samples were analysed for arginine, ADMA and SDMA, using high performance liquid chromatography-tandem mass spectrometry (HPLC-MS). Clinical and laboratory data were evaluated applying structured questionnaire and routine methods.

Results: Serum arginine was significantly lower in patients with EH than in the control group ($p < 0.001$). ADMA levels were significantly higher in the hypertensive group ($p = 0.002$), while SDMA levels were not different ($p = 0.15$). ADMA levels were significantly higher in EH patients associated with diabetes mellitus ($p = 0.009$) as compared with the remaining EH patients.

Conclusion: This study demonstrated a positive association between serum arginine and ADMA levels with EH in the Sudanese patients. Lowering serum ADMA levels or increasing the arginine levels might be a novel therapeutic target in these individuals.

Keywords: ADMA, Essential Hypertension, Association, Sudanese patients

A1990 NOVEL MECHANISM OF SALT-SENSITIVE HYPERTENSION: CD8 T CELLS STIMULATE SODIUM CHLORIDE CO-TRANSPORTER IN THE KIDNEY

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Objectives: The kidney plays a key role in salt-sensitive hypertension. Recent studies also suggest a role for T lymphocytes in hypertension. However, whether T cells contribute to renal sodium retention is an important question, which if answered, could reveal a critical relationship between immunity and pathogenesis of salt-sensitive hypertension. Here, we propose a novel mechanism of salt-sensitive hypertension: that renal-infiltrating T cells interact with distal renal tubules, enhancing sodium retention via stimulating sodium transporter.

Methods: Wild type and knockout mice were used in DOCA-salt model or T cell-adoptive transferred model. In-vitro study we co-cultured mouse distal convoluted tubule cells (DCTs) with T cells. Immuno-blot was used to detect protein expression; multi-color staining and 3D-Super-resolution SIM microscopy (Figure 1) were used to demonstrate direct interaction between cell types in-vitro and in-vivo; siRNAs were used to knockdown molecules to explore signaling pathways.

Results: We found that renal infiltrated CD8 T cells interact with DCTs in the kidney via a direct cell-cell contact (Figure 1), which upregulates sodium-chloride co-transporter (NCC) in DCTs via Src kinase-induced up-regulation of the K+ channel Kir4.1, and stimulation of the Cl- channel ClC-K. The later event increases chloride efflux, leading to compensatory chloride influx via NCC activation at the cost of increasing sodium retention. Moreover, interrupting above pathway by knockout of Kir4.1 in renal tubules prevented NCC upregulation and consequent development of salt-induced salt-sensitive hypertension.

Conclusion: Our findings provide a novel mechanism for involvement of adaptive immunity in the kidney defect in sodium handling, which contributes to the pathogenesis of salt-sensitive hypertension.

Keywords: hypertension, salt-sensitive hypertension, T cells, CD8 T cells, sodium trtention, sodium chloride co-transporter, adaptive immunity

A2022 DISTURBANCE OF MITOCHONDRIAL TRPC3-MEDIATED CALCIUM HANDLING IN THE VASCULATURE FROM HYPERTENSIVE RATS

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Objectives: Mitochondrial Ca2+ homeostasis is fundamental to the regulation of mitochondrial ROS generation, which is correlated with the pathogenesis of hypertension. Transient receptor potential channel, canonical type 3 (TRPC3), localized in membrane of mitochondria play a role in maintaining mitochondrial calcium homeostasis. The aim is to determine whether mitochondrial TRPC3 participates in hypertension by increasing mitochondrial calcium handling.

Methods: Eight-week-old male SHRs and normotensive WKY rats were fed with normal diet for 12 weeks. Vascular constriction was measured using wire myograph. Mitochondrial calcium uptake was measured from primary vascular smooth muscle cells (VSMCs). Western blotting and immunofluorescence were used to detect the expression and distribution of TRPC3.

