

Overall research theme:

Importance of proximal tubular fluid output in regulating urinary sodium excretion in health and disease

Latest update:

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Senior staff member(s):	Position(s):	Degrees:	E-mail addresses:
Klaus Thomsen Martin Bak	Senior Research Associate Physician	PhD, Dr. Med. Sci. PhD	klt@psykiatri.aaa.dk mb@dadlnet.dk

Department/institution/address/telephone/fax:

Institute for Basic Psychiatric Research, Department of Biological Psychiatry, Aarhus University Hospital, Skovagervej 2, DK-8240 Risskov
Tel.: 7789 3512 Fax: 7789 3549

Characteristics of the research group:

Our group is mostly interested in the physiological mechanisms that regulate the proximal tubular fluid output (V_{prox}) and the importance of this variable in regulating sodium excretion. We use the lithium clearance technique for monitoring V_{prox} and we use the rat model with chronic catheterisation of arteria, vena and bladder that was originally developed at the Department of Pharmacology, Panum Institute. The model allows continuous monitoring of sodium and water excretion during the experiment in conscious rats. It furthermore offers the opportunity of full or partial sodium and/or fluid replacement by a PC-controlled servo-system. The experimental setup includes four additional infusion pumps, an auto-sampler for urine collection and a modem for messages. All this is operated automatically by another PC through a pre-entered time schedule.

Running projects: Titles and abstracts:

Effect of adenosine A_1 receptor inhibition on proximal tubular fluid output in hypertensive Dahl salt sensitive rats

Adenosine A_1 receptor inhibitors are a promising group of drugs for treatment of arterial hypertension and congestive heart failure. The drugs are supposed to inhibit the physiological regulation of the tubuloglomerular feed-back system and increase V_{prox} . The aim of the study is to investigate whether V_{prox} is increased by treatment with an adenosine A_1 receptor blocker and whether an increase in V_{prox} is maintained during chronic treatment with the drug. Our hypothesis is that a chronic increase in V_{prox} is not compatible with maintenance of the sodium balance. V_{prox} will eventually return to normal due to development of a slight sodium deficiency and the blood pressure will decrease to a level that depends on dose of drug.

Importance of the renin-angiotensin system and the NO system in excreting a small saline load

The kidneys are essential for excreting any excess sodium and fluid from the body. Failure in this mechanism(s) may lead to oedema formation and/or hypertension. Accumulating evidence suggests that V_{prox} is important in this process and that V_{prox} is regulated by the balance between the renin-angiotensin system and the NO system. It is likely, that excretion of a small excess of saline requires the combined effect of reduced renin-angiotensin activity and increased NO activity. We will examine this hypothesis in our unique rat model with and without servo control of the sodium and fluid balance.

Recent publications related to the projects described above:

Thomsen K, Shalmi M. Effect of adrenalectomy on distal nephron lithium reabsorption induced by potassium depletion. *Kidney and Blood Press Res* 1997; 20: 31-37.
Krusell LR, Jespersen LT, Christensen CK, Thomsen K, Pedersen OL. Proximal tubular function in essential hypertensives on beta-blocker therapy with atenolol. *Blood Pressure* 1997; 6: 166-170.
Thomsen K, Shirley DG. The validity of lithium clearance as an index of sodium and water delivery from the proximal tubules. *Nephron* 1997; 77: 125-138.

- Spannow J, Thomsen K, Petersen JS, Haugan K, Christensen S. Influence of renal nerves and sodium balance on the acute antidiuretic effect of bendroflumethiazide in rats with diabetes insipidus. *J Pharmacol Exp Ther* 1997; 282: 1155-1162.
- Shalmi M, Jonassen T, Thomsen K, Kibble JD, Bie P, Christensen S. Model explaining the relation between distal nephron Li^+ reabsorption and urinary Na^+ excretion in rats. *Am J Physiol* 1998; 274: F445-F452.
- Thomsen K, Bak M, Shirley DG. Chronic lithium treatment inhibits amiloride-sensitive sodium transport in the rat distal nephron. *J Pharmacol Exp Ther* 1999; 289: 443-447.
- Thomsen K. Renal lithium excretion in man and its role in the development of lithium intoxication. In Birch NJ, Gallicchio VS, Becker R, editors. *Lithium: 50 years of Psychopharmacology*. Cheshire, Connecticut: Weidner Publishing Group 1999: 100-115.
- Thomsen K, Schou M. Avoidance of lithium intoxication: Advice based on knowledge about the renal lithium clearance under various circumstances. *Pharmacopsychiat* 1999; 32: 83-86.
- Emamifar M, Shalmi S, Thomsen K, Christensen S. Mechanisms of distal nephron Li^+ reabsorption during dietary K^+ restriction in rats. *Kidney and Blood Press Res* 2000; 23: 83-88.
- Bak M, Thomsen K, Christiansen, T, Flyvbjerg A. Renal enlargement precedes renal hyperfiltration in early experimental diabetes in rats. *J Am Soc Nephrol* 2000; 11: 1287-1292.
- Thomsen K, Shirley DG. Importance of proximal tubular fluid output in regulating long-term urinary sodium excretion in health and disease. *Nephron* 2000; 90: 121-132.
- Bak M, Thomsen K, Flyvbjerg A. Effects of the somatostatin analogue octreotide on renal function in conscious diabetic rats. *Nephrol Dial Transplant* 2001; 16: 2002-2007.
- Janjua N, Jonassen TEN, Langhoff S, Thomsen K, Christensen, S. The role of sodium depletion in the acute antidiuretic effect of bendroflumethiazide in rats with nephrogenic diabetes insipidus. *J Pharmacol Exp Ther* 2001; 299: 307-313.
- Hansen TK, Møller J, Thomsen K, Frandsen E, Dall R, Jørgensen JO, Christiansen JS. Effects of growth hormone on renal tubular handling of sodium in healthy humans. *Amer J Physiol, Endocrinology* 2001; 281: E1326-E1332.
- Thomsen K, Jonassen TEN, Christensen S, Shirley DG. Amiloride inhibits proximal tubular reabsorption in conscious euvoletic rats. *Eur J Pharmacol* 2002; 437: 85-90.
- Thomsen K, Nielsen CB, Flyvbjerg A. Effects of glycine on GFR and segmental tubular handling of sodium in conscious rats. *Clin Exp Pharmacol Physiol* 2002; 29: 449-454.