



Universiteit
Leiden
The Netherlands

Mineralocorticoid receptor gene variants : implications for stress, blood pressure and personality

Leeuwen, N. van

Citation

Leeuwen, N. van. (2010, November 9). *Mineralocorticoid receptor gene variants : implications for stress, blood pressure and personality*. Retrieved from <https://hdl.handle.net/1887/16122>

Version: Corrected Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/16122>

Note: To cite this publication please use the final published version (if applicable).

Reference List

- Anseau, M., Leboulle, D., Sulon, J., von Frenckell, R., Legros, J.J., 1993. Oral contraceptives and the dexamethasone suppression test. *Psychoneuroendocrinology* 18 (1), 37-43
- Arai, K., Nakagomi, Y., Iketani, M., Shimura, Y., Amemiya, S., Ohyama, K., Shibasaki, T., 2003. Functional polymorphisms in the mineralocorticoid receptor and amiloride-sensitive sodium channel genes in a patient with sporadic pseudohypoaldosteronism. *Human Genetics* 112, 91-97.
- Arriza, J.L., Weinberger, C., Cerelli, G., Glaser, T.M., Handelin, B.L., Housman, D.E., Evans, R.M., 1987. Cloning of human mineralocorticoid receptor complementary DNA: structural and functional kinship with the glucocorticoid receptor. *Science* 237, 268-275.
- Arvat, E., Maccagno, B., Giordano, R., Pellegrino, M., Broglio, F., Gianotti, L., Maccario, M., Camanni, F., Ghigo, E., 2001. Mineralocorticoid receptor blockade by canrenoate increases both spontaneous and stimulated adrenal function in humans. *J.Clin.Endocrinol.Metab* 86, 3176-3181.
- Asselin-Labat, M.L., David, M., Biola-Vidamment, A., Lecoecuche, D., Zennaro, M.C., Bertoglio, J., Pallardy, M., 2004. GILZ, a new target for the transcription factor FoxO3, protects T lymphocytes from interleukin-2 withdrawal-induced apoptosis. *Blood* 104, 215-223.
- Atkinson, H.C., Wood, S.A., Castrique, E.S., Kershaw, Y.M., Wiles, C.C.R., Lightman, S.L., 2008. Corticosteroids mediate fast feedback of the rat hypothalamic-pituitary-adrenal axis via the mineralocorticoid receptor. *American Journal of Physiology-Endocrinology and Metabolism* 294, E1011-E1022.
- Azizi, M., Boutouyrie, P., Bissery, A., Agharazii, M., Verbeke, F., Stern, N., Bura-Riviere, A., Laurent, S., henc-Gelas, F., Jeunemaitre, X., 2005. Arterial and renal consequences of partial genetic deficiency in tissue kallikrein activity in humans. *J.Clin.Invest* 115, 780-787.
- Backhaus, J., Junghanns, K., Hohagen, F., 2004. Sleep disturbances are correlated with decreased morning awakening salivary cortisol. *Psychoneuroendocrinology* 29, 1184-1191.
- Bardeleben, U., Holsboer, F., 1989. Cortisol response to a combined dexamethasone-human corticotrophin-releasing hormone challenge in patients with depression. *J.Neuroendocrinol.* 1, 485-488.
- Barrett, J.C., Fry, B., Maller, J., Daly, M.J., 2005. Haploview: analysis and visualization of LD and haplotype maps. *Bioinformatics* 21, 263-265.
- Bartels, M., van den, B.M., Sluyter, F., Boomsma, D.I., de Geus, E.J., 2003. Heritability of cortisol levels: review and simultaneous analysis of twin studies. *Psychoneuroendocrinology* 28, 121-137.
- Bhagwagar, Z., Hafizi, S., Cowen, P.J., 2003. Increase in concentration of waking salivary cortisol in recovered patients with depression. *Am.J.Psychiatry* 160, 1890-1891.
- Bijl, R.V., Ravelli, A., van Zessen, G., 1998. Prevalence of psychiatric disorder in the general population: results of The Netherlands Mental Health Survey and Incidence Study (NEMESIS). *Soc.Psychiatry Psychiatr.Epidemiol.* 33, 587-595.
- Bloem, L.J., Guo, C., Pratt, J.H., 1995. Identification of a splice variant of the rat and human mineralocorticoid receptor genes. *J.Steroid Biochem.Mol.Biol.* 55, 159-162.
- Born, J., Steinbach, D., Dodt, C., Fehm, H.L., 1997. Blocking of central nervous mineralocorticoid receptors counteracts inhibition of pituitary-adrenal activity in human sleep. *Journal of Clinical Endocrinology and Metabolism* 82, 1106-1110.
- Bradbury, M.J., Akana, S.F., Dallman, M.F., 1994. Roles of type I and II corticosteroid receptors in regulation of basal activity in the hypothalamo-pituitary-adrenal axis during the diurnal trough and the peak: evidence for a nonadditive effect of combined receptor occupation. *Endocrinology* 134, 1286-1296.

- Brinks, V., Berger, S., Gass, P., de Kloet, E.R., Oitzl, M.S., 2009. Mineralocorticoid receptors in control of emotional arousal and fear memory. *Horm.Behav.* 56, 232-238.
- Broderick, J.E., Arnold, D., Kudielka, B.M., Kirschbaum, C., 2004. Salivary cortisol sampling compliance: comparison of patients and healthy volunteers. *Psychoneuroendocrinology* 29, 636-650.
- Buckby, J.A., Yung, A.R., Cosgrave, E.M., Cotton, S.M., 2007. Distinguishing between anxiety and depression using the Mood and Anxiety Symptoms Questionnaire (MASQ). *Br.J.Clin.Psychol.* 46, 235-239.
- Buckley, T.M., Mullen, B.C., Schatzberg, A.F., 2007. The acute effects of a mineralocorticoid receptor (MR) agonist on nocturnal hypothalamic-adrenal-pituitary (HPA) axis activity in healthy controls. *Psychoneuroendocrinology* 32, 859-864.
- Caprio, M., Feve, B., Claes, A., Viengchareun, S., Lombes, M., Zennaro, M.C., 2007. Pivotal role of the mineralocorticoid receptor in corticosteroid-induced adipogenesis. *FASEB J.* 21, 2185-2194.
- Carey, M.P., Deterd, C.H., de Koning, J., Helmerhorst, F., de Kloet, E.R., 1995. The influence of ovarian steroids on hypothalamic-pituitary-adrenal regulation in the female rat. *J.Endocrinol.* 144, 311-321.
- Carroll, B.J., Martin, F.I.R., Davies, B., 1968. Resistance to Suppression by Dexamethasone of Plasma 11-Ohcs Levels in Severe Depressive Illness. *British Medical Journal* 3, 285-&.
- Castren, M., Patchev, V.K., Almeida, O.F., Holsboer, F., Trapp, T., Castren, E., 1995. Regulation of rat mineralocorticoid receptor expression in neurons by progesterone. *Endocrinology* 136 (9), 3800-3806
- Chida, Y., Steptoe, A., 2008. Cortisol awakening response and psychosocial factors: A systematic review and meta-analysis. *Biol.Psychol.*
- Clark, L.A., Watson, D., Mineka, S., 1994. Temperament, personality, and the mood and anxiety disorders. *J.Abnorm.Psychol.* 103, 103-116.
- Clow, A., Thorn, L., Evans, P., Hucklebridge, F., 2004. The awakening cortisol response: methodological issues and significance. *Stress* 7, 29-37.
- Conway-Campbell, B.L., McKenna, M.A., Wiles, C.C., Atkinson, H.C., de Kloet, E.R., Lightman, S.L., 2007. Proteasome-dependent down-regulation of activated nuclear hippocampal glucocorticoid receptors determines dynamic responses to corticosterone. *Endocrinology* 148, 5470-5477.
- Costa, P.T., Jr., Bagby, R.M., Herbst, J.H., McCrae, R.R., 2005. Personality self-reports are concurrently reliable and valid during acute depressive episodes. *J.Affect.Disord.* 89, 45-55.
- Costa, P.T., McCrae, R.R., 1992. NEO PI-R. Professional manual. Psychological Assessment Resources, Inc, Odessa, FL
- Cui, J.S., Hopper, J.L., Harrap, S.B., 2003. Antihypertensive treatments obscure familial contributions to blood pressure variation. *Hypertension* 41, 207-210.
- de Beurs, E., den Hollander-Gijsman, M.E., Helmich, S., Zitman, F.G., 2007. The tripartite model for assessing symptoms of anxiety and depression: psychometrics of the Dutch version of the mood and anxiety symptoms questionnaire. *Behav.Res.Ther.* 45, 1609-1617.
- de Kloet, C.S., Vermetten, E., Geuze, E., Kavelaars, A., Heijnen, C.J., Westenberg, H.G.M., 2006. Assessment of HPA-axis function in posttraumatic stress disorder: Pharmacological and non-pharmacological challenge tests, a review. *Journal of Psychiatric Research* 40, 550-567.
- de Kloet, E.R., van, d., V, De Wied, D., 1974. The site of the suppressive action of dexamethasone on pituitary-adrenal activity. *Endocrinology* 94, 61-73.
- de Kloet, E.R., Vreugdenhil, E., Oitzl, M.S., Joels, M., 1998. Brain corticosteroid receptor balance in health and disease. *Endocrine Reviews* 19, 269-301.

