Controlling arterial tone and blood flow in the brain

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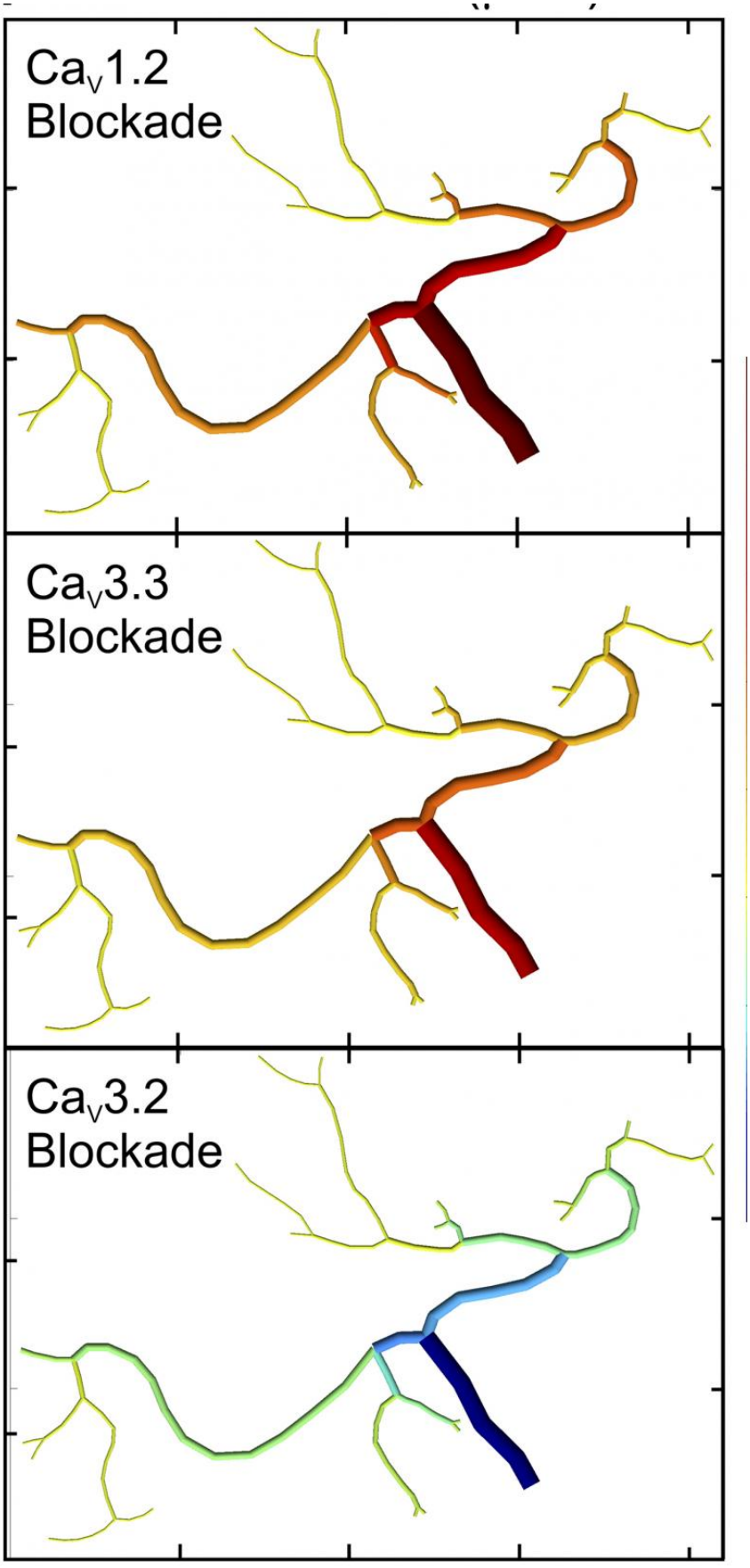
$Ca_V1.2$
Blockade
$Ca_V3.3$
Blockade
$Ca_V3.2$
Blockade

This computation model reveals that blocking $Ca_V1.2$ or $Ca_V3.3$ dilates cerebral arteries and increases blood flow, whereas blocking $Ca_V3.2$ constricts arteries and decreases cerebral blood flow. Credit: Harraz et al., 2015

Researchers have performed the first human-based study to identify calcium channels in cerebral arteries and determine the distinct role each channel plays in helping control blood flow to the brain. The study appears in the May issue of *The Journal of General Physiology*.

The contractile activity of smooth muscle cells in the walls of cerebral arteries determines the degree of constriction they experience (known as arterial tone) and thereby controls blood flow. Arterial tone is regulated in large part by the influx of calcium through voltage-gated calcium (Ca_V) channels, which are found in the membranes of excitable cells throughout the body. However, much of what is known about the identity and function of brain arterial Ca_V channels comes from experiments in rodents.

To uncover the identities and roles of these channels in humans, Donald Welsh and colleagues from the University of Calgary investigated smooth muscle cells from cerebral arteries harvested from patients undergoing brain surgery. As in rodents, the researchers found one L-type ("long-lasting") channel ($Ca_V1.2$) and two T-type ("transient") channels ($Ca_V3.2$, and 3.3) in the human smooth muscle cells.

Welsh and colleagues found that, although $Ca_V1.2$ and $Ca_V3.3$ are different channel types, they both mediate constriction so that blocking them dilates the arteries and increases blood flow, with $Ca_V1.2$ playing a bigger role at higher pressures and $Ca_V3.3$ at lower pressures. Using a

computational model to analyze the effects of blocking these channels, they determined that blocking $Ca_V1.2$ would have a particularly dramatic effect on blood flow in larger arteries, which have higher pressure. In marked contrast, the model shows that $Ca_V3.3$ has the opposite effect on blood flow. This channel promotes vasodilation so that blocking it constricts arteries and decreases the flow of blood.

The findings reveal that each of the channel subtypes in human cerebral arteries play a different role in the regulation of arterial tone. Moreover, this is the first study that implicates T-type channels in the regulation of blood flow in human cerebral arteries. Understanding all of these distinctions will be important to the development of drugs that manipulate specific channels to either suppress or enhance regional blood flow.

More information: Harraz, O.F., et al. 2015. *J. Gen. Physiol.* DOI: 10.1085/jgp.201511361

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