Serum Concentrations of Luteinizing Hormone (LH) and Follicle Stimulating Hormone (FSH) in *KISS1* Knockout Gilts Treated with Neurokinin B, Kisspeptin, and GnRH hormone analogs.

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Kisspeptin knockout (*KISS1*$^{-/-}$) pigs exhibit hypogonadotropic hypogonadism. Hormone analogs stimulate gonadotropin secretion and ovulation in mice and humans with induced or naturally occurring mutations in the *KISS1* gene. It is unknown how such agonists affect gonadotropin secretion in *KISS1*$^{-/-}$ gilts. The goal was to characterize LH and FSH secretion in gilts treated with hormone analogs activating the hypothalamic-pituitary-gonadal axis. Gilts (254 d of age) were jugular catheterized for serial blood collection before and after treatments. Concentrations of LH and FSH were quantified with RIA. Data were analyzed as repeated measures with genotype and time as fixed effects. In Experiment 1, baseline hormone secretion was established for 6 h, then gilts were treated with a neurokinin 3 receptor (NK3R) agonist (senktide; 10 mg/kg, i.v.) to activate *KISS1* neurons. In Experiment 2, gilts were estrus synchronized with altrenogest (18 mg/d, 14 d) and treated with PG600 (1000 IU hCG, 2000 IU PMSG, i.m.) 12 h after altrenogest withdrawal to synchronize follicular development. At 112 h after PG600, a kisspeptin receptor agonist (C6; 0.3 nMol/kg, i.m.) was administered to activate GnRH neurons. In Experiment 3, gilts were treated with GnRH (Cystorelin; 150 ng/kg, i.v.) to stimulate gonadotroph cells. In Experiment 4, gilts received an estradiol implant and GnRH with increasing frequency every 2 wk (1500 ng/kg, 1/d; 1000 ng/kg, 2/d; 500 ng/kg, 4/d, i.v.) followed with PMSG (1000 IU) and hCG (1000 IU) 78 h apart to induce follicular development and ovulation. LH and FSH pulse amplitude, but not pulse frequency, was greater in *KISS1*$^{+/-}$ and *KISS1*$^{+/+}$ gilts compared with *KISS1*$^{-/-}$ gilts, which had reduced serum LH and FSH concentrations ($P < 0.01$). LH but not FSH concentrations in *KISS1*$^{+/-}$ and *KISS1*$^{+/+}$ gilts were increased for 60 min following senktide ($P < 0.001$), which did not affect LH or FSH in *KISS1*$^{-/-}$ gilts. C6 treatment did not affect FSH but increased circulating LH in *KISS1*$^{+/-}$ and *KISS1*$^{+/+}$ gilts for approximately 24 h ($P < 0.05$), but C6 did not affect LH in *KISS1*$^{-/-}$ gilts. The C6 treatment induced ovulation in all *KISS1*$^{+/+}$ gilts but none of the *KISS1*$^{-/-}$ gilts. A single acute injection of GnRH increased LH in *KISS1*$^{+/-}$ and *KISS1*$^{+/+}$ gilts but not in *KISS1*$^{-/-}$ gilts ($P < 0.001$). LH secretion in *KISS1*$^{-/-}$ gilts was increased modestly with a greater dose and frequency of GnRH ($P < 0.05$). One *KISS1*$^{-/-}$ gilt ovulated 2 follicles after hCG and one had luteinized follicles, but the rest failed to ovulate. A single functional *KISS1* allele is sufficient to confer normal reproductive endocrine function in pigs. This is the first report to confirm NK3R regulates LH secretion in gilts. Lack of GnRH-induced LH secretion in *KISS1*$^{-/-}$ gilts may result from insufficient

releasable pools of LH due to lack of sufficient GnRH priming. Optimization of treatments will be required to induce full ovulation in *KISS1*$^{-/-}$ gilts. Funding FFAR 552176 and CRIS 3040-31320-001-000D. The USDA is an equal opportunity provider and employer.