- de Kloet, R., DeRijk, R.H., Meijer, O.C., 2007. Therapy Insight: is there an imbalanced response of mineralocorticoid and glucocorticoid receptors in depression? *Nature Clinical Practice Endocrinology & Metabolism* 3, 168-179.
- de Kloet, R., Wallach, G., McEwen, B.S., 1975. Differences in corticosterone and dexamethasone binding to rat brain and pituitary. *Endocrinology* 96, 598-609.
- De, V.W., Olf, M., Van Amsterdam, J.G., Kamphuis, J.H., Emmelkamp, P.M., 2003. Physiological differences between burnout patients and healthy controls: blood pressure, heart rate, and cortisol responses. *Occup. Environ. Med.* 60 Suppl 1, i54-i61.
- Deng, H.W., Chen, W.M., Recker, R.R., 2000. QTL fine mapping by measuring and testing for Hardy-Weinberg and linkage disequilibrium at a series of linked marker loci in extreme samples of populations. *Am.J.Hum.Genet.* 66, 1027-1045.
- DeRijk, R.H., Schaaf, M.J., Turner, G., Datson, N.A., Vreugdenhil, E., Cidlowski, J., de Kloet, E.R., Emery, P., Sternberg, E.M., Detera-Wadleigh, S.D., 2001. A human glucocorticoid receptor gene variant that increases the stability of the glucocorticoid receptor beta-isoform mRNA is associated with rheumatoid arthritis. *J.Rheumatol.* 28, 2383-2388.
- DeRijk, R.H., van Leeuwen, N., Klok, M.D., Zitman, F.G., 2008. Corticosteroid receptor-gene variants: modulators of the stress-response and implications for mental health. *Eur.J.Pharmacol.* 585, 492-501.
- DeRijk, R.H., Wüst, S., Meijer, O.C., Zennaro, M.C., Federenko, I.S., Hellhammer, D.H., Giacchetti, G., Vreugdenhil, E., Zitman, F.G., de Kloet, E.R., 2006. A common polymorphism in the mineralocorticoid receptor modulates stress responsiveness. *Journal of Clinical Endocrinology and Metabolism* 91, 5083-5089.
- Deuschle, M., Weber, B., Colla, M., Muller, M., Kniest, A., Heuser, I., 1998. Mineralocorticoid receptor also modulates basal activity of hypothalamus-pituitary-adrenocortical system in humans. *Neuroendocrinology* 68, 355-360.
- Di, S., Malcher-Lopes, R., Halmos, K.C., Tasker, J.G., 2003. Nongenomic glucocorticoid inhibition via endocannabinoid release in the hypothalamus: a fast feedback mechanism. *J.Neurosci.* 23, 4850-4857.
- Dickerson, S.S., Kemeny, M.E., 2004. Acute stressors and cortisol responses: a theoretical integration and synthesis of laboratory research. *Psychol.Bull.* 130, 355-391.
- Dressendorfer, R.A., Kirschbaum, C., Rohde, W., Stahl, F., Strasburger, C. J., 1992. Synthesis of a cortisol-biotin conjugate and evaluation as a tracer in an immunoassay for salivary cortisol measurement. *J. Steroid Biochem. Mol. Biol.* 43 (7), 683-692
- Dodt, C., Kern, W., Fehm, H.L., Born, J., 1993. Antimineralocorticoid canrenoate enhances secretory activity of the hypothalamus-pituitary-adrenocortical (HPA) axis in humans. *Neuroendocrinology* 58, 570-574.
- Droste, S.K., de Groote, L., Atkinson, H.C., Lightman, S.L., Reul, J.M.H.M., Linthorst, A.C.E., 2008. Corticosterone levels in the brain show a distinct ultradian rhythm but a delayed response to forced swim stress. *Endocrinology* 149, 3244-3253.
- Edwards, C.R., Stewart, P.M., Burt, D., Brett, L., McIntyre, M.A., Sutanto, W.S., de Kloet, E.R., Monder, C., 1988. Localisation of 11 beta-hydroxysteroid dehydrogenase--tissue specific protector of the mineralocorticoid receptor. *Lancet* 2, 986-989.
- Epel, E.S., McEwen, B., Seeman, T., Matthews, K., Castellazzo, G., Brownell, K.D., Bell, J., Ickovics, J.R., 2000. Stress and body shape: stress-induced cortisol secretion is consistently greater among women with central fat. *Psychosom.Med.* 62, 623-632.
- Fagart, J., Huyet, J., Pinon, G.M., Rochel, M., Mayer, C., Rafestin-Oblin, M.E., 2005. Crystal structure of a mutant mineralocorticoid receptor responsible for hypertension. *Nat.Struct.Mol.Biol.* 12, 554-555.
- Federenko, I.S., Schlotz, W., Kirschbaum, C., Bartels, M., Hellhammer, D.H., Wüst, S., 2006. The heritability of perceived stress. *Psychological Medicine* 36, 375-385.
- Fernandes-Rosa, F.L., Bueno, A.C., Molina de, S.R., de, C.M., Dos Santos, J.E., Foss, M.C., Zennaro, M.C., Bettiol, H., Barbieri, M.A., Antonini, S.R., 2009. Mineralocorticoid Receptor p.I180V Polymorphism: Association with Body Mass Index and LDL-cholesterol Levels. *J.Endocrinol.Invest* (In press),

