



## Review article

# The first model of keeping energy balance and optimal psycho affective development: Breastfed infants



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## ABSTRACT

**Background:** Breastfed infants follow a peculiar growth fashion characterized by a rapid weight gain in the first weeks of life, then followed by a fast decrease in growth rates, a capacity to self-regulate the sense of hungry and satiety, and a minor propensity towards overweight and obesity later on, in parallel with a better neurodevelopmental performance.

**Methods:** We searched studies investigating the relationship between the feeding mode in infancy and the energy balance, so the possible associations with total energy expenditure and intake regulation. We focused the research on the interaction with the neuropsychological development and the possible role of microbiome in determining the normal generation and regular functioning of the brain through the so named "gut-brain axis".

**Results:** Total energy expenditure (TEE) is different for breast-fed and formula-fed infants, in particular the feeding mode seems to affect the sleep organisation. Long-term breastfeeding, is one of the most studied factors of neurodevelopment, several studies reporting beneficial effects on child neuropsychological development. Probably this effect is modulated by genetic variations in fatty acid metabolism. Increasing data also showed that the intestinal microbiome exerts several functions which are able to influence neurodevelopment.

**Limitations:** There is considerable controversy over whether nutrition in early life has a long-term influence on neurodevelopment. Other studies are needed to confirm the association between breastfeeding and brain development.

**Conclusions:** The key points of energy disposal, the role and effects of the intestinal flora represent promising fields of investigation possibly leading to indications for the wide area of preventive medicine.

## 1. Introduction

Growth and development represent the key vital processes in the first phases of life. If either fails, consequences will have long-lasting effects, dramatically limiting the individual genetic potential. Within this context, breastfeeding and/or human milk, as either behaviour or food habit, is today believed to represent the element optimally

connecting in the best way the requirements for growth and development. Accordingly, breastfed infants have traditionally been reported to follow a peculiar growth fashion characterized by a rapid weight gain in the first weeks of life, then followed by a fast decrease in growth rates, a capacity to self regulate the sense of hungry and satiety, and a minor propensity towards overweight and obesity later on, in parallel with a better neurodevelopmental performance.

**Abbreviations:** TEE, Total energy expenditure; EE, energy expenditure; SMR, sleeping metabolic rate; AA, amino acid; NREM, nonrapid eye movement; REM, rapid eye movement; TEF, thermic effect of food; IQ, intelligence quotient; LC-PUFA, long chain polyunsaturated fatty acids; WAIS, Wechsler Adult Intelligence Scale; BPP, Borge Priens Prove; VLBW, very low birth weight; HM, human milk; OMM, own mother's milk; ADHD, attention deficit hyperactivity disorder; CNS, central nervous system; HFD, High Fat Diet; SCFAs, short-chain fatty acids; EC, enterochromaffin

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Considering the way by which breastfed infants may keep their energy balance may help in understanding the biologic plausibility of these observations.

## 2. Energy requirements in infancy

Infant energy requirements are the sum of total energy expenditure (TEE) and energy stored during growth. TEE includes the energy needs for basal metabolism, diet-induced thermogenesis and physical activity, and is influenced largely by age, sex and body size (Butte, 2005). The increase in energy expenditure induced by growth results from the expenditure for protein and lipid synthesis and their deposition in newly-formed tissue and it is significant only in rapidly growing infants and children. The mean energy cost of growth is 20 kJ/g at 3 months and  $\approx$ 10 kJ/g weight gain (Butte et al., 2000b). On the basis of the changes in body composition of Fomon's term infant reference (Fomon et al., 1982), the energy cost of growth falls from 19 to 8 kJ/g in the first year of life. Accordingly, the energy cost of growth represents a major issue only during the first half of infancy, during which energy deposition contributes significantly to energy requirements. At ages 3 and 6 months, the energy cost of growth represents 22% and 6%, respectively, of total energy requirements; thereafter, it contributed negligibly (2–3%) to total energy requirements (Butte et al., 2000b). Growth is a sensitive indicator of whether energy requirements are met.

Published mean data on the TEE of infants living in developed and developing countries show that TEE increases linearly with age, and, standardised by body mass, ranges from 255 to 393 kJ/kg (61–94 kcal/kg) per day (EFSA, 2013).

Energy intakes based on the mean milk intakes of exclusively breastfed infants appear to meet mean energy requirements during the first 6 months of life.

## 3. Feeding mode and total energy expenditure

Feeding mode affects TEE as well as body composition and growth in infancy, and these effects are likely to influence energy requirements (Nielsen et al., 2013).

