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Mice deficient in pituitary adenylate cyclase activating polypeptide (PACAP) show increased susceptibility to in vivo renal ischemia/reperfusion injury

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Pituitary adenylate cyclase activating polypeptide (PACAP) is a neuropeptide with well-known cytoprotective effects. We have reported earlier that PACAP decreases mortality and the degree of tubular atrophy in renal ischemia/reperfusion injury. Recently, we have shown that kidney cultures isolated from PACAP deficient mice show increased susceptibility to oxidative stress. Based on these previous studies, we raised the question whether PACAP deficient mice display increased sensitivity to in vivo renal ischemia/reperfusion. PACAP -/- mice underwent 45 or 60 min renal ischemia followed by 2 weeks reperfusion. Kidneys were processed for histological analysis. In other sets of experiments, tissue cytokine expression and the level of superoxide dismutase (SOD) were also determined after 60 min ischemia/reperfusion. Our results show that while intact kidneys were not different between wild-type and PACAP deficient mice, marked differences were observed in the histological structures in groups that underwent ischemia/reperfusion. PACAP deficient mice had significantly worse histological outcome. Cytokine expression was also markedly different between wild-type and PACAP deficient mice. In addition, the level of SOD was significantly lower in PACAP -/- animals after ischemia/reperfusion. In conclusion, the lack of endogenous PACAP leads to higher susceptibility to in vivo renal ischemia/reperfusion, suggesting that PACAP has an endogenous renoprotective effect.