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REVIEW ARTICLE

Functional Significance of Hormonal Changes in Mammalian Fathers

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In the 5–10% of mammals in which both parents routinely provide infant care, fathers as well as mothers undergo systematic endocrine changes as they transition into parenthood. Although fatherhood-associated changes in such hormones and neuropeptides as prolactin, testosterone, glucocorticoids, vasopressin and oxytocin have been characterised in only a small number of biparental rodents and primates, they appear to be more variable than corresponding changes in mothers, and experimental studies typically have not provided strong or consistent evidence that these endocrine shifts play causal roles in the activation of paternal care. Consequently, their functional significance remains unclear. We propose that endocrine changes in mammalian fathers may enable males to meet the species-specific demands of fatherhood by influencing diverse aspects of their behaviour and physiology, similar to many effects of hormones and neuropeptides in mothers. We review the evidence for such effects, focusing on recent studies investigating whether mammalian fathers in biparental species undergo systematic changes in (i) energetics and body composition; (ii) neural plasticity, cognition and sensory physiology; and (iii) stress responsiveness and emotionality, all of which may be mediated by endocrine changes. The few published studies, based on a small number of rodent and primate species, suggest that hormonal and neuropeptide alterations in mammalian fathers might mediate shifts in paternal energy balance, body composition and neural plasticity, although they do not appear to have major effects on stress responsiveness or emotionality. Further research is needed on a wider variety of biparental mammals, under more naturalistic conditions, to more fully determine the functional significance of hormone and neuropeptide profiles of mammalian fatherhood and to clarify how fatherhood may trade off with (or perhaps enhance) aspects of organismal function in biparental mammals.

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Introduction

During the transition to motherhood, female mammals undergo a series of hormonal changes that prepare the body and brain for the myriad challenges of parenting. These hormonal changes involve predictable fluctuations in circulating concentrations of steroids (e.g. oestrogens, progestagens, androgens, glucocorticoids), as well as peptides (e.g. prolactin and other lactogenic hormones, oxytocin, vasopressin, gonadotrophins). The functional effects of these endocrine changes fall into three broad categories. First, they directly regulate the physiological processes in the mother necessary for the production and maintenance of offspring (i.e. pregnancy, parturition and lactation) through actions on the reproductive tract and accessory tissues. During gestation, for example, oestrogen and progesterone act on the uterus to regulate endometrial morphology and function, and thereby play a critical role in maintaining the pregnancy, whereas, during lactation, prolactin and oxytocin act on the mammary glands to stimulate the synthesis and release of milk (1–3). Second, the so-called maternal hormones directly stimulate maternal behaviour through actions on the central nervous system. Importantly, these actions involve the same hormones involved in the physiological regulation of pregnancy, parturition and lactation. Thus, oestrogen, progesterone, prolactin and oxytocin, amongst other hormones and neuropeptides, all act within the brain to activate or, in some cases, inhibit the expression of maternal behaviour (4). Third, these same hormones and neuropeptides can indirectly facilitate maternal care and/or maternal survival via a host of centrally and/or peripherally mediated effects. For example, pregnancy

and lactation are accompanied by changes in maternal energy balance (5,6), immune function (7), neural plasticity (8–11), cognition (8,12,13), sensory physiology (13,14), emotional regulation (12,15) and stress responsiveness (12,16), and these alterations have been hypothesised, or in some cases demonstrated, to be mediated by the endocrine profile of motherhood.

Although the vast majority of mammalian fathers play no systematic role in infant care, males in approximately 5–10% of mammalian genera routinely help to rear their young (17,18). Paternal care appears to have evolved independently multiple times among mammals, and is assumed to evolve under conditions in which males are more likely to increase the number of offspring fathered and/or the likelihood of offspring survival by assisting with infant care than by abandoning their mates and seeking additional mating opportunities (17–19). The largest numbers of biparental mammals have been identified among the rodents, primates and carnivores (17). Depending on the species, paternal care in mammals can entail a broad range of behaviours involved in transporting, defending, playing with, socialising, grooming and warming offspring, as well as providing them with food, shelter or other resources (17). In some species, fathers spend at least as much time interacting with their offspring as do mothers, and paternal care can have important consequences for the survival, growth and development of young (18–21). Some components of paternal care may have considerable energetic costs (22) and may differ quantitatively and/or qualitatively from behaviour performed by nonbreeding males (20). In biparental mammals, therefore, the onset of fatherhood, similar to motherhood, can entail pronounced shifts in parents' behaviour and physiology.

Not surprisingly, then, fathers in biparental species, similar to mothers, undergo systematic endocrine changes in association with the onset of parenthood. These changes, in such hormones and neuropeptides as prolactin, testosterone and vasopressin, have been characterised to a greater or lesser extent in a number of rodent and primate species; however, their functions are not well understood (4,23). Obviously, these endocrine events do not subserve obligatory changes in reproductive physiology comparable to pregnancy, parturition and lactation in females (i.e. the first category above). Therefore, their functional significance, if any, is likely to lie in either directly promoting paternal care (the second category) or indirectly facilitating paternal care or paternal survival through centrally and/or peripherally mediated effects that help fathers meet the demands of parenting (the third category). Over the last three decades, numerous investigators have used correlational or, less commonly, experimental approaches to evaluate possible effects of these fatherhood-induced endocrine changes on the expression of paternal behaviour (4,23). Only in the last few years, however, have researchers begun to examine other possible effects of these hormonal and neurochemical changes as males undergo the transition to fatherhood. Thus, the extent to which the endocrine sequelae of fatherhood influence behaviour and physiology in fathers is still largely unknown.

