Comparison of the pretranslational regulation of FSH synthesis by gonadal steroids in rats and mice

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ABSTRACT

There are significant differences between rats and mice in the gonadal regulation of several aspects of gonadotroph function. To investigate whether these extend to the pretranslational regulation of FSH synthesis by gonadal steroids, we have measured FSH-β mRNA levels following gonadectomy and sex-steroid replacement and have related these to serum and pituitary FSH as a reflection of overall hormone synthesis.

In ovariectomized rats, FSH-β mRNA levels increased by 8 h, decreased, and then rose progressively over the next 28 days. A similar pattern of response was observed in orchidectomized rats. In mice, there were progressive increases in FSH-β mRNA levels in both males and females following gonadectomy, without evidence of the early peaks observed in rats. In both species, the change in FSH-β mRNA levels after gonadectomy was greater in females than in males. These changes in FSH-β mRNA following gonadectomy were paralleled by changes in the serum FSH concentration. In ovariectomized female rats and mice, pituitary FSH stores increased by 8 h and 3 days respectively, whereas in male rats, pituitary FSH content did not rise until 10 days after orchidectomy. The most striking species difference was the marked and prolonged reduction of pituitary FSH after orchidectomy of mice.

Treatment of rats and mice from the time of ovariectomy, with a dose of oestradiol that prevented increases in serum LH, only partially attenuated the rises in FSH-β mRNA and serum FSH and did not prevent the increase in pituitary FSH content. Treatment of intact or orchidectomized rats with testosterone suppressed FSH-β mRNA levels to 50% below intact control values without affecting pituitary FSH content. In mice, testosterone treatment for 10 days reduced the post-castration increase in FSH-β mRNA by only 26%, and prevented the fall in pituitary FSH content, although the increased serum concentration of FSH was unaffected.

In conclusion: (1) there is a good correlation between FSH-β mRNA levels and overall FSH biosynthesis in male and female rats and female mice, but this relationship is less obvious in male mice where pituitary FSH stores are not increased; (2) the inability of oestradiol to prevent completely the post-ovariectomy increase in FSH-β mRNA and FSH synthesis in female rats and mice indicates either that other gonadal products are necessary or that higher doses of oestradiol are required than for complete suppression of LH synthesis; (3) whilst the post-gonadectomy increases in FSH-β mRNA are larger in the female of both species, there are no major differences between rats and mice in the regulation of FSH-β gene expression by sex steroids.

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INTRODUCTION

Gonadal steroids assume major importance in the modulation of gonadotroph function, acting directly on the gonadotrophs, or indirectly by altering the pattern of gonadotrophin-releasing hormone (GnRH) release (Knobil, 1980; Plant, 1986; Rodin, Laloz & Clayton, 1989a; Saade, London & Clayton, 1989a). Oestradiol has both positive- and negative-feedback effects on gonadotrophin secretion in females (Jaffe & Keye, 1974; Knobil, 1974, 1980; Drouin, Lagace & Labrie, 1976; Plant, 1986), while testosterone is the major component of the negative-feedback loop in males (Plant, 1982; Steiner, Bremner & Clifton, 1982; Plant & Dubey, 1984). However, in both males (Plant, 1986) and females...
(Goodman, Pickover & Karsch, 1981; Alexander & Miller, 1982; Batra & Miller, 1985) gonadal steroids do not prevent the post-gonadectomy increase in serum follicle-stimulating hormone (FSH), which requires the synergistic action of gonadal proteins of the inhibin family (Mercer, Clements, Funder & Clarke, 1987; McLachlan, Robertson, de Kretser & Burger, 1988; Ying, 1988; Attardi, Keeping, Winters et al. 1989).

There is evidence for species differences in the regulation of gonadotroph function by gonadal steroids between rats and mice. The rise in serum gonadotrophin concentrations after gonadectomy is associated with increased pituitary luteinizing hormone (LH) content in both male and female rats (Gay & Midgley, 1969; Yamamoto, Diebel & Bogdanove, 1970; Badger, Wilcon, Meyer et al. 1978; Clayton & Catt, 1981; Frager, Pieper, Tonetta et al. 1981). However, in mice, while serum LH concentrations increased in both sexes after gonadectomy, pituitary LH content is persistently reduced after orchidectomy but increased after ovariectomy (Naik, Young, Charleston & Clayton, 1984a,b). It is not clear whether changes in pituitary FSH content after gonadectomy of mice parallel those of LH, since the only study in which this issue has been addressed showed only a small decrease (<20%) in pituitary FSH 10 days after castration (Charlton, Jones, Ward et al. 1987). In addition, gonadotroph GnRH receptors rise after gonadectomy of rats (Clayton & Catt, 1981; Frager et al. 1981) but decrease in castrated mice (Naik et al. 1984a,b).

