Resource allocation in reproductive rabbit does: genetic strategies for a suitable performance[§]

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ABSTRACT: This article reviews how frequent feeding and selection programmes could be affecting resource allocation in reproductive rabbit does. The possible consequences of these changes and the central role of body condition for suitable female performance are analysed considering genetic level, health and welfare. Resources allocation between functions, and consequently body condition, must be genetically driven in reproductive rabbit does. The body condition of females changes during the reproductive cycle and throughout their reproductive life according to their genetically determined level. The problems appear when the animals are forced to diverge from this appropriate level, increasing susceptibility to disease, other stress factors and eventual failure. Negative energy balances detected during lactation do not seem to have the strength of those observed in late pregnancy. Genetic selection in rabbit for litter size at weaning has increased prolificacy, but also the ability to obtain resources without compromising the survival of rabbit females. However, it could have also increased the susceptibility of animals to the environment, focusing more on the maternal investment in the future litter rather than the current one under restricted conditions to maximise their selection success, “the number”. Rabbit does selected for reproductive longevity have a greater soma, which enables them to better cope with the possible productive challenges. There is also evidence that they have greater plasticity in using their soma, making them more robust to overcome demanding situations. In addition, there seems to be evidence of a possible improvement of immune system modulation in robust animals.

Key words: Rabbit female, Genetic selection, Nutrient partitioning, Body condition.

INTRODUCTION

Rabbit health may be considered one of the main handicaps to current rabbit production under commercial conditions. Rabbit susceptibility to diseases is similar to other intensively farmed animals such as pigs, with similar on-farm mortality risk (Lebas, 2000; Rosell and de la Fuente, 2009). However, the appearance of a new challenge in minor species, such as epizootic rabbit enteropathy (ERE), usually requires devoting a greater part of the scientific effort to reducing the economical impact. For example, many works have focused on increasing the knowledge of the influence of nutrition on intestinal health of growing rabbits in recent years, with the main results recently being included in acknowledged revisions (Gidenne and Garcia, 2006; Carabaño et al., 2008, 2009).

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In any case, this effort should not lead us away from the study of current breeding systems for reproductive rabbit does, which could be unbalancing nutrient partitioning and affecting the global health and welfare of the farm, and their possible implication in the incidence of specific illnesses. In the last two decades, we have moved on from more or less traditional production systems to other more intensive ones using modern prolific lines, which have made it necessary to adjust the nutritional requirements of the animals in line with the new demands (Maertens, 1992). It is true that the nutritional requirements of weaned rabbit have changed as a result of selection by growth rate - between +0.45 and 1.23 g/day per generation of selection (Baselga, 2004) - although it is the reproductive doe that has suffered the effects of these improvements and the new production systems to a greater extent.

Genetic selection programmes in reproductive rabbit does have mainly focused on improving litter size, either at partum or weaning. These programmes bring about an effective increase of between 0.05 and 0.13 live-born kits per generation of selection (Rochambeau et al., 1994; Gómez *et al*., 1996). This selection criterion, along with artificial insemination (AI) of the does with semen from males selected for growth rate, has clearly increased the litter’s demand for milk. On the other hand, the frequent intensification of the reproductive rhythms gives rise to competition between the mammary glands and foetuses, which is usually detrimental to foetal growth if the needs are not well covered (Fortun and Lebas, 1994). The requirements of reproductive rabbit does may therefore have increased considerably in recent years, affecting nutrient partitioning and perhaps compromising body condition, lifespan and general health of the farm.

In this sense, some works have even suggested a possible effect of doe health status on the potential risk of their kits suffering digestive troubles during the growing period. Quevedo *et al*. (2003), in a trial with five thousand kits from five reproductive cycles, described an increase in mortality during the growing period with the mother’s age (from 5 to 29%), with 22% of females being responsible for 50% of the mortality observed. In fact, García *et al*. (2005) observed a significant effect of the litter on the microbiotic profile of young rabbits, with siblings showing a high similarity rate.

For this reason and in the current productive context, new breeding systems must be defined with more emphasis on the welfare of the animals and the general health status of the farm. The search for long-term and globalised strategies to uphold these criteria would take into account the possible collateral effects resulting from isolated strategies (Pascual, 2004). A suitable strategy for the feeding and genetic selection of reproductive does would therefore have to consider short-term productive criteria - such as litter size, milk production or the interval between parturitions - as well as long-term - for example body condition, life expectancy and health status of the doe - while evaluating the possible effect on subsequent litter development (transition at weaning, gastrointestinal health...).

Both reproduction (litter size, milk yield, fertility…) and survival (health, welfare, lifespan…) are energetically expensive. Especially in mammals, body reserves are involved both in successful reproduction and in maintaining the soma and thereby survival (Theilgaard, 2006). Thus, the body condition of the rabbit females might be an important factor when addressing the association between reproduction and survival, and consequently may play a central role in the definition of appropriate genetic selection programmes. The present work firstly examines the particularities of rabbit does’ nutrient partitioning, and thereafter how selection programmes may be affecting the allocation of resources in reproductive rabbit does, the possible consequences resulted from these changes, and the central role of body condition for suitable female performance considering genetic level, health and welfare.

