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Female reproductive maturation in the absence of kisspeptin/GPR54 signaling

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Abstract: Puberty onset is initiated in the brain by activation of gonadotropin-releasing hormone (GnRH) neurosecretion. Different permissive signals must be integrated for the initiation of reproductive maturation; however, the neural circuits controlling timely awakening of the reproductive axis are not understood. The identification of the neuropeptide kisspeptin as a potent activator of GnRH neuronal activity suggests that kisspeptin-releasing neurons might coordinate puberty onset. To test this hypothesis, we generated mice that specifically lack kisspeptin cells. Puberty onset in females was unaffected by kisspeptin neuron ablation. Furthermore, the animals were fertile, albeit with smaller ovaries. Consistent with this, female mice lacking neurons that express the kisspeptin receptor GPR54 were also fertile. Acute ablation of kisspeptin neurons in adult mice inhibited fertility, suggesting that there is compensation for the loss of kisspeptin neurons early in development. Our data indicate that the initiation and completion of reproductive maturation can occur in the absence of kisspeptin/GPR54 signaling.

Statement: Puberty is a universal phenomenon among mammals that has been studied intensively, and yet the neural circuits that control its onset and completion are unclear. The most important advance in our understanding of how the brain controls fertility came in 2003 when two clinical research groups reported that humans with mutations in the receptor for the neuropeptide kisspeptin were infertile. This suggested that kisspeptin-producing neurons in the brain might control puberty onset and sparked a worldwide explosion of interest in these cells. Surprisingly, our findings demonstrate that the initiation and completion of reproductive maturation can occur in the absence of kisspeptin neurons.

This work was performed at the Institute of Neural Signal Transduction in the group of Ulrich Boehm. It is part of the PhD thesis of Dipl. Biol. Christian Mayer and supported by the DFG grants BO1743/2, BO1743/3, BO1743/4 to U.B. Ulrich Boehm's group at the ZMNH is interested in the neural circuitry underlying reproductive behavior and physiology in the brain.