Since several studies have demonstrated the physiological relevance of changes in gene expression in the regulation of LH and FSH synthesis in rats (Gharib, Bowers, Need & Chin, 1986; Gharib, Wierman, Badger & Chin, 1987; Abbot, Docherty & Clayton, 1988a,b), we sought to determine whether this also applies to mice. In addition, as there are differences in LH synthesis and other aspects of gonadotroph function after gonadectomy between male rats and mice, we wanted to know whether these also applied to FSH.

**MATERIALS AND METHODS**

**Animals**

Adult male and female Sprague–Dawley rats and adult male and female BALB/c mice were housed under conditions of 14 h light and 10 h darkness, at ambient temperature (20±2°C) and with food and water freely available. Operations were performed under light metaphane anaesthesia. Animals were orchidectomized through the scrotum or through transverse abdominal incisions. Ovariectomy was performed through dorsal incisions without reference to the stage of the oestrous cycle. Animals were killed by decapitation at the end of each experiment. Pituitary glands were removed rapidly, snap-frozen in liquid nitrogen and then stored at −70°C until used. Trunk blood was collected and serum saved at −20°C until assayed.

**Hormone treatments**

For female rats, 1 μg 17β-oestradiol, 2.5 mg progesterone or a combination of the two (Sigma Chemical Co., Poole, Dorset, U.K.) were dissolved in 200 μl sesame oil and injected s.c. once daily. Testosterone propionate (250 μg; Sigma Chemical Co.) was dissolved in 100 μl sesame oil for s.c. injection in male rats. In the steroid-replacement experiments in mice, 17β-oestradiol, progesterone and testosterone propionate were diluted in sesame oil to final concentrations of 300 ng/100 μl, 370 μg/100 μl and 25 μg/100 μl respectively, and 100 μl aliquots were administered s.c. These doses are sufficient to prevent the post-gonadectomy increases in GnRH receptors and serum and pituitary LH concentrations (Clayton & Catt, 1981; Naik et al. 1984a,b), but it is not known whether they will suppress serum FSH to intact levels. In all the steroid-replacement experiments, intact and gonadectomized control animals were injected with sesame oil.

**Measurements of FSH-β mRNA by dot-blot hybridization**

Individual pituitary glands were homogenized in 200 μl homogenization buffer (0.15 m, NaCl, 10 mm Tris–HCl (pH 7.5), 1 mm MgCl₂ and 0.1% (v/v) Triton) and an aliquot (20 μl) was saved for measurement of pituitary FSH content. Cytoplasmic RNA was then extracted from individual pituitary glands as described previously (Abbot et al. 1988a; Lalloz, Detta & Clayton, 1988). The total RNA yield from each pituitary gland was determined from the optical density at 260 nm. Rat FSH-β cDNA (provided by Dr R. Maurer, University of Iowa, Iowa City, I.A., U.S.A.) was excised from its plasmid vector, purified and 25 ng cDNA were labelled with [32P]dCTP (NEN Research Products, Boston, MA, U.S.A.) by random primer extension (Multiprime RPN.1601; Amersham International plc, Amersham, Bucks, U.K.) (Feinberg & Vogelstein, 1983) to a specific activity of 1–5 × 10⁸ c.p.m./μg DNA. Plasmids containing a rat growth hormone (GH) cDNA insert (Dr C. Bancroft, Mount Sinai School of Medicine, New York, NY, U.S.A.) were also labelled with [32P]dCTP to a specific activity of 1–3 × 10⁸ c.p.m./μg DNA. This probe was used as a control to ascertain the
specificity of the effects of sex hormones on mRNA levels.