Here, we review the evidence, almost all of which comes from rodents and primates, suggesting that endocrine changes in mammalian fathers influence diverse aspects of fathers' behaviour and physiology. First, we briefly describe the hormone and neuropeptide changes that have been reported to occur in biparental mammalian fathers. We next summarise the evidence that these endocrine and neurochemical events of fatherhood play a causal role in the activation of paternal care, emphasising the results obtained from experimental studies. We then review recent findings that suggest mammalian fathers in biparental species may undergo systematic changes in (i) energetics and body composition; (ii) neural plasticity, cognition and sensory physiology; and (iii) stress responsiveness and emotionality, all of which are likely mediated by endocrine changes. Finally, we discuss the limitations and implications of these findings, as well as future directions for studying the physiological and behavioural consequences of parenthood for mammalian fathers.

Hormonal changes in biparental mammalian fathers

Males in a number of biparental mammals, specifically, several rodent and primate species, have been shown to undergo changing hormonal profiles during their mates' pregnancy and lactational periods. These changes appear to mimic the hormonal fluctuations that are occurring in their mates. Importantly, many of the endocrine changes in mammalian fathers are modulated by paternal experience (22,24,25). Hormonal changes in mammalian fathers have been reviewed elsewhere (4,23) and therefore are summarised only briefly here.

Prolactin

In biparental Mongolian gerbils (*Meriones unguiculatus*) (26), California mice (*Peromyscus californicus*) (27) and Djungarian hamsters (*Phodopus campbelli*) (28), circulating prolactin concentrations are significantly higher in fathers living with their mate and pups than in virgin males, newly mated males and/or expectant fathers. Moreover, male Djungarian hamsters have increased prolactin receptor mRNA transcript levels in the choroid plexus of the hypothalamus during their mate's early postpartum period, indicating elevated prolactin activity in the brain during the period when males are interacting with pups (29).

Biparental male nonhuman primates also show increases in circulating or excreted prolactin levels during their mate's gestational period, and even more pronounced prolactin elevations during the postpartum period, when fathers are directly involved in caring for infants. The cotton-top tamarin (*Saguinus oedipus*) and common marmoset (*Callithrix jacchus*), cooperatively breeding, biparental, New World monkeys, both show elevated prolactin levels during their mate's pregnancy, with mid-gestational elevations and highest levels in the final month of pregnancy [e.g. tamarin (30); marmoset (31)]. Once the infants are born, fathers maintain significantly higher prolactin levels throughout the period of infant dependency than during the gestational phase (31,32). Similarly, a recent study found that human fathers have significantly higher prolactin levels than other men (33).

Androgens

Testosterone generally shows a negative relationship with paternal care. In some biparental mammals, testosterone levels of expectant

fathers rise across the mate's pregnancy [e.g. cotton-top tamarin (25); Djungarian hamster (28)]. Following the birth of infants, however, paternal testosterone concentrations drop precipitously in biparental primate fathers, including common marmosets (31), cotton-top tamarins (34) and humans (35). Similarly, rodent fathers undergo pronounced declines in testosterone levels following the birth of their pups [e.g. Mongolian gerbil (26); Djungarian hamster (28); California mouse (36)].

Oestrogen and progesterone

Few studies have characterised changes in oestrogen signalling in mammalian fathers, and in the small number of species that have been studied, no consistent picture has emerged. In male Djungarian hamsters, serum oestradiol levels do not appear to change with paternal status (37), and oestrogen receptor α-immunoreactivity in several brain regions [medial preoptic area, bed nucleus of the stria terminalis (BNST) and medial amygdala] does not appear to differ between fathers and non-fathers (38). By contrast, mandarin vole (*Microtus mandarinus*) fathers have lower levels of oestrogen receptor α-immunoreactivity in the medial preoptic area and the BNST, and higher levels in the ventromedial hypothalamus, compared to non-fathers (39). Among the biparental primates, experienced but not first-time cotton-top tamarin fathers show significant increases in urinary oestrone and oestradiol concentrations in the final month of their mate's gestation (34), and black-tufted-ear marmoset (*Callithrix kuhlii*) fathers show significant but transient drops in urinary oestradiol concentrations following the birth of their infants (40).

The findings for progesterone, similar to those for oestrogen, are sparse and inconsistent. Male Djungarian hamsters show a significant increase in circulating progesterone levels at the end of the mate's pregnancy (37), whereas circulating progesterone levels in California mice are significantly lower in fathers than in virgin males (36).

Glucocorticoids

Glucocorticoid (cortisol or corticosterone) levels rise during the mate's mid- to late gestational period in expectant fathers of several biparental mammals, including Djungarian hamsters (28), cotton-top tamarins (34) and humans (41). Glucocorticoid levels decline again shortly after parturition, however, so that studies of basal glucocorticoid concentrations typically find no differences between fathers and nonbreeding males [e.g. California mouse (42,43); prairie vole (22); human (44,45)].

