Title: Piezo1: Enough pressure to open a new door of possibilities for cardiovascular male and female differences.

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Structured Abstract:

Introduction: Piezo receptors are transmembrane proteins specialized in detecting mechanosensitive stimuli. Associated with Pathophysiology of Hypertension (inward eutrophic remodeling) due to altered fiber organization and cell orientation; Heart Failure & Peripheral Vascular Disease (increased Exercise pressor reflex). As we have progressed in our project, we have seen how male and female expresion and function of piezo receptors, contribute to the inherent transduction of mechanichal stimuli that regulate the cardivascular system, and may contribute to the known incidence reduction in females, to present cardiovascular pathologies.

Hypothesis: Piezo1 channel activation is not essential to induce myogenic control and FID differences between males and females. Piezo1 channel sensitivity is not significant between different tissue comparisons.

Methods: Total n=30 Sprague-Dawley rats for Gracilis and Middle Cerebral Arteries for ex-vivo vessel preparations and n=3 Intravital videomicroscopy were we could observe in-vivo Gluteus Max network in-vivo alterations. As control, the arterioles are subjected to an increasing set of pressures and flow challenges in order to quantify the homestatic ability of the arterioles. The same set of pressure/flow changes are repeated after incubation of a spider toxin (GsMTx4), which blocks Piezo1 protein receptors. The same concentration of a GsMTx4 infusion alters the vascular homestatic mechanisms in the Gluteus Maximus preparation. Both experimental methods were repeated after Piezo1 activation with Yoda1, showing return to normal fuction of the vessels involved in the Gluteus prep and issolated vessels. For data analysis we used Linear regression with a p-value=.05 for both ends of the curve, and SD with SEM.

Results: After selective inhibition of Piezo1 receptor with GsMTx4, we see a marked increase in male reduction in the Middle cerebral artery (22.92% in males vs. 5.45% in females) but no significant difference between male & females for peripheral arterioles. Also, after GsMTx4 we were surprised for a decrease of slope in correlation with time in all arterioles, predominately in cerebral arteries, corresponding to a decrease of an effective flow induced changes in the diameter of the vessel, and a probable increased presence of Piezo1 in males.

Discussion: This marked reduction of homestatic regulation in arterioles in males compared against females by blocking of the Piezo1 channels, impact the capacity of the vessels to adjust in phisiologycal settings. As we know CVD's impact earlier to male subjects and the repetitive results proving a greater affection of Myogenic control and FID in said subjects vs. Females, that haven't been exposed that long to hormonal variations, can open a new door of possibilities about previous hypothesis, where estrogens or hormonal variations are responsible of the cardioprotective effect in females.