RNA samples were denatured with formaldehyde and then applied to GeneScreen hybridization membrane (NEN Research Products) at two dilutions as described previously (Abbot et al. 1988a; Laloz et al. 1988). Rat RNA samples were diluted to 1/10 and 1/20 of a pituitary, and mouse samples were diluted to 1/5 and 1/20 of a pituitary. Filters were prehybridized at 42°C for 22 h and then hybridized with the heat-denatured 32P-labelled FSH-β cDNA probe for a further 22 h at 42°C. In the rat experiments, filters were washed in 30 mM sodium chloride, 3 mM sodium citrate (pH 7.0; 2 × SSC) plus 0.1% (w/v) sodium dodecyl sulphate (SDS) for 30 min at 20°C, 1 × SSC plus 0.1% SDS for 30 min at 20°C, 0.1 × SSC plus 0.1% SDS for 30 min at 20°C, and 0.1 ± 0.1% SSC plus 0.1% (w/v) SDS for 30 min at 55°C. In the mouse experiments the washing conditions were: 2 × SSC plus 0.1% SDS for 30 min at 20°C, 1 × SSC plus 0.1% SDS for 30 min at 20°C twice, and 1 × SSC plus 0.1% SDS for 30 min at 42°C. Separate filters were prepared for use with the GH cDNA probe. These were hybridized and washed using the same conditions as for the FSH-β probe.

Hybridized filters were exposed to X-ray film, with intensifying screens, at −70°C for 1–4 days. The intensity of the dots on the autoradiographs was quantified by scanning densitometry, corrected for differences in total RNA of the individual samples and expressed as a percentage of the intact control values (designated as 100%). This allowed results from several similar experiments to be pooled.

**Measurement of pituitary FSH content and serum FSH concentration**

The pituitary FSH content and serum FSH concentration were determined by double-antibody radioimmunoassay using reagents and methods supplied by NIADDK (Bethesda, MD, U.S.A.). Results are expressed in terms of the RP-2 rat FSH standard. Intra- and interassay coefficients of variation were <8% and <12% respectively.

**Statistical analysis**

All data were analysed by analysis of variance and Tukey’s multiple range analysis (Tukey, 1949). Differences between groups were considered significant if P < 0.05.

**RESULTS**

In both rats and mice, FSH-β mRNA was measured by hybridization to a rat cDNA probe, and similar hybridization and washing conditions were used. Linearity of the signal was demonstrated over a range of dilutions of total pituitary RNA applied to the hybridization membrane. Growth hormone mRNA levels were unaltered by gonadectomy or steroid replacement, indicating the specificity of the changes in FSH-β mRNA levels (data not shown).

**Changes in FSH-β mRNA, pituitary FSH content and serum FSH concentration after ovariectomy of female rats** (Fig. 1)

To examine changes in FSH-β mRNA levels following ovariectomy, groups of rats were killed at

![Figure 1](image-url)
intervals from 8 h to 28 days after operation. Levels of FSH-β mRNA increased over eightfold by 8 h, but then declined to approximately twice intact control values at 24 and 48 h. By 4 days after ovariectomy, however, FSH-β mRNA levels increased again to six times intact control values and then rose further to 9-5 times intact control values at 28 days. Pituitary FSH content increased significantly by 8 h and exceeded five times intact control values after 28 days. The serum FSH concentration increased significantly by 12 h and rose steadily to 3-4 times intact control values after 28 days.

**Changes in FSH-β mRNA, pituitary FSH content and serum FSH concentration after ovariectomy of female mice (Fig. 2)**

In mice, there was a twofold increase in FSH-β mRNA levels 12 and 24 h after ovariectomy. After 3 days, FSH-β mRNA levels had increased ninefold, rising to 12-fold at 10 days. Pituitary FSH content first increased at 3 days after ovariectomy, and reached 3-7 times intact control values after 10 days. Serum FSH increased more than fivefold by 2 days after ovariectomy and remained at this level for 10 days.

**Changes in FSH-β mRNA, pituitary FSH content and serum FSH concentration after orchidectomy of male rats (Fig. 3)**

Groups of male rats were killed 8 h to 28 days after orchidectomy. There was a twofold increase in FSH-β mRNA levels by 12 h after orchidectomy followed by a fall to intact control levels after 24 h. However, by 48 h there was a further significant rise in FSH-β mRNA levels and values remained three to fivefold greater than those of intact controls for 28 days. Pituitary FSH content decreased to 17.5% below intact control values after 2 days. Then, 10 days after orchidectomy, there was an increase in pituitary FSH content which reached 2.5 times intact control levels after 28 days. Serum FSH was increased after 8 h and rose to 9.5 times intact control values at 28 days.

