Prémio Pedro Eurico Lisboa SPD/Lilly 2018: Resumos dos Trabalhos Premiados

Pedro Eurico Lisboa SPD/Lilly Prize 2018: Abstracts of the Awarded Works

> 1º PRÉMIO

Referência

Sacramento JF, Ribeiro MJ, Rodrigues T, Olea E, Melo BF, Guarino MP, Fonseca-Pinto R, Ferreira CR, Coelho J, Obeso A, Seiça R, Matafome P, Conde SV. Functional abolition of carotid body activity restores insulin action and glucose homeostasis in rats: key roles for visceral adipose tissue and the liver. Diabetologia. 2017 Jan; 60(1): 158-168.

Autores e Instituições

Sacramento JF[1], Ribeiro MJ[1], Rodrigues T[2], Olea E[3], Melo BF[1], Guarino MP[1,4], Fonseca-Pinto R[5,6], Ferreira CR[1], Coelho J[1], Obeso A[3], Seiça R[2], Matafome P[2,7], Conde SV[8]

1 - Centro Estudos Doenças Crónicas (CEDOC), Faculdade Ciências Médicas, NOVA Medical School, Universidade Nova de Lisboa, Lisboa, Portugal.

2 - Laboratório de Fisiologia, Instituto Biomédico de Investigação de Luz e Imagem (IBILI), Faculdade de Medicina, Universidade de Coimbra, Coimbra, Portugal.

3 - Departamento de Bioquímica y Biología Molecular y Fisiología, Universidad de Valladolid, Facultad de Medicina. Instituto de Biología y Genética Molecular, Consejo Superior de Investigaciones Científicas (CSIC), Instituto de Salud Carlos III (ISCIII), Valladolid, España.

4 - Unidade de Investigação em Saúde (UIS), Escola Superior de Saúde de Leiria, Instituto Politécnico de Leiria, Leiria, Portugal.

5 - Escola Superior de Tecnologia e Gestão, Instituto Politécnico de Leiria, Leiria, Portugal.

6 - Instituto de Telecomunicações, Leiria, Portugal.

7 - Instituto Politécnico de Coimbra, Escola Superior de Tecnologia da Saúde (ESTeSC), Departmento de Ciências Complementares, Coimbra, Portugal.

8 - Centro Estudos Doenças Crónicas (CEDOC), Faculdade Ciências Médicas, NOVA Medical School, Universidade Nova de Lisboa, Lisboa, Portugal.

Abstract

Aims/Hypothesis: We recently described that carotid body (CB) over-activation is involved in the aetiology of insulin resistance and arterial hypertension in animal models of the metabolic syndrome. Additionally, we have demonstrated that CB activity is increased in animal models of insulin resistance, and that carotid sinus nerve (CSN) resection prevents the development of insulin resistance and arterial hypertension induced by high-energy diets. Here, we tested whether the functional abolition of CB by CSN transection would reverse pre-established insulin resistance, dyslipidaemia, obesity, autonomic dysfunction and hypertension in animal models of the metabolic syndrome. The effect of CSN resection on insulin signalling pathways and tissue-specific glucose uptake was evaluated in skeletal muscle, adipose tissue and liver.
Methods: Experiments were performed in male Wistar rats submitted to two high-energy diets: a high-fat diet, representing a model of insulin resistance, hypertension and obesity, and a high-sucrose diet, representing a lean model of insulin resistance and hypertension. Half of each group was submitted to chronic bilateral resection of the CSN. Age-matched control rats were also used.
Results: CSN resection normalised systemic sympathetic nervous system activity and reversed weight gain induced by high-energy diets. It also normalised plasma glucose and insulin levels, insulin sensitivity lipid profile, arterial pressure and endothelial function by improving glucose uptake by the liver and perienteric adipose tissue.
Conclusions/Interpretation: We concluded that functional abolition of CB activity restores insulin sensitivity and glucose homeostasis by positively affecting insulin signalling pathways in visceral adipose tissue and liver.