NUTRIENT PARTITIONING IN REPRODUCTIVE RABBIT DOES

The different metabolic functions of a rabbit female (growth, gestation, milking, health…) must be covered from the available resources (food or body reserves). The process whereby available nutrients are channelled, in varying proportions, to these functions is known as nutrient partitioning (Friggens and Newbold, 2007). Nutrient partitioning changes depending on the physiological stage, with linked changes in the endocrine profile (Bauman, 2000) which also controls body fatness throughout the reproductive cycle (Vernon *et al.*, 2001), and with the age of the animal, as the relative priorities for the different life functions change throughout the female's life (Martin and Sauvant, 2010). Thus, it is widely accepted that resource allocation between functions, and consequently body condition, must be genetically driven.

Although mobilisation could be environmentally driven (e.g. when voluntary feed intake is limited under heat stress conditions), there is a lot of evidence of the independence between nutrient availability and mobilisation. In fact, there are numerous studies where additional energy supply by dietary energy enrichment has not yielded appreciable results to avoid reserves mobilisation in cows (Gagliostro and Chilliard, 1991; Andersen *et al.*, 2003), but also in rabbits (Fortun-Lamothe, 1997; Xiccato *et al.*, 1999; Pascual *et al.*, 2000, 2003). Instead, when the feed intake was successfully increased, this extra energy boost is frequently addressed to milk production (Xiccato *et al.*, 1995; Parigi-Bini *et al.*, 1996). For example, the traditional view is that primiparous rabbit does have limited their voluntary feed intake as their growth is not completed, which could lead to mobilisation of body reserves during lactation (Xiccato, 1996; Pascual *et al.*, 2003; Fortun-Lamothe, 2006). However, there does not seem to be a relevant relationship between body weight (BW) and daily feed intake during the first lactation (Figure 1), as primiparous does with a 1 kg difference in BW present a similar feed intake.

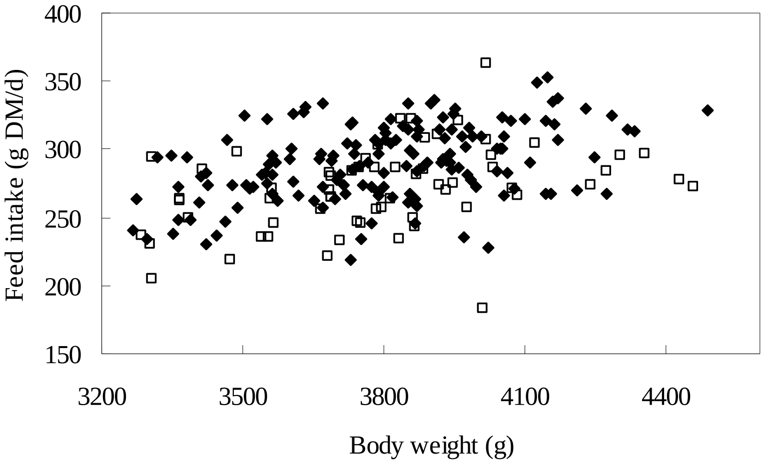

Figure 1 – Relationship between dry matter intake (g DM/d) and body weight (g) of primiparous rabbit does (data from ☐ Pascual *et al.*, 2002 and ◆ Quevedo *et al.*, 2006b)

If we accept that there is a genetic component driving temporal changing of body reserves, the occasional negative energy balance is occurring in rabbit females should not be considered a malfunction in the animal, but rather a possible natural adaptation designed to maximise the chances of evolutionary success (Friggens and Newbold, 2007). From an evolutionary point of view, rabbit selection has focused on maximising the number of viable litters produced in a lifetime. To achieve this goal, the optimum trade-off between number of pregnancies and postnatal investment in litter viability must be defined (Friggens, 2003), i.e. the optimal trade-off between the maternal investment addressed to the current and future litters.

The female rabbit usually has a great decision-making ability on whether to become pregnant or not depending on the resources available, which could also be assisted by hormonal and bio-stimulation methods (Theau-Clément, 2007). However, the female does not know what the future available resources will be when the reproduction effort is increased (end of pregnancy and onset of lactation). Thus, the pregnant doe store reserves for the forthcoming litter (similar to other mammals; Oftedal, 2000), as resources available for foetal growth and early suckling will clearly affect the litter's chances of survival. Body reserves mobilisation observed around parturition is mainly addressed to this task (Savietto, 2013), and it seems to be independent of the resources available at this point, as the additional fat build-up is for transfer to the litter and maintaining a heavier soma is energetically costly, reduces mobility and increases the risk of being predated (McNamara and Houston, 1990). On the other hand, yielding more milk than that required at the end of lactation will not improve the litter's chances of survival. Therefore, milk yield is decreased as the priority of restoring reserves for the future litter starts to increase.

