Long Lasting Microvascular Tone Alteration in Rat Offspring Exposed In Utero to Maternal Hyperglycaemia

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Résumé en anglais	Epidemiologic studies have demonstrated that cardiovascular risk is not only determined by conventional risk factors in adulthood, but also by early life events which may reprogram vascular function. To evaluate the effect of maternal diabetes on fetal programming of vascular tone in offspring and its evolution during adulthood, we investigated vascular reactivity of third order mesenteric arteries from diabetic mother offspring (DMO) and control mother offspring (CMO) aged 3 and 18 months. In arteries isolated from DMO the relaxation induced by prostacyclin analogues was reduced in both 3- and 18-month old animals although endothelium (acetylcholine)-mediated relaxation was reduced in 18-month old DMO only. Endothelium-independent (sodium nitroprusside) relaxation was not affected. Pressure-induced myogenic tone, which controls local blood flow, was reduced in 18-month old CMO compared to 3-month old CMO. Interestingly, myogenic tone was maintained at a high level in 18-month old DMO even though agonist-induced vasoconstriction was not altered. These perturbations, in 18-months old DMO rats, were associated with an increased pMLC/MLC, pPKA/PKA ratio and an activated RhoA protein. Thus, we highlighted perturbations in the reactivity of resistance mesenteric arteries in DMO, at as early as 3 months of age, followed by the maintenance of high myogenic tone in older rats. These modifications are in favour of excessive vasoconstrictor tone. These results evidenced a fetal programming of vascular functions of resistance arteries in adult rats exposed in utero to maternal diabetes, which could explain a re-setting of vascular functions and, at least in part, the occurrence of hypertension later in life.

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