**ESSENTIAL ROLE OF ROS IN MEDIATING STRETCH-INDUCED LEPTIN SECRETION AND VASCULAR SMOOTH MUSCLE HYPERTROPHY**

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Obesity is associated with hypertension and increased leptin production that contribute to cardiovascular pathology. Mechanical stretch (MS) has been shown to contribute to vascular remodeling through various mechanisms, including production of leptin and vascular smooth muscle (VSMC) hypertrophy. We used rat portal vein (RPV) organ culture to investigate the effect of mechanical stretch (mimicking hypertension) on autocrine secretion of leptin and the effect of exogenous leptin (3.1 nM) on VSMC. Stretching the RPV for 2, 3 6 or 12h significantly up-regulated leptin gene expressions. In addition, stretching RPV for 24h significantly increased leptin secretion. MS significantly increased ROS production (10 fold increase), effects that was significantly attenuated by the coadministration of an anti-leptin receptor antibody (166 ng/ml), the ROCK inhibitor Y-27632 (10 microM) as well the RhoA inhibitor C3, (30 microg/ml). Disruption of actin microfilaments with 50nM latrunculin B significantly attenuated mechanical stretch-induced ROS production. The role of ROS in MS-induced leptin secretion and expression was further established when pretreatment of NADPH oxidase inhibitor apocynin (1 mM) potently attenuated leptin expression and secretion induced by MS. In addition, MS significantly increased polymerization of actin in unstretched blood vessels, as reflected by an increase in the F-/G-actin ratio, effects that were significantly attenuated by apocynin. The hypertrophic effect of mechanical stretch was significantly attenuated by an anti-leptin receptor antibody, and apocynin. Our results indicate that the activation RhoA pathway and ROS production plays a pivotal role in MS signaling, leading to leptin secretion and the development of VSMC hypertrophy.