Given these considerations, under non-limiting resource conditions, the traditional view of body reserves mobilisation in reproductive rabbit does as a response to feed intake must give way to an animal viewpoint, where feed intake must be considered more as an "output" resulting from the allocation of resources in the female to ensure current and future litter viability.

Resource allocation in reproductive rabbit does

The body condition of young rabbit females rises till the end of first pregnancy, reaching the peak 10 days before kindling. From this moment to kindling, reproductive rabbit does seem to suffer the highest body reserves mobilisation, with the body condition at parturition showing the lowest level [see Figure 2 adapted from Pereda (2010) and Savietto (2013)]. This fact was recently confirmed by different works, where the evolution of body condition was controlled by different in vivo methods such as perirenal fat thickness (PFT; Quevedo *et al*., 2005, 2006a; Theilggard 2006, 2009), total body electrical conductivity (TOBEC; Bolet and Fortun-Lamothe, 2002) and bioelectrical impedance analysis (BIA; Pereda, 2010). In fact, Pereda (2010) describes how the blood concentration in non-esterified fatty acids (NEFA) of primiparous rabbit does reached a higher level at partum (in average 0.9 mmol/L) compared to that shown at 17 weeks of age (0.22 mmol/L) and even at 21 days of lactation (0.33 mmol/L). This is mainly because rabbit foetuses show most of their growth in late pregnancy (almost doubled in the last 3 days; Moce *et al*., 2004), while the maternal body is subject to intense catabolism (Parigi-Bini *et al*., 1990). In fact, episodes of pregnancy toxaemia can be surmised in primiparous rabbit does, sometimes linked to ad libitum feeding systems, which lead females to higher mobilisation of reserves in late pregnancy, higher risk of death or culling and lower litter size at birth (Rommers *et al.*, 2004; Martínez-Paredes *et al.*, 2012).

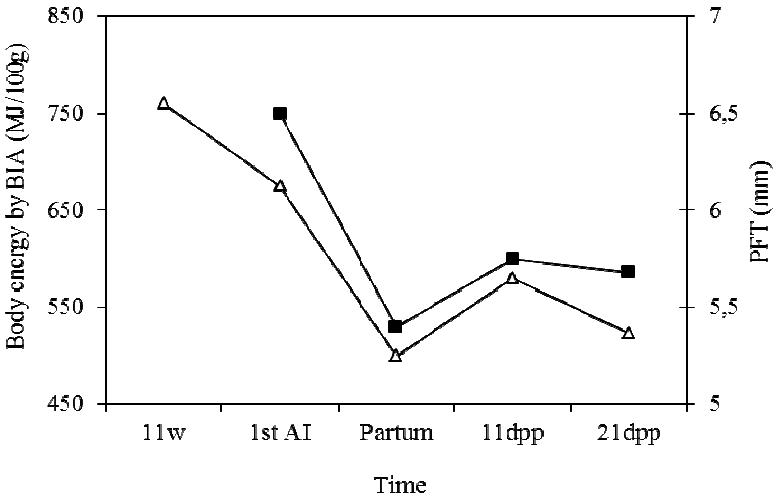

Figure 2 – Evolution of the body energy estimated by BIA (bioelectrical impedance analyse) and perirenal fat thickness (PFT) measured by ultrasounds in primiparous rabbit does [adapted from Pereda (2010) and Savietto (2013)]

Subsequently, body reserves are recovered during the first stage of lactation (Figure 2) and reach a maximum around day 10 in lactation (Bolet and Fortun-Lamothe, 2002; Quevedo *et al.*, 2006b; Theilgaard *et al.*, 2006, 2009; Pereda, 2010; Savietto, 2013). Thus, rabbit females would prioritise the current offspring till kindling (devoting a great pre-partum effort), but would prioritise the next offspring immediately afterwards (promoting their quick recovery after partum). This time course of the body reserves around kindling is slightly different from other species, where the body fatness is highest just before parturition (e.g. sows: Sigfridson, 1996; dairy cows: Nielsen *et al.*, 2003), perhaps related to their different evolutionary success. For example, dairy cows usually have only one offspring per year and sows recover LH pulse only after weaning, so addressing more body reserves to the current offspring at early lactation could be expected.

However, the evolutionary success of rabbits seems to be more related to the “number” (litter size and reproduction frequency), being one of the few animals with fertile acceptance at post-partum day, which could explain their early recovery of reserves. In this respect, it is worth remembering that the shapes of curves for feed intake and milk yield in rabbit does are completely different to those observed in other species (e.g. dairy cows; NRC, 1989). During the first week of lactation, the feed intake curve slope (+50 g DM per day) seems to be higher than that observed for milk yield (+30 g of milk per day), which would allow the recovery of body reserves.