Vasopressin

Vasopressin in fathers has been studied most thoroughly in the prairie vole, with a strong emphasis on vasopressin signalling within the brain. In this species, new fathers have reduced densities of vasopressin-immunoreactive fibres in the lateral septum and lateral habenular nucleus compared to both sexually naïve males and males housed with late-pregnant mates; this finding appears to reflect increased synthesis and release of vasopressin from the BNST and medial amygdaloid nucleus following both copulation and parturition (46,47). Prairie vole fathers (as well as mothers) also exhibit elevated vasopressin mRNA levels in the hypothalamic paraventricular nucleus (PVN) and supraoptic nucleus (SON) in the postpartum period compared to sexually naïve controls (48). In the California mouse, in contrast, vasopressin mRNA levels in the PVN do not differ between fathers and virgin males or males housed with tubally ligated females (49). In common marmosets, fathers have a greater abundance of vasopressin V1a receptors in the prefrontal cortex than males that have not sired offspring (50). The effects of fatherhood on vasopressin signalling therefore appear to differ across species and might be clarified by additional studies.

Oxytocin

Several studies have investigated changes in intracerebral oxytocin signalling or peripheral oxytocin concentrations in rodent fathers. In the facultatively biparental meadow vole, sexually and paternally experienced, paternally behaving males were found to have significantly higher oxytocin receptor binding in several brain regions (accessory olfactory nucleus, lateral septum, BNST and lateral amygdala) than sexually and paternally inexperienced, nonpaternally behaving males; however, it could not be determined whether these neural differences were caused by differences in sexual activity, cohabitation with a female and/or paternal experience (51). Similarly, fathers have increased numbers of oxytocin-immunoreactive fibres in the PVN and SON in biparental mandarin voles, compared to virgin males; however, similar effects were seen in non-fathers that were either exposed briefly to pups or housed with a female prior to parturition (39). Among biparental male prairie voles, in contrast, neither oxytocin gene expression in the hypothalamus nor oxytocin receptor binding in a number of brain regions was found to differ between sexually naïve males and new fathers (48). Male California mice exhibit elevated circulating oxytocin concentrations during the first half of their mate's pregnancy, although oxytocin levels decline prior to parturition and remain low throughout the postpartum period (52); however, it is unclear whether circulating oxytocin levels reliably reflect levels in the brain (53). Thus, the effects of fatherhood on the brain's oxytocin system appear to be inconsistent across species and, where effects have been detected, they may correspond to cohabitation with a female rather than fatherhood *per se*.

In conclusion, whereas hormonal changes in mothers apparently evolved to subserve the physiological processes of gestation, parturition and lactation, and thus appear to be broadly similar across eutherian mammals, hormonal changes in fathers are much less constrained. Not surprisingly, the endocrine profile of fatherhood is quite variable among the handful of biparental mammals that have been studied in detail. Although fathers in all or most of the species studied show increases in prolactin and decreases in testosterone concentrations during the mate's perinatal period, changes in oestrogen, progesterone, vasopressin and oxytocin signalling are less consistent.

Effects of hormonal changes in fathers on paternal behaviour

As described above, fathers in biparental mammalian species undergo species-specific changes in several hormone and neuropeptide systems as they prepare for and subsequently engage in paternal care**.** This has led to the hypothesis that these hormonal and neurochemical changes pay a role in the suppression of infanticidal behaviour and the activation of paternal behaviour (23,54). Consequently, numerous studies have evaluated possible effects of these hormones and neuropeptides on males' behavioural responses to infants, often relying on correlational analyses of hormone–behaviour relationships (4,23). Here, we briefly review the evidence that suggests endocrine profiles of fatherhood play a causal role in activating paternal care, focusing primarily on experimental studies.

Prolactin

By contrast to numerous studies demonstrating positive correlations between circulating prolactin levels and paternal behaviour, pharmacological experiments generally do not support a causal role of prolactin in the onset or maintenance of paternal care (23). Roberts *et al.* (55) found that treatment of common marmosets with the dopamine receptor agonist bromocriptine to suppress prolactin secretion reduced retrieval of infants; however, the study used parentally inexperienced animals, most of which were females, rather than fathers. By contrast, in a study using experienced marmoset fathers, suppression of prolactin secretion using the dopamine D_2 receptor agonist cabergoline caused no changes in infant-care behaviours during observations made within the family context (56). A more recent, longitudinal study provides further insights into the role of prolactin in marmoset paternal behaviour. Ziegler *et al.* (31) tested experienced common marmoset fathers across three consecutive litters, during which each father underwent treatment, in randomised order, with cabergoline, human recombinant prolactin or nothing. Neither of the prolactin manipulations significantly altered fathers' infant-carrying or other parenting behaviours within the family, although both significantly reduced fathers' responsiveness to infant distress calls when fathers were tested away from the family.

Studies in rodents, similar to those in marmosets, have failed to yield compelling evidence indicating that prolactin influences paternal care in biparental species. Although prolactin has been shown to promote paternal behaviour in the uniparental rat (*Rattus norvegicus*) (57), no such effect was found in biparental Djungarian hamsters, in which treatment of first-time fathers with either cabergoline or bromocriptine did not alter fathers' pup-retrieval behaviour, or the growth and survival of pups (58).

