Imagine waking up in the morning and not knowing where you are, what should you do next? Choose clothes… but which one? How to dress yourself, how to tie shoes? Someone just entered the room, but who is that person? Is it your loved one or an oppressor…

It starts with minor mistakes: errors in calculating house expenses, problems with remembering names of relatives and friends, problems with recalling yours yesterday's activities, performing basic, routine duties in everyday life or with choosing the appropriate words in a conversation. This description may refer to our future self or any person we know. If it will not happen tomorrow – but may come within a few or a dozen of years. Statistics are alarming: according to the World Health Organization (WHO), there are around 50 million people with dementia worldwide, and the data predict that up to 152 million people will be affected by 2050. The aging-associated diseases are becoming an increasing burden for a rapidly aging societies.

Alzheimer's disease (AD) is a neurodegenerative disease affecting the nervous system and causing a progressive dementia – slow weakening and finally total impairment of cognitive functions including attention, memory and behavioral control. AD leads also to a mental impairment and personality changes. Dementia prevents the affected person from living a full and happy life and significantly affects the life of his/her relatives and caregivers. Alzheimer's disease has an unexpected onset and the symptoms inevitably increase over time.

Typically AD affects people over 60 years of age – this type of AD is called *sporadic* or *late-onset* Alzheimer's disease (LOAD). Exactly this type of AD is the subject of the proposed research. Patients are usually diagnosed after the onset of clinical symptoms, when the changes in the brain are already advanced. Due to the late diagnosis, effective treatment is not possible. There is no known existing drug or treatment that would reverse the neurodegenerative changes in the brain. Current therapies are aimed only at delaying the inevitable progression of the disease and improving quality of patient's everyday life. For these reasons, it seems to be extremely important to study and deepen the knowledge about the early mechanism triggering (or delaying) the development of LOAD. Dementia is caused by many interacting factors, including genetic ones. It was proven that the risk of developing late form of Alzheimer's disease is higher among people with specific variants of particular genes (variant ε4 of the APOE gene and specific variants of additional genes: PICALM, CLU and CR1). If we have these gene variants, we have them from the very beginning of our lives. However, it is not known if they are responsible only for neurodegenerative processes observed in late age, or they affect the functioning of the brain throughout life – long before any clinical signs of dementia can be spotted.

In our project, we intend to study executive functions and attention in healthy middle-aged people, who however bear the burden of genetic factors that increase the risk of developing Alzheimer's disease. For this purpose, we will perform genetic screening on a larger group in search of people characterized by having two selected variants of the APOE and PICALM genes. We are going to investigate, whether and how, the brain activity of these people is different from an age-matched control group. We want to evaluate the functioning of the brain areas responsible for attention and executive control (including the cingulate cortex and the cingulo-fronto-parietal cognitive network). For this purpose we will use a computer task in which conflicting information should activate mentioned brain areas. We are going to examine these activations using two neuroimaging techniques: functional magnetic resonance imaging (fMRI) and multichannel electroencephalography (EEG). Apart from standard data analysis, we plan to apply *machine learning* technique – a method that allows to efficiently detect specific patterns in a large-scale data.

We hope that this will bring us closer to finding, in the EEG and/or fMRI results, functional, biological biomarker of the earliest cognitive impairment that may precede the development of clinical Alzheimer's disease.