Therefore, it could be hypothesised that an adequate amount of body reserves around kindling seems to be important in support of reproduction in rabbit females. Quevedo *et al.* (2006b) proposed that body condition of rabbit does at partum could condition the AI success at 10 days of lactation, as the greater the loss of pre-partum reserves, the greater the post-partum recovery (r=+0.29; P<0.001) and the lower the fertility during lactation. Savietto (2013) depicted the PFT evolution of rabbit females that were effectively and non-effectively inseminated at 11 days of lactation separately. Females that were not effectively inseminated presented significantly greater PFT losses in late pregnancy, lower PFT at partum and greater recovery in early lactation.

In recent decades, several works have supported the idea that rabbit does are susceptible to body energy deficit during lactation, especially the highly productive commercial hybrids whose voluntary feed and energy intake is insufficient to cover nutrient requirements for lactation and pregnancy (Xiccato, 1996; Pascual *et al*., 2006). However, many of the studies carried out in recent years with in vivo technologies to control body condition call this assertion into question. Several trials performing comparative slaughters among parturitions (Xiccato *et al*., 1992, 2004, 2005; Parigi-Bini *et al*., 1996) describe frequent negative balances of lactating pregnant rabbit does during their first reproductive cycles. However, in our opinion, the low recovery time after weaning and the large mobilisation occurring at late pregnancy could be more responsible for this negative balance than lactation effort.

In fact, negative balances have sometimes been detected during first lactation; especially in non-pregnant rabbit does which promote milk yield more than body recovery in late lactation (Parigi-Bini *et al*., 1996; Xiccato *et al*., 1999; Pascual *et al*., 2002; Bolet and Fortun-Lamothe, 2002). Under these conditions, Pascual (2006) indicated the suitability of energy diets that clearly increased the energy intake of does in lactation (+15%; Pascual *et al*., 1998), although energy seems to be used more to increase their productivity (Pascual *et al*., 1999) than to recover their body condition.

However, the energy balance during lactation seems to be different in the case of multiparous rabbit does, where no relevant energy deficit seems to occur (Pascual, 2006). Furthermore, fat mobilisation during lactation was sometimes difficult to correlate with the lactation effort (reproductive rhythm, litter size, milk yield, …), with no significant differences in body condition at weaning being detected in spite of the different feeding and management programmes used (Theilggard *et al*., 2009; Pereda, 2010). In these two experiments, and regardless of the differences in body condition at partum, animals seemed to reach a similar target level of body fatness at weaning. Similar results were observed by Garnsworthy and Topps (1982) in dairy cows, where females with different levels of body fatness at calving, receiving the same feed and yielding similar amounts of milk, reached the end of the milking period with similar body condition scores. As a possible explanation for the different energy balance behaviour observed in lactating rabbit does, Friggens (2003) proposed that animals could be re-adjusting the size of their body reserves to optimise the cost-benefit trade-off of having this safety factor (an excess of reserves is costly and a deficit of reserves is dangerous). Therefore, the main risk of imbalance for reproductive rabbit does should be those programmes which would not allow recovery of the adequate soma of the female 10 days before partum, as the effort will be strong and inevitable. In fact, one of the factors conditioning the energy intake after weaning is the body condition of the female (Pascual, 2004).

Traditionally, concurrence of lactation and pregnancy has been associated with higher productive effort, and consequently higher body reserves mobilisation. It could be true for young reproductive rabbit does, when energy balance between parturitions is determined (Xiccato *et al*., 1999), as concurrence reduces the weaning to next parturition period and consequently the time needed to prepare the female for the pre-partum mobilisation. However, lactation-pregnancy concurrence has frequently been associated with the recovery of body reserves during late lactation, as pregnant rabbit does increase their priority to store reserves for the next litter, the main consequence being the reduction of milk yield (priority for the current litter).

Theilgaard *et al*. (2006) observed how the relative risk of culling was significantly ($P<0.001$) higher from weaning to kindling (7.16) than during lactation (2.44) and empty state (1.00) in reproductive rabbit does. Rosell and de la Fuente (2009), analysing the data on 366,162 females from 18 commercial farms, described the gestation stage as one of the main factors affecting mortality, with the risk of mortality per day being increased as pregnancy progressed and reaching maximum around kindling.

The evidence of the negative effect of fat reserves being too low is clear, as this may imply insufficient resources to be mobilised, but animals carrying excess fat reserves may also show a negative effect. For example, animals which are very fat at parturition have a higher risk of metabolic diseases and lower feed intake in early lactation (pigs: Revell *et al*., 1994; Brandt *et al*., 1999; cows: Broster and Broster, 1998; rabbits: Pascual *et al*., 1999). Theilgaard *et al*. (2006) analysed the relative risk of reproductive rabbit does being culled on the basis of their fatness level at the maximum body condition day in lactation (Figure 3).

