Abstract

Obesity and related disorders are thought to have their roots in metabolic thirftiness that evolved to combat periodic starvation. The failure to detect any thrifty genes and the observation that low birth weight is associated with type 2 diabetes in later life, caused a shift in the concept from thrifty gene to thrifty phenotype and fetal programming. This hypothesis assumes that if a fetus faces undernutrition in intra-uterine life, the body is programmed to be thrifty, predicting and preparing for starvation in later life. However, there are reproductive costs associated with this programming since it is associated with reduced ovulation and defective spermatogenesis. We examine here, with the help of a simple mathematical model, the conditions under which thrifty genes or fetal programming could evolve. Results of the model suggest that the conditions for evolution of fetal programming are very restricted. For species with longer life spans, programming for thriftiness is unlikely to evolve if starvation is decided by seasonality or stochastic annual climatic variations since the correlations between intra-uterine and life-time conditions are poor. On the other hand, if starvation is governed by longer periodicity cycles such as population oscillations, fetal programming can evolve. Social inequality and poverty can also lead to strong correlations between intrauterine and life time conditions. Therefore seasonal and climatic "feast and famine" are unlikely to be the selective force behind the evolution of thrifty genotype or phenotype. Social and population processes are more likely to have selected for fetal programming since such processes can lead to better correlation between intra-uterine and life time conditions.

The model:

- □ We consider 3 genotypes namely wildtype having no mechanism for thriftiness (n), thrifty genotype (tg) and genotype for capacity of fetal programming for thriftiness (tp).
- Environmental variables affecting food abundance vary randomly. For simplicity we consider two discrete states 'feast' and 'famine' with probabilities of famine (*pf*) and probability of feast (1-*pf*).
- □ In feast season, the fitness of an individual with non-thrifty genotype (nf1) is greater than that of thrifty genotype (tf1). (nf1 > tf1)
- □ In famine season, the fitness of an individual with non-thrifty genotype (nf0) is less than that of thrifty genotype (tf0). (nf0 < tf0)</p>
- ☐ The lifetime fitness of an individual is given by following equations:
- ☐ For individuals with non-thrifty genotype:

$$Ln = pf \times nf 0 + (1 - pf) \times nf 1$$

☐ For individuals with thrifty genotype:

$$Ltg = pf \times tf 0 + (1 - pf) \times tf 1$$

For individuals with thrifty phenotype or fetal programming: assuming no correlation between birth and life time conditions. The total lifetime fitness is calculated as a sum of all years with the assumption that in the birth year the phenotype is best suited for the given conditions. For the rest of the lifespan (S) fitness fluctuates according to the randomly fluctuating environmental conditions.

$$Ltp = \frac{1}{S}(pf \times tf0) + (1-pf) \times nf1) + \frac{S-1}{S}(pf \times Ltg) + (1-pf) \times Ln$$

If there is correlation (r) between birth conditions and lifetime conditions, the model changes to:

$$pfr0 = (1 - pf) \times r + pf$$

$$pfr1 = pf - (pf \times r)$$

$$Ltpr0 = \frac{tf 0 + (S - 1) \times [pfr0 \times Ltgr0 + (1 - pfr0) \times Lnr0]}{S}$$