- Fernandes-Rosa, F.L., de Castro, M., Latronico, A.C., Sippell, W.G., Riepe, F.G., Antonini, S.R., 2006. Recurrence of the R947X mutation in unrelated families with autosomal dominant pseudohypoaldosteronism type 1: evidence for a mutational hot spot in the mineralocorticoid receptor gene. *J.Clin.Endocrinol.Metab* 91, 3671-3675.
- Flint, J., 2004. The genetic basis of neuroticism. *Neurosci.Biobehav.Rev.* 28, 307-316.
- Fries, E., Dettenborn, L., Kirschbaum, C., 2009. The cortisol awakening response (CAR): facts and future directions. *Int.J.Psychophysiol.* 72, 67-73.
- Funder, J.W., 2009. Reconsidering the roles of the mineralocorticoid receptor. *Hypertension* 53, 286-290.
- Funder, J.W., Pearce, P.T., Smith, R., Smith, A.I., 1988. Mineralocorticoid action: target tissue specificity is enzyme, not receptor, mediated. *Science* 242, 583-585.
- Geller, D.S., Farhi, A., Pinkerton, N., Fradley, M., Moritz, M., Spitzer, A., Meinke, G., Tsai, F.T., Sigler, P.B., Lifton, R.P., 2000. Activating mineralocorticoid receptor mutation in hypertension exacerbated by pregnancy. *Science* 289, 119-123.
- Geller, D.S., Rodriguez-Soriano, J., Vallo, B.A., Schifter, S., Bayer, M., Chang, S.S., Lifton, R.P., 1998. Mutations in the mineralocorticoid receptor gene cause autosomal dominant pseudohypoaldosteronism type I. *Nat.Genet.* 19, 279-281.
- Gold, P.W., Kling, M.A., Whitfield, H.J., Rabin, D., Margioris, A., Kalogeras, K., Demitrack, M., Loriaux, D.L., Chrousos, G.P., 1988. The clinical implications of corticotropin-releasing hormone. *Adv.Exp.Med.Biol.* 245, 507-519.
- Grossi, G., Perski, A., Ekstedt, M., Johansson, T., Lindstrom, M., Holm, K., 2005. The morning salivary cortisol response in burnout. *J.Psychosom.Res.* 59, 103-111.
- Grossmann, C., Scholz, T., Rochel, M., Bumke-Vogt, C., Oelkers, W., Pfeiffer, A.F., Diederich, S., Bahr, V., 2004. Transactivation via the human glucocorticoid and mineralocorticoid receptor by therapeutically used steroids in CV-1 cells: a comparison of their glucocorticoid and mineralocorticoid properties. *Eur.J.Endocrinol.* 151, 397-406.
- Guglielmi, R.S., Tatrow, K., 1998. Occupational Stress, Burnout, and Health in Teachers: A Methodological and Theoretical Analysis. *Review of Educational Research* 69, 61-99.
- Haller, J., Millar, S., Kruk, M.R., 1998. Mineralocorticoid receptor blockade inhibits aggressive behaviour in male rats. *Stress* 2, 201-207.
- Halushka, M.K., Fan, J.B., Bentley, K., Hsie, L., Shen, N., Weder, A., Cooper, R., Lipshutz, R., Chakravarti, A., 1999. Patterns of single-nucleotide polymorphisms in candidate genes for blood-pressure homeostasis. *Nat.Genet.* 22, 239-247.
- Heuser, I., Deuschle, M., Weber, A., Kniest, A., Ziegler, C., Weber, B., Colla, M., 2000. The role of mineralocorticoid receptors in the circadian activity of the human hypothalamus-pituitary-adrenal system: effect of age. *Neurobiol.Aging* 21, 585-589.
- Heuser, I., Yassouridis, A., Holsboer, F., 1994. The combined dexamethasone/CRH test: a refined laboratory test for psychiatric disorders. *J.Psychiatr.Res.* 28, 341-356.
- Holsboer, F., 1986. Corticotropin-releasing hormone--a new tool to investigate hypothalamic-pituitary-adrenocortical physiology in psychiatric patients. *Psychopharmacol.Bull.* 22, 907-912.
- Holsboer, F., 2000. The corticosteroid receptor hypothesis of depression. *Neuropsychopharmacology* 23, 477-501.
- Ising, M., Depping, A.M., Siebertz, A., Lucae, S., Unschuld, P.G., Kloiber, S., Horstmann, S., Uhr, M., Muller-Myhsok, B., Holsboer, F., 2008. Polymorphisms in the FKBP5 gene region modulate recovery from psychosocial stress in healthy controls. *Eur.J.Neurosci.* 28, 389-398.
- Joels, M., Karst, H., Derijk, R., de Kloet, E.R., 2008. The coming out of the brain mineralocorticoid receptor. *Trends in Neurosciences* 31, 1-7.

- Karssen, A.M., Meijer, O.C., Berry, A., Pinol, R.S., de Kloet, E.R., 2005. Low doses of dexamethasone can produce a hypocorticosteroid state in the brain. *Endocrinology* 146, 5587-5595.
- Karssen, A.M., Meijer, O.C., van der Sandt, I.C.J., Lucassen, P.J., De Lange, E.C.M., De Boer, A.G., de Kloet, E.R., 2001. Multidrug resistance P-glycoprotein hampers the access of cortisol but not of corticosterone to mouse and human brain. *Endocrinology* 142, 2686-2694.
- Karst, H., Berger, S., Turiault, M., Tronche, F., Schutz, G., Joels, M., 2005. Mineralocorticoid receptors are indispensable for nongenomic modulation of hippocampal glutamate transmission by corticosterone. *Proc.Natl.Acad.Sci.U.S A* 102, 19204-19207.
- Karst, H., Joels, M., 2005. Corticosterone slowly enhances miniature excitatory postsynaptic current amplitude in mice CA1 hippocampal cells. *Journal of Neurophysiology* 94, 3479-3486.
- Kendler, K.S., Gardner, C.O., Prescott, C.A., 2002. Toward a comprehensive developmental model for major depression in women. *Am.J.Psychiatry* 159, 1133-1145.
- Kendler, K.S., Kuhn, J.W., Prescott, C.A., 2004. Childhood sexual abuse, stressful life events and risk for major depression in women. *Psychol.Med.* 34, 1475-1482.
- Kirschbaum, C., Kudielka, B.M., Gaab, J., Schommer, N.C., Hellhammer, D.H., 1999. Impact of gender, menstrual cycle phase, and oral contraceptives on the activity of the hypothalamus-pituitary-adrenal axis. *Psychosom.Med.* 61, 154-162.
- Kovacs, K.J., Foldes, A., Sawchenko, P.E., 2000. Glucocorticoid negative feedback selectively targets vasopressin transcription in parvocellular neurosecretory neurons. *Journal of Neuroscience* 20, 3843-3852.
- Kozak, M., 1986. Influences of mRNA secondary structure on initiation by eukaryotic ribosomes. *Proc.Natl.Acad.Sci.U.S A* 83, 2850-2854.
- Kudielka, B.M., Bellingrath, S., Hellhammer, D.H., 2007a. Further support for higher salivary cortisol levels in "morning" compared to "evening" persons. *Journal of Psychosomatic Research* 62, 595-596.
- Kudielka, B.M., Broderick, J.E., Kirschbaum, C., 2003. Compliance with saliva sampling protocols: Electronic monitoring reveals invalid cortisol daytime profiles in noncompliant subjects. *Psychosomatic Medicine* 65, 313-319.
- Kudielka, B.M., Buchtal, J., Uhde, A., Wüst, S., 2007b. Circadian cortisol profiles and psychological self-reports in shift workers with and without recent change in the shift rotation system. *Biological Psychology* 74, 92-103.
- Kudielka, B.M., Hellhammer, D.H., Wüst, S., 2009. Why do we respond so differently? Reviewing determinants of human salivary cortisol responses to challenge. *Psychoneuroendocrinology* 34, 2-18.
- Kudielka, B.M., Schmidt-Reinwald, A.K., Hellhammer, D.H., Kirschbaum, C., 1999. Psychological and endocrine responses to psychosocial stress and dexamethasone/corticotropin-releasing hormone in healthy postmenopausal women and young controls: The impact of age and a two-week estradiol treatment. *Neuroendocrinology* 70, 422-430.
- Kumsta, R., Entringer, S., Koper, J.W., van Rossum, E.F., Hellhammer, D.H., Wüst, S., 2007. Sex specific associations between common glucocorticoid receptor gene variants and hypothalamus-pituitary-adrenal axis responses to psychosocial stress. *Biol.Psychiatry* 62, 863-869.
- Kumsta, R., Entringer, S., Koper, J.W., van Rossum, E.F., Hellhammer, D.H., Wüst, S., 2008. Glucocorticoid receptor gene polymorphisms and glucocorticoid sensitivity of subdermal blood vessels and leukocytes. *Biol.Psychol.* 79, 179-184.
- Kuningas, M., de Rijk, R.H., Westendorp, R.G.J., Jolles, J., Slagboom, P.E., van Heemst, D., 2007. Mental performance in old age dependent on cortisol and genetic variance in the mineralocorticoid and glucocorticoid receptors. *Neuropsychopharmacology* 32, 1295-1301.
- Lai, M., Bae, S.E., Bell, J.E., Seckl, J.R., Macleod, M.R., 2009. Mineralocorticoid receptor mRNA expression is increased in human hippocampus following brief cerebral ischaemia. *Neuropathol.Appl.Neurobiol.* 35, 156-164.