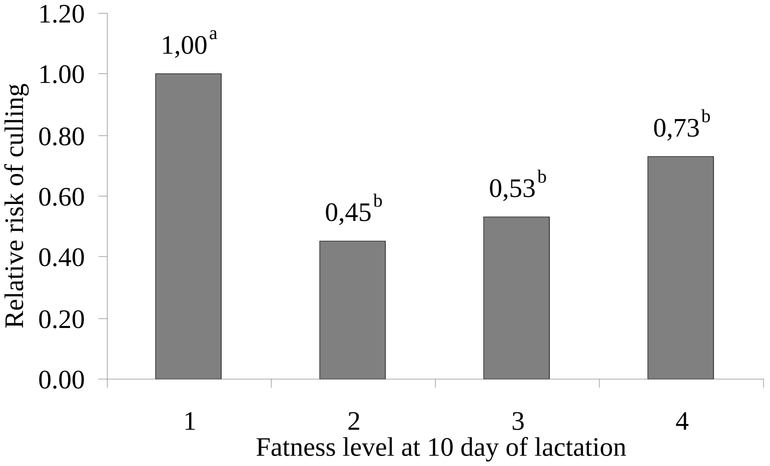

Figure 3 – Relative risk estimates of being culled of reproductive does over 6 reproductive cycles according to fatness level (adapted from Theilgaard *et al.*, 2006)

They observed that the highest reproductive cost in terms of survival was found for the animals belonging to the lowest fatness group. This could indicate that the animals also need a certain amount of fat in early lactation to ensure enough resources to maintain the litter without loss in other body functions, such as lifespan cost. In addition, and although no significant differences were found, relative risk of being culled increased along with the fatness level. The higher risk of culling for both the highest and the lowest fatness groups suggests that there is an optimum level of fat reserves where reproduction has a lower cost, and that perhaps animal deviations from this optimum level could have negative consequences in reproduction.

GENETIC SELECTION AND RESOURCE ALLOCATION

Through genetic selection programmes, a considerable improvement in the productive level of our animals is being achieved. However, in some species it is frequently observed that selection by exclusively productive criteria has had some associated effects, such as lower fertility, higher rates of metabolic diseases in the animals and lower viability of their offspring (in dairy cows, Royal *et al*., 2002; sows, Dourmad *et al*., 1994; hens, Lui *et al*., 1995). Meat rabbits are no strangers to this phenomenon, since some selected lines present worse reproductive rates, the replacement rate of breeding females is around 110% (Rosell and de la Fuente, 2009) and one major handicap in rabbit production is the frequent appearance of digestive disorders in the kits after weaning (Rosell, 2003).

Selection for growth rate

One example of the possible effects of selection on reproduction is the selection for growth rate. Feed conversion ratio during the growing period is one of most important traits to be considered for genetic selection, as post-weaning feeding constitutes around 40% of total production costs in rabbit farming (Baselga and Blasco, 1989). As selection for feed conversion ratio is expensive and the expected genetic correlation with growth rate is high −0.61 to −0.68 (Lampo and Van der Broeck, 1975; Randi and Scossiroli, 1980; Moura *et al*., 1997), genetic selection programmes of paternal lines in rabbits have traditionally focused on selection for growth rate. However, recent works have highlighted that this genetic correlation seems to be lower (−0.48, even with phenotypic correlations lower than −0.20), questioning indirect selection (Piles *et al*., 2004).

In any case, it is well accepted that genetic groups coming from lines selected for growth rate are heavier, have greater growth rate and feed intake and show better feed conversion ratio than those coming from lines selected for litter size (Orengo *et al*., 2009). In consequence, animals from these paternal lines have a tendency to show higher fatness level (Larzul *et al*., 2005; Pascual and Pla, 2007). Although there is evidence of the importance of body reserves for reproduction, an excessive fatness has also been related to negative effects on reproduction (Theilgaard *et al*., 2006). For example, in swine, the fattest sows at mating time had fewer piglets at parturition and weaning (Tibau *et al*., 2003), or in dairy cattle, where females with higher fat reserves presented delayed oestrus (De Vries and Veerkamp, 2000). On the other hand, daily gain has been observed to be low or negatively associated with longevity (Theilgaard, 2006). For example, López-Serrano *et al*. (2000) obtained negative correlations between daily gain and stayability both in Large White and Landrace sows (−0.06 and −0.32, respectively), and similar results of low or negative correlation were observed by Tholen *et al*. (1996) in an Australian pig population (0.02 to −0.13).

