

We are aging society.

Nowadays, the study of aging is of increased interest to scientists due to demographic changes and the expanding of senior population in many European countries, including Poland. As advancing age is usually associated with poorer mental resources, it may be expected that because of such demographic shift more individuals will suffer from declined cognition. Such statement is supported by a large body of experimental data indicating clearly in elderly (even in normal healthy elderly without any signs of neurodegenerative diseases) the progressive loss of function across multiple cognitive systems, including new learning, memory, perception, attention, language, motor control, problem solving, etc. Furthermore, our previous studies indicated that these age-related declines are accompanied by deteriorated temporal dynamic of information processing which provides a frame for human mental activity. Hence, '*cognitive aging*', as well as so called '*healthy aging*' is in the centre of interest in modern neuroscience. It refers to declines in various mental functions that markedly changed after 65 years of age in normal healthy elderly. Our Project is in line with these studies and offers an innovative approach to verify the effectiveness of different training methods in amelioration of cognitive function, considering also the changes in the neural basis of our brains.

The traditional view assumed that functional decline in aging is unavoidable, because it is a direct consequence of brain machinery wearing down. In recent years, a new viewpoint argues that the improvement of mental function in elderly is still possible using appropriately designed training programs. The challenging finding was that cognitive declines in elderly can be reduced because their brain is still able to reorganize its structure and function. Such reorganization is due to the plasticity of the nervous system which still dominates brain function.

At this point one should mention that the term '*plasticity*' of the nervous system was introduced into the scientific world by the Polish Scholar – Jerzy Konorski who worked in the Nencki Institute – the Leader of the Consortium which will realize the present Project. Existing studies on adult brain plasticity have shown that following the applied therapy improvement of cognitive function may be possible. Up to data, it remains still an open question which type of intervention would be most beneficial for elderly. Moreover, of special interest is the transferability of benefits into the broad cognitive spectrum which remained untrained during the intervention. These questions are still a neglected topic and the existing publications cannot be conclusive.

These findings start a big discussion which type of therapy and, if so, which intensity of performed exercise would be most prominent for the improvement of mental activity. Such discussion has been reflected not only in existing scientific publications, but also in the public interest, programs of the European Commission in Brussels, media, as well as in government politics considering the needs of aging society. In light of these important problems of XXI century, as well as the needs of the modern society, the present Project offers a novel approach to improvement of cognitive function in elderly and aims at comparison of benefits for amelioration of mental function following two different types of intervention, i.e. the cognitive training (applied in the experimental Group A) and physical activity training (experimental group B), as compared to two control groups (C and D). Group C will obtain the placebo training and Group D will be served as non-active controls obtaining no training.

All training procedures, i.e. the cognitive, physical or placebo will be conducted with protocols as matched as possible. The major trump is that the cognitive training is not focussed on particular cognitive functions (called '*closed skill training*'), but on underlying neural mechanisms creating a situation of the '*open skill training*' with benefits transferable to other untrained cognitive domains. The cognitive training will be performed in laboratory setting and consists of (1) selected modules from the existing therapy program "Dr Neuronowski" already developed in our Laboratory, and (2) action computer games. The physical training comprises strength and stretching exercises which will be performed in a gym under supervision of a professional trainer instructor and monitored by the cooperating geriatrician. The placebo training comprises watching educational films in the laboratory setting. Both the cognitive and placebo training (Groups A and C) will be supervised by the experimenter. Each kind of training will be performed in 3- subject subgroups for 8 weeks with the intensity of 3 sessions per week and 45 min duration per each session.

To verify the effectiveness of each training kind, we apply the complex interdisciplinary diagnostic assessment, comprising geriatric, psychological, physical, neuropsychological and neuroimaging investigations. The geriatric assessment will focus on the health status of tested subjects. The psychological assessment includes the application of life quality questionnaire. The assessment of the physical status will be evaluated using Six-Minute Walk Test (6MWT). The neuropsychological assessment will be focused on evaluation of the broad aspects of cognitive functions on the basis of 15 tasks that measure associates learning, short term and working memory, attention, executive functions, and temporal information processing as a basic logistic function underlying human cognition. Neuroimaging assessment will be performed to learn and understand the neuroplastic changes following the applied therapy, using modern neuroimaging methods, like structural (MRS, DTI) and functional (rsMRI, fMRI) Magnetic Resonance Imaging (MRI). These methods are characterized by the good spatial resolution, but poor temporal resolution and will be accompanied by electrophysiological assessment characterized by the good temporal resolution but the poor spatial one. These multidisciplinary assessment aims at understanding better the mental space for individual cognition that contributes significantly to our mental wellbeing and life quality.

All these diagnostic methods will be applied before- and after the training to compare the effectiveness of applied interventions. Non-active controls (Group D) will complete the pre-and post-testing assessment in the time span related to the training in groups A, B, C. To verify the stability of obtained improvements over a longer period of time, a follow-up assessment will be conducted after 8 weeks.

Subjects are ca. 96 elderly volunteers (male, female), aged between 65 and 69 years in relatively good health without any signs of mental retardation (geriatric diagnosis). They will be randomly assigned to one of the groups described above (A, B, C, D).

Following realization of this Project we expect to provide a new knowledge on improvement of both mental and physical fitness in elderly. Specifically, we assume the significant stable over time improvements in the cognitive status following both the cognitive and physical training. These improvements will comprise new learning, short term and working memory, attention, executive functions and temporal information processing. These cognitive benefits will be accompanied by neuroplastic changes

verified in electrophysiological, MRI and fMRI assessments. Furthermore, we anticipate significant correlations between results of particular cognitive tests (or life quality questionnaire) and neuroimaging data. Because of the high impact of the complex cognitive training, its application may result in more transparent improvements and more pronounced neuroplastic changes than the physical exercise. On the other hand, the physical training will result in improvement of the physical fitness, as it improves directly the particular body muscles. Following the placebo training, as well as in non-active controls neither cognitive nor physical improvements are expected. The modified behaviour following the applied training may be used in every-day activities, evidenced in the applied life quality questionnaire.

These results may provide important insights not only into age- or training-related changes, but also into the dynamic flow of information in our brains.