

Brain, being an important and fragile organ, needs special protection. One of its defences against potentially toxic substances and pathogens, which could be circulating in the blood, is a mechanism called blood-brain barrier (BBB). Specialised cells and proteins which are the building blocks of the BBB constitute a specialised border between blood and brain tissue, only letting some of the circulating substances and cells through. However, at times, the permeability of the BBB might not be balanced properly – resulting, for example by such modulation of blood-brain substance exchange which significantly impacts brain metabolism and promotes inflammatory processes within it (which might be one of the mechanisms leading to depression). There are many factors which may influence the permeability of the BBB – most importantly inflammation (both local and systemic) and physical exercise. One potential disease associated with inflammation, is depression as it may develop as a result of the actions of cytokines and inflammatory mediators in the brain. We can mark increased levels of cytokines and other markers of inflammation in the blood of depressed individuals, as well as the latest neuroimaging technologies enable us to observe some changes in brain neurotransmitters among depressed patients. The current recommendations for depression treatment typically involve pharmacologic treatment, usually with a selective serotonin reuptake inhibitor (SSRI), but there is increasing interest in the effect of alternative therapies, such as physical exercise, which can reduce symptoms of depression and reduction of inflammation.

The main objective of the project is to find out how physical exercise influences both BBB permeability and brain metabolism in depressed patients. We are going to check that by taking 50 patients who have been diagnosed with major depressive disorder and randomly assigning them into two groups. First group, will be receiving a standard antidepressant therapy. The second group will also receive standard antidepressant therapy, however, after 6 weeks they will start regular gym trainings, performing special type of exercise called ‘resistance exercise training’. They will then attend the gym twice a week, for 24 weeks. Both groups will be regularly assessed by measuring their intensity of psychiatric symptoms. More importantly, however, their brain metabolism (by MRI spectroscopy) and certain inflammatory process markers in the blood will be tested twice (at the beginning of treatment and after 6 months). We will then compare the results between those groups, answering the research questions we have stated.

We expect that:

- Physical exercise will diminishes the inflammatory process within the brain
- Adding physical exercise to standard antidepressant treatment in patients with major depressive disorder will diminish the permeability of the BBB
- Brain metabolism in the experimental (second) group will be altered