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Chimpanzees under pressure–Selection of a left ventricular structural and functional phenotype

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We are grateful for the interest and comments provided by Jensen and Wang (1) related to our recent paper (2). As previously noted, obtaining true resting blood pressure (BP) measurements in chimpanzees is challenging, if not impossible (1). In our study, and as described in detail in the SI Appendix of ref. 2, BP was measured at least three times in each animal, and the average of these measures was used for analysis (2). We specifically excluded measurements taken within the 20-min period immediately following anesthetic delivery, in order to minimize the effects of the stress associated with anesthetic induction and the initial hypertensive response to medetomidine that we have previously shown (3). Despite this careful aspect of our study design, we fully concur that any reported measures of cardiovascular function may have been influenced by anesthesia. However, until chimpanzees can be persuaded to rest quietly for the collection of BP measurements and cardiac ultrasonographic data, there is no feasible way to eliminate the possibility that anesthesia is a potential confounder. Within our paper, we posit that left ventricular (LV) structural characteristics of chimpanzees were selected to help manage periodic spikes in BP associated with activities such as climbing and fighting, while the human LV structure was differentially selected to enhance end diastolic volume and the corollary stroke volume required for endurance activities. Specifically, larger LV relative wall thickness suggests a pressure-adapted heart in chimpanzees, and the complete lack of LV apical rotation suggests chimpanzees, unlike humans, do not require diastolic untwisting to facilitate LV filling. We have recently confirmed these findings in a larger cohort of chimpanzees including males and females of all ages who were anesthetized using a range of different protocols with and without medetomidine. Specifically, the highly trabeculated LV apex and absence of apical rotation that was observed in almost all animals in our original study (2) was confirmed in this larger cohort. Basic echocardiographic parameters from this cohort have been published (4), and data on trabeculations and rotational mechanics will follow in due course. Confirmation of marked apical trabeculation in chimpanzees across the full age spectrum, including those anesthetized with and without medetomidine, strongly supports the hypothesis that this phenotype represents a defining structural characteristic of the derived chimpanzee heart. In contrast, marked apical LV trabeculation and reduced apical rotation are comparatively rare in humans and exist only in the context of certain forms of genetic heart disease (5), or as phenotypic responses to the marked and sustained hemodynamic stressors that may occur during intense athletic training (6), and during pregnancy (7). Importantly, there are no data to suggest that LV apical trabeculations, either in humans or in other mammals, emerge in response to an acute bout of hypertension. We share Jensen and Wang's interest in further understanding the link between LV structure and function in chimpanzees. Future work, including detailed cardiac MRI studies, will be required to confirm the relationship between LV apical trabeculation, cardiomyocyte fiber alignment, and functional rotational measures in chimpanzees, humans, and other mammals.

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