In conclusion, although prolactin is elevated in fathers of several biparental mammals and has been referred to as the 'hormone of paternity' (59), the findings from experimental studies provide little support for the hypothesis that prolactin plays a key role in activating paternal behaviour in male mammals. Instead, the role of prolactin in fathers before and during periods of infant care may be more closely related to some of its other known functions, such as increasing food intake, stimulating neurogenesis and reducing anxiety.

Testosterone and oestrogen

Although circulating or excreted testosterone levels correlate negatively with measures of paternal behaviour in several mammals (4,23), experimental studies indicate that effects of testosterone on paternal care differ markedly across species. In the Djungarian hamster (60) and in one study of prairie voles (61), for example, castration had no detectable effect on paternal behaviour, whereas castrated male Mongolian gerbils engaged in significantly more paternal behaviour than either castrated, testosterone-treated males or sham-castrated males (62). The opposite pattern has been found in another study of prairie voles (63) and in California mice (64), in which castration reduced and testosterone treatment restored paternal behaviour. In the California mouse, this effect is mediated by aromatisation of testosterone to oestrogen within the brain: paternal behaviour of castrated, reproductively experienced males was restored by treatment with testosterone or oestrogen, but not by treatment with the non-aromatisable androgen dihydrotestosterone (65). Moreover, fathers had higher aromatase activity within the medial preoptic area of the brain, which is a region strongly implicated in paternal behaviour (66,67), than non-fathers (36). Thus, even though California mouse fathers have lower circulating concentrations of testosterone than non-fathers, they might have higher local concentrations of oestrogen within the brain.

Progesterone

In the uniparental house mouse (*Mus* spp.), progesterone signalling has been shown to promote infanticide and inhibit paternal behaviour in adult males (68,69). Progesterone receptor knockout mice, as well as mice treated with the progesterone receptor antagonist RU486, showed markedly reduced aggression toward pups and enhanced paternal behaviour, whereas progesterone treatment of wild-type males significantly increased aggression toward pups. To our knowledge, however, the effects of progesterone on paternal care have not been tested in biparental mammals.

Glucocorticoids

Very few studies have examined effects of glucocorticoids on paternal care. To characterise the effects of acute glucocorticoid elevations, Harris *et al.* (70) injected California mouse fathers with high doses of corticosterone and found neither short-term effects on paternal behaviour, nor longer-term effects on pup survival or development. Similarly, in free-ranging, cooperatively breeding meerkats (*Suricata suricatta*), glucocorticoid injections had no effect on provisioning of pups or time spent in proximity to pups in non-breeding male alloparents (71). To determine the effects of chronic stress, including chronic elevations of circulating corticosterone levels, on paternal care, Harris *et al.* (72) subjected California mouse fathers to a chronic variable stress paradigm for 7 days. Stressed fathers showed both significant elevations in plasma corticosterone

levels and subtle reductions in their interactions with their mate and pups compared to control fathers, although no differences were detected in pup survival or development. These findings suggest that neither acute nor chronic glucocorticoid elevations have pronounced effects on parental or alloparental care in males, although additional data are clearly needed from other species.

Vasopressin

Both within and among species, paternal behaviour correlates with patterns of vasopressin-immunoreactivity and vasopressin binding, especially in the lateral septum and other parts of the 'extended amygdala' (48,51,73,74). Moreover, central infusion of vasopressin or vasopressin receptor antagonists promotes or inhibits paternal behaviour, respectively, in the biparental prairie vole (75) and in the facultatively biparental meadow vole (*Microtus pennsylvanicus*: 76). Nonetheless, castration of male prairie voles almost eliminates vasopressin-immunoreactivity in the lateral septum and lateral habenula but does not affect paternal behaviour, suggesting that vasopressin signalling in these areas is not essential for the expression of paternal care (61).

Oxytocin

Several experimental studies support a role of oxytocin in paternal behaviour. In humans, intranasal oxytocin treatment of fathers modulates several aspects of father–child interaction (77–79); however, the extent to which intranasally administered oxytocin enters the brain and gains access to oxytocin-responsive regions is unclear (53). In virgin male prairie voles, paternal behaviour is inhibited by combined treatment with a vasopressin receptor antagonist and an oxytocin receptor antagonist but not either antagonist alone (80). Finally, in free-ranging meerkats, peripheral injections of oxytocin increased adults' feeding of pups and time spent in proximity to pups; however, the study included both breeding and nonbreeding animals of both sexes, and, again, the extent to which oxytocin entered the brain is unknown (81). Further studies utilising direct manipulation of intracerebral oxytocin signalling are needed to clarify the effects of the brain's oxytocin system on paternal behaviour.

In summary, experimental studies provide limited and inconsistent support for the hypothesis that the hormone and neuropeptide changes occurring in mammalian fathers are important in the expression of paternal behaviour. What, then, can we conclude about the functional significance of parenthood-associated hormonal and neurochemical alterations in biparental mammalian fathers? Although the answer is still far from clear, we explore several possibilities below, based on known effects of these same hormones and neuropeptides in mammalian mothers, and on observed morphological, physiological, neurobiological and behavioural changes in fathers.

