Role of PPARα in the Contribution of the Brain Renin-Angiotensin System (RAS) to Blood Pressure

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Absence of the PPARα gene abolishes hypertension in the Tsukuba Hypertensive Mouse (THM) - a hypertensive model due to transgenic expression of the human RAS. Although these animals have reduced circulating renin, this alone cannot account for the entire effect. A significant reduction in hypothalamic renin mRNA in these animals, suggests a decrease in the activity of the brain RAS which might provide additional protection from hypertension.
Aim: To compare PPARα null to C57/Bl6 mice subjected to the aldosterone-salt model. Under these conditions the systemic RAS is typically shut down whereas the brain RAS is upregulated.
Methods: A week after unilateral nephrectomy, mice were implanted with a minipump that delivered a pressor dose of aldosterone for 4 weeks. Mice had access to 1% NaCl as their drinking water. Blood pressure was recorded, mice were studied in metabolic cages, and the expression of the hypothalamic RAS components (renin, angiotensinogen, ACE, AII receptor) was analyzed by realtime PCR
Results: Under aldosterone, blood pressure increased significantly in the C57/Bl6 mice (135.5±2.7 vs 108.7±2.8 mm Hg, *P*=0.0001), but not in the PPARα null animals. C57/BL6 animals drank more than PPARα null mice (23.2±1.2 vs 18.4±1.3 ml/20 g BW respectively, *P*=0.01). Hypothalamic renin was decreased by 65%-70% in the PPARα null mice, both in control and under aldosterone, compared to C57/Bl6 (*P*=0.003). Other components of the RAS were not significantly affected.
Conclusions: Our data support the notion that in addition to its effect on the classic RAS, PPARα centrally raises blood pressure by upregulating brain RAS thereby driving thirst and salt appetite.