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Scientists find what might be responsible for slow heart function under general anesthesia

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Anesthesia is used every day, but surprisingly little is known about one of its most dangerous side effects—depressed heart function. Now, thanks to a team of Johns Hopkins researchers who published a new research article in *The FASEB Journal*, this mystery is clarified as they identify which proteins in heart muscle are affected by anesthesia. This, in turn, opens the doors to the development of new anesthetics that would not have depressed heart function as a side effect.

"General anesthetics are the most dangerous group of drugs that physicians use, in part because of effects like that studied here," said Wei Dong Gao, M.D., Ph.D., a researcher involved in the work from the Johns Hopkins University School of Medicine in Baltimore, Maryland. "A detailed understanding of how the anesthetic drug produces this effect helps the physician to understand how to predict and counteract it, as well as to understand how to alter the anesthetic itself to minimize it."

In their study, Gao and colleagues conducted two series of experiments. In one series, excised rat heart muscle tissue was mounted onto a device that directly measured the force of contraction at the same time as intracellular calcium concentration. These muscles were then treated with the anesthetic and their force production was recorded. In the second series of experiments, protein extracts of heart muscle were treated with special light-reactive anesthetics and subjected to light in order to "glue" the anesthetic to the particular material with which it was complexed. Although the anesthetics became bound to all of the various proteins, the most extensive binding was observed in three proteins,

including actin and myosin- the muscle force producing proteins. The investigators then used mass spectrometry to home in on the particular regions in each protein to which the anesthetics were bound and these turned out to be domains that are critical for the proteins' contractile function. Although this study was a basic laboratory investigation, the results emphasize that careful attention to heart performance is required when deploying general anesthesia, especially for patients with at risk for heart failure or with any other condition that compromises heart pumping function.

"This report is a great example of how discoveries in the laboratory could translate into advances in human health," said Thoru Pederson, Ph.D., Editor-in-Chief of The *FASEB Journal*. "Now that we have this very plausible basis for why anesthesia causes depressed heart function, scientists can begin to develop new drugs without this dangerous effect."

More information: T. Meng et al, Molecular mechanism of anesthetic-induced depression of myocardial contraction, *The FASEB Journal* (2016). DOI: 10.1096/fj.201600290RR

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