- Lai, M., Horsburgh, K., Bae, S.E., Carter, R.N., Stenvers, D.J., Fowler, J.H., Yau, J.L., Gomez-Sanchez, C.E., Holmes, M.C., Kenyon, C.J., Seckl, J.R., Macleod, M.R., 2007. Forebrain mineralocorticoid receptor overexpression enhances memory, reduces anxiety and attenuates neuronal loss in cerebral ischaemia. *Eur.J.Neurosci.* 25, 1832-1842.
- Langelaan, S., Bakker, A.B., Schaufeli, W.B., van, R.W., van Doornen, L.J., 2006. Do burned-out and work-engaged employees differ in the functioning of the hypothalamic-pituitary-adrenal axis? *Scand.J.Work Environ.Health* 32, 339-348.
- Lazarus, R.S., Launier, R., 1978. Stress-related transactions between person and environment. *Perspectives in Interactional Psychology* (ed.L.A.Pervin andM.Lewis)287-327.
- Lee, W.C., 2003. Searching for disease-susceptibility loci by testing for Hardy-Weinberg disequilibrium in a gene bank of affected individuals. *Am.J.Epidemiol.* 158, 397-400.
- Licht, C.M., de Geus, E.J., Seldenrijk, A., van Hout, H.P., Zitman, F.G., van, D.R., Penninx, B.W., 2009. Depression is associated with decreased blood pressure, but antidepressant use increases the risk for hypertension. *Hypertension* 53, 631-638.
- Lightman, S.L., Wiles, C.C., Atkinson, H.C., Henley, D.E., Russell, G.M., Leendertz, J.A., McKenna, M.A., Spiga, F., Wood, S.A., Conway-Campbell, B.L., 2008. The significance of glucocorticoid pulsatility. *Eur.J.Pharmacol.* 583, 255-262.
- Linkowski, P., Van Onderbergen, A., Kerkhofs, M., Bosson, D., Mendlewicz, J., Van Cauter, E., 1993. Twin study of the 24-h cortisol profile: evidence for genetic control of the human circadian clock. *Am.J.Physiol* 264, E173-E181.
- Mancia, G., Parati, G., 2004. Office compared with ambulatory blood pressure in assessing response to antihypertensive treatment: a meta-analysis. *J.Hypertens.* 22, 435-445.
- Martinez, F., Mansego, M.L., Escudero, J.C., Redon, J., Chaves, F.J., 2009. Association of a Mineralocorticoid Receptor Gene Polymorphism With Hypertension in a Spanish Population. *Am.J.Hypertens.*
- Maslach, C., Schaufeli, W.B., Leiter, M.P., 2001. Job burnout. *Annu.Rev.Psychol.* 52, 397-422.
- Mcewen, B.S., Davis, P.G., Parsons, B., Pfaff, D.W., 1979. The brain as a target for steroid hormone action. *Annu.Rev.Neurosci.* 2, 65-112.
- Mcewen, B.S., Stellar, E., 1993. Stress and the individual. Mechanisms leading to disease. *Arch.Intern.Med.* 153, 2093-2101.
- Mehdi, U.F., ms-Huet, B., Raskin, P., Vega, G.L., Toto, R.D., 2009. Addition of angiotensin receptor blockade or mineralocorticoid antagonism to maximal angiotensin-converting enzyme inhibition in diabetic nephropathy. *J.Am.Soc.Nephrol.* 20, 2641-2650.
- Meijer, O.C., De Lange, E.C.M., Breimer, D.D., De Boer, A.G., Workel, J.O., de Kloet, E.R., 1998. Penetration of dexamethasone into brain glucocorticoid targets is enhanced in *mdr1A* P-glycoprotein knockout mice. *Endocrinology* 139, 1789-1793.
- Melamed, S., Shirom, A., Toker, S., Berliner, S., Shapira, I., 2006. Burnout and risk of cardiovascular disease: evidence, possible causal paths, and promising research directions. *Psychol.Bull.* 132, 327-353.
- Menard, J., Gonzalez, M.F., Guyene, T.T., Bissery, A., 2006. Investigation of aldosterone-synthase inhibition in rats. *J.Hypertens.* 24, 1147-1155.
- Miller, S.A., Dykes, D.D., Polesky, H.F., 1988. A Simple Salting Out Procedure for Extracting Dna from Human Nucleated Cells. *Nucleic Acids Research* 16, 1215-1215.
- Minelli, C., Thompson, J.R., Abrams, K.R., Thakkinstian, A., Attia, J., 2008. How should we use information about HWE in the meta-analyses of genetic association studies? *Int. J. Epidemiol.* 37 (1), 136-146
- Mommersteeg, P.M., Heijnen, C.J., Verbraak, M.J., van Doornen, L.J., 2006. Clinical burnout is not reflected in the cortisol awakening response, the day-curve or the response to a low-dose dexamethasone suppression test. *Psychoneuroendocrinology* 31, 216-225.

