Neuro-endocrinology

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BRIEFINGS

The Mother Load of Lactation

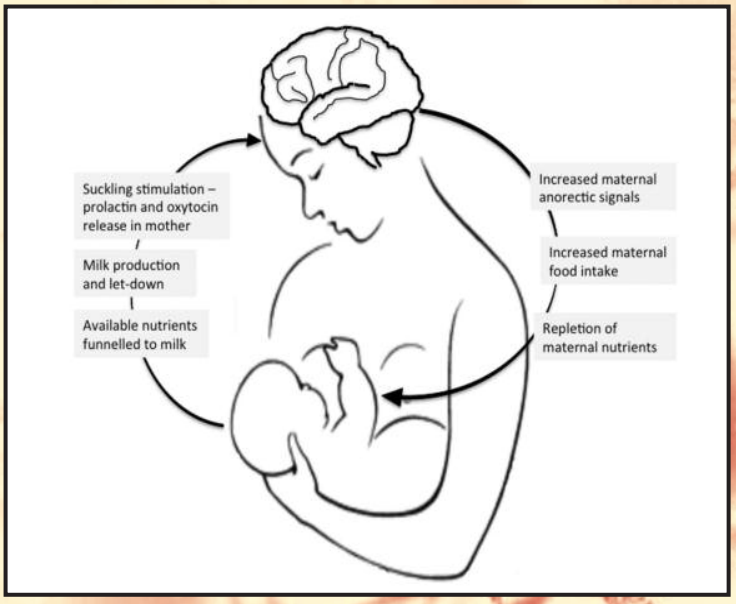
SUMMARY

Providing milk to support their growing young is a tremendous energetic drain on mammalian females. They meet this challenge by recruiting multiple hormone-dependent mechanisms both in peripheral tissue and in the brain that conserve nutrients for milk production and facilitate increases in food intake. In addition, the negative energy balance associated with milk delivery itself results in changes in central pathways controlling metabolism that drive increases in food intake.

Our likelihood of developing metabolic and cardiovascular diseases like diabetes and high blood pressure does not only depend on the decisions we make as adults. There is increasing evidence that the nutritional environment before and after birth also affects risk for disease in adulthood. As such, variations in the amount and quality of milk produced by the mother, a mammal's only source of nutrition in early life, can have wide ranging and subtle effects on her young. The task of providing adequate nutritional resources to offspring is complicated because the needs of the young change depending on their age and the environment. Thus, successful lactation depends on the mother's ability to obtain and properly convert enough food to provide sufficient milk, and also on her responses to signals from the young that reflect their changing needs.

Signals from the young

Lactation has two components – the first is milk production in the breast, the second is letdown – where milk is transported from the breast to the nipple. Suckling stimulation from offspring is the primary signal for milk production and letdown in the mother. Although the mammary gland begins to develop in pregnancy, full lactation is only achieved at birth in most species and not until 2-4 days postpartum in women. Suckling stimulation from the neonate induces the release of the hormones prolactin and oxytocin from the maternal pituitary gland to stimulate milk production and milk ejection respectively. The amount of prolactin released and hence the drive for milk production is a function of the amount of stimulation received which reflects, in turn, the frequency and duration of nursing episodes



Suckling stimulation acts on the mother's brain to release hormones that stimulate milk production and letdown. They also contribute to metabolic and behavioral changes in the mother that provide nutrients for milk.

as well as, in species with multiple young, the number of nipples stimulated. The bolus release of oxytocin required to induce milk letdown results from the ability of suckling to induce phasic activity of hypothalamic oxytocin neurons. In the absence of the removal of milk from the mammary gland the synthetic processes underlying its production cease but the ability of suckling stimulation to elicit pituitary hormone production persists.

Maternal responses

Women who choose to breastfeed exclusively may produce as much as 750g of milk/day. Female rats produce 75g of milk/day to nourish an average litter of eight pups in rats. This huge demand is associated with a doubling of the mother's metabolic rate. Meeting these requirements begins with an increase in maternal fat stores during pregnancy. A growth in the absorptive surface of the gut at this time allows more efficient utilization of ingested food in general and changes in some enzymes increase the ability to absorb calcium. Thus when the demand for milk production arises after parturition the mother is equipped with a store of fat and calcium, both of which are mobilized to offset the energetic cost of lactation.

The energetic requirements of milk production are also partially offset by decreases in energy expenditure in brown fat thermogenesis and physical activity as well as a variable period of reproductive suppression during which the mother cannot become pregnant again. Funneling of available energy into milk production is ensured by decreased insulin sensitivity in maternal fat depots and glucose utilization in skeletal muscle while insulin sensitivity in the mammary gland is maintained.

In a few species these strategies are sufficient to underwrite the costs of milk production, however, for most mothers, obtaining enough resources to support milk output requires alterations in food choice as well as an increase in overall food intake. Lactating rats, for example, increase their food intake by approximately 300% and this change in behavior is accompanied by alterations in the neurochemical mechanisms controlling appetite.

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Circulating concentrations of both insulin and leptin, which act at the hypothalamus to decrease food intake are reduced, with the result that there is less influence of these anorectic signals. In contrast, there is an increase in hypothalamic density of receptors for ghrelin, a hormone that acts centrally to increase food intake suggesting an increased influence of orexigenic signals. Consistent with this, levels of related brain signals like the neuropeptide proopiomelanocortin that acts to reduce food intake are decreased in lactating rats whereas levels of neuropeptide Y and agouti-related peptide, which stimulate food intake, are increased.

Role of hormones

The energy demands of producing milk play a key role in adaptation of maternal energy balance systems to lactation but lactational hormones also have a role. In rodent models, preventing milk delivery does not completely eliminate the increased food intake seen in lactation. Suppressing prolactin release pharmacologically after this surgical manipulation, however, does suppress food intake to non-lactating levels and this effect is reversed if prolactin is administered into the brain. This suggests that suckling-induced prolactin release can act in the brain to increase food intake. Because prolactin has this effect when fat stores and leptin levels are high it has been suggested that one route through which prolactin may increase food intake is by altering the response to leptin. The suckling-induced suppression of ovarian cyclicity may also favour increased food intake because it results in lower levels of estrogen an anorectic hormone.

Thus adequate milk production depends on the interaction of multiple mechanisms. Disruptions in any of these, whether conditions in the young that prevent adequate suckling stimulation, or in the mother that limit her hormonal response can limit neonatal growth and have long-term consequences on the health of the offspring.

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