In female rabbits, it has been observed that an intermediate body fat level is optimum for fertility and that when the fat level is lower or higher than this level, it leads to a reduction in fertility of around 10-12% (Castellini *et al*., 2006). Paternal lines selection is done according to daily weight gain in the fattening phase, and some of these lines currently present deterioration in their reproductive features, which are clearly inferior to maternal lines (Khalil and Baselga, 2002). However, estimates of genetic correlations within breeds given in the literature (Camacho and Baselga, 1990; Gomez *et al*., 1998; Garreau *et al*., 2000; García and Baselga, 2002a; Piles and Tusell, 2012) among litter size or fertility and growth traits are low or zero.

The majority of these paternal lines are addressed to AI, and the most recent results associate a possible increase in abnormal spermatozoa and a high risk of fertility problems with the increase in weight of the breeding bucks (Du Plessis *et al*., 2010). On the other hand, individuals with higher weight present a drop in androgen levels and high levels of oestrogens (Hammoud *et al*., 2008), and obesity affects the GnRH-LH-FSH pulses, altering Leydig and Sertoli cell functions, and in turn modifying sperm maturation (Bélanger *et al*., 2002). These modifications in the hormone profiles could explain the increased risk of altering the seminal parameters in males as their weight increases (Hammoud *et al*., 2008).

These controversial results reveal the importance of further scientific research into the possible effect of selection for growth rate on resource allocation and the possible effect on reproduction and lifespan, as well as on the genetic relationships of growth rate and reproduction (Garreau *et al*., 2004).

Selection for litter size

From the above proposed deductions for body condition and reproduction relationship, it could be expected that selection for improved litter size (reproduction), frequently used in rabbits (García and Baselga, 2002a, 2002b; Tudela *et al*., 2003), should have changed the ability of rabbit females to obtain resources. On the contrary, negative consequences on body condition and survival should be expected.

Using freezing and transfer techniques (García-Ximénez *et al*., 1996), Quevedo *et al*. (2005 and 2006b) studied the effect of selection for litter size at weaning on the performance and physiological and productive characteristics of rabbit does by the contemporary comparison of crossbred does with 12 generations of differential selection (Table 1). As mentioned above, current females presented a greater number of live-born kits (+1.1 kits) than older ones. However, when these females are subjected to the same productive pressure (standardised litter), differences in feed intake and milk production are observed at the onset of lactation in favour of the animals selected more for litter size.

Table 1 – Effect of selection for litter size at weaning on reproductive does and their litters (adapted from Quevedo *et al*., 2006b)

Type of females		Old	Current
Nº born alive:	Primiparous	8.31^a	10.76^b
	Multiparous	9.18	9.90
Intake (g DM $kg^{-0.75}$ d^{-1}):	0-21 d lactation	113^a	117^b
	21-28 d lactation	112	112
Milk production (g d^{-1}):	0-7 d lactation	156^a	165^b
	8-28 d lactation	215	218

[a,b] Measures without letters in common are significantly different at P<0.05.

These results could explain a possible change in the use of available resources by the animal as a result of the selection. In this way, when selecting the animals by litter size at weaning, we would be selecting both prolificacy (and in fact more kits are born) and maternal aptitude criteria (survival of the kits). Survival in lactation is mainly determined by what happens in the first days after parturition, and is clearly related to the ingestion of energy by the kits in that period, which is why the increase in milk production as a result of the greater ingestion of the does would be favourable.

Mammals have evolved a breeding strategy where they fuel their reproduction from energy gained earlier and stored in body reserves. The body reserves are subsequently used to sustain the reproduction cycle, usually at the time of greatest energy demand, e.g. to ensure foetal growth at late pregnancy or nursing in the form of milk for the litter at early lactation. Selection experiments show evidence of a relationship between reproduction and body reserves, as selection for prolificacy increases the demand of energy to the litter; selection for litter size therefore increases body fatness (e.g. pigs: Holl and Robinson, 2003; Estany *et al.*, 2002). In fact, Quevedo *et al.* (2005) proposed a possible increase in the efficacy of use of energy feed for foetus growth as a consequence of selection by reproduction criteria (0.29 and 0.33 for old and current does, respectively). The product of pregnancy was clearly higher in the selected does, despite they not showed greater energy ingestion, nor greater mobilisation of reserves. In addition, Quevedo *et al.* (2006b) observed that more selected animals for litter size presented a greater PFT at 10th day of lactation (+0.12±0.06 mm; $P<0.05$), considered as the maximum body condition day. Thus, it could be that the selection of the animals by reproduction has produced a response correlated in the capacity of the animals to obtain resources (van Noordwijk and de Jong, 1986; Reznick *et al.*, 2002).

Similar results have recently been obtained by Savietto (2013), where more selected rabbit females (plus 20 generations of selection for litter size at weaning), under conditions of unlimited resources, presented a significantly higher daily feed intake and milk yield in the first week of lactation, and a lower milk yield in the last week of lactation. Friggens (2003) proposed that maternal investments for the current litter reach the maximum around parturition in order to contribute to the viability of the newborn litter (Figure 4). Selection for litter size at weaning could have affected the relative priority for the current litter, flattening the shape around kindling to ensure adequate development of larger but probably less mature litters.