**Changes in FSH-β mRNA, pituitary FSH content and serum FSH concentration after orchidectomy of male mice (Fig. 4)**

There was a 43% increase in FSH-β mRNA levels by 24 h after orchidectomy. This was followed by a progressive rise to a peak of more than three times intact control values at 8 and 10 days, and then a slight decline to about twice intact levels at 14 and 21 days. Pituitary FSH content fell progressively to 43% of intact values at 14 and 21 days. Serum FSH

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**Figure 2. Effects of ovariectomy for 12 h to 10 days on**

(a) FSH-β mRNA levels, (b) pituitary FSH content and

(c) serum FSH concentration in female mice. Values are means ± S.E.M. for 9-15 animals per group, except for the intact control groups where n = 26. P < 0.05 vs: a, intact controls (hatched bars); b, 12 h; c, 24 h; d, 2 days; e, 3 days; f, 6 days; g, 8 days (ANOVA and Tukey's multiple range analysis).

rose by more than threefold at day 1 and remained at similar values at each of the time-points examined.

**Effect of oestrogen and progesterone treatment for 10 days from the time of ovariectomy in female rats and mice**

(Table 1)

Groups of ovariectomized rats were treated with oestradiol, progesterone or both steroids together for 10 days, commencing at the time of operation. The 9.5-fold increase in FSH-β mRNA 10 days after ovariectomy was attenuated by 50% by treatment with oestradiol or oestradiol and progesterone, but not by progesterone alone. The increased pituitary
progesterone combined with oestradiol, or treatment with oestradiol alone resulted in a 27–30% increase in pituitary FSH. Serum FSH increased 3.4-fold by day 10 after ovariectomy. Oestradiol replacement limited this increase to 2.4-fold and, when combined with progesterone, further attenuated this response to a 1.7-fold increase.

**Effect of testosterone treatment for 10 days from the time of orchidectomy in male rats and mice (Table 2)**

In this experiment, groups of intact and orchidectomized male rats were treated with testosterone for 10 days from the time of operation. Orchidectomy increased FSH-β mRNA levels by only 46% (compare with Fig. 3), although testosterone treatment of intact and orchidectomized rats suppressed FSH-β mRNA levels to 51% and 60% of intact
DISCUSSION

The changes in FSH-β mRNA levels in rats in response to gonadectomy and sex-steroid replacement have been demonstrated indirectly in cell-free translation assays (Counis, Corbani & Jutisz, 1983) and by direct hybridization (Gharib et al., 1987; Wierman, Gharib, & LaRovere et al., 1988). There is, however, no published information about the role of pretranslational events in FSH synthesis in the response to gonadectomy in mice. That there may be major species differences in sex-steroid regulation of FSH synthesis was suggested by earlier observations of differences between rats and mice in various aspects of gonadotroph function (see Introduction), and this has been investigated in this study.

Following ovariectomy of rats, there was an increase in FSH-β mRNA within 8 h, followed by a fall and then a further rise which was sustained for 28 days. Gharib et al. (1987) showed five- to six-fold increases in FSH-β mRNA levels between 3 and 28 days after ovariectomy of rats, but the earlier changes have not been reported previously. In mice,

### TABLE 1. Effects of 17β-oestradiol (OE2) and progesterone (Prog) treatment immediately after ovariectomy (OVX) of rats and mice. Values are means ± S.E.M.

<table>
<thead>
<tr>
<th>Female rats</th>
<th>FSH-β mRNA (% of intact)</th>
<th>Pituitary FSH (μg/pituitary)</th>
<th>Serum FSH (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intact</td>
<td>1000 ± 196</td>
<td>0.67 ± 0.04</td>
<td>5.80 ± 0.84</td>
</tr>
<tr>
<td>OVX</td>
<td>956 ± 78</td>
<td>4.45 ± 0.20</td>
<td>33.18 ± 1.35</td>
</tr>
<tr>
<td>OVX + OE2</td>
<td>4108 ± 61.6†</td>
<td>4.08 ± 0.42</td>
<td>18.90 ± 1.45†</td>
</tr>
<tr>
<td>OVX + Prog</td>
<td>824 ± 850**</td>
<td>5.50 ± 0.88</td>
<td>34.32 ± 2.94†</td>
</tr>
<tr>
<td>OVX + OE2 + Prog</td>
<td>3570 ± 73.2**††</td>
<td>3.76 ± 0.39</td>
<td>12.53 ± 0.46††</td>
</tr>
</tbody>
</table>

*P<0.05 compared with intact controls; †P<0.05 compared with OVX controls; ‡P<0.05 compared with OVX + OE2; ††P<0.05 compared with OVX + Prog (ANOVA and Tukey’s multiple range analysis).

