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THE TIME FRAME OF VASCULAR REMODELLING IS DISSOCIATED WITHIN THE BRAIN AND THE KIDNEY AND MAY BE EXPLAINED BY THE VARIABILITY OF miRNAs EXPRESSION IN TYPE 2 DIABETES MELLITUS PATIENTS

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INTRODUCTION AND AIMS: Atherosclerosis and microangiopathy within the brain parallel diabetic nephropathy (DN) in the course of Type 2 diabetes mellitus (DM). The aim of our study was to evaluate the time frame of vascular remodelling in the course of Type 2 diabetes mellitus (DM) in two vascular territories, the kidney and the brain, both affected by diabetic vasculopathic complications. The pattern of vascular involvement was evaluated in relation to miRNAs profile.

METHODS: Seventy-six patients with Type 2 DM and 19 healthy subjects were assessed concerning urine albumin: creatinine ratio (UACR); urinary nephrin, podocalyxin, and synaptopodin as biomarkers of podocye injury; urinary N-acetyl-β-D-glucosaminidase (uNAG), urinary kidney injury molecule-1 (uKIM-1) as biomarkers of proximal tubule dysfunction; eGFR. MiRNAs were quantified in blood and urine by a real-time PCR System. The neurosonology methods included intima-media thickness (IMT) in the common carotid arteries, the resistance index (RI) in the internal carotid arteries and the middle cerebral arteries; the cerebrovascular reactivity was assessed through the breath-holding index (BHI).

RESULTS: Within the kidney miRNA21 and miRNA125a correlated directly with podocalyxin, uNAG, UACR, and indirectly with eGFR (R^2=0.702; p<0.0001); miRNA124, miRNA126, and miRNA146a correlated directly with podocalyxin, synaptopodin, uNAG, KIM-1, UACR, and indirectly with eGFR (R^2=0.761; p<0.0001); miRNA192 correlated indirectly with synaptopodin, uNAG, UACR, and directly with eGFR (R^2=0.881; p<0.0001). With regard to the cerebral haemodynamics indices, miRNA21 and miRNA192 correlated directly with IMT and RI, and indirectly with BHI (R^2=0.792; p<0.0001), pointing to negative effects of these miRNAs to cerebral vessels remodelling; miRNA124, miRNA125a, miRNA126, miRNA146a correlated indirectly with IMT, RI, and directly with BHI (R^2=0.835; p&lt0.0001), suggesting neuroprotective effects.These observations were consistent across all groups studied, even in normoalbuminuric patients.

CONCLUSIONS: In Type 2 DM patients the time frame of vascular remodelling is dissociated within the brain and the kidney. Sequentially, changes to the cerebral vessels appear to precede renal involvement in early DN. This phenomenon may be explained by the variability of miRNAs expression within the two organs.