- Munck, A., Guyre, P.M., Holbrook, N.J., 1984. Physiological functions of glucocorticoids in stress and their relation to pharmacological actions. *Endocr.Rev.* 5, 25-44.
- Murray, C.J., Lopez, A.D., 1997. Alternative projections of mortality and disability by cause 1990-2020: Global Burden of Disease Study. *Lancet* 349, 1498-1504.
- Myles, K., Funder, J.W., 1996. Progesterone binding to mineralocorticoid receptors: in vitro and in vivo studies. *Am.J.Physiol* 270, E601-E607.
- Nystrom, A.M., Bondeson, M.L., Skanke, N., Martensson, J., Stromberg, B., Gustafsson, J., Anneren, G., 2004. A novel nonsense mutation of the mineralocorticoid receptor gene in a Swedish family with pseudohypoaldosteronism type I (PHA1). *J.Clin.Endocrinol.Metab* 89, 227-231.
- Oakley, R.H., Sar, M., Cidlowski, J.A., 1996. The human glucocorticoid receptor beta isoform. Expression, biochemical properties, and putative function. *J.Biol.Chem.* 271, 9550-9559.
- Oitzl, M.S., de Kloet, E.R., 1992. Selective corticosteroid antagonists modulate specific aspects of spatial orientation learning. *Behav.Neurosci.* 106, 62-71.
- Ormel, J., Rosmalen, J., Farmer, A., 2004. Neuroticism: a non-informative marker of vulnerability to psychopathology. *Soc.Psychiatry Psychiatr.Epidemiol.* 39, 906-912.
- Otte, C., Jahn, H., Yassouridis, A., Arlt, J., Stober, N., Maass, P., Wiedemann, K., Kellner, M., 2003a. The mineralocorticoid receptor agonist, fludrocortisone, inhibits pituitary-adrenal activity in humans after pre-treatment with metyrapone. *Life Sci.* 73, 1835-1845.
- Otte, C., Moritz, S., Yassouridis, A., Koop, M., Madrischewski, A.M., Wiedemann, K., Kellner, M., 2007. Blockade of the mineralocorticoid receptor in healthy men: effects on experimentally induced panic symptoms, stress hormones, and cognition. *Neuropsychopharmacology* 32, 232-238.
- Otte, C., Yassouridis, A., Jahn, H., Maass, P., Stober, N., Wiedemann, K., Kellner, M., 2003b. Mineralocorticoid receptor-mediated inhibition of the hypothalamic-pituitary-adrenal axis in aged humans. *J.Gerontol.A Biol.Sci.Med.Sci.* 58, B900-B905.
- Panarelli, M., Holloway, C.D., Fraser, R., Connell, J.M., Ingram, M.C., Anderson, N.H., Kenyon, C.J., 1998. Glucocorticoid receptor polymorphism, skin vasoconstriction, and other metabolic intermediate phenotypes in normal human subjects. *J.Clin.Endocrinol.Metab* 83, 1846-1852.
- Pascual-Le Tallec, L., Demange, C., Lombes, M., 2004. Human mineralocorticoid receptor A and B protein forms produced by alternative translation sites display different transcriptional activities. *Eur.J.Endocrinol.* 150, 585-590.
- Pascual-Le Tallec, L., Lombes, M., 2005. The mineralocorticoid receptor: a journey exploring its diversity and specificity of action. *Mol.Endocrinol.* 19, 2211-2221.
- Penninx, B.W., Beekman, A.T., Smit, J.H., Zitman, F.G., Nolen, W.A., Spinhoven, P., Cuijpers, P., De Jong, P.J., van Marwijk, H.W., Assendelft, W.J., van der, M.K., Verhaak, P., Wensing, M., De, G.R., Hoogendijk, W.J., Ormel, J., van, D.R., 2008. The Netherlands Study of Depression and Anxiety (NESDA): rationale, objectives and methods. *Int.J.Methods Psychiatr.Res.* 17, 121-140.
- Peri, S., Pandey, A., 2001. A reassessment of the translation initiation codon in vertebrates. *Trends Genet.* 17, 685-687.
- Pinon, G.M., Fagart, J., Souque, A., Auzou, G., Vandewalle, A., Rafestin-Oblin, M.E., 2004. Identification of steroid ligands able to inactivate the mineralocorticoid receptor harboring the S810L mutation responsible for a severe form of hypertension. *Mol.Cell Endocrinol.* 217, 181-188.
- Pitt, B., 2005. Role of aldosterone blockade in heart failure. *Heart Fail.Clin.* 1, 49-56.
- Portella, M.J., Harmer, C.J., Flint, J., Cowen, P., Goodwin, G.M., 2005. Enhanced early morning salivary cortisol in neuroticism. *Am.J.Psychiatry* 162, 807-809.
- Pruessner, J.C., Hellhammer, D.H., Kirschbaum, C., 1999. Burnout, perceived stress, and cortisol responses to awakening. *Psychosom.Med.* 61, 197-204.

- Pruessner, M., Hellhammer, D.H., Pruessner, J.C., Lupien, S.J., 2003. Self-reported depressive symptoms and stress levels in healthy young men: associations with the cortisol response to awakening. *Psychosom.Med.* 65, 92-99.
- Pujo, L., Fagart, J., Gary, F., Papadimitriou, D.T., Claes, A., Jeunemaitre, X., Zennaro, M.C., 2007. Mineralocorticoid receptor mutations are the principal cause of renal type 1 pseudohypoaldosteronism. *Hum.Mutat.* 28, 33-40.
- Ratka, A., Sutanto, W., Bloemers, M., de Kloet, E.R., 1989. On the role of brain mineralocorticoid (type I) and glucocorticoid (type II) receptors in neuroendocrine regulation. *Neuroendocrinology* 50, 117-123.
- Raubenheimer, P.J., Young, E.A., Andrew, R., Seckl, J.R., 2006. The role of corticosterone in human hypothalamic-pituitary-adrenal axis feedback. *Clin.Endocrinol.(Oxf)* 65, 22-26.
- Riepe, F.G., Krone, N., Morlot, M., Ludwig, M., Sippell, W.G., Partsch, C.J., 2003. Identification of a novel mutation in the human mineralocorticoid receptor gene in a german family with autosomal-dominant pseudohypoaldosteronism type 1: further evidence for marked interindividual clinical heterogeneity. *J.Clin.Endocrinol.Metab* 88, 1683-1686.
- Riepe, F.G., Krone, N., Morlot, M., Peter, M., Sippell, W.G., Partsch, C.J., 2004. Autosomal-dominant pseudohypoaldosteronism type 1 in a Turkish family is associated with a novel nonsense mutation in the human mineralocorticoid receptor gene. *J.Clin.Endocrinol.Metab* 89, 2150-2152.
- Roberts, A.D., Wessely, S., Chalder, T., Papadopoulos, A., Cleare, A.J., 2004. Salivary cortisol response to awakening in chronic fatigue syndrome. *Br.J.Psychiatry* 184, 136-141.
- Rohleder, N., Joksimovic, L., Wolf, J.M., Kirschbaum, C., 2004. Hypocortisolism and increased glucocorticoid sensitivity of pro-inflammatory cytokine production in Bosnian war refugees with posttraumatic stress disorder. *Biol.Psychiatry* 55, 745-751.
- Rohleder, N., Kirschbaum, C., 2006. The hypothalamic-pituitary-adrenal (HPA) axis in habitual smokers. *Int.J.Psychophysiol.* 59, 236-243.
- Rosano, G.M., Vitale, C., Marazzi, G., Volterrani, M., 2007. Menopause and cardiovascular disease: the evidence. *Climacteric.* 10 Suppl 1, 19-24.
- Rosmond, R., Chagnon, Y.C., Chagnon, M., Perusse, L., Bouchard, C., Bjorntorp, P., 2000. A polymorphism of the 5'-flanking region of the glucocorticoid receptor gene locus is associated with basal cortisol secretion in men. *Metabolism* 49, 1197-1199.
- Rosner, W., 1990. The functions of corticosteroid-binding globulin and sex hormone-binding globulin: recent advances. *Endocr.Rev.* 11, 80-91.
- Rozeboom, A.M., Akil, H., Seasholtz, A.F., 2007. Mineralocorticoid receptor overexpression in forebrain decreases anxiety-like behavior and alters the stress response in mice. *Proc.Natl.Acad.Sci.U.S A* 104, 4688-4693.
- Rupprecht, R., Reul, J.M., Van steensel, B., Spengler, D., Soder, M., Berning, B., Holsboer, F., Damm, K., 1993. Pharmacological and functional characterization of human mineralocorticoid and glucocorticoid receptor ligands. *Eur.J.Pharmacol.* 247, 145-154.
- Sarabdjitsingh, R.A., Isenia, S., Polman, A., Mijalkovic, J., Lachize, S., Datson, N., de Kloet, E.R., Meijer, O.C., 2010. Disrupted corticosterone pulsatile patterns attenuate responsiveness to glucocorticoid signaling in rat brain. *Endocrinology* 151, 1177-1186.
- Sarabdjitsingh, R.A., Meijer, O.C., Schaaf, M.J., de Kloet, E.R., 2009. Subregion-specific differences in translocation patterns of mineralocorticoid and glucocorticoid receptors in rat hippocampus. *Brain Res.* 1249, 43-53.
- Sartorato, P., Khaldi, Y., Lapeyraque, A.L., Armanini, D., Kuhnle, U., Salomon, R., Caprio, M., Viengchareun, S., Lombs, M., Zennaro, M.C., 2004. Inactivating mutations of the mineralocorticoid receptor in Type I pseudohypoaldosteronism. *Mol.Cell Endocrinol.* 217, 119-125.
- Schjolden, J., Basic, D., Winberg, S., 2009. Aggression in rainbow trout is inhibited by both MR and GR antagonists. *Physiol Behav.*