Ovariectomized rats (five or six per group) and mice (five to ten per group) were treated with 17β-oestradiol, progesterone or both by s.c. injection for 10 days from the time of operation.

<table>
<thead>
<tr>
<th>Female mice</th>
<th>FSH-β mRNA (% of intact)</th>
<th>Pituitary FSH (μg/pituitary)</th>
<th>Serum FSH (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intact</td>
<td>1000 ± 186</td>
<td>88.17 ± 9.31</td>
<td>7.35 ± 1.01</td>
</tr>
<tr>
<td>OVX</td>
<td>1765 ± 144.8*</td>
<td>275.00 ± 31.25*</td>
<td>25.28 ± 1.84*</td>
</tr>
<tr>
<td>OVX + OE2</td>
<td>875 ± 108.7†</td>
<td>348.83 ± 15.28*</td>
<td>17.70 ± 1.81*‡</td>
</tr>
<tr>
<td>OVX + Prog</td>
<td>1979 ± 186.9†</td>
<td>255.40 ± 24.18*‡</td>
<td>28.40 ± 3.78*‡</td>
</tr>
<tr>
<td>OVX + OE2 + Prog</td>
<td>736 ± 103.1‡‡†</td>
<td>356.83 ± 6.85*‡‡</td>
<td>12.50 ± 0.72‡‡</td>
</tr>
</tbody>
</table>

*P<0.05 compared with intact control; †P<0.05 compared with intact + TP; ‡P<0.05 compared with ORCH (ANOVA and Tukey’s multiple range analysis).

Ovariectomized and intact rats (five or six per group) and ovariectomized mice (nine per group) were treated with testosterone propionate by s.c. injection for 10 days from the time of operation.

**TABLE 2. Effect of testosterone propionate (TP) treatment immediately after orchidectomy (ORCH) of rats and mice. Values are means ± S.E.M.**

<table>
<thead>
<tr>
<th>Male rats</th>
<th>FSH-β mRNA (% of intact)</th>
<th>Pituitary FSH (μg/pituitary)</th>
<th>Serum FSH (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intact</td>
<td>1000 ± 80</td>
<td>4.37 ± 0.61</td>
<td>—</td>
</tr>
<tr>
<td>Intact + TP</td>
<td>513 ± 4.9*</td>
<td>3.61 ± 0.29</td>
<td>—</td>
</tr>
<tr>
<td>ORCH</td>
<td>1459 ± 10.4†</td>
<td>3.42 ± 0.37</td>
<td>—</td>
</tr>
<tr>
<td>ORCH + TP</td>
<td>596 ± 66.6†</td>
<td>3.51 ± 0.23</td>
<td>—</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Male mice</th>
<th>FSH-β mRNA (% of intact)</th>
<th>Pituitary FSH (μg/pituitary)</th>
<th>Serum FSH (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intact</td>
<td>1000 ± 189</td>
<td>2.34 ± 0.14</td>
<td>12.89 ± 1.64</td>
</tr>
<tr>
<td>ORCH</td>
<td>2661 ± 26.9*</td>
<td>1.38 ± 0.04</td>
<td>28.24 ± 1.87*</td>
</tr>
<tr>
<td>ORCH + TP</td>
<td>1976 ± 17.4**</td>
<td>2.07 ± 0.23</td>
<td>26.70 ± 2.10*</td>
</tr>
</tbody>
</table>

*P<0.05 compared with intact control; †P<0.05 compared with intact + TP; ‡P<0.05 compared with ORCH (ANOVA and Tukey’s multiple range analysis).
however, there was a progressive increase in FSH-β mRNA levels after ovariectomy, with no evidence of the initial peak observed in rats. The earlier rise in FSH-β levels after ovariectomy of rats was associated with increased pituitary FSH stores and increased FSH release whereas, in mice, it was 3 days before both storage and release of FSH increased.

