Local auto-amplification of cortisol actions in human carotid atheroma is in link with arterial remodeling and stroke

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High cortisol and aldosterone increase cardiovascular risk but the respective roles of local cortisol and aldosterone in the arterial wall remain controversial. The hypothesis that increased local cortisol production within the arterial wall may act through illicit activation of the mineralocorticoid receptor in atherosclerotic remodeling was investigated. Gene expression studies of the corticoid system components and marker genes of the atherosclerotic process in human carotid atheroma plaque and nearby macroscopically intact tissue (MIT) were associated with clinical data and compared to pharmacological stimulation of human vascular smooth muscle cells (VSMC) in a contractile or lipid storing phenotypes.

The components for corticoid production and action were present and active within the human carotid wall and VSMC. Atheroma plaque and lipid storing VSMC expressed 11β-HSD1 at 2 to 10-fold higher level than MIT or contractile VSMC. The 11β-HSD1 expression was stimulated by cortisol and cortisone, especially in lipid storing VSMC. MR, under-expressed in atheroma and lipid storing VSMC, was down-regulated via MR by aldosterone and also cortisol. Cortisol up-regulated collagen I and MCP-1 mRNAs, via GRα exclusively, in both VSMC phenotypes whereas fludrocortisone stimulated the collagen I expression only in lipid storing VSMC. The GRα mRNA in MIT was higher in patients with previous stroke, correlated, positively with the collagen I mRNA, and negatively with diastolic blood pressure. Parietal GRα expression and cortisone-cortisol conversion could be relevant from the first step of atherosclerotic remodelling increasing collagen I and macrophage contents thus favouring stroke, and could auto-amplify with transdifferentiation of VSMC during atheroma progression.