Effects of fatherhood on energy balance and body composition

Female mammals show a direct relationship between reproduction and energy balance (82). Pregnancy and lactation are energetically expensive; without access to adequate calories, females will either terminate reproductive attempts or continue them at the expense of self-maintenance (83,84). Several hormones are involved in the energetics of pregnancy and induce coordinated adaptations to physiological functions in the mother. In particular, prolactin and placental lactogen appear to be involved in the leptin resistance that occurs beginning at mid-pregnancy, and prolactin induces hyperphagia (85). Oestradiol increases energy utilisation (86) but inhibits food intake (87), whereas progesterone increases food intake and body weight during pregnancy (88). During lactation, mild leptin resistance may persist, whereas sensitivity to ghrelin appears to increase, thereby stimulating hyperphagia (6,89). Prolactin also acts centrally to stimulate hyperphagia during the lactational period, complemented by elevated basal levels of the orexigenic glucocorticoid hormones and low levels of the anorexigenic oestrogens (6). Thus, the endocrine changes in pregnancy and lactation provide signals to reset maternal homeostatic mechanisms, facilitating shifts in feeding behaviour and energy utilisation to meet increased metabolic demands (6,85).

Although males in biparental species obviously do not undergo pregnancy or lactation (with the exception of some species of fruit bats in which males lactate) (90), hormonal changes in fathers nonetheless appear to interact with paternal homeostatic mechanisms, and males may show changes in body mass and body composition similar to those in their mates (Table 1). In two biparental primates, the common marmoset and the cotton-top tamarin, expectant fathers undergo significant weight gain, especially in the final month of the mate's gestation, concurrent with elevations in prolactin concentrations (91,92). Fathers engage in infant care beginning shortly after parturition, including extensive carrying of multiple infants, and lose weight during the period of infant dependency (31,93). Prolactin has been shown to limit weight loss in common marmoset fathers in the first few weeks postpartum: fathers treated with the dopamine D_2 receptor agonist cabergoline

Table 1. Effects of Fatherhood on Energy Balance and Body Composition in Males of Biparental Mammalian Species.

Dependent variable	Species	Effect of fatherhood	Reference
Body mass	Common marmoset	Increase across mate's pregnancy, especially in final month; decrease during period of infant care	31,91
Body mass	Cotton-top tamarin	Increase across mate's pregnancy, especially in final month; decrease during period of infant care	91–93
Body mass	California mouse	Increase during mate's pregnancy; decrease during period of infant care	70
Body mass, subcutaneous fat	Prairie vole	Decrease during period of infant care	22

to lower their circulating prolactin levels lost significantly more weight during the infant-care period than males given prolactin implants (31). It is possible, therefore, that prolactin has orexigenic effects in fathers providing infant care, as in pregnant and lactating mothers.

Similar to marmosets and tamarins, California mouse fathers show significant increases in body weight towards the end of their mate's pregnancy, followed by weight loss during the postpartum period (70). Prairie vole fathers also lose weight when caring for pups, and undergo a significant loss of subcutaneous fat and a significant decline in plasma leptin concentrations (22). These morphological and endocrine changes in prairie vole fathers are associated with an increased preference for sucrose solution over water and increased time spent feeding, but no change in physical activity levels (22).

In summary, findings from biparental monkeys and rodents demonstrate that fathers undergo systematic decreases in body weight and, in at least one species, reductions in subcutaneous fat and circulating leptin levels when rearing infants, suggesting that providing paternal care is energetically costly. Importantly, these findings were obtained from captive animals housed under nonchallenging conditions, with ample food, comfortable ambient temperatures and an absence of predators. Studies of biparental mammals living in natural or semi-natural environments would likely reveal even more pronounced energetic costs of fatherhood.

Effects of fatherhood on neural plasticity, cognition and olfaction

Reproduction in female mammals governs plasticity in the brain. During pregnancy and lactation, mothers undergo molecular, electrophysiological, neurochemical and morphological changes in brain regions associated with the expression of maternal behaviour, as well as in regions involved in cognition, sensory processing and emotional regulation (8–12). In recent years, interest has focused particularly on effects of motherhood on neurogenesis. Neuronal proliferation in the dentate gyrus of the hippocampus declines during the early lactational period in rats, mice and sheep, compared to control females, and this effect appears to be mediated by hormonal and/or neurochemical events, including reductions in oestrogen and elevations in glucocorticoid levels. By contrast, in the subventricular zone, which produces neurones that migrate to the olfactory bulb, the proliferation of neurones is enhanced during both pregnancy and lactation in rats and mice as a result of stimulatory effects of prolactin but is suppressed in lactating ewes (10). Although the functional significance of these motherhood-induced changes in neural plasticity is not yet known, they have been proposed to mediate changes in cognition (e.g. spatial memory), sensory processes (e.g. olfactory recognition of offspring) and emotional regulation (e.g. anxiety reduction) in mothers, potentially enhancing mothers' ability to meet the demands of parenthood (8–12).

In the past decade, a handful of studies have indicated that fatherhood, similar to motherhood, modulates plasticity in brain regions subserving cognitive, affective and sensory functions (Table 2). Kozorovitskiy *et al.* (50) found that, in the common marmoset, both first-time and experienced fathers had higher densities of dendritic spines on pyramidal neurones in the prefrontal cortex, a region involved in goal-directed behaviour, compared to age-matched males that had not sired offspring. The functional significance of this difference is not known.