Orchidectomy of rats produced a similar pattern of change in FSH-β mRNA to that observed in ovariectomized rats while, in male mice, FSH-β mRNA levels increased progressively from 24 h after orchidectomy without the initial rise seen in rats. In both rats and mice, the changes in FSH-β mRNA levels were greater in females than in males. The post-orchidectomy changes in FSH-β mRNA which we have described are consistent with two previous reports (Corbani, Counis, Starzec & Jutisz, 1984; Wierman et al. 1988) but differ from another (Gharib et al. 1987) in which FSH-β fell to intact levels by 28 days. In both rats and mice, there were early and sustained increases in serum FSH concentrations following orchidectomy. The most striking difference between these species was the change in pituitary mRNA stores after orchidectomy. In orchidectomized rats, an initial small reduction was followed by an increase by 10 days, whereas in mice, pituitary FSH content fell by 24 h after orchidectomy and remained low. Thus any increase in FSH synthesis in orchidectomized mice results in enhanced release rather than storage.

The time-courses of the changes in FSH-β mRNA levels, pituitary FSH and serum FSH following gonadectomy of male and female rats bear strong similarities to the changes reported for LH-β mRNA, pituitary LH and serum LH (Abbot et al. 1988a,b). In ovariectomized mice, FSH-β mRNA increases earlier than LH-β mRNA levels. The pattern of change in FSH release and storage is very similar to the change observed for LH, except that there is a shorter delay before pituitary FSH stores increase (Saade, London, Lallov et al. 1989b). The post-orchidectomy changes in FSH-β mRNA and pituitary and serum FSH in mice parallel the reported relationships between LH-β mRNA, pituitary LH and serum LH (Saade et al. 1989b). The persistent depletion of pituitary FSH stores in orchidectomized mice is reminiscent of previous studies which show that pituitary LH content and GnRH receptors fall after castration in mice and remain low for at least 1 month (Naik et al. 1984a; Charlton et al. 1987).

Treatment of rats and mice with oestradiol for 10 days from the time of ovariectomy partially suppressed FSH-β mRNA levels, although progesterone had no effect. This corroborates previous reports of cell-free translation (Alexander & Miller, 1982; Counis et al. 1983) and dot-blot hybridization assays (Maurer, 1987). The incomplete suppression of FSH synthesis/secretion in response to this steroid replacement may indicate that other ovarian products, such as inhibin (Mercer et al. 1987; McLachlan et al. 1988; Ying, 1988), are important components of the feedback loop regulating FSH-β gene expression. Furthermore, similar treatments prevent completely the increases in LH-β mRNA and serum LH (Abbot et al. 1988a; Saade et al. 1989b), suggesting that gonadal steroid negative feedback may be more important in the regulation of LH synthesis and secretion in female rats and mice than they are in the control of FSH synthesis and release. An alternative explanation may be that higher doses of oestradiol are required to suppress FSH synthesis than LH synthesis.

In rats treated with testosterone for 10 days from the time of orchidectomy, and in intact rats treated with testosterone, FSH-β mRNA levels were suppressed to 50% below normal intact levels. In mice, however, replacement with testosterone for 10 days following orchidectomy attenuated the rise in FSH-β mRNA levels only slightly. The failure of testosterone to suppress the post-orchidectomy increase in FSH-β mRNA in mice lends support to a role for inhibin in this feedback loop, while the reduction in FSH-β mRNA levels in intact and orchidectomized rats does not exclude a role for gonadal peptides in the control of FSH-β gene expression in the male rat. In both rats and mice, treatment with testosterone for 10 days after orchidectomy normalized LH-β mRNA levels (Abbot et al. 1988b; Saade et al., 1989b), suggesting a possible difference between the regulation of FSH and LH synthesis in these species.

These studies have confirmed the importance of pretranslational events in the regulation of FSH synthesis by gonadal steroids by demonstrating a good qualitative correlation between overall FSH synthesis (as indicated by pituitary and serum FSH concentrations) and FSH-β mRNA levels. The major difference between these species is the persistent depletion of pituitary FSH stores in orchidectomized mice. The differences in the timing and magnitude of the changes in FSH-β mRNA after gonadectomy of rats and mice are generally minor, although the early peaks in FSH-β mRNA levels observed in rats may be of significance. The failure of gonadal steroid replacement to restore FSH-β mRNA levels to normal suggests that other gonadal factors, such as inhibin, are required for the regulation of FSH-β gene expression and FSH synthesis in vivo.
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