

At the turn of the 20th and 21st centuries addictions were no longer 'niche' disorders, which were typical of some social groups, but became a global, social and economic problem. Who has no immediate or distant relative or a friend who is addicted, or has witnessed tragic consequences of the addiction?

Addiction has become a popular term in everybody's vocabulary. It is very often that we can hear: "I think I am hopelessly addicted to it". This term is used both colloquially and in the non-scientific context as well. But what about people who drink a lot and lose their true 'self'? They are very often called 'drunkards'. Those who habitually smoke cannabis are called *potheads*, and people who take illegal drugs, such as heroin, are called 'drug-addicts' or 'junkies'. These pejorative terms point out that the drug-takers 'are not some of us' and that the problem with drugs is their own fault and that they should be punished for that. Such people are either 'evil', 'mad' or 'stupid' and in order to stop using drugs they should simply become 'good', 'healthy' or 'educated'. However, is this transformation simple or possible, if at all? Is it either biological, genetic or environmental factors or maybe a desire to find relief and pleasure that plays the main role? Is addiction a sin, brain or soul disease or emotional dysfunction? What is behind a drug addict who is still suffering? Haplotypes, genotypes, changes in the level of methylation in the DAT1 gene promoter region or just a pain of their soul which is not connected with genetic factors? We still do not know that. However, it is a fact that thousands of people suffer trying to get out of their habit and at the same time are still in it. We still know too little to provide effective help for patients. That is why we have made our decision to do this research. We want to examine 300 people, mainly from the MONAR centres, who are addicted to psychoactive substances and 300 healthy people who will form a control group. Psychological tests, biological material sampling in order to isolate DNA and examination of polymorphisms of the genes in the dopaminergic system (DRD2 and DRD4 dopamine receptors and DAT1 dopamine transporter) will be carried out in both groups. Apart from that we will examine the level of DNA methylation in the DAT1 promoter region, which we previously examined in the people who are addicted to alcohol, and we received promising results. We would like to use the obtained results of genetic research to create haplotypes in order to find a haplotype predisposing to addiction. Why dopamine?

Chemical compounds, which are potentially addictive, are distinguished by their capacity to stimulate dopamine release, e.g. in the nucleus accumbens via other neural pathways. Additionally, a combination of unfavourable external factors, including stress and failure, with hereditarily weakened dopaminergic conductivity in the reward system results in a heightened sensitivity to the occurrence of addictions. The consolidated receptor changes in the dopaminergic system, on which sensitization is based, can contribute to the increased risk of recurrence. The dopaminergic system in the limbic region generates subjective pleasurable sensations in response to the stimuli related to eating, having sex or unnatural stimuli such as drugs or alcohol.

It is an enormous challenge, but one should be persistent in their efforts to understand the aetiology of this multifactorial disorder and use knowledge, which is gained in this manner, to control it. This project, which focuses on identification of genetic determinants of addictions, is supposed to be one step towards this direction.