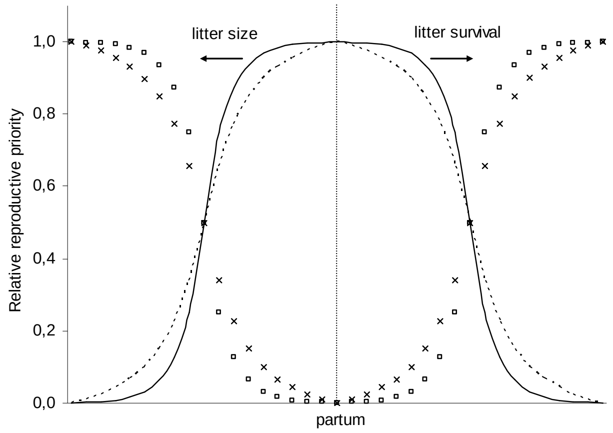

Figure 4 – Proposal for evolution of the relative reproductive priority for the current [less (······) and more (——) selected for litter size] and future litter [less (× × ×) and more (☐ ☐ ☐) selected for litter size] in rabbit females from conception to weaning. The priority accorded the current litter is assumed to be the maternal investment rate scaled from 0 to 1 (Friggens, 2003)

Increasing priority for the current litter at the end of pregnancy leads to an extra effort to ensure adequate foetal development, which could be related with the higher reduction in the lactation effort observed at the end of lactation in the previous reproductive cycle and the high mobilisation observed at the end of pregnancy in this species (Savietto, 2013). In addition, the flattening of the priority shape would allow a greater maternal investment after parturition (higher milk yield), as kit survival index is mainly determined by what happens in early life, being clearly related with the energy intake of kits during these days (Quevedo *et al*., 2006b). After that, priority for the current litter would be reduced, as producing milk in excess of that required for the litter –when it becomes progressively less dependent on maternal milk– will not improve the litter's chances of survival.

Therefore, when prolific animals are selected for reproduction, those characteristics of the animal that ensure their selection success, which we could call "the number", such as prolificacy and the ability to manage the resources more appropriately when they are not limited, seem to be enhanced to ensure the viability of their larger litter but without negative effects on the future one.

However, under a nutritionally restricted environment, Savietto (2013) observed how more selected animals for litter size at weaning showed a higher delay in adjusting their feed intake to compensate low dietary DE content, which also led to a lower milk yield. In contrast, the main female body traits controlled were less affected by the feeding restriction in more selected animals. These results seem to indicate that selection for litter size could increase the susceptibility of animals to this type of environmental challenge, which led to a change in nutrient partitioning to reduce the performance under this situation of restriction.

But why does selection for litter size lead to more environmentally sensitive animals? As proposed above, the fitness characteristics enhanced under this selection criterion are "the number". When the resources available are limited at the present, the success of the current litter could be questioned, so the animal probably decides to reduce the priority for the current litter (relatively addressing a lower amount of resources to those traits directly related to the current litter performance, such as energy intake and milk yield), while the next litter seems to be prioritised (relatively increasing the fuel for the future litter, the body reserves). Therefore, when animals are selected for reproductive traits such as litter size and the resources available are limited to the present, they are unable to ensure the success of the current litter, so maternal investment for the current litter is reduced (and in consequence the animals are less robust –or more sensitive to the environment–) to concentrate their efforts on ensuring the next one (Friggens, 2003), when perhaps resources and environment could be improved.

Selection for longevity

Longevity reflects the animal's ability not to be culled or die. The main culling reasons in animal production include diseases, low fertility and low production (Vollema, 1998). In recent decades there has been a considerable rise in livestock production per animal. This increase is largely due to successful selection for productive traits (e.g. milk yield, growth, litter size) in combination with an improved dietary formulation and management. Focusing almost exclusively on production traits has had some associated negative side effects such as lower fertility, higher frequency of metabolic diseases for the animal and lower viability of the offspring. However, positive relationships between productive traits and longevity are also still frequently reported (Lynch and Walsh, 1998). So, it is still not clear when to expect positive or negative relationships between production, reproduction and survival.

In rabbit production, the main traits of interest are growth rate, litter size and fertility. Selection for reproduction performance has so far not been reported to have negative consequences on longevity. For example, it was reported that high litter sizes were positively associated with longevity in meat type does (Garreau *et al*., 2001; Sánchez *et al*., 2006). Also, in an experiment comparing a rabbit line selected for litter size over seven generations with a control line, no difference in longevity was found (Rinaldo and Bolet, 1988). The only work in rabbit production estimating the genetic correlation between reproductive performance and survival found that this correlation was no different from zero (Sánchez *et al*., 2006).

