Did you have a good time? We know where you'll store the memory of it

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Where do you go for a tasty bite and where the food is not so good? Where are you likely to meet an attractive partner and where you risk damage to your health? For every person – but also for animals – the information about pleasant and unpleasant experiences is of key importance. Researchers from the Nencki Institute in Warsaw discovered how and where nice memories are stored.

As shown by researchers from the Nencki Institute of Experimental Biology in Warsaw, Poland, nice memories are stored in an area of the brain known as the central nucleus of the amygdala. The results obtained by the group of Prof. Leszek Kaczmarek and Dr. Ewelina Knapska, which were published in the well-known *Journal of Neuroscience* show that just one protein plays the key role in the process of memorizing pleasant experiences. In the future these results may help design more effective treatment of addictions, depression and schizophrenia.

"We want our research to help us understand the relation between the mind and the brain by studying memory, which is of fundamental importance for the mind. Without memory there is no mind", Prof. Kaczmarek explains context of the research.

Neurobiologists differentiate between many types of memory, the most basic types of which are characterized by clear duality. For example we have short and long term memories, declarative (referring to events/data) and procedural (memory of actions). Researchers from the Nencki Institute focused on another dichotomy of great importance to every

animal. They focused on appetitive memory related to memories of pleasant experiences and aversive memory related to unpleasant experiences.

Experimental research on human memory often comes across a very basic problem: there are no volunteers for the experiments. No one of sound mind will agree to participate in experiments involving his or her own memory. Fortunately having a mind is not limited to humans. Many mental activities typical for humans take place also in the minds of animals. Therefore scientists from the Nencki Institute conducted their experiments on mice.

These novel experiments on memory have been conducted on mice placed in the so-called IntelliCages. In each corner of such cage two water bottles have been placed. In order to get water a mouse has to get to the corner and nose poke on a small gate of a given bottle. Depending on the type of experiment, the mouse will either get water or harmless but unpleasant puff of air on the nose. All mice in the cage have individual ID chips and therefore researchers are able to tell exactly what decisions are made by each mouse.

IntelliCages make it possible to conduct different experiments. If for example in one corner sweet water (that is an appetitive stimulus) bottles are placed, the effectiveness of spatial memory in mice can be investigated. More subtle experiments are also possible by placing only one sweet water bottle in a selected corner. Then the mouse needs to remember not only the corner where the sweet water bottle is, but also which of two bottles contains sweet water.

Twenty five years ago Nencki researchers have observed changes in the activity of a gene known as *c-fos* in the nervous cell nuclei during learning. One of the proteins, the production of which is regulated by a protein encoded by the *c-fos* gene, is the MMP-9 enzyme active outside

of the cell. Researchers decided to investigate the role of MMP-9 in memorizing pleasant and unpleasant experiences. In order to do this a series of experiments was conducted on control mice and on mice either lacking this protein entirely or with its selective blocking only within the central amygdala.

The amygdala is a small structure within the cerebral hemisphere and it is located at the base of the brain, close to the hippocampus. It consists of two groups of nuclei responsible for innate and acquired emotional reactions, such as laughter or fear.

Researchers were surprised by the experiments. When placed in the IntelliCages, the control mice after three days of learning almost always chose the corner with sweet water. Mice lacking MMP-9 behaved distinctly different: they showed no preference for any of the corners. At the same time all mice equally well remembered the corner where they received the unpleasant puff on their noses. Furthermore, selective blocking of MMP-9 just in the central amygdala produced the same effect – the memory for the sweet water location could not be formed.

"The results are clear. Pleasant experiences are memorised due to changes in plasticity within the neurons of the central nucleus of the amygdala. At the same time we have shown that just one protein, the MMP-9, is responsible for learning about pleasant experiences themselves and memorizing them. At the same time this protein has no impact on the memory of unpleasant experiences. These are important discoveries and to tell the truth making them was... very pleasant", says Prof. Kaczmarek.

These research results, which stem from experiments conducted at the Nencki Institute for the past 25 years, hold great scientific significance for they explain the processes of learning and appetitive memory by referring to two seemingly very distant domains of neurobiology: system

– investigating entire neuronal structures (such as the central nucleus of the amygdala) – and molecular, investigating physical and chemical processes responsible for various functions of nervous cells (in which the MMP-9 protein takes part).

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