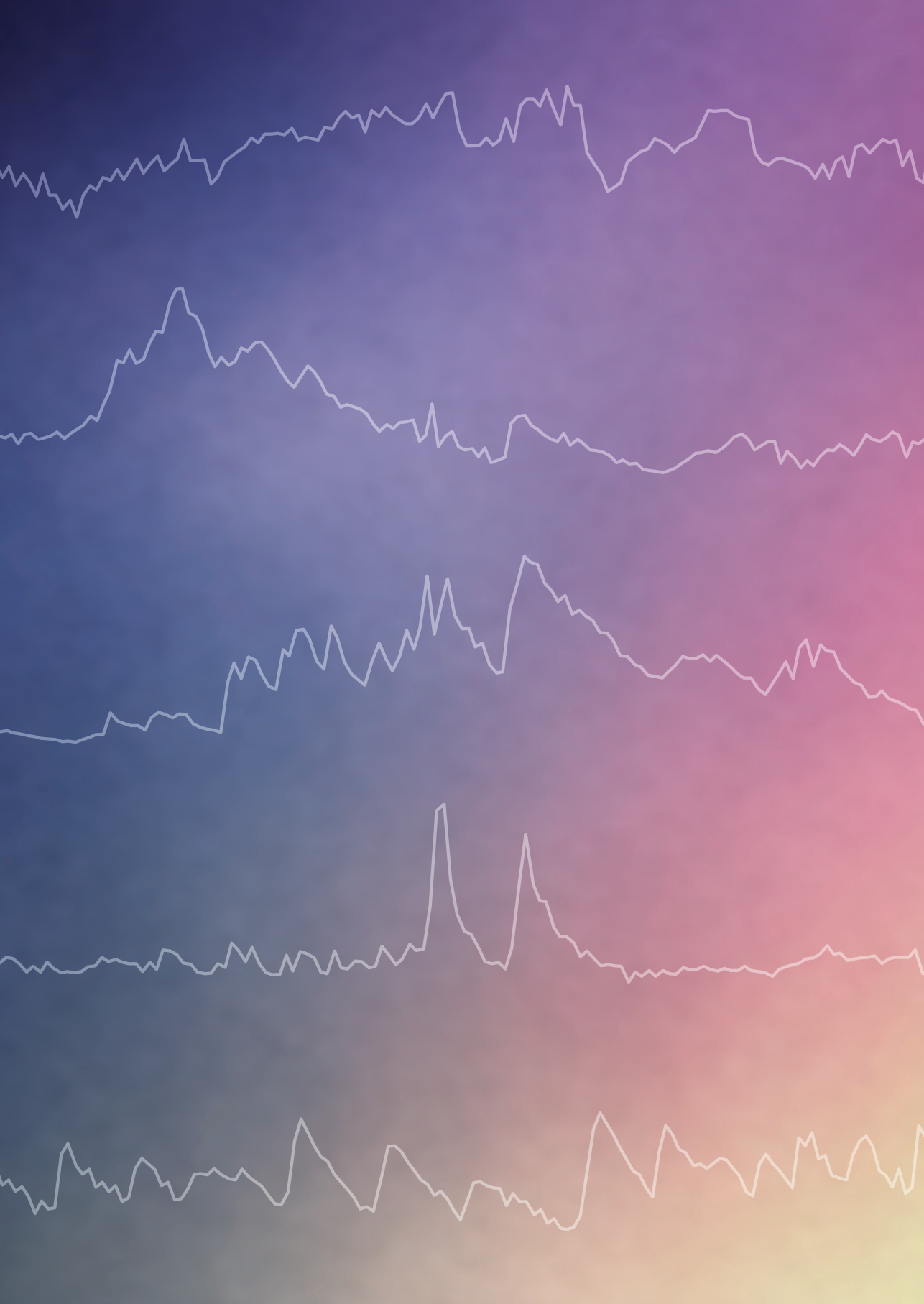
The endocrinology of familial longevity : time series analyses of different hormonal axes and their interrelationships

Spoel, E. van der



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English summary

Nederlandse samenvatting

List of publications

List of co-authors

Curriculum Vitae

Dankwoord

ENGLISH SUMMARY

In **Chapter 2**, we investigated whether circulating insulin-like growth factor 1 (IGF-1) axis parameters associate with old age survival and functional status in nonagenarian siblings from the LLS. We found that lower IGF-1/IGF binding protein 3 (IGFBP3) molar ratios were associated with lower hazard ratios, indicating improved survival. Furthermore, nonagenarians in the lowest quartile of IGF-1/IGFBP3 ratios had the highest scores for both Activities of Daily Living (ADL) scales and Instrumental ADL scales, indicating better functional status. In **Chapter 3**, we measured circulating growth hormone (GH) concentrations in blood withdrawn every 10 min and IGF-1 and IGFBP3 every 4 h in healthy offspring of long-lived families and their partners. We found an association between lower total and basal GH secretion and familial longevity. GH secretion was tighter controlled in offspring of long-lived families compared with their partners. No significant differences were observed in circulating levels of IGF-1 and IGFBP3 between offspring and controls, although these tended to be somewhat lower in the offspring. In **Chapter 4**, we investigated in healthy male middle-aged participants whether familial longevity is associated with altered endocrine features in the hypothalamic-pituitary-gonadal axis using luteinizing hormone (LH) and testosterone concentrations measured in blood withdrawn every 10 during 24 h. We found no major differences in the LH and testosterone secretion between male offspring of long-lived families and the control group. In **Chapter 5**, we investigated the interrelationships between hormones from the different hypothalamic-pituitary-target gland axes and confirmed that within interlinked hormonal axes, adrenocorticotropic hormone (ACTH) and cortisol concentrations are correlated, as well as LH and testosterone concentrations. Between hormonal axes, we observed a negative correlation between cortisol and thyroid stimulating hormone (TSH), and a positive correlation between TSH and GH. The joint pattern synchrony between GH and cortisol, and between GH and LH, are the greatest of all hormone combinations. These results are indications that there is interplay between hormonal axes in healthy older individuals. In **Chapter 6**, the 24-h profiles of bone markers in healthy older subjects were determined. We confirmed that C-terminal cross-linked telopeptide of type 1 collagen (CTX) and osteocalcin levels display a circadian rhythm. N-terminal propeptide of type 1 procollagen (P1NP) and sclerostin levels, although not exhibiting a circadian rhythm, varied as well during the day. For Dickkopf-related protein 1 (DKK1), no reliable conclusion on the absence or presence of a 24-h rhythm could be drawn because of the large intraindividual variation. Although levels differed between men and women, timing of the 24-h rhythm of all bone markers did not differ between men and women.