> MENÇÕES HONROSAS

Referência

Rodrigues T, Matafome P, Sereno J, Almeida J, Castelhano J, Gamas L, Neves C, Gonçalves S, Carvalho C, Arslanagic A, Wilcken E, Fonseca R, Simões I, Conde SV, Castelo-Branco M, Seiça R. Methylglyoxal-induced glycation changes adipose tissue vascular architecture, flow and expansion, leading to insulin resistance. Sci Rep. 2017 May 10; 7(1): 1698.

Autores e Instituições

Rodrigues T[1], Matafome P[2,3], Sereno J[4], Almeida J[1], Castelhano J[4], Gamas L[1], Neves C[1], Gonçalves S[4], Carvalho C[1], Arslanagic A[1], Wilcken E[1], Fonseca R[1], Simões I[5], Conde SV[6], Castelo-Branco M[4,7], Seiça R[1]

1 - Laboratory of Physiology, CNC.IBILI and Faculty of Medicine, University of Coimbra, Coimbra, Portugal.

2 - Laboratory of Physiology, CNC.IBILI and Faculty of Medicine, University of Coimbra, Coimbra, Portugal.

3 - Instituto Politécnico de Coimbra, Coimbra Health School (ESTeSC), Department of Complementary Sciences, Coimbra, Portugal.

4 - Institute of Nuclear Sciences Applied to Health (CIBIT-ICNAS), University of Coimbra, Coimbra, Portugal.

5 - Serviço de Anatomia Patológica, University Hospital Center of Coimbra, Coimbra, Portugal.

6 - CEDOC, NOVA Medical School - Faculty of Medical Sciences, New University of Lisbon, Lisbon, Portugal.

7 - Laboratory of Visual Neuroscience, CNC.IBILI and Faculty of Medicine, University of Coimbra, Coimbra, Portugal.

Abstract

Microvascular dysfunction has been suggested to trigger adipose tissue dysfunction in obesity. This study investigates the hypothesis that glycation impairs microvascular architecture and expandability with an impact on insulin signalling. Animal models supplemented with methylglyoxal (MG), maintained with a high-fat diet (HFD) or both (HFDMG) were studied for periepididymal adipose (pEAT) tissue hypoxia and local and systemic insulin resistance. Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) was used to quantify blood flow in vivo, showing MG-induced reduction of pEAT blood flow. Increased adipocyte size and leptin secretion were observed only in rats feeding the high-fat diet, without the development of hypoxia. In turn, hypoxia was only observed when MG was combined (HFDMG group), being associated with impaired activation of the insulin receptor (Tyr1163), glucose intolerance and systemic and muscle insulin resistance. Accordingly, the adipose tissue angiogenic assay has shown decreased capillarization after dose-dependent MG exposure and glyoxalase-1 inhibition. Thus, glycation impairs adipose tissue capillarization and blood flow, hampering its expandability during a high-fat diet challenge and leading to hypoxia and insulin resistance. Such events have systemic repercussions in glucose metabolism and may lead to the onset of unhealthy obesity and progression to type 2 diabetes.

Referência

Monteiro-Soares M, Ribas R, Pereira da Silva C, Bral T, Mota A, Pinheiro Torres S, Morgado A, Couceiro R, Ribeiro R, Dias V, Moreira M, Mourão P, Oliveira MJ, Madureira M, Paixão-Dias V, Dinis-Ribeiro M. Diabetic foot ulcer development risk classifications' validation: A multicentre prospective cohort study. Diabetes Res Clin Pract. 2017 May; 127: 105-114.

Autores e Instituições

Monteiro-Soares M[1], Ribas R[2], Pereira da Silva C[2], Bral T[2], Mota A[2], Pinheiro Torres S[2], Morgado A[2], Couceiro R[2], Ribeiro R[2], Dias V[3], Moreira M[3], Mourão P[3], Oliveira MJ[4], Madureira M[5], Paixão-Dias V[5], Dinis-Ribeiro M[6]

1 - MEDCIDES/CINTESIS - Departamento de Medicina da Comunidade Informação e Decisão em Saúde, Oporto University Faculty of Medicine, Oporto, Portugal.

2 - Unidade de Saúde Familiar Aquae Flaviae, Chaves, Portugal.