More recently, two studies have examined possible effects of fatherhood on neural plasticity and cognition in the biparental California mouse, with contrasting results. Glasper *et al.* (94) injected the cell-division marker bromodeoxyuridine (BrdU) into adult males 1 week following the birth of the males' offspring, and euthanised the fathers 3 weeks later. Compared to control males, fathers had fewer BrdU-labelled cells and, specifically, fewer BrdU-labelled neurones, in the dentate gyrus, suggesting that fatherhood inhibits hippocampal neurogenesis; no differences were seen in the subventricular zone. The functional significance of this difference, if any, is not clear: no significant correlations were found between number of BrdU-labelled cells and measures of paternal behaviour, and performance in two hippocampus-dependent cognitive tests, the object-recognition test and the novelty-suppressed feeding test, did not differ between fathers and controls.

Table 2. Effects of Fatherhood on Neural Plasticity, Cognition and Olfaction in Males of Biparental Mammalian Species.

Dependent variable (interpretation)	Species	Effect of fatherhood	Reference
Density of dendritic spines on pyramidal neurones in prefrontal cortex (structural reorganisation)	Common marmoset	Increase	50
BrdU-labelled neurones in dentate gyrus (neurogenesis)	California mouse	Decrease	94
BrdU-labelled neurones in subventricular zone (neurogenesis)	California mouse	No effect	94
Performance in object-recognition test and novelty-suppressed feeding test (hippocampal function)	California mouse	No effect	94
Nestin, Ki-67, doublecortin and glial fibrillary acidic protein in hippocampus (neural plasticity)	California mouse	No effect	95
Performance in dry land maze, exploratory behaviour in dry land maze (spatial learning)	California mouse	Increase	95
BrdU-labelled cells in amygala, dentate gyrus and ventromedial hypothalamus (survival of new cells)	Prairie vole	Decrease	96
BrdU-labelled cells in main olfactory bulbs (survival of new cells)	Prairie vole	No effect	96
Ki67-labelled cells in amygdala, dentate gyrus and ventromedial hypothalamus (cell proliferation)	Prairie vole	No effect	96
BrdU-labelled cells in subventricular zone and dentate gyrus (neurogenesis)	House mouse (uniparental)	Increase	98

BrdU, bromodeoxyuridine.

Franssen *et al.* (95) similarly investigated effects of fatherhood on hippocampal plasticity and function in California mice, comparing neural and cognitive measures among fathers, pup-naïve virgin males and virgin males that had been exposed to a pup for 10 min on each of seven consecutive days. Fathers performed significantly better in a dry land maze than both pup-exposed and pup-naive virgins, whereas pup-exposed virgins performed significantly better than pup-naïve virgins. Fathers also showed increased exploratory behaviour in the maze and, subsequently, had enhanced Fos-immunoreactivity in the CA1, CA3 and dentate gyrus of the hippocampus, compared to one or both control groups. No differences were found between fathers and non-fathers, however, in markers of neural plasticity, including hippocampal expression of nestin (a marker of restructuring in mature neurones), Ki-67 (a marker of cell proliferation), doublecortin (an index of the number of new neurones) and glial fibrillary acidic protein (a marker of glial responsiveness).

As in the California mouse, fatherhood has been found to modulate neural plasticity in the prairie vole. Lieberwirth *et al.* (96) injected male voles with BrdU daily for 14 days before assigning them to mixed-sex pairs, same-sex pairs or individual housing. Voles were euthanised the day after the birth of the breeding males' second litters, and brains were analysed for BrdU labelling to characterise the survival of new cells. Compared to one or both control groups, fathers had significantly fewer BrdU-labelled cells in the central, cortical and medial amygdala but not the basolateral amygdala. Fathers also had significantly fewer BrdU-labelled cells in the dentate gyrus, as well as the ventromedial hypothalamus. No differences were found in the main olfactory bulbs. These results suggest that fatherhood reduces the survival of new cells in the amygdala, dentate gyrus and hypothalamus of male prairie voles. These results could not be attributed simply to fathers' interactions with pups: in male prairie voles pair-housed with oestrogen-treated, ovariectomised females, neither acute (20 min on 1 day), nor chronic (20 min on each of 10 consecutive days) exposure to a pup altered survival of new cells in these brain regions (96,97).

Finally, an elegant series of studies in the uniparental house mouse indicates that interactions of an adult male mouse with its own pups stimulate neurogenesis in the father's subventricular zone and dentate gyrus under the influence of prolactin signalling (98). Some of the new cells mature into olfactory interneurones in the olfactory bulb, where they respond preferentially to offspring odours and appear to subserve recognition of mature offspring.

Taken together, these findings indicate that several aspects of plasticity, including the proliferation and survival of neurones, as well as neuronal morphology, can be altered by parental experience in male mammals. To date, the only documented functional consequence of this fatherhood-induced plasticity is olfactory recognition of offspring in male house mice (98). Clearly, additional work is needed to more fully characterise the effects of fatherhood on the paternal brain; the sensory, behavioural and endocrine mechanisms mediating these effects; and the functional significance of fatherhood-induced neural plasticity for fathers' physiology and behaviour.

