Feel-good hormone helps to jog the memory

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The feel-good hormone dopamine improves long-term memory. This is the finding of a team lead by Emrah Düzel, neuroscientist at the German Center for Neurodegenerative Diseases and the University of Magdeburg. The researchers investigated test subjects ranging in age from 65 to 75 years, who were given a precursor of dopamine. Treated subjects performed better in a memory test than a comparison group, who had taken a placebo. The study provides new insights into the formation of long lasting memories and also has implications for understanding why memories fade more rapidly following the onset of Alzheimer's disease. The results appear in the *Journal of Neuroscience*.

Dopamine is a multi-faced neurotransmitter. It provides communication between nerve cells as well as between nerve and muscle cells. If this signal transmission becomes disturbed, the consequences can be dramatic. This is illustrated by Parkinson's disease, whose symptoms – akinesia and other movement disorders – can be traced back to a lack of dopamine. On the other hand, when someone is pleased or motivated, a flood of dopamine is released in the brain, which is why the term "feel-good hormone" has become popular. There have already been indications of the special role of dopamine in forming long-lasting memories for some time. The signs came from various studies and also from the fact that rewarding incidents and other important events can usually be remembered for a long time. Researchers led by Düzel, who is also affiliated with University College London, have now been able to confirm this effect in older people.

"Our investigations for the first time prove that dopamine has an effect

on episodic memory. This is the part of long-term memory, which allows us to recall actual events. Occurrences in which we were personally involved," Düzel says. The Site Speaker of the DZNE in Magdeburg and Director of the Institute of Cognitive Neurology and Dementia Research at the University of Magdeburg adds: "Episodic memory is that part of our capacity to remember, which is first affected in Alzheimer's dementia. This is why our results can contribute to a better understanding of the disease."

Recognising pictures

In particular animal studies have indicated that to store experiences permanently the brain has to release dopamine. Düzel and his colleagues examined whether this also applies to humans: the task of the test subjects ranging in age from 65 to 75 years was to recognise photos which they had been shown previously. Half of the test participants had first taken a placebo and the remainder had taken Levodopa. This substance, also known as L-DOPA, is able to reach the brain from the bloodstream, and there it is converted into dopamine. In this way the researchers could exercise a targeted influence over dopamine levels in the brains of the test subjects. "Neurons, which produce dopamine, decline with age," Düzel says. "Increasing dopamine levels in these elderly subjects, should show a clear effect." The neuroscientist mentions another reason for undertaking the study with older people: "In old age the episodic memory declines. This is why the topic we are investigating is particularly relevant for elderly people."

The participants were first shown black and white photos of indoor scenes and landscapes. They were to differentiate these images from others, which they had not seen before. When they first viewed the pictures brain activity of the participants was monitored using fMRT, a special form of magnetic resonance tomography. The photos which triggered hardly any activity in the memory centre were of particular

interest to the neuroscientists. The reason: If this brain area is only slightly active, then it should cause little or no dopamine release. "In such cases the memory of these pictures should gradually fade. As they have been encoded only weakly," Düzel says, "we wanted to find out whether the memory of these pictures could nevertheless persist."

Effect after six hours

Two and six hours after the participants had memorized the photos, they were requested to recognise and distinguish them from new images.

In the test after two hours there was no significant difference between participants who had taken Levodopa and those who had consumed a placebo. However, after six hours memory performance changed. Test subjects with Levodopa recognised up to 20 per cent more photos than the members of the comparison group. The ratio between the amount of Levodopa taken and the body weight of the test subjects proved to be decisive for an optimal dose. "This confirms our assumption that dopamine contributes to anchoring memories in the brain on a permanent basis. You might say it improves the survival chances of memory content," Düzel indicates. "Our study also shows that the survival of memories can be regulated, regardless of how strong these were originally encoded. This is a new finding."

But why did the effect emerge only after six hours? Düzel sees the cause in the way in which the brain stores memories. "When memories are encoded, certain changes take place at the nerve endings, the so-called synapses," he explains. "This activation is however only temporary, and afterwards the state of synapses change back again. This is unless dopamine is available so that newly formed synapses can be stabilised over a long period of time." The test after two hours must still have taken place during the period of short-term synaptic activation, according to the neuroscientist. Both test subject groups therefore had

similarly good results. However, at the later time the memories of the test participants with the placebo had already started to fade. Now, the influence of the dopamine was noticeable for the other test subjects.

Future outlook

In this study participants had taken the dopamine precursor before memorizing. The finding that the persistence of memories can be influenced – independent of whether memory encoding was weak or strong – might open the way to further investigation. "It is conceivable that participants might receive the supplement at a later stage," Düzel says. "The idea is that they learn something, then take dopamine afterwards and still don't forget what they have learnt."

In addition, the study gives food for thought for the treatment of Alzheimer's dementia. "The episodic memory suffers substantially when affected by Alzheimer's. Our results show that in addition to current forms of treatment, which chiefly target certain protein deposits in the brain, other aspects should also be taken into consideration", Düzel says. "Here dopamine and the so-called neuromodulatory systems, which release chemical messengers into the brain are of particular importance. But so far, research into this topic is still in its infancy."

More information: "Dopamine Modulates Episodic Memory Persistence in Old Age", Rumana Chowdhury, Marc Guitart-Masip, Nico Bunzeck, Raymond J. Dolan, and Emrah Düzel, *The Journal of Neuroscience*, online at: www.jneurosci.org/content/32/41/14193

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