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## PRESS RELEASE

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### SEROTONIN'S EARLY ROLE IN THE AS- SEMBLY OF BRAIN CIRCUITS

Although the genetic bases for vulnerability to mental illnesses are starting to come to light, the underlying biological mechanisms are still poorly understood. During the development of the cortex, different kinds of neurons must migrate to attain their final destinations, before forming the essential neural circuits necessary for good cognitive and emotional function. But early dysregulation in the serotonin system -an essential neurotransmitter in mood regulation- has been associated with a higher risk of developing psychiatric problems, and seems to disturb this neurodevelopmental process. Researchers at the University of Geneva (UNIGE) have discovered the crucial role of a serotonin receptor in this phenomenon, which has also allowed a better understanding of the key role early serotonin plays in the assembly of brain circuits. Read the results in *Nature Communications*.

A lot of research has shown that poor regulation of the serotonin system, caused by certain genetic variations, can increase the risk of developing psychiatric illnesses such as autism, depression, or anxiety disorders. Furthermore, genetic variations in the components of the serotonin system can interact with stress experienced during the foetal stages and/or early childhood, which can also increase the risk of developing psychiatric problems later on.

In order to better understand serotonin's influence in the developing brain, Alexandre Dayer's team in the Psychiatry and Fundamental Neuroscience Departments of UNIGE's Faculty of medicine examined a particular receptor for this neurotransmitter, and its role in the formation of brain circuits. The researchers were able to show that this receptor, which is expressed in inhibitory interneurons (cells that regulate excitement in order to avoid potentially pathological cerebral over activity), was indispensable in order for neurons to find their correct location in the developing cortex.

#### Psychological vulnerability caused by incorrectly assembled cortical circuits?

Through a series of experiments in mice, scientists were able to demonstrate that stimulating this receptor modifies the activity and migration of the interneurons during a specific phase in their migratory process. This mechanism allows them to position themselves correctly in the different layers of the cortex, a key step in the development of brain circuits. Conversely, a poorly functioning receptor can change the setup of the circuits, and could potentially explain the behavioural problems observed in the mice. Identifying the role of this receptor in the migration of cortical interneurons therefore makes it possible

how **early dysregulation of serotonin can alter the assembly of cortical circuits**, and potentially cause increased **vulnerability to mental illnesses**

to propose a new mechanism for better understanding how early dysregulation of serotonin can alter the assembly of cortical circuits, and potentially cause increased vulnerability to mental illnesses.

This study opens the door to larger studies on the role of serotonin in brain development. “Our discovery poses several important questions,” emphasised Alexandre Dayer, “including about the use of medicine by pregnant women which could modify foetal serotonin levels. We also want to understand how early stress acts on this receptor and modifies the function of the neurons in question.” Professor Dayer’s team is now working on these questions as part of the national “*Synapsy*” National Centre of Competence in Research.

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