resting metabolic rate and muscle strength were not confirmed by this study.

http://dx.doi.org/10.1016/j.pbj.2017.07.023

PS146

Titin phosphorylation by protein kinase G as a novel mechanism of diastolic adaptation to acute load

R. Rocha1,*, J. Almeida-Coelho1, A.M. Leite-Moreira1, J.S. Neves1, N. Hamdani3, I. Falcão-Pires1, A.P. Lourenço1,4, W.J. Paulus5, W.A. Linke3, A.F. Leite-Moreira1,6

1 Department of Physiology and Cardiothoracic Surgery & Cardiovascular Research Center, Faculty of Medicine, University of Porto, Portugal
2 Department of Endocrinology, São João Hospital Center, Porto, Portugal
3 Department of Cardiovascular Physiology, Ruhr University Bochum, Germany
4 Department of Physiology, Institute for Cardiovascular Research, VU University Medical Center, Amsterdam, The Netherlands
5 Department of Anesthesiology, São João Hospital Center, Porto, Portugal
6 Department of Cardiothoracic Surgery, São João Hospital Center, Porto, Portugal
E-mail address: rafaelm_rocha@hotmail.com
(R. Rocha).

Aim: To evaluate acute adaptions of myocardial stiffness to acute stretch and characterize the underlying mechanisms.

Introduction: Systolic adaption to myocardial stretch/volume overload is known, but whether the heart is also able to modulate its stiffness following such challenges remains unknown.

Methods: Left ventricle (LV) of intact rat Langendorff hearts, rabbit papillary muscles and myocardial strips from cardiac surgery patients were acutely stretched. Skinned cardiomyocytes from stretched and non-stretched myocardium were studied. Stretch by increased venous return or volume loading was assessed by echocardiography in healthy volunteers; pressure-volume dynamics in cardiac surgery patients and in a rat model of LV hypertrophy. Myocardial cGMP, phosphorylated vasodilator-stimulated phosphoprotein (VASP) and titin phosphorylation were quantified. Pharmacological studies assessed the role of NO and natriuretic peptides (NP).

Results: After stretch, end-diastolic pressure (EDP) or passive tension (PT) decreased over 15 min in all preparations. Skinned cardiomyocytes from stretched hearts showed decreased PT – abrogated by protein phosphatase incubation – those from non-stretched hearts showed decreased PT after protein kinase (PKG) incubation. Stretched samples showed increased cGMP levels and phosphorylation of VASP. Titin phosphorylation was increased in stretched samples – attenuated by PKG inhibition (PKGI). PT decay after stretch was blunted by PKGI or by joint NP antagonism, NO synthase inhibition and NO scavenging. Moreover, it was remarkably attenuated in hypertrophic rat hearts which showed reduced titin phosphorylation and no increase with stretch. Healthy volunteers and cardiac surgery patients showed E/E’ and EDP decrease after sustained stretch maneuvers, respectively.

Conclusion: We describe a novel physiological mechanism whereby myocardial compliance is increased in response to stretch/volume overload, by titin phosphorylation through cGMP-PKG signaling. The mechanism was translated to human physiology and may be abolished in the hypertrophic heart (potential role in the pathophysiology of heart failure with preserved ejection fraction).

http://dx.doi.org/10.1016/j.pbj.2017.07.024

PS172

Cannabis sativa tetrahydrocannabinol (THC) impact on placental endocrine function

L. Midão1,3,*, J. Maia1,2, M. Almada1,2, B. Fonseca1,2, D. Gonçalves4, J. Braga4, N. Teixeira1,2, G. Correia-da-Silva1,2

1 Laboratório de Bioquímica, Faculdade de Farmácia Universidade do Porto, Porto, Portugal
2 UCIBIO-REQUIMTE, Porto, Portugal
3 Departamento de Química, Universidade de Aveiro, Aveiro, Portugal
4 Departamento da Mulher e da Medicina Reprodutiva, Serviço de Obstetricia, Centro Materno-Infantil do Norte- Centro Hospitalar do Porto, Porto, Portugal
E-mail address: midao@ua.pt
(L. Midão).

Aim: The main goal of this work is to understand the impact of THC on placenta endocrine function.

Introduction: Cannabis sativa-based medicines have been used to help ease pain, nausea and loss of appetite in cancer and HIV patients. Endocannabinoid system plays an important role in the regulation of female fertility and pregnancy. This system is implicated in proliferation, differentiation and apoptosis of placental stem cells, the trophoblasts (1). These mediate critical steps such as hormone production, fetal immune protection and increase in maternal vascular blood flow. Previous studies have shown that cannabis consumption during pregnancy is associated with intrauterine growth restriction, preterm labor and low birth weight. Moreover, tetrahydrocannabinol (THC), the main psychoactive compound of cannabis, is able to cross the placental barrier. However its effect on trophoblasts turnover and hormone production are unknown.

Methods: Term placental explants were treated with THC [1–40 μM] for 24 h to 72 h. The relative mRNA levels of 3β-HSD, aromatase, leptin and PP13 were determined by qRT-PCR. The protein expression levels of 3β-HSD, aromatase and leptin were assessed by Western Blot. Progesterone, estradiol and β-human chorionic gonadotropin (β-hCG) levels were measured by ELFA.

Results: After stretch, end-diastolic pressure (EDP) or passive tension (PT) decreased over 15 min in all preparations. Skinned cardiomyocytes from stretched hearts showed decreased PT – abrogated by protein phosphatase incubation – those from non-stretched hearts showed decreased PT after protein kinase (PKG) incubation. Stretched samples showed increased cGMP levels and phosphorylation of VASP. Titin phosphorylation was increased in stretched samples – attenuated by PKG inhibition (PKGI). PT decay after stretch was blunted by PKGI or by joint NP antagonism, NO synthase inhibition and NO scavenging. Moreover, it was remarkably attenuated in hypertrophic rat hearts which showed reduced titin phosphorylation and no increase with stretch. Healthy volunteers and cardiac surgery patients showed E/E’ and EDP decrease after sustained stretch maneuvers, respectively.

Conclusion: These findings suggest that THC may impair trophoblast turnover and endocrine function which may affect pregnancy outcome. Moreover these results may contribute to disclose the cellular effects of cannabis-derived drugs.

Acknowledgements: Work financed by FEDER through COMPETE and FCT through PTDC/TP-PTO/5651/2014-POCI-01-0145-FEDER-016562; FCT/MEC and FEDER, under PT2020 (UID/01/0145/FERD/007728) and CCDR-N/NORTE2020/Portugal 2020 (norte-01-0145-FEDER-000024).