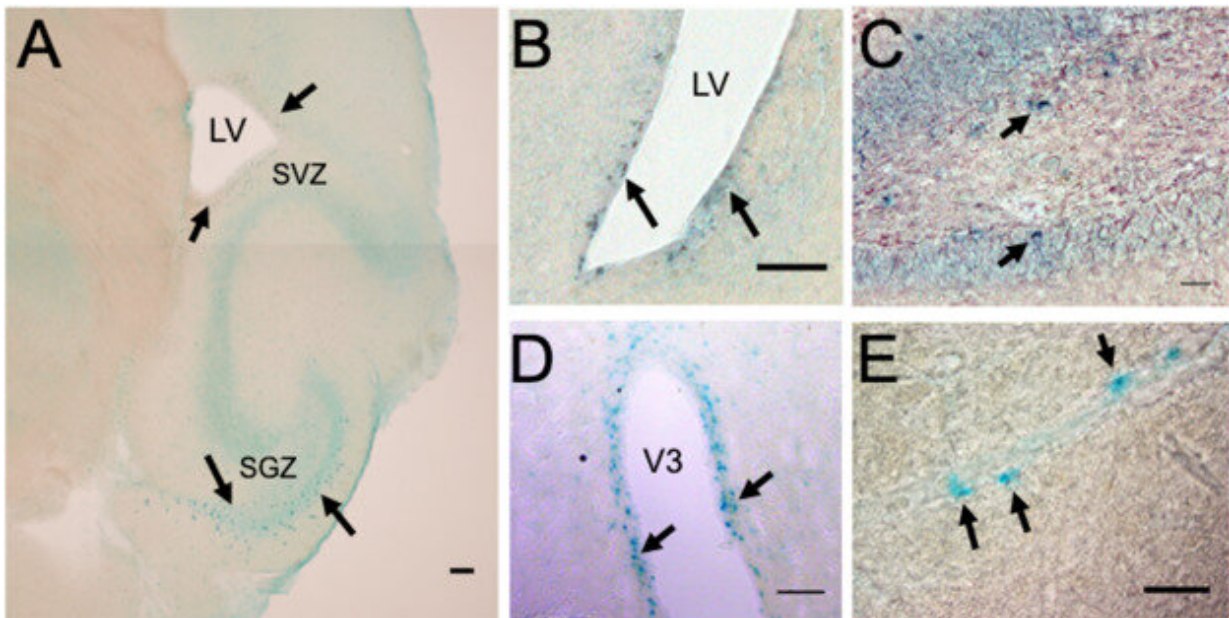


# Trace amine-associated receptor 5 (TAAR5) works to rewire your brain naturally

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TAAR5 is detected in the brain regions that are associated with adult neurogenesis. Credit: SPbU

St Petersburg University researchers, led by Professor Raul R. Gainetdinov, Director of the Institute of Translational Biomedicine and Academic Supervisor of the St Petersburg University Hospital, have found a new role for recently discovered neurotransmitter system that uses the trace amine-associated receptor 5 (TAAR5) for neurotransmission. It has been observed that lack of TAAR5 in mice

leads to a higher number of dopamine neurons and an increase in adult neurogenesis, i.e. the process by which new neurons are formed in the brain. This may provide a new treatment opportunity for neurodegenerative disorders such as Parkinson's disease.

Today, many clinically used drugs affect neurotransmission, that is the process of how the [neurons](#) communicate between each other or pass signals to other cells via chemicals. Among the well-studied neurotransmitters, i.e. chemical messengers which transmit signals across [nerve endings](#) in the body, are dopamine, norepinephrine, serotonin, histamine, and glutamate to name but a few. Earlier this year, the same group of researchers reported the discovery of a new neurotransmitter system that transmits signals from nerve cells to target cells via trace amine-associated receptor 5 (TAAR5).

"Trace amine-associated receptors (TAARs) are a class of receptors that detect biogenic amines, which are the products of decarboxylation of amino acids. In other words, each amino acid has its amine," says Professor Gainetdinov. "As a rule, the acid part is removed by the enzymes (decarboxylases) that catalyze decarboxylation. They are found in our body or in certain bacteria that metabolize amino acids, for example, when bacteria break down tissues. Little wonder, the trace amines are abundant in fermented foods, such as cheese, wine, beer, and cured meats."

The majority of TAARs have been described mainly in the [olfactory epithelium](#) in the nose and considered to be olfactory receptors sensing innate odors (decaying tissue, pheromones, predators). Yet TAARs are also found in certain [brain areas](#) and involved in the regulation of our emotions, as discovered by scientists from the Institute of Translational Biomedicine at the University. The experiments revealed that TAAR5 knockout mice with a 'switched off' gene that encodes the TAAR5 protein demonstrate antidepressant—and antianxiety-like behaviors and

alterations in brain serotonin transmission.

Further detailed investigations focused on how TAAR5 can influence dopamine neurons in the substantia nigra of the brain. Certain neurodegenerative disorders, including Parkinson's disease, are associated with the loss of dopamine neurons. The research findings were quite unexpected, scientists say.

"The number of dopamine neurons in the substantia nigra and dopamine content increased by 30% in mice lacking TAAR5 compared to wild type animals. Such an increase in the number of dopamine neurons can occur either during development or via alterations in adult neurogenesis. Some neurons are known to form in the neurogenic areas of the brain such as the subventricular zone (SVZ) and the subgranular zone (SGZ) in adult mammals. The analysis showed that TAAR5 is present in these canonical neurogenic areas as well as in potentially neurogenic zone surrounding the 3rd ventricle. It is known also that adult neurogenesis can be regulated via serotonin receptors, dopamine receptors, and adrenoceptors and it can be increased during antidepressant treatment. In fact, we found out that TAAR5 knockout mice show increased adult neurogenesis," says Professor Gainetdinov.

TAARs may serve as intra-brain 'olfactory' sensors to detect decarboxylated amino acids and thereby provide a neurotransmitter mechanism for triggering a neurogenic reaction in response to various pathological processes in the brain. Thus, TAARs may not only modulate emotional behaviors but also regulate adult neurogenesis. Targeting TAAR5 can provide a new treatment opportunity for neurodegenerative disorders, including Parkinson's disease and Alzheimer's disease.

Yet much is to be done. Scientists are striving to evaluate future selective TAAR5 antagonists on adult neurogenesis. Further detailed investigations are necessary to clarify the molecular mechanism leading

to an increased number of [dopamine](#) neurons in the substantia nigra of TAAR5 knockout mice.

**More information:** Evgeniya V. Efimova et al, Increased dopamine transmission and adult neurogenesis in trace amine-associated receptor 5 (TAAR5) knockout mice, *Neuropharmacology* (2020). [DOI: 10.1016/j.neuropharm.2020.108373](#)

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