Effects of fatherhood on stress responsiveness and emotionality

In at least several mammalian species, mothers exhibit blunted hormonal, neural and behavioural responses to stressors during late pregnancy and lactation (16,99,100). Late-pregnant and lactating rats, for example, have reduced corticosterone and/or adrenocorticotrophic hormone responses to numerous psychological and physiological stressors compared to virgin females. Pregnant and lactating rats also show attenuated stress-induced increases in corticotrophin-releasing hormone (CRH) mRNA, vasopressin mRNA and c-fos mRNA expression in the PVN. The mechanisms underlying these reductions in hormonal and neural responsiveness during pregnancy and lactation are not fully understood; however, increased activity of the brain's prolactin and, to a lesser extent, oxytocin systems and decreased noradrenergic stimulation of the PVN have been implicated (16,100).

Pregnant and lactating rats, mice and, arguably, women also exhibit reduced anxiety and fearfulness (15,100,101). Compared to nulliparous females, for example, postpartum rats and/or mice show reduced acoustic startle responses, increased locomotion in the open field, increased time in the open arms of the elevated plus maze, increased time in the light compartment of a light/dark chamber and reduced fleeing from an intruder. The mechanisms of decreased emotionality in mothers are not fully understood but, similar to reduced stress-responsiveness, are considered to involve intracerebral prolactin and oxytocin, which tend to have anxiolytic effects, as well as intracerebral CRH and vasopressin, which tend to be anxiogenic (100–102).

The function of diminished stress responsiveness and emotionality in mothers is not known. Hypotheses include the protection of infants from exposure to high glucocorticoid levels through the placenta or breast milk (99,100), the protection of mothers from mood disorders (100,101) and the protection of maternal behaviour and/or lactation from stress-induced inhibition (16,99,102). Because fathers in biparental species, similar to mothers, presumably undergo selection to provide infant care under stressful circumstances, and because these fathers, similar to mothers, may undergo changes in prolactin, oxytocin and vasopressin signalling with the onset of parenthood (4,103), the question arises as to whether fathers, too, exhibit blunted stress responsiveness and reduced emotionality compared to their nonbreeding counterparts. This question has been addressed in recent studies using the California mouse and prairie vole (Table 3).

An acute stressor, handling plus 5-min exposure to predator urine, elicited a marked elevation in plasma corticosterone concentrations in male California mice; however, the magnitude of this elevation did not differ between new fathers (housed with their pairmate and first litter of pups) and either virgin males (housed in with another male) or pair-housed, nonbreeding males [intact males housed with a tubally ligated female (43) or vasectomised males housed with an intact female (42)]. These results were obtained whether the males were tested individually or with their cagemate (s) present. In a separate study, Fos expression in three brain regions associated with stress (the PVN, central nucleus of the

Table 3. Effects of Fatherhood on Responses to Stressors and Anxiety-like Behaviour in Males of Biparental Mammalian Species.

Stressor/test (interpretation)	Dependent variable	Species	Effect of fatherhood	Reference
Handling + 5-min exposure to predator urine (acute stress response)	Plasma corticosterone	California mouse	No effect	42,43
Handling + 5-min exposure to predator urine (acute stress response)	Fos in PVN, CeA, BNST	California mouse	No effect	104
Handling + 5-min exposure to predator urine (acute stress response)	Behaviour	California mouse	Decrease	42
Novel-object test (neophobia)	Behaviour	California mouse	No effect	104
Novel-object open-field test (anxiety-like behaviour)	Disruptions in patterning of behaviour	California mouse	Decrease	105
3-min exposure to TMT (acute stress response)	Behaviour	California mouse	No effect	105
Chronic variable stress paradigm (chronic stress response)	Plasma corticosterone	California mouse	No effect	49,72
Chronic variable stress paradigm (chronic stress response)	CRH mRNA and AVP mRNA in PVN	California mouse	No effect	49
Elevated plus maze (anxiety-like behaviour)	Behaviour	Prairie vole	Decreased ratio of time in open arms to total time in arms; no other significant differences	96
Open-field test (anxiety-like behaviour)	Behaviour	Prairie vole	Increased time in corners of open field; no other significant differences	96
Forced-swim test (depression-like behaviour)	Behaviour	Prairie vole	Increased latency to immobility, number of immobility bouts and duration of immobility (in fathers and mated males)	96

AVP, vasopressin; BNST, bed nucleus of stria terminalis; CeA, central nucleus of amygdala; CRH, corticotrophin-releasing hormone; PVN, paraventricular nucleus of hypothalamus; TMT, 2,5-dihydro-2,4,5-trimethylthiazoline (component of fox faeces).

amygdala and BNST) did not differ between new fathers and either expectant fathers or virgin males, either under baseline conditions or after exposure to predator urine (104).

Fatherhood also does not appear to alter hormonal or neural responses to chronic stress in California mice. A 7-day chronic variable stress paradigm elicited a transient elevation in plasma corticosterone concentrations and an increase in vasopressin mRNA (but not CRH mRNA) expression in the PVN; however, these effects did not differ between new fathers, nonbreeding males pair-housed with a tubally ligated female, and virgin males pair-housed with another male (49).

