(SMT 1 μm) or a piégeur du peroxynitrite (Acide urique, 100 μm). La vasorelaxation endothélial indépendante a été évaluée dans l’ensemble des cuves avant et après incubation d’H2O2 par ajout d’une dose de SNP (10-5M).

**Résultats** — Dans des conditions standards, 4 semaines d’exposition au CO ne sont pas à l’origine d’une altération de la voie de vasorelaxation NO-cGMP. Il est par contre intéressant de noter, que les rats CO présentent une sensibilité accrue au stress oxydant provoqué par l’incubation d’H2O2 dans les cuves. En effet, les rats CO présentent suite à ce stress oxydant une altération significativement plus marquée de la vasorelaxation endothélial dépendante (Ctrl rats : 18 % ; CO rats : 55 %) sans modification de la vasorelaxation endothélial indépendante. L’utilisation d’un inhibiteur spécifique de la NOS2 au cours du stress oxydant permet de prévenir les effets aggravants du CO.

**Conclusion** — Les effets d’une exposition prolongée au CO à des concentrations telles que rencontrées en environnement urbain, sont masqués dans des conditions standards, mais apparaissent majeurs et délétères consécutivement à un stress oxydant aigu au H2O2. La NOS2 semble être impliquée de manière majeure dans les effets délétères du CO.

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**C002 INCREASE OF AORTIC NITRIC OXIDE PRODUCTION IN METABOLIC SYNDROME**

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We demonstrated an increase of nitric oxide (NO) production in aortas of Zucker obese fatty rat (ZOF). Metabolic syndrome is associated with an attenuation of acetylcholine (ACh) response. The impairment of ACh induced vasodilation suggests a decrease in nitric oxide (NO) bioavailability. The aim of this work was to assess whether a reduced NO production is involved in the drop of NO bioavailability. Male Zucker obese fatty (ZOF, n=8) and lean (n=9) rats, 31 weeks old, were anesthetized and thoracic aortic segments harvested. The NO produced by aortic rings was assayed by EPR spectroscopy using colloid Fe/EDTA/2 spin-trapping. The EPR spectra were obtained using a X-Band EPR spectrometer. Basal NO production was significantly (p=0.0001) increase (126%) in ZOF rats (306±201AU/h/mg) from lean controls (135±101AU/h/mg). Addition of ACh (3.10-6M) induced an increase in NO levels in aortic rings of both ZOF and lean rats, this relative increase was significantly smaller in ZOF (162±10 vs 270±26 %, p=0.002). However the level was higher in ZOF (4905±360 vs 3500±213AU/h/mg, p=0.004). Without endothoim derived NO production was detected in ZOF aortas. A specific inhibitor of neuronal NOS, Nw-Propyl-L-arginine (PLA; 0,1 μm), was unable to decreased both NO productions : the basal NO production and the ACh-stimuluated NO production in ZOF aortas. A similar result was obtained with the specific inhibitor of inducible NOS suggesting the only involvement of eNOS in increase of NO production observed in ZOF. We conclude that the vascular dysfunction observed in metabolic syndrome is not due to a decrease in NO production but may be at least in part due to a reduced sensitivity to ACh stimulation.

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**C003 CYCLOOXYGENASE-2 PRESERVES FLOW-MEDIATED REMODELING IN OLD OBESE ZUCKER RATS**

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Resistance arteries have a key role in the control of local blood flow. They are able to remodel in response to chronic increases in flow during growth, exercising or in ischemic diseases. Flow-mediated remodelling is governed by the endothelium. The incidence of metabolic syndrome increases with age and these 2 risk factors reduce endothelium integrity, because of an inflammatory process. We hypothesized that inflammation possibly through the induction of cycloxygenase-2 (COX2), might affect remodeling in old obese rats. In 12-month old obese and lean Zucker rats mesenteric resistance arteries were alternatively ligated in vivo so that one artery was submitted to high flow (HF), compared to normal flow (NF) vessels. After 21 days, outward hypertrophic remodelling in HF arteries occurred in obese rats (498±20 in HF arteries vs 443±18 μm in HF arteries, P<0.01), not in lean rats (454±17 vs 432±14, NS ; n=12 per group). Endothelium-dependent (acetylcholine)-relaxation (AMR) was reduced in obese control compared to lean rats. AMR was reduced by NO-synthesis blockade (L-NAME) in all groups and eNOS expression was higher in HF than in NF arteries without difference between lean and obese rats. Indomethacin further reduced AMR in HF from obese rats without significatly affecting arteries from lean animals. As COX2 immunostaining and expression level was evidenced in arteries from obese rats, COX2 inhibition (NS398) was tested on AMR. NS398 signficantly reduced AMR in HF arteries in obese rats only. In obese rats chronically treated (3 weeks) with NS398 outward remodelling did not occurred in HF arteries. Thus, COX2 preserved arterial remodelling in response to a chronic rise in blood flow in old obese rats. This adaptation is in favor of a better tissue perfusion.

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**C004 CYCLOOXYGENASE-2 INHIBITION RESTORED ENDOTHELIAL-MEDIATED RELAXATION IN OLD OBESE**

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End-organs perfusion is altered in metabolic diseases due in part to a decreased endothelium-mediated relaxation in resistance arteries (RA). Inflammatory factors including cycloxygenase-2 (COX2) derived agents affect the endothelium to different degrees in aging and obesity but the effect of their association on the endothelium is not fully understood. We hypothesized that COX2 derivatives might reduce endothelium-mediated relaxation in aging associated with obesity. RA from 4 and 12 month-old obese Zucker rats RA were isolated to measure acetylcholine (endothelium)-mediated relaxation (AMR), in vitro, using wire-myography. Impaired with obesity in young rats, AMR was further reduced with aging in old obese rats (89 versus 77 % maximal relaxation, young versus old lean rats and 72 versus 51 %, old young versus young old obese rats).
old obese rats). Endothelial NO-synthase (eNOS) blockade (L-NAME) was reduced in obese rats although eNOS expression level was unaffected. However, indomethacin improved AMR in old obese rats only, suggesting that vasoconstrictor prostanoids were involved. Similarly, COX2 inhibition (NS398) and Tx2A2/PGH2 receptor blockade (SQ29548) increased AMR in arteries from old obese rats only. Old obese rats presented the highest levels of blood Tx2B (Tx2A2 metabolite) associated with an increased COX2 immunostaining and expression level. Chronic inhibition of COX2 with NS398 (3 weeks) restored AMR in old obese rats (78% versus 57% in control obese rats) to the level observed in solvents对不起，图像中的内容无法正常显示。