From happiness to pain: Understanding serotonin's function

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In a study published today, in the scientific journal *PLoS One*, researchers at the Champalimaud Neuroscience Programme establish the effect of serotonin on sensitivity to pain using a combination of advanced genetic and optical techniques.

"Serotonin is a small molecule known to be implicated in a wide range of brain functions, from the control of sleep and appetite, to the regulation of complex emotional behaviours, This neurotransmitter is also popularly thought to contribute to feelings of well being and happiness, as some anti-depression medications work through increasing serotonin in the brain." – says Zachary Mainen, CNP director and principal investigator of the Systems Neuroscience Lab.

Serotonin's great importance led researchers to seek ways of understanding its function, but studying it has been a long-standing challenge.

"Most of the cells that produce serotonin are located in a defined cell group called the Dorsal Raphe Nucleus (DRN)" – explains Zachary Mainen. "This cell group is small and located deep in the brain, which makes targeting it difficult. In addition, other cells that produce and release different molecules are also present in the DRN, which means that general stimulation of the area may result in the release of other molecules besides serotonin."

"To overcome the limitations of previous studies and explore the specific function of serotonin, we used a combination of light and genetics, an approach called optogenetics" – says Guillaume Dugue?, a former postdoctoral researcher in the lab of Zachary Mainen. Using genetic techniques, the researchers expressed a light-sensitive protein specifically in the serotonin-producing cells of mice, so that when the researchers shone light on these cells, the cells released serotonin.

"The effect of the serotonin was clear" – says Guillaume Dugue?. "Mice that we stimulated to release serotonin showed a significant decrease in sensitivity to pain, when compared with mice in the control group."

"We devoted substantial efforts to optimising light activation of serotonin-producing cells. Overall these results provide a new level of evidence on the importance of serotonin in gating the influence of sensory inputs to behavioural outputs, a key physiological role that will help define large-scale theories of serotonin function. Moreover, it has possible implications for better understanding chronic pain treatment." – concludes Zachary Mainen.

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