$$Lnr0 = pfr0 \times nf0 + (1 - pfr0) \times nf1$$

$$Lnr1 = pfr1 \times nf \ 0 + (1 - pfr1) \times nf \ 1$$

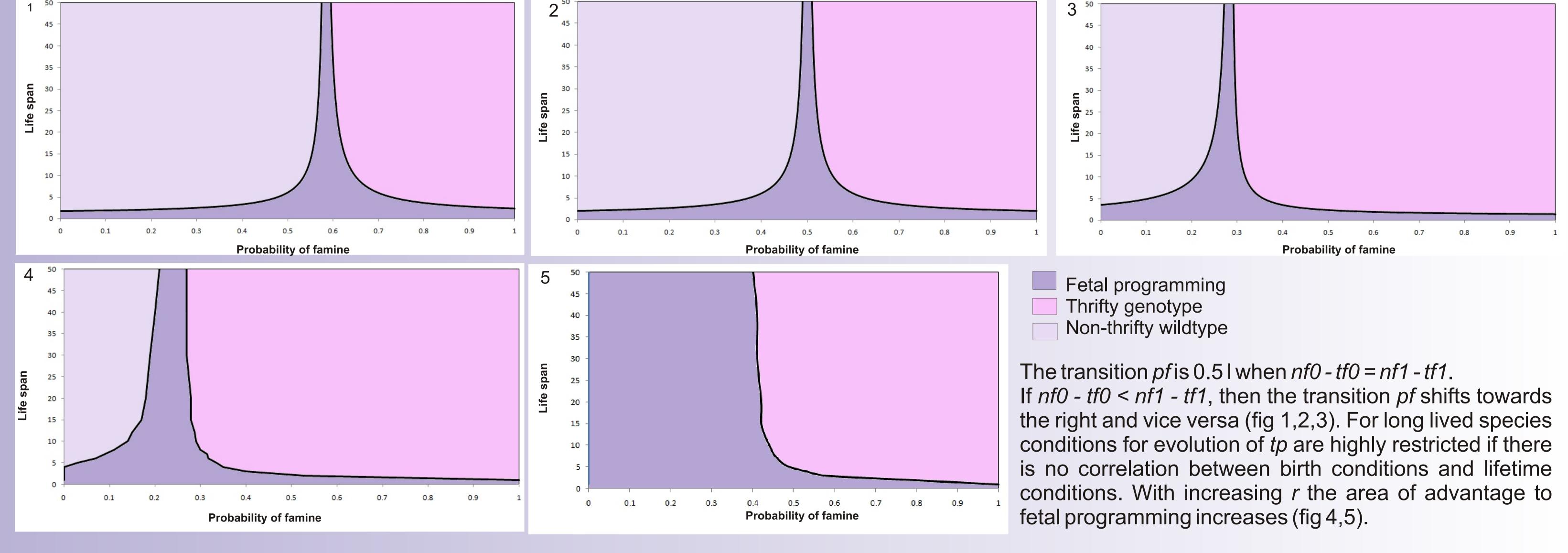
$$Ltpr1 = \frac{nf1 + (S - 1) \times [pfr1 \times Ltgr1 + (1 - pfr1) \times Lnr1]}{S}$$

$$Ltgr0 = pfr0 \times tf \ 0 + (1 - pfr0) \times tf \ 1$$

$$Ltgr1 = pfr1 \times tf0 + (1 - pfr1) \times tf1$$

$$Ltpr = pf \times Ltpr0 + (1 - pf) \times Ltpr1$$

Results: The figures represent the parameter area in which the corresponding genotypes predominate.



Conclusions:

Results of the model suggest that under no condition thrifty and non-thrifty genes would co-exist stably in a population. Fetal programming for thriftiness is also very unlikely to evolve particularly for species with longer life span, if starvation is decided by seasonality or stochastic annual climatic variations. Since the correlations between intra-uterine and life-time conditions are poor fetal programming can be maladaptive. On the other hand, if starvation is governed by longer periodicity cycles such as population oscillations or heritable social hierarchy, fetal programming can evolve.

Therefore seasonal and climatic "feast and famine" are unlikely to be the selective force behind the evolution of thrifty genotype or phenotype. Social and population processes are more likely to have selected for fetal programming since such processes can lead to better correlation between intra-uterine and life time conditions. However in that case population and social cues are equally likely to have evolved along with nutritional ones. Also implied is the possibility that fetal programming did not evolve for thriftiness but for a different function. Alternatives for thriftiness hypothesis have been suggested and a comparative critical evaluation of the alternative hypotheses is needed.