Results: Compared with WKY, TRPC3 expression in the mitochondria was increased in VSMC from SHR. Furthermore, increased cellular and mitochondrial ROS production, enhanced H2O2 production, but impaired ATP synthesis were identified in SHR compared with WKY. Specifically, mitochondrial calcium uptake stimulated by ATP or histamine in VSMCs was significantly increased in VSMCs from SHRs compared with WKY rats, whereas the administration of angiotensin II receptor blocker, telmisartan or TRPC3 inhibitor (Pyr3) significantly attenuated these parameters. Furthermore, mitoTEMPO or telmisartan inhibited increases in store-operated calcium entry in the VSMCs of SHRs, as well as suppressed the excessive vasoconstriction induced by either phenylephrine or U46619 in SHRs.

Conclusion: These results suggest that mitochondrial TRPC3 mediated calcium regulation is dysfunction in the vasculature from SHRs. Modulation of mitochondrial TRPC3 is a promising target for antihypertension.

Keywords: mitochondrial Ca2+ homeostasis, TRPC3, SHR, VSMC

A0984 EFFECT OF LOW-DOSE LEVAMLODIPINE BESYLATE IN THE TREATMENT OF VASCULAR DEMENTIA

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Objectives: Vascular dementia (VaD) is a heterogeneous brain disorder for which there are no effective approved pharmacological treatments available. We aimed to evaluate theeffect of Levamlodipine Besylate in the treatment of vascular dementia on cognitive impairment in mice after eight weeks-right unilateral common carotid arteriesocclusion (rUCCAO).

Methods: Levamlodipine Besylate (0.1 or 0.5 mg/kg) was given to rUCCAO mice for eight weeks. Administration of Levamlodipine Besylate (0.1 mg/kg) reduced escape latency in space exploration and working memory test compared with the vehicle group.

Results: Vehicle-treated mice showed reduced phospho-CaMKII (Thr286) levels in the hippocampus, whereas partially restored by Levamlodipine Besylate (0.1 mg/kg) treatment. No significant effect on microglia and astrocyte activation was observed following Levamlodipine Besylate (0.1 mg/kg) treatment.

Conclusion: These data disclose novel findings about the therapeutic potential of low-dose Levamlodipine Besylate significantly enhanced the cognitive function in VaD mice.

Keywords: vascular dementia, cognitive impairment, Levamlodipine Besylate, low-dose, calcium channel blocker

A3016 CENTRALLY ANGIOTENSIN-(1-7) DECREASES WITH AGE

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Objectives: The depressor axis of the renin-angiotensin system (RAS) exerts cerebroprotective effects. We hypothetized that a centrally dysbalance exists between both axis that may contribute to hypertension development and cognitive dysfunction with age. Our aim was to determine Ang-(1-7) and Ang II levels in different areas of the brain in normotensive and spontaneously hypertensive (SHR) rats of different ages

Methods: Hypothalamus (HT), brain stem (BS), hippocampus (HC) and brain cortex (C) from 1, 3 and 12-months-old rats were isolated. Ang levels were quantified by radioimmunoassay

Results: Ang-(1-7) levels decreased with age in HT, BS and C from normotensive rats. Regarding SHR, an increase in Ang-(1-7) levels with age was observed in BS, HC and HT when 1 and 3 months-old rats were compared but not significant differences were observed between 3 and 12 months-old rats, except in brainstem where Ang-(1-7) decreased. Ang-(1-7) levels in C did not significantly change with age in SHR. In all the studied areas Ang-(1-7) levels in 1-month-old rats were greater in normotensive than in SHR. Ang II levels increased with age in all the studied areas both in normotensive and SHR. However, AngII levels in HT, BS and C of 12-months-old rats decreased in comparison to 3-months-old rats. 1-month-old SHR showed greater Ang II levels in BS and C in comparison to normotensive young rats. On the contrary, Ang II levels in HT of young SHR were lower than in normotensive

Conclusion: Our results show that brain Ang-(1-7) levels in normotensive rats decreased while Ang II levels increased with age. The fact that Ang-(1-7) increased with age in hypertension may be due to a compensatory mechanism.

Keywords: angiotensin-(1-7), brain, hypertension, angiotensin II