- Schlotz, W., Hellhammer, J., Schulz, P., Stone, A.A., 2004. Perceived work overload and chronic worrying predict weekend-weekday differences in the cortisol awakening response. *Psychosom.Med.* 66, 207-214.
- Schmidt-Reinwald, A., Pruessner, J.C., Hellhammer, D.H., Federenko, I., Rohleder, N., Schurmeyer, T.H., Kirschbaum, C., 1999. The cortisol response to awakening in relation to different challenge tests and a 12-hour cortisol rhythm. *Life Sci.* 64, 1653-1660.
- Schulman, I.H., Aranda, P., Rajj, L., Veronesi, M., Aranda, F.J., Martin, R., 2006. Surgical menopause increases salt sensitivity of blood pressure. *Hypertension* 47, 1168-1174.
- Schulz, P., Schlotz, W., 1999. The Trier Inventory for the Assessment of Chronic Stress (TICS): Scale construction, statistical testing, and validation of the scale work overload. *Diagnostica* 45, 8-19.
- Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., Dunbar, G.C., 1998. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J.Clin.Psychiatry* 59 Suppl 20, 22-33.
- Sonnenschein, M., Mommersteeg, P.M., Houtveen, J.H., Sorbi, M.J., Schaufeli, W.B., van Doornen, L.J., 2007. Exhaustion and endocrine functioning in clinical burnout: an in-depth study using the experience sampling method. *Biol.Psychol.* 75, 176-184.
- Spath-Schwalbe, E., Gofferje, M., Kern, W., Born, J., Fehm, H.L., 1991. Sleep disruption alters nocturnal ACTH and cortisol secretory patterns. *Biol.Psychiatry* 29, 575-584.
- Strazzullo, P., Galletti, F., Dessi-Fulgheri, P., Ferri, C., Glorioso, N., Malatino, L., Mantero, F., Manunta, P., Semplicini, A., Ghiadoni, L., Zoccali, C., 2000a. Prediction and consistency of blood pressure salt-sensitivity as assessed by a rapid volume expansion and contraction protocol. *J Nephrol* 13, 46-53.
- Strazzullo, P., Galletti, F., Dessi-Fulgheri, P., Ferri, C., Glorioso, N., Malatino, L., Mantero, F., Manunta, P., Semplicini, A., Ghiadoni, L., Zoccali, C., 2000b. Prediction and consistency of blood pressure salt-sensitivity as assessed by a rapid volume expansion and contraction protocol. Salt-Sensitivity Study Group of the Italian Society of Hypertension. *J.Nephrol.* 13, 46-53.
- Sugiyama, T., Kato, N., Ishinaga, Y., Yamori, Y., Yazaki, Y., 2001. Evaluation of selected polymorphisms of the Mendelian hypertensive disease genes in the Japanese population. *Hypertens.Res.* 24, 515-521.
- Sullivan, P.F., de Geus, E.J., Willemsen, G., James, M.R., Smit, J.H., Zandbelt, T., Arolt, V., Baune, B.T., Blackwood, D., Cichon, S., Coventry, W.L., Domschke, K., Farmer, A., Fava, M., Gordon, S.D., He, Q., Heath, A.C., Heutink, P., Holsboer, F., Hoogendijk, W.J., Hottenga, J.J., Hu, Y., Kohli, M., Lin, D., Lucae, S., Macintyre, D.J., Maier, W., McGhee, K.A., McGuffin, P., Montgomery, G.W., Muir, W.J., Nolen, W.A., Nothen, M.M., Perlis, R.H., Pirlo, K., Posthuma, D., Rietschel, M., Rizzu, P., Schosser, A., Smit, A.B., Smoller, J.W., Tzeng, J.Y., van, D.R., Verhage, M., Zitman, F.G., Martin, N.G., Wray, N.R., Boomsma, D.I., Penninx, B.W., 2009. Genome-wide association for major depressive disorder: a possible role for the presynaptic protein piccolo. *Mol.Psychiatry* 14, 359-375.
- Tajima, T., Ma, X.M., Bornstein, S.R., Aguilera, G., 1999. Prenatal dexamethasone treatment does not prevent alterations of the hypothalamic pituitary adrenal axis in steroid 21-hydroxylase deficient mice. *Endocrinology* 140, 3354-3362.
- Tempfer, C.B., Jirecek, S., Riener, E.K., Zeisler, H., Denschlag, D., Hefler, L., Husslein, P.W., 2004. Polymorphisms of thrombophilic and vasoactive genes and severe preeclampsia: a pilot study. *J.Soc.Gynecol.Investig.* 11, 227-231.
- Tobin, M.D., Tomaszewski, M., Braund, P.S., Hajat, C., Raleigh, S.M., Palmer, T.M., Caulfield, M., Burton, P.R., Samani, N.J., 2008. Common variants in genes underlying monogenic hypertension and hypotension and blood pressure in the general population. *Hypertension* 51, 1658-1664.
- Tomlinson, J.W., Sinha, B., Bujalska, I., Hewison, M., Stewart, P.M., 2002. Expression of 11beta-hydroxysteroid dehydrogenase type 1 in adipose tissue is not increased in human obesity. *J.Clin.Endocrinol.Metab* 87, 5630-5635.
- Turner, B.B., 1990. Sex difference in glucocorticoid binding in rat pituitary is estrogen dependent. *Life Sci.* 46, 1399-1406.

