[gw22-e0683] **AGEING-RELATED CHANGES IN ENDOTHELIN-1 RECEPTOR SUBTYPES IN RAT HEART AND KIDNEY**

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Objective Ageing is associated with a decline in renal and cardiac function. Endothelin (ET) system plays an important role in the ageing process. The purpose of this study was to determine changes in density and subtypes of ET-1 receptors in kidneys and hearts of aged rats.

Methods Twenty Fisher 344xBrown Norway (F1) rats (male, 27 months) were divided into an Old Impaired group (n=9) and an Old Intact group (n=11) according to a cognitive function test. A group of 12-month-old rats (n=10) was used as a Young Intact group. Blood was collected for measuring serum creatinine and ET-1 concentration. Renal and cardiac histology was evaluated using PAS staining and trichrome staining. ET receptors (ETA and ETB) in renal cortex and medulla and myocardium were assessed by immunohistochemistry and western-blotting.

Results Plasma creatinine was increased significantly in the Old Impaired group
(2.32±0.20 mg/dl vs 1.18±0.12 mg/dl $p<0.01$), suggesting impaired renal function. Aged rats showed glomerulosclerosis and tubulointerstitial fibrosis. The glomerulosclerosis score and collagen area fraction were significantly higher in old impaired group than those in old intact, (3.34±0.26 vs 2.02±0.15, $p<0.01$); (5.62±0.36% vs 3.76±0.29%, $p<0.05$), and they were significantly higher than those in young intact group (1.01±0.09, $p<0.05$, $p<0.01$); (2.42±0.16%, $p<0.05$, $p<0.001$). Aged rats also displayed collagen deposit around vessels in hearts. These pathological changes were markedly aggravated in the old cognitively impaired than in the old cognitively intact animals. The level of the circulating ET-1 was not altered. ETA receptor protein expression was upregulated in renal cortex and medulla in aged rats. While ETB receptor protein expression was downregulated in medulla. Interestingly, the ratio of ETA: ETB in renal medulla in aged rats was double that of in young rats ($p<0.01$). Conversely, ETA receptor protein expression was downregulated in myocardium in aged rats and the ratio of ETA:ETB was significantly decreased in myocardium in aged rats ($p<0.01$). Notably, these changes were more visible in the old impaired than in the old intact rats.

Conclusions The ageing-related kidney damage and cardiac damage paralleled with the cognitive function impairment. The ETA protein expression and the ration of ETA; ETB were upregulated in aged kidney, in contrast, those were

downregulated in aged heart. These findings indicate an alteration of ET-1 receptors in kidney and heart associated with ageing.