

Neuropeptide may be real cause of migraines

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Migraine is thought to be caused by abnormal activation of a cluster of neurons



that relays sensory information, including pain signals, from the head. Researchers now find that these neurons are triggered by activity in the central, and not peripheral, nervous system.Credit: C. Bickel / Science Translational Medicine

A pair of researchers, one with New York University College of Dentistry in New York, the other with King's College in the U.K. has found that a neuropeptide may be responsible for the onset of migraines. In their paper published in *Science Translation Medicine*, Simon Akerman and Peter Goadsby describe their experiments with two neuropeptides on rats and what it could mean for the development of a cure for migraines.

Migraines do not get a lot of press, and people that get them are not always given the attention or sympathy they deserve because it is so difficult for people that do not get them to understand how debilitating they can be. Scientists over time have come to believe that they are caused by widening of <u>blood vessels</u> in the head, and because of that, treatment has focused on constricting those blood vessels—but now it appears such thinking may be wrong, and drugs that are used to treat them, only work by accident. This new work by Akerman and Goadsby suggests that <u>migraine pain</u> is actually caused by the over excitation of neurons deep in the brain. If their results turn out to apply to people, it could mean a cure is on the horizon, offering hope to those who suffer from the condition.

Prior research has shown that when people have a migraine, there are increased levels of the neuropeptides VIP and PACAP in their blood, suggesting their presence may be a cause. To find out if that is true, the researchers administered each to test rats while monitoring both blood vessels and neurons that are known to be involved in headaches. They



found that both caused the blood vessels to widen, but only one, PACAP caused an increase in <u>neural activity</u>, fingering it as the real culprit in causing migraines.

To relieve the neural activity they had instigated, the researchers fed a compound known to block the receptors that PACAP binds to (PAC1), but that did not work, so they injected it directly into the rats' brain, and that did cause the over-active nerves to quiet.

At this point, it is still not known if the results the research pair found apply to humans, and it will be difficult to find out—it is not really possible to inject drugs directly into a patient's brain. Further research will thus have to be directed at finding a way to carry a compound through the <u>blood-brain barrier</u> that can reach the over-active nerves and to find out what causes PACAP levels to rise in the first place.

More information: S. Akerman et al. Neuronal PAC1 receptors mediate delayed activation and sensitization of trigeminocervical neurons: Relevance to migraine, *Science Translational Medicine* (2015). DOI: 10.1126/scitranslmed.aaa7557

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