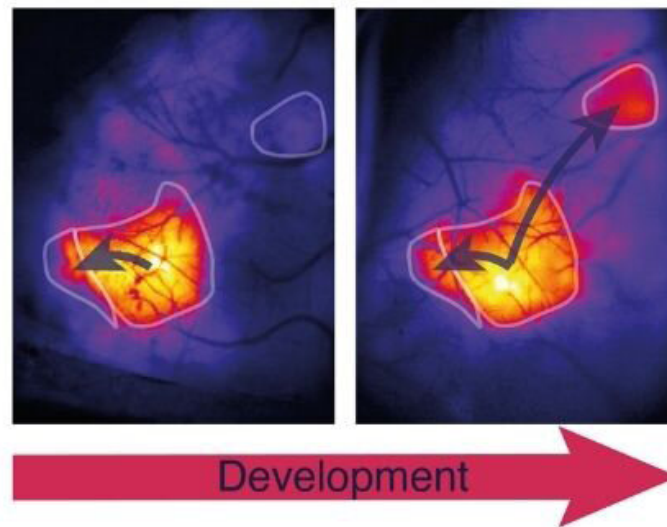


# Brain connections have their own tempo

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The activation of cerebral cortex areas increases progressively during postnatal development. In this study, the authors unraveled the genetic bases for the establishment of such connectivity. Credit: UNIGE – Laboratoire Denis Jabaudon

The cerebral cortex, located at the surface of the brain, handles the cognitive, language, and complex functions that allow us to represent the world or project ourselves into the future. By being able to categorize and associate the stimuli it receives from our five senses, the cortex links this information together to make sense of it. To do this, different types of neurons establish cortical connections during embryonic development and early postnatal life. What is the biological mechanism by which this

delicate assembly is created? A team from the University of Geneva (UNIGE), Switzerland, has now deciphered this process: although neurons are anatomically distinct, their genetic programs remain very similar. It turns out that the differences emerge during the molecular maturation of these neurons, which must follow a precise rhythm to establish the right connections. These surprising results can be discovered in the journal *Nature*.

The various functions managed by the [cerebral cortex](#) are not randomly distributed, but instead are organized according to a precise map. For instance, [visual areas](#) are located at the back of the head, while touch is represented on the side, and [motor control](#) in the front. To perform their different functions, however, these areas must communicate effectively. "And this is continually verified: to catch a ball, for example, visual and motor areas must coordinate," explains Denis Jbabaudon, a professor in the Department of Basic Neurosciences at the UNIGE Faculty of Medicine, who led this research. These connections are essential for human beings to construct a coherent vision of the world. However, choices must be made so that associations are not erroneous and the most useful associations are selected.

## **A common genetic partition played at a different tempo**

Connections between cortical areas are provided by so-called 'inter-areal cortical projection neurons' (ICPN), which send electrical signals to their cortical target(s). "For cortical areas to communicate, the system must connect precisely," Denis Jbabaudon points out, "and for this to happen, different types of connections must be established at the right place and at the right time." To understand how this phenomenon takes place, Dr. Esther Klingler, a researcher in Denis Jbabaudon's team, and their colleagues studied how the connections between the areas responsible

for touch and motor skills are established in mice after birth. "To our great surprise, the [genetic programs](#) of the two ICPN populations were not different overall, despite their anatomical dissimilarities. However, the tempo governing their expression varied considerably."

Thus, neurons making connections of a given type develop more rapidly, while others developing more slowly, connect to other cortical areas.

"Our work suggests that creating diversity in neurons does not always require major genetic diversity. It seems that in this case, the score sheet is similar, only the rhythm of the music changes."

To confirm their discovery, the scientists modified the execution of this genetic program by expressing, over a long period of time, a gene that is normally expressed only at the beginning of the process. Mice then showed abnormal sensorimotor connectivity, as well as an unusual exploration of their environment. This single change disrupted the entire system.

## **Touch-movement relationship comes first**

Distinct neuronal types thus have distinct maturation rhythms, that are reflected in the order in which connections between [brain](#) areas appear.

"In mice, active exploration of the environment only emerges progressively during the first two weeks of life, corresponding to the order of connections between the corresponding brain areas," Denis Jabaudon explains. "The sequential development of these different neurons allows sensory abilities to emerge according to a similar schedule: the newborn mouse first needs to suckle—and will, therefore, first develop the touch relationship—and then to move, it will develop motor abilities that are processed by other cerebral areas." Step by step, the cortex learns to establish connections only when they are necessary, to be able to process the information correctly. In the brain, too, there is a time and place for everything.

**More information:** Denis Jabaudon, Temporal controls over interareal cortical projection neuron fate diversity, *Nature* (2021). [DOI: 10.1038/s41586-021-04048-3](https://doi.org/10.1038/s41586-021-04048-3).  
[www.nature.com/articles/s41586-021-04048-3](https://www.nature.com/articles/s41586-021-04048-3)

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