On the other hand, two studies have found that California mouse fathers show attenuated behavioural responses to acute stressors, compared to non-fathers. Bardi *et al.* (105) found no differences in behavioural responses to 3-min exposure to 2,5-dihydro-2,4,5-trimethylthiazoline (a component of fox faeces) among experienced fathers, virgin males with no previous exposure to pups and virgin males that had been exposed to pups on three previous days. When tested in an open field containing a novel object, however, the three groups showed several significant differences in the patterning of behaviour, with fathers showing the lowest and pup-naïve virgins showing the highest numbers of interrupted grooming bouts, behavioural transitions and changes in direction of locomotion (105). By contrast, Chauke *et al.* (104) found no differences among fathers, expectant fathers, paired virgins and isolated virgins in behavioural responses in a novel-object test. Chauke *et al.* (104) did find, however, that in males tested with their familiar cagemates, 5-min exposure to predator urine elicited acute changes in several behaviours in virgin males and nonbreeding males but not in fathers. In the California mouse, therefore, mixed evidence suggests that fathers may show blunted behavioural responses to acute stressors, and this effect does not appear to depend upon the immediate presence of the fathers' mate and pups; however, no evidence to date indicates that California mouse fathers have attenuated hormonal or neural responses to acute or chronic stressors.

By contrast to California mice, prairie vole fathers may show increased anxiety-like behaviour, according to a recent study. Compared to virgin males housed in same-sex pairs and mated males housed with an ovariectomised, oestrogen-primed female, fathers spent significantly more time in the corners of an open field, and a significantly lower proportion of time in the open arms of the elevated plus maze (96). These differences were subtle, however, and most behavioural measures in both tests did not differ among groups, calling into question the biological significance of the effects. Prairie vole fathers also showed increased depression-like behaviour in the forced-swim test (i.e. shorter latency to immobility, more bouts of immobility, increased duration of immobility) compared to virgin males; however, these measures did not differ between fathers and nonbreeding mated males, suggesting that depression-like behaviour was increased by pair-bonding or cohabitation with a female, rather than by fatherhood *per se* (96).

Taken together, these results from California mice and prairie voles suggest that parenthood may not have pronounced effects on stress responsiveness or emotionality in fathers, in contrast to the well documented effects of pregnancy and lactation in mothers. Given that gestational and lactational hyporesponsiveness to stress have not been documented in female California mice (42) or prairie voles, this apparent difference between mothers and fathers might instead reflect differences among species. On the other hand, if gestational and lactational hyporesponsiveness to stress evolved as a mechanism to protect fetuses and pups from exposure to high levels of glucocorticoids via the placenta and mother's milk, then the lack of similar hyporesponsiveness in males would make sense, from a functional perspective. Studies of additional biparental species, including intraspecific comparisons of mothers and fathers, would be informative.

Conclusions

Behavioural endocrinologists have recognised for three decades that mammalian fathers can undergo systematic endocrine changes in association with infant care (32). These changes commonly appear to include shifts in circulating prolactin and testosterone levels, and may additionally include changes in peripheral oestrogen, progesterone and glucocorticoid concentrations, as well as in the intracerebral vasopressin and oxytocin systems. In recent years, however, it has become increasingly clear that the hormonal and neuropeptide profiles of fatherhood may be quite variable among species and might not play important, direct, causal roles in the expression of paternal behaviour (4,23). Several investigators have suggested, therefore, that the hormonal and neurochemical sequelae of fatherhood in biparental mammals may indirectly facilitate paternal care and/or paternal survival through diverse actions on fathers' behaviour and physiology (9,106); however, the study of such effects is still in its infancy.

The endocrine consequences of fatherhood, as well as their physiological and behavioural sequelae, are likely to differ within and among species, in association with the specific demands on fathers. These, in turn, may depend on such factors as ecological and demographic parameters (e.g. abundance and distribution of food, intensity of predation pressure, and availability of alloparents), as well as the quality, quantity and energetic costs of infant care provided by fathers.

Several important caveats should be kept in mind when considering hormonal and neurochemical changes in mammalian fathers and their potential significance. First, our understanding of such effects comes almost entirely from only a small number of species, primarily several muroid rodents and callitrichid primates (i.e. marmosets and tamarins). Clearly, data are needed from a broader range of taxa, including the heavily biparental canids (17).

Second, hormonal correlates of fatherhood, as well as their possible physiological and behavioural consequences, have been studied almost exclusively in captive animals, which face few energetic demands such as finding food, thermoregulating, detecting or escaping from predators, defending a territory, or competing for mates. Studies of biparental mammals in natural or semi-natural environments would provide valuable insights into the physiological and behavioural impacts of parenthood on mammalian fathers.

Despite these limitations, as reviewed above, recent evidence suggests that fathers in biparental mammalian species undergo systematic changes in body weight, body composition and neurogenesis, all of which are likely to be mediated by hormonal profiles of fatherhood. The mechanisms, functional significance and frequency in nature of these effects remain to be determined. Moreover, endocrine changes in biparental mammalian fathers are likely to induce additional physiological and behavioural alterations in such functions as thermoregulatory ability, osmoregulation (106), immune function (49), exercise physiology and performance ability. Characterising such impacts of fatherhood on male mammals in biparental species would significantly enhance our understanding of male reproductive strategies as well as mammalian life histories, and poses an exciting challenge for behavioural endocrinology.

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