- Van Eekelen, J.A., Rots, N.Y., Sutanto, W., de Kloet, E.R., 1992. The effect of aging on stress responsiveness and central corticosteroid receptors in the brown Norway rat. *Neurobiol.Aging* 13, 159-170.
- van Leeuwen, N., Kumsta, R., Entringer, S., de Kloet, E.R., Zitman, F.G., DeRijk, R.H., Wüst, S., 2010. Functional mineralocorticoid receptor (MR) gene variation influences the cortisol awakening response after dexamethasone. *Psychoneuroendocrinology* 35, 339-349.
- Van Rossum, E.F.C., Binder, E.B., Majer, M., Koper, J.W., Ising, M., Modell, S., Salyakina, D., Lamberts, S.W.J., Holsboer, F., 2006. Polymorphisms of the glucocorticoid receptor gene and major depression. *Biological Psychiatry* 59, 681-688.
- Van Rossum, E.F.C., Feelders, R.A., van den Beld, A.W., Uitterlinden, A.G., Janssen, J.A.M.J., Ester, W., Brinkmann, A.O., Grobbee, D.E., de Jong, F.H., Pols, H.A.P., Koper, J.W., Lamberts, S.W.J., 2004a. Association of the ER22/23EK polymorphism in the glucocorticoid receptor gene with survival and C-reactive protein levels in elderly men. *American Journal of Medicine* 117, 158-162.
- Van Rossum, E.F.C., Koper, J.W., Huizenga, N.A.T.M., Uitterlinden, A.G., Janssen, J.A.M.J., Brinkmann, A.O., Grobbee, D.E., de Jong, F.H., van Duyn, C.M., Pols, H.A.P., Lamberts, S.W.J., 2002. A polymorphism in the glucocorticoid receptor gene, which decreases sensitivity to Glucocorticoids in vivo, is associated with low insulin and cholesterol levels. *Diabetes* 51, 3128-3134.
- Van Rossum, E.F.C., Voorhoeve, P.G., Velde, S.J.T., Koper, J.W., Delemarre-Van De Waal, H.A., Kemper, H.C.G., Lamberts, S.W.J., 2004b. The ER22/23EK polymorphism in the glucocorticoid receptor gene is associated with a beneficial body composition and muscle strength in young adults. *Journal of Clinical Endocrinology and Metabolism* 89, 4004-4009.
- van Vliet, I., de Beurs, E., 2007. [The MINI-International Neuropsychiatric Interview. A brief structured diagnostic psychiatric interview for DSM-IV en ICD-10 psychiatric disorders]. *Tijdschr.Psychiatr.* 49, 393-397.
- Vandewalle, A., Lelongt, B., Geniteau-Legendre, M., Baudouin, B., Antoine, M., Estrade, S., Chatelet, F., Verroust, P., Cassingena, R., Ronco, P., 1989. Maintenance of proximal and distal cell functions in SV40-transformed tubular cell lines derived from rabbit kidney cortex. *J.Cell Physiol* 141, 203-221.
- Viau, V., Chu, A., Soriano, L., Dallman, M.F., 1999. Independent and overlapping effects of corticosterone and testosterone on corticotropin-releasing hormone and arginine vasopressin mRNA expression in the paraventricular nucleus of the hypothalamus and stress-induced adrenocorticotrophic hormone release. *J. Neurosci.* 19 (15), 6684-6693
- von Have, M., Oppelt, P.G., Müller, A., Beckmann, M.W., Binder, H., 2005. Kontrazeption. *Geburtsh Frauenheilk* 65 (09), R173-R199
- Watson, S., Gallagher, P., Smith, M.S., Ferrier, I.N., Young, A.H., 2006. The dex/CRH test--is it better than the DST? *Psychoneuroendocrinology* 31, 889-894.
- Weber, A., 2004. Krankheitsbedingte Frühpensionierungen von Lehrkräften, Early retirement of teachers as a result of health problems. *Psychosomatische Erkrankungen bei Lehrerinnen und Lehrern Hillert and E. Schmitz, Editors*, 22-38.
- Weinstock, L.M., Whisman, M.A., 2006. Neuroticism as a common feature of the depressive and anxiety disorders: a test of the revised integrative hierarchical model in a national sample. *J.Abnorm.Psychol.* 115, 68-74.
- Wellhoener, P., Born, J., Fehm, H.L., Dodt, C., 2004. Elevated resting and exercise-induced cortisol levels after mineralocorticoid receptor blockade with canrenoate in healthy humans. *J.Clin.Endocrinol.Metab* 89, 5048-5052.
- Wessa, M., Rohleder, N., Kirschbaum, C., Flor, H., 2006. Altered cortisol awakening response in posttraumatic stress disorder. *Psychoneuroendocrinology* 31, 209-215.
- Wilhelm, P., Born, J., Kudielka, B.M., Schlotz, W., Wüst, S., 2007. Is the cortisol awakening rise a response to awakening? *Experimental and Clinical Endocrinology & Diabetes* 115, S51-S51.
- Wüst, S., Federenko, I., Hellhammer, D.H., Kirschbaum, C., 2000. Genetic factors, perceived chronic stress, and the free cortisol response to awakening. *Psychoneuroendocrinology* 25, 707-720.

- Wüst, S., Wolf, J.M., Hellhammer, D.H., Kirschbaum, C., 2001. The free cortisol response to awakening: Normal values and recent findings. *Journal of Psychophysiology* 15, 152-152.
- Yehuda, R., 2002. Post-traumatic stress disorder. *N.Engl.J.Med.* 346, 108-114.
- Young, E.A., Lopez, J.F., Murphy-Weinberg, V., Watson, S.J., Akil, H., 1998. The role of mineralocorticoid receptors in hypothalamic-pituitary-adrenal axis regulation in humans. *J.Clin.Endocrinol.Metab* 83, 3339-3345.
- Zaykin, D.V., Westfall, P.H., Young, S.S., Karnoub, M.A., Wagner, M.J., Ehm, M.G., 2002. Testing association of statistically inferred haplotypes with discrete and continuous traits in samples of unrelated individuals. *Hum.Hered.* 53, 79-91.
- Zemunik, T., Boban, M., Lauc, G., Jankovic, S., Rotim, K., Vatauvuk, Z., Bencic, G., Dogas, Z., Boraska, V., Torlak, V., Susac, J., Zobic, I., Rudan, D., Pulanic, D., Modun, D., Mudnic, I., Gunjaca, G., Budimir, D., Hayward, C., Vitart, V., Wright, A.F., Campbell, H., Rudan, I., 2009. Genome-wide association study of biochemical traits in Korcula Island, Croatia. *Croat.Med.J.* 50, 23-33.
- Zennaro, M.C., Caprio, M., Feve, B., 2009. Mineralocorticoid receptors in the metabolic syndrome. *Trends Endocrinol.Metab* 20, 444-451.
- Zennaro, M.C., Keightley, M.C., Kotelevtsev, Y., Conway, G.S., Soubrier, F., Fuller, P.J., 1995. Human mineralocorticoid receptor genomic structure and identification of expressed isoforms. *J.Biol.Chem.* 270, 21016-21020.
- Zennaro, M.C., Souque, A., Viengchareun, S., Poisson, E., Lombes, M., 2001. A new human MR splice variant is a ligand-independent transactivator modulating corticosteroid action. *Mol.Endocrinol.* 15, 1586-1598.
- Zuker, M., 2003. Mfold web server for nucleic acid folding and hybridization prediction. *Nucleic Acids Res.* 31, 3406-3415.