3 - Unidade de Saúde Familiar Santo André de Canidelo, Vila Nova de Gaia, Portugal.

4 - Diabetic Foot Clinic, Endocrinology, Diabetes and Metabolism Department, Centro Hospitalar de Vila Nova de Gaia/Espinho EPE, Vila Nova de Gaia, Portugal.

5 - Diabetic Foot Clinic, Internal Medicine Department, Centro Hospitalar de Vila Nova de Gaia/Espinho EPE, Vila Nova de Gaia, Portugal.

6 - MEDCIDES/CINTESIS - Departamento de Medicina da Comunidade Informação e Decisão em Saúde, Oporto University Faculty of Medicine, Oporto, Portugal.

Revista Portuguesa de Diabetes. 2018; 13 (1): 41-43

Abstract

Aims: To prospectively validate the existing classifications to stratify subjects with diabetes mellitus (DM) by their risk of diabetic foot ulcer (DFU), in high and low risk settings.
Methods: A prospective multicentre cohort study was conducted, including 446 subjects with DM without active DFU followed in the hospital or primary care setting. Demographic, clinical characterization variables, and those included in the classifications were collected at baseline. Subjects were followed for 1year, until DFU or death.
Results: In our sample, with a mean age of 65years, 52% were male; 32 developed a DFU, 7 required an amputation and 18 died. Differences were found between participants' characteristics and classifications' accuracy according to the setting. The great majority of the variables were associated with higher DFU risk. Globally, classifications were highly and equally valid, positive predictive values (PV) were inferior to 40%, negative PV superior to 90% and area under the receiver operating characteristic curve superior to 0.75.
Discussion: All the existing classifications are valid to be applied in high risk clinical context and have a very high capacity to categorize as low risk those subjects that will not develop a DFU. Further research is needed in the primary care setting.

Referência

Moura J, Rodrigues J, Gonçalves M, Amaral C, Lima M, Carvalho E. Impaired T-cell differentiation in diabetic foot ulceration. Cell Mol Immunol. 2017 Sep; 14(9): 758-769.

Autores e Instituições

Moura J[1], Rodrigues J[2,3], Gonçalves M[2,3], Amaral C[2], Lima M[2,3,4], Carvalho E[1,5,6,4]

1 - Center for Neuroscience and Cell Biology (CNC), University of Coimbra, Coimbra, Portugal.

2 - Hospital de Santo António (HSA), Centro Hospitalar do Porto (CHP), Porto, Portugal.

3 - Unidade Multidisciplinar de Investigação Biomédica (UMIB/ICBAS/UP), Porto, Portugal.

4 - These authors contributed equally to this work.

5 - Department of Geriatrics, University of Arkansas for Medical Sciences (UAMS), Little Rock, AR, USA.

6 - Arkansas Children's Hospital Research Institute (ACHRI), Little Rock, AR, USA.

Abstract

Foot ulceration is one of the most debilitating complications associated with diabetes, but its cause remains poorly understood. Several studies have been undertaken to understand healing kinetics or find possible therapies to enhance healing. However, few studies have been directed at understanding the immunological alterations that could influence wound healing in diabetes. In this study, we analysed the T-cell receptor (TCR) repertoire diversity in TCR-αβ+ T cells. We also analysed the distribution and phenotype of T cells obtained from the peripheral blood of healthy controls and diabetic individuals with or without foot ulcers. Our results showed that diabetic individuals, especially those with foot ulcers, have a significantly lower naive T-cell number and a poorer TCR-Vβ repertoire diversity. We also showed that the reduced TCR-Vβ repertoire diversity in diabetic individuals was mainly owing to the accumulation of effector T cells, the major source of tumour necrosis factor-α production, which was even more pronounced in patients with acute foot ulceration. Moreover, the expression of several inflammatory chemokine receptors was significantly reduced in diabetic patients. In conclusion, effector T-cell accumulation and TCR repertoire diversity reduction appear to precede the development of foot ulcers. This finding may open new immunological therapeutic possibilities and provide a new prognostic tool in diabetic wound care.