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Effects of growth hormone in the hippocampus and cortex of adult rodents

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i Förmaket, Vita stråket 12, onsdagen den 18 januari 2017, klockan 09:00

av Marion Walser, Msc, leg BMA

Fakultetsopponent:

Professor Kerstin Brismar

Karolinska institutet, Stockholm

Avhandlingen baseras på följande delarbeten

I. Walser M, Hansén A, Svensson PA, Jernås M, Oscarsson J, Isgaard J, Åberg ND. Peripheral administration of bovine GH regulates the expression of cerebrocortical beta-globin, GABAB receptor 1, and the Lissencephaly-1 protein (LIS-1) in adult hypophysectomized rats. Growth Horm IGF Res. 2011 Feb; 21(1):16-24

II. Walser M, Samà MT, Wickelgren R, Åberg M, Bohlooly-Y M, Olsson B, Törnell J, Isgaard J, Åberg ND. Local overexpression of GH and GH/IGF1 effects in the adult mouse hippocampus. J Endocrinol. 2012 Nov; 215(2):257-68

III. Walser M, Schiöler L, Oscarsson J, Åberg MA, Svensson J, Åberg ND, Isgaard J. Different modes of GH administration influence gene expression in the male rat brain. J Endocrinol. 2014 May 28; 222: 181-90

IV. Walser M, Schiöler L, Oscarsson J, Åberg MA, Wickelgren R, Svensson J, Isgaard J, Åberg ND. Mode of GH administration influences gene expression in the female rat hippocampus and parietal cortex. 2016, manuscript

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Effects of growth hormone in the hippocampus and cortex of adult rodents

Marion Walser

Department of Internal Medicine, Institute of Medicine
Sahlgrenska Academy at the University of Gothenburg, Göteborg, Sweden.

Abstract

Background and Aims: Growth hormone (GH) affects proliferation, regeneration and specific plasticity in the adult brain. We aimed to investigate new mechanisms of local and circulating GH in the brain, and to explore the effects of different modes of administration of GH in rodents.

Methodology: GH transgenic male mice (GH-Tg) overexpressing astroglial GH were used. Hypophysectomised (Hx) female and male rats were substituted with GH. DNA microarrays were used to screen for transcripts responding to GH. Quantitative reverse transcription polymerase chain reaction (Q-RT-PCR) was used to confirm expression of transcripts and western blots to detect protein. Effects of GH were analysed with a statistical model allowing analysis of single transcripts, as well as categories of transcripts.

Results: In the hippocampus, GH-Tg did not influence selected neuronal transcripts whereas there was a modest effect on astroglial transcripts. Using DNA microarrays, we identified 24 single transcripts in the female cerebral cortex that were normalized by infusions of GH in Hx rats as compared to intact rats. Three transcripts were highly regulated by GH and confirmed by Q-RT-PCR. Of these three, only hemoglobin β (Hbb) was regulated in the hippocampus. In male and female rats, different modes of GH administration elicited robust responses on Hbb, twice-daily injections being more efficient than infusions. Effects on other transcripts were smaller, injections of GH were more effective in increasing or restoring overall transcript levels in the hippocampus and male cortex while GH infusions were more effective in the female cortex.

Conclusions: The Hbb transcript is robustly regulated by GH administration. Other transcripts were regulated by GH to a lesser degree but differently comparing hippocampus and cortex and in females and males. These effects probably have implications for normal cognitive physiology as well as for brain injuries. Further studies addressing different modes of GH-treatment in injuries are therefore warranted.

Keywords: growth hormone; mode of administration; sex; transcript; polymerase chain reaction

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