Publications and Presentations

Publications

Functional Mineralocorticoid Receptor (MR) gene variation influences the cortisol awakening response after dexamethasone *N. van Leeuwen, R. Kumsta, S. Entringer, E.R. de Kloet, F.G. Zitman, R.H. DeRijk, & S. Wüst* *Psychoneuroendocrinology* 2010, 339-349

The functional -2 C variant of the Mineralocorticoid receptor modulates basal and salt-dependent rennin and aldosterone levels and associates with lower blood pressure *N van Leeuwen*, M Caprio*, C Blaya, F Fumeron, P Sartorato, G Giacchetti, F Mantero, FL Fernandes-Rosa, C Simian, S Peyrard, FG Zitman, R de Kloet, M Azizi, X Jeunemaitre, RH DeRijk & MC Zennaro* *Hypertension*, epub 20 September 2010

Corticosteroid receptor- gene variants: Modulators of the stress-response and implications for mental health. *R.H. deRijk, N. van Leeuwen, M.D. Klok, F.G. Zitman* *European Journal of pharmacology* 2008, 492-50

Human Mineralocorticoid Receptor (MR) gene haplotypes modulate MR expression and transactivation: implication for the stress response. *N. van Leeuwen*, S. Bellingrath*, E.R. de Kloet, F.G. Zitman, R.H. DeRijk, B.M. Kudielka & S. Wüst* *Psychoneuroendocrinology* (*in press*)

Mineralocorticoid Receptor gene-variants as determinants of HPA axis regulation and behavior. *R.H. DeRijk, E.R.de Kloet, F. G. Zitman and N. van Leeuwen* *Endocrine book series*, 2010 (*in press*)

Presentations

MR gene variants *in vitro* and *in vivo*. Marius Tausk Masterclass 2009 Oegstgeest

An *in vitro* functional mineralocorticoid receptor (MR) gene variant is associated with the cortisol response to psychosocial stress. Spring School the ABC of Stress 2009 Dresden Germany

An *In vitro* functional SNP in the human Mineralocorticoid Receptor (MR) is associated with the cortisol awakening response (CAR) after 0.25mg dexamethasone. ISPNE 2008 Dresden, Germany

Mineralocorticoid receptor (MR) gene variants modulate the CAR. Dutch EndoNeuroPsycho meeting meeting 2008 Doorwerth

Stress: de invloed van genetische variatie in de mineralocorticoid receptor (MR). NVVP 2008 Amsterdam

Functionele polymorfismen in de mineralocorticoid receptor in stress respons en psychopathologie. NVVP 2007 Maastricht

The role of single nucleotide polymorphisms (SNPs) in the Mineralocorticoid Receptor (MR) in stress response and psychopathology. First prize poster competition Dutch EndoNeuroPsycho meeting meeting 2007 Doorwerth

Functional analysis of human mineralocorticoid receptor variants associated with stress responsiveness. Dutch EndoNeuroPsycho meeting meeting 2006 Doorwerth

Curriculum vitae

Nienke van Leeuwen werd op 22 december 1975 geboren in Haarlem. In 1993 behaalde zij haar HAVO diploma aan het Linnaeus college te Haarlem. In 1993 begon zij aan de HBO opleiding medische biologie aan de Hogeschool van Amsterdam waar zij in 1997 het diploma behaalde. Haar afstudeer stage heeft zij uitgevoerd bij TNO, afdeling preventie en gezondheid onder leiding van Dr. I. Meulenbelt en Prof. dr. P.E. Slagboom. Vervolgens is zij in 1997 met de studie biologie begonnen aan de Vrije Universiteit in Amsterdam waar zij in 1998 haar bachelor en in 1999 haar doctoraal diploma behaalde in de afstudeer richting medische biologie. Haar afstudeer stage van deze studie heeft zij uitgevoerd op de Vrije Universiteit, afdeling oncologie onder leiding van Dr. V.W. van Beusechem en Prof. dr. W.R. Gerritsen. Voor zij in 2005 begon met het in dit proefschrift beschreven promotie onderzoek bij de afdeling Medische Farmacologie van het Leiden/ Amsterdam Center for Drug Research (LACDR) en het Leids Universitair Medisch Centrum (LUMC) onder leiding van Prof. dr. E.R. de Kloet, Prof. Dr. F.G. Zitman en Dr. R.H. de Rijk is zij werkzaam geweest bij Crucell en psychiatrisch ziekenhuis Rivierduinen. Na haar promotie onderzoek is zij twee maanden blijven werken bij de afdeling Medische Farmacologie waar zij onder leiding van Dr. E. Vreugdenhil microRNA technieken opgezet heeft. Sinds december 2010 werkt zij bij de afdeling Moleculaire Celbiologie van het LUMC onder leiding van Dr. L.H. 't Hart. Hier doet zij onderzoek naar de gentica van type 2 diabetes. Met behulp van *in vitro* technieken probeert zij het moleculaire mechanisme van recent geïdentificeerde diabetes genen te achterhalen. Bovendien voert zij in een groot cohort met diabetes patiënten farmacogenetisch onderzoek uit om na te gaan of het succes van de behandeling voorspeld kan worden op basis van het genotype van een patiënt.

Dankwoord

Ik wil iedereen die me geholpen heeft met mijn onderzoek heel erg bedanken. Dat zijn ten eerste alle stagiaires die ik zelf begeleid heb maar ook de stagiaires van Roel bleken erg behulpzaam bij mijn onderzoek. Dus bedankt Andrew, Daniël, Marc, Dennis, Birgitta, Nicola, Heleen, Julian, Panos, Charly en Rudie. Secondly, I would like to thank Stefan Wüst, Brigitte Kudielka, Silja Bellingrath and Robby Kumsta from the University of Trier and Christina Zennaro from the University of Paris for their collaboration en Melly Oitzl voor het coördineren van de IRTG Trier-Leiden samenwerking. Ook wil ik Wendy Rodgers bedanken voor het corrigeren van de introductie en discussie. Verder wil ik natuurlijk mijn begeleider Roel de Rijk bedanken voor alle hulp bij het onderzoek.

Ik wil natuurlijk ook al mijn andere collega's bij Medische Farmacologie bedanken. Met name Liane (de andere aio van Roel en dus helemaal op de hoogte van mijn onderzoek en problemen tijdens het onderzoek), Erno (hij heeft me een tijdelijke baan gegeven toen mijn aio contract afliep, ik vond het miRNA onderzoek erg interessant om te doen), Jessica (zij heeft me geholpen bij het uitzoeken van de high tea locatie door na het samen sporten mee te gaan naar de verschillende locaties) en Theo, Sanne, Jessica, Anette en Ethan (mijn kamergenootjes).

Mijn nieuwe collega's wil ik bedanken voor het geduld afgelopen jaar. Nu mijn proefschrift af is kan ik eindelijk beginnen met het schrijven van mijn eerste diabetes farmacogenetica artikel.

Verder wil ik mijn vrienden en familie bedanken!