Elucidation of the mechanism for abnormal blood pressure responses during exercise in pre-hypertension

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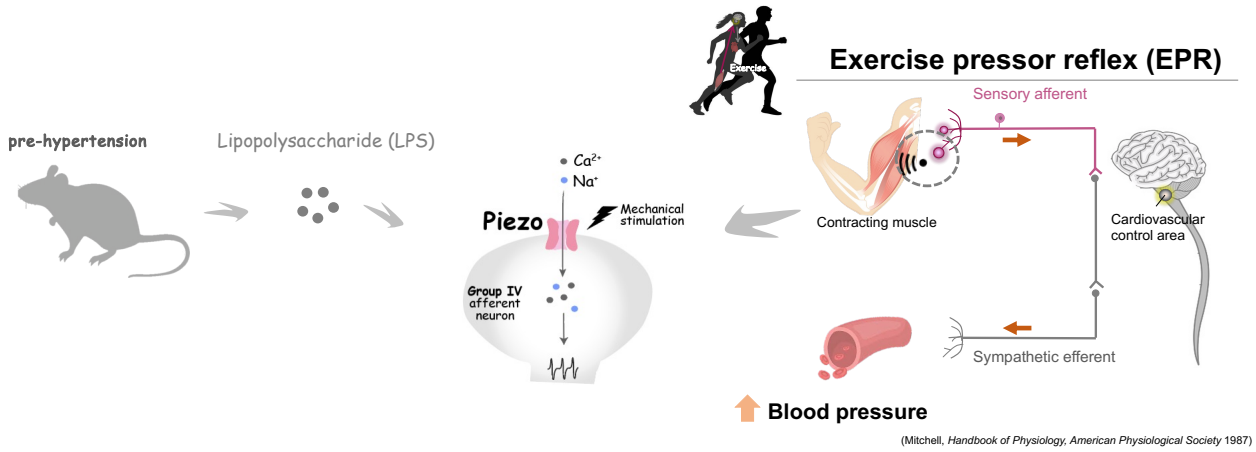
Graphic abstract



Background and Purpose

Skeletal muscle reflex-induced increases in blood pressure are exaggerated during exercise in pre-hypertension. However, the underlying mechanisms remain unclear. Piezo1 channels are known to be mechanically-activated ion channels that play crucial roles in mechanotransduction. Moreover, these channels are expressed in dorsal root ganglion located in the peripheral nervous system. Lipopolysaccharide (LPS), a toxic substance produced by gut-negative bacterium, is increased in pre-hypertension. A recent study indicated that LPS excites nodose ganglion neurons via a transient receptor potential channel 1 (TRPA1) mechanoreceptor activation. Moreover, a receptor of LPS, toll like receptor 4 (TLR4), drives the innate immune response via Piezo1 activation in macrophage. Thus, it is logical to further suggest that LPS may sensitize the sensory afferents in skeletal muscle via activation of mechanoreceptor ion channel that would lead to increased pressor response to exercise. Taken together, the purpose in this study is to investigate the **impact of acute high-LPS on neuronal responses to Piezo1 activities and mechanical stimulation in group IV afferents.**

Methods

< Impacts of LPS on Piezo1-induced neuronal response in normal rats>

- Healthy male Sprague-Dawley rats (8-10 weeks old)
- The extensor digitorum longus (EDL) muscle attached to peroneal nerve
- Mechanosensitive group IV fiber (Conduction velocity ≦ 2.0 m/s)
- 10 mg/mL LPS injection to receptive field
- Measurements
  1. Mechanical stimulation (0-196 mN) for 10 seconds to receptive field
  2. 200 μM Yoda1 (a specific Piezo1 agonist) injection for 30 seconds to receptive field

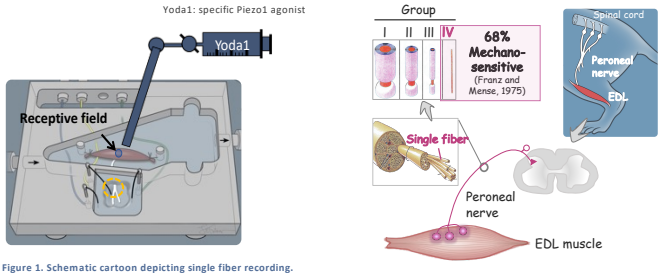


Figure 1. Schematic cartoon depicting single fiber recording.

Results

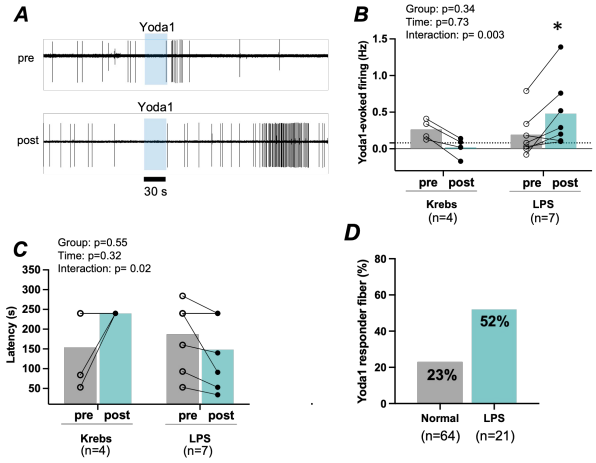


Figure 1. Piezo1 channel activities by lipopolysaccharide (LPS) in group IV fibers from normal rats. A, Representative raw recording of individual group IV fiber activity in response to a 200 μM Yoda1 administration for 30 s (blue shading) pre- and post-LPS injection. Peak in Yoda1-induced firing and the latency in group IV muscle afferent in Krebs (vehicle) and LPS injections are shown in B and C, respectively. D, Percentage of group IV fibers that responded to Yoda1 in LPS administration.

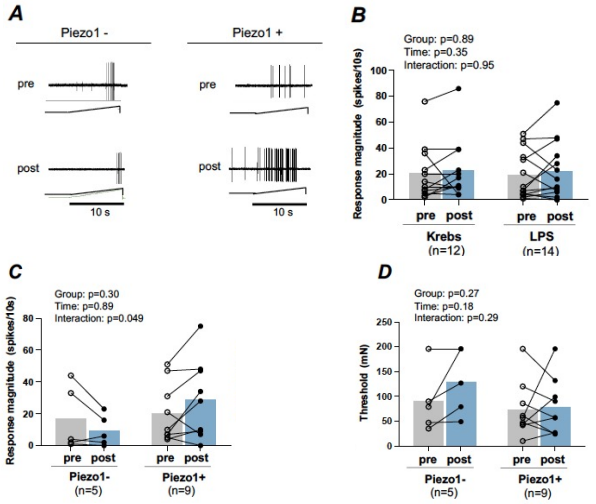


Figure 2. Piezo1 channel activities and neuronal responses to mechanical stimulus by lipopolysaccharide (LPS) in group IV fibers from normal rats.
. Representative raw recording of individual group IV fiber activity (A) and the response magnitude (B) to a ramp-shaped mechanical stimulation (0-196 mN for 10 s) in Krebs and LPS injection. Change in the response magnitude to a mechanical stimulation and the latency by LPS administration in Piezo1-negative and Piezo1-posivibe group IV afferent are shown in C and D, respectively.

Conclusion

These findings suggest that LPS increased the Piezo1 activities and neuronal discharge to mechanical stimulus in group IV fiber. Thereby, these alterations could contribute to the potentiated circulatory response to physical exercise in pre-hypertensive.

Acknowledgements & Correspondence

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