Wishart et al., 2006). Collectively, the results of the latest research allow us to assume the existence of common molecular and cellular mechanisms for neurological diseases that are directly linked to these processes. The article contains a detailed description of synaptic disorders in Alzheimer’s disease, Parkinson’s disease, prion diseases, Huntington’s disease, autism, and amyotrophic lateral sclerosis. The role of synaptic dysfunctions in aging is also discussed.

ALZHEIMER’S DISEASE

Alzheimer’s disease (AD) represents the most frequent advanced-age NDD; it is characterized by a progressive loss of memory, speech disorders, and
decreased content of synaptophysin was detected at Terry, 1993; Davidsson and Blennow, 1998). Thus, a gene expression and synaptic proteins (Masliah and et al., 1999). Note that violations in the structure of synapses and in the expression of genes of synaptic proteins reflect the earliest AD stages and precede the formation of amyloid plaques and neurofibrillary tangles (Catado et al., 2000).

According to current views, the formation of toxic oligomers Aβ is the basis for the causal loss and dysfunction of synapses in AD. In fact, the synapse loss occurs in close vicinity to amyloid tangles; therefore, they can be the source of toxic Aβ oligomers (Tsai et al., 2004).

The detailed mechanism of Aβ oligomerization and the structure of intermediate compounds formed during the formation of amyloid fibrils are still studied insufficiently. Nevertheless, it has been established that, among oligomers, there are soluble dimers, trimmers, dodecamers, and oligomers of a higher order, designated in the literature as Aβ-derived diffusible ligands (ADDLs) and protofibrils (Lambert et al., 1998; Walsh et al., 1999). Synthetic Aβ-oligomers or oligomers, extracted from the medium of cell cultures expressing mutant APP, initiate synaptic dysfunctions both, in vivo and in vitro (Enya et al., 1999; Walsh et al., 1999). In addition, Aβ dimers and trimmers have the most expressed effect of inhibiting long-term potentiation (LTP) (Townsend, et al., 2006; Shankar et al., 2007). Note that Aβ oligomers cause significant disorders in cognitive functions in animals, both during injections into the brain (O’Hare et al., 1999; Cleary et al., 2005) and on transgenic models (Mucke et al., 2000).

The synapse dysfunction caused by Aβ oligomers has a very complex mechanism associated with the disturbance of Ca2+ homeostasis and the functions of N-methyl-D-aspartate (NMDA) receptors (Liu et al., 2004; Mucke et al., 2000; Citri et al., 2008). Long-term potentiation depends physiologically on the Ca2+ inflow through the NMDA receptors and occurs when its concentration increases (Kullmann and Lamsa, 2007; Citri et al., 2008). Interestingly, mutations in the gene of presenilin 1 (PS1), which cause an early familial AD form, amplify the Ca2+ accumulation in the endoplasmic reticulum and lead to LTP defects (Popugaeva et al., 2012). The Aβ oligomers inhibit LTP induction and cause the disturbance of the structure of dendrites and the collapse of synapses, which show up in cognitive defects (Palop and Mucke, 2010). Thus, injections of synthetic and natural Aβ oligomers into the brain change the behavior of animals, including their memory and cognitive functions (O’Hare et al., 1999; Cleary et al., 2005). The neutralization of soluble Aβ oligomers using Aβ antibodies normalizes behavioral anomalies in various lines of transgenic animals (Kotilinek et al., 2002; Dodart et al., 2002; Klyubin et al., 2005).

![Diagram](attachment:image.png)

**Fig. 1.** Amyloidogenic synaptic proteins cause synaptic dysfunctions and neurodegeneration (after Masliah et al., 2001, with modifications).