Prolactin as a key regulator of Growth Hormone pulsatility in lactation, acting *via* somatostatin

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Growth hormone (GH) is an anabolic pituitary hormone that is critically involved in the regulation of energy flux. In lactation GH acts to promote the deposition of fatty acids in maternal milk. It remains unclear whether endogenous GH levels change in lactation, and whether alterations in GH release occur in response to maternal hormones associated with lactation. Prolactin is a key maternal hormone that regulates events underlying lactation. While the actions of prolactin in respect to milk production are well defined, it remains unknown whether prolactin promotes milk production indirectly though regulating the anabolic actions of GH. To address this we characterised the pulsatile release of GH in lactating female mice and investigated the role of prolactin in regulating the pulsatile release of GH.

Following established methodology (Steyn *et al.*, 2011), we assessed pulsatile GH release in C57Bl/6J mice at days 10 and 17 of lactation. Observations were compared to non-lactating virgin and reproductively experienced mice. We observed a significant increase in total GH release in lactating mice when compared to non-lactating mice. At day 10 of lactation the overall rise in GH release was coupled to a rise in peak pulsatile GH secretion and by day 17 of lactation we observed an overall rise in basal GH secretion. The number of GH pulses seen during the 6-hour sampling interval increased significantly during lactation, suggesting that events specific to lactation altered interactions between hypothalamic regulators of GH pulsatility. This was verified by the return of pulse frequency following weaning. The pulsatile pattern of GH release is under the reciprocal control of hypothalamic inhibitory somatostatin (SRIF) and stimulatory growth hormone releasing hormone (GHRH). We anticipated that the rise in GH pulse frequency in lactation is coupled to an overall shift in the interaction between these hypothalamic regulators of GH release. To address this we assessed the onset of peak GH release in mice following a single peripheral (i.p.) injection of prolactin (1mg/kg.bw and 3mg/kg.bw). Injections were delivered immediately following the cessation of a GH pulse, corresponding to an anticipated period of elevated somatostatin release. Observations show the advancement of the onset of a GH secretory event. This was not associated with a rise in peak or total GH release.

Collectively, our observations suggest that PRL modifies somatostatin interactions within the hypothalamus, potentially reversing the suppressive effects of somatostatin on GHRH induced GH release. These measures are complemented by site-specific assessment of somatostatin activity and through the validation of hypothalamic expression of Srif and Ghrh mRNA throughout lactation. Collectively, our observations confirm that PRL is a key regulator of GH release in lactation, acting predominantly through somatostatin neurons to modulate GH pulse frequency.

Steyn FJ, Huang L, Ngo ST, Leong JW, Tan HY, Xie TY, Parlow AF, Veldhuis JD, Waters MJ, Chen C. (2011) *Endocrinology*, **152**: 3165-3171.