Introduction

- Hypertension in human is a polygenic disorder and the prevalent cause of cardiovascular disease leading to cardiac failure and, ultimately, death.
- The transgenic rat model used in this study is a generation of rat line bearing the murine Ren-2 gene i.e. (mRen2)27 with suppressed concentrations of active renin, angiotensin I (AngI) and AngII.
- The cascade of physiologic events which lead to hypertension is not fully understood. However, treatment with angiotensin converting enzyme (ACE) inhibitors or AngII receptor antagonists is extremely efficient.
- mRen27 model of hypertension is mediated through AngII and favors the concept of extrarenal Renin-Angiotensin system (RAS).
- Studies have shown that sympathetic synaptic transmission correlates with sustained pressure and it is uncertain the causality of this correlation.
- Thus, the objective is to study the neuroplastic behavior and AngII receptor expression at the ganglion level.

Scheme

Renin Angiotensin-aldosterone system

Methods

(a) Isolation of superior cervical ganglia from the HnSD and m(Ren2)27,
(b) SGC extracellular recording of post synaptic responses,
(c) Neuronal cell isolation by disassociating SCG,
(d) Confocal microscopy to study surface receptors and (e) SGC western blotting.

Results

Figure 1: Renin-Angiotensin System has major effects in fluid homeostasis and cardiorespiratory functions through AT1 receptor activation in brain, kidney, and heart. (Front. Pediatr. 2019 July; 7: 296). https://doi.org/10.3389/fped.2019.00296

Figure 2: (A) Systolic Blood Pressure and (B) Heart Rate were measured in m(Ren2)27 (n=12) and HnSD (n=10) rats via tail cuff plethysmograph. SEM. **P<0.0001.

Figure 3: Time course of decay of synaptic potentiation recorded in ganglia isolated from (mRen2)27 (n=6) and control HnSD (n=7) rats in the presence of angiotensin II. Values are expressed as the mean ± SEM. There is a significant difference compared with the other group, P<0.05.

Figure 4: Angiotensin II (n=6) significantly enhanced the decay time constant of Long-Term Potentiation (LTP), an index of synaptic strength, in SCG isolated from (mRen2)27 rats compared with its control in Locke’s solution (N=4). There is a statistically significant difference between the two groups. Values are expressed as the mean ± SEM. *P<0.05.

Figure 5: (A) Angiotensin Type 1 Receptor Protein Assessment via Immunocytochemistry, (B) Angiotensin Type 1a Receptor Protein Assessment via Western blot (N=4; **p<0.05).

Conclusion

- Blood pressure progressively increased in (mRen2)27 animals with no significant change in heart rate compared to HnSD animals (Figure 2).
- AngII potentiated synaptic transmission via AT1R and was abolished by candesartan, AT,R antagonist (Figure 3).
- Thus, AngII in the local environment of the ganglia may contribute to the synaptic strength and enhanced LTP that facilitates ganglionic transmission (Figures 4 & 5A).
- There is significantly higher AT1 expression of in the SCG of (mRen2)27 (Figure 5B).
- Thus, we expect that the mechanisms that regulate tissue dependent differences in AngII receptor expression in the sympathetic nervous system will provide better insights to the pathogenesis of hypertension.

Reference