It is generally accepted that TEE is different for breast-fed and formula-fed infants. Indeed, energy intakes of the breast-fed infants are lower than those of the formula-fed infants after the first few months of life (Butte et al., 1990). Differing energy intakes between feeding groups imply that energy absorption, expenditure, and (or) deposition between groups also differ.

Differences in the macronutrient composition of human milk and formula, combined with quite heterogeneous levels of milk intake, result in significant differences in protein, lactose, and fat intake and may also influence energy utilization by infants.

TEE of breast-fed infants was shown to be lower than that of formula-fed infants (Butte et al., 1990, 2000a; Davies et al., 1990; Jiang et al., 1998), however differences in TEE between the groups diminished after the first year of life. Butte et al. reported that TEE was 12%, 7%, 6% and 3% higher in formula-fed compared to breast-fed infants at 3, 6, 9 and 12 months, respectively, suggesting that energy requirements of formula-fed infants may be accordingly different than those of breast-fed infants (Butte et al., 2000a).

Lubetzky et al. (2003) found that feeding preterm infants with human milk results in significantly lower energy expenditure (EE) as compared with feeding with formula too, consistent with data in term infants.

For infants during the first half year of life (until six months of age), energy requirements are considered to be equal to the energy supply from human milk (EFSA, 2013).

## 4. Feeding mode and sleeping metabolic rate

In infants, sleeping metabolic rate (SMR) is  $\approx$ 60% of TEE, and the metabolic expenditure of the brain contributes to around 70% of SMR (Holliday, 1971).

The feeding mode seems to affect the sleep organisation: the synthesis of brain neurotransmitters involved in the induction and maintenance of sleep is influenced by normal postprandial fluctuations in the availability of amino acid (AA) (Butte et al., 1992). Plasma AA levels in breast-fed infants have been shown to differ from those in formula-fed infants; in particular, the plasma tryptophan and tryptophan/sum of large neutral AA levels are higher in the breast-fed than in the formula-fed infants. Diet-induced alterations in plasma AA ratios have, in fact, been shown to affect infant sleep behaviour (Butte et al., 1992).

Several studies found higher SMR in formula-fed compared with breast-fed infants (Wells and Davies, 1995; Butte et al., 2000b, 1990). Butte et al. (1992) found that nonrapid eye movement (NREM) sleep time is greater for infants fed human milk than for infants fed a casein-predominant formula; conversely, rapid eye movement (REM) sleep time is greater for formula fed infants. The energy expenditure of infants generally has been shown to be higher during REM than during NREM sleep. The increase in energy costs during REM sleep is consistent with the physiologic and biochemical changes that occur in the transition from NREM to REM (Montplaisir and Godbout, 1990): heart rate and respiration rates are more variable, blood pressure increases and regional blood flow to the thalamus, hypothalamus and brainstem are higher during REM than NREM sleep (Cote and Haddad, 1990). CNS VO<sub>2</sub> and glucose use increase diffusely during REM sleep and result in increased brain temperature. During REM sleep, there is considerable physical activity which consists of facial, limb, and whole body movements (Anders et al., 1971). In their study Butte et al. (1992) found that energy expenditure was clearly higher during REM sleep and a distinct pattern of energy expenditure was also evident during the REM phases.

Another possible mechanism could be through the thermic effect of food (TEF). Infant formulas prepared using cow's milk often have a higher protein content than breast milk, and protein contributes more to TEF than lipids and carbohydrates (Haisma et al., 2005). However, Butte et al. (1990) measured TEF as part of SMR measurements in breast- and formula-fed infants, and found no difference.

## 5. Feeding mode and the energy intake regulation

Infants' ability to regulate intake or the caretakers' encouragement to feed, which may alter later regulation of intake, differs between breastfed and formula-fed infants (Butte, 2001).

Infants naturally regulate their energy intake, but their parents' behaviour can override cues for hunger and satiety. Mothers who breastfeed may develop feeding styles that are less controlling feeding habits, thus promoting in their children the development of self-regulatory mechanisms of energy intake and the response to internal appetite cues.

Birch and Fisher, (1998) reported that highly controlling feeding practices by parents were directly associated with poorer self-regulation of energy intake among children 3–5 years of age. Experimental studies have shown that restricting children's access to preferred foods increases the probability that children will consume those foods when given free access (Fisher and Birch, 1999a, 1999b).

Taveras et al. (2004) found that mothers who fed their infants breast milk in the first 6 months of life or who breastfed them for longer periods had decreased odds of restricting their children's food intake at 1 year, suggesting a virtuous circle between prolonged breastfeeding and self controlled eating behaviors.

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