Recently, Theilgaard *et al*. (2007) evaluated genetic differences in reproductive performance and body condition traits during successive parities between a longevous productive (LP) line [consisting of hyper selection of animals with an extremely high number of parities (at least 25) and an average reproductive performance] compared to a line (V) selected for 31 generations for litter size at weaning. Both lines were found to have an equal reproductive performance in the first three cycles, but when animals were subjected to a non-programmed restricted environment (change of nutritional management to feed restriction after weaning) in one of the farms from the third reproductive cycle, litter size at birth of V line females was depleted as of this moment, while those from the LP line maintained their prolificacy at the expense of a reduction in their greater soma (Figure 5). Theilgaard *et al*. (2007) hypothesised that the higher body soma of adult LP females (+250 g than adult V females) allows them a greater body buffer capacity, reducing their environmental sensitivity.

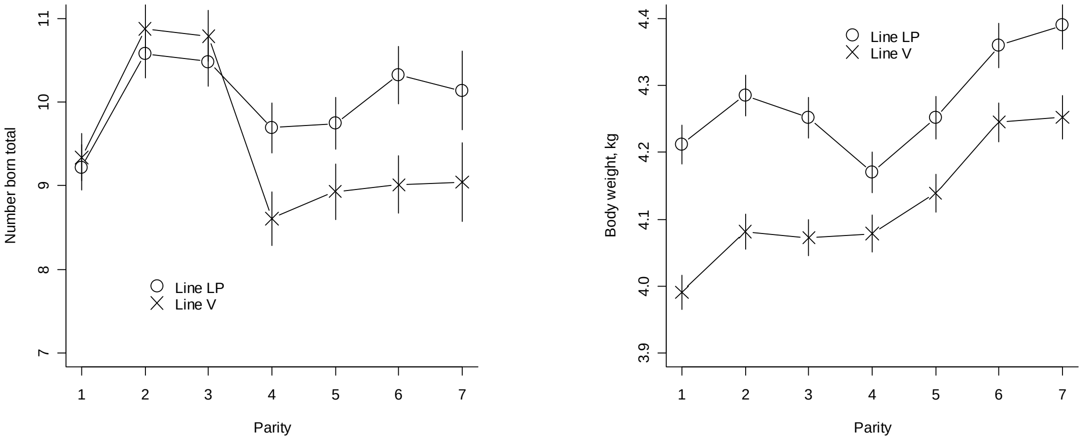

Figure 5 – Effect of genetic line (LP and V) on the evolution of the total number born and female body weight at partum (adapted from Theilgaard *et al*., 2007)

Therefore, hyper selection for reproductive longevity and average prolificacy could delay reproductive senescence, as this newly founded line seems to show less environmental sensitivity. Nevertheless, no indication of a trade-off between reproduction and survival was found in these experiments in any case. When sufficient resources are provided, the female should be better able to meet the demands of both reproduction and maintenance without compromising either. Failure to provide enough energy for maintenance will have a deteriorative effect on her physiological condition, and continued reproduction under such conditions will likely increase the susceptibility to disease and other stress factors (Friggens, 2003). So, these animals might be less robust and show an increased susceptibility to disease, other stress factors and eventual failure.

In rabbits, Theilgaard *et al*. (2007) observed that the LP line was heavier than the V line (4.27 vs. 4.12 kg; $P<0.05$) throughout 6 reproductive cycles, in agreement with experiments where selecting for reproductive longevity in mice (Nagai *et al*., 1995) and on late reproduction in flies (Partridge and Fowler, 1992) also increased BW, suggesting that selection for longer life favours extended growth to produce a more durable adult soma.

To confirm these results, Theilgaard *et al*. (2009) compared the performance and body condition traits of LP and V does subjected to different productive effort levels (previous AI at partum or weaning, and litter sizes of 5 or 9 pups) during their second lactation. LP does were again significantly heavier than the V line, but also showed a better body condition (+0.50±0.09 mm of PFT; $P<0.05$) and a lower mobilisation (-0.11±0.03 mmol of NEFA/L; $P<0.05$) at the beginning of lactation, confirming the greater soma of this type of animals to confront productive and environmental challenges. In fact, LP does showed a greater milk yield than V does, even per kg of metabolic weight (+5±2 g kg^{-1} $BW^{0.75}$ day^{-1}; $P<0.05$), and especially when lactation pressure increased (9 pups).

This greater soma of rabbit females selected for reproductive longevity seems to allow them to better cope with the possible productive challenges that they may meet in the course of their productive life. They seem to present a greater plasticity, enabling them to use their greater soma to overcome these demanding situations, reflected in the fact that the greater the productive effort, the lower the differences observed in BW between lines. So, rabbit females selected for reproductive longevity are more “robust” in these situations (more milk for the offspring) and their risk of early culling for low productivity is consequently reduced.

Robustness

It seems that when the availability of resources is not limited, more selected animals can successfully cope with most of their higher needs without too many negative consequences. In fact, it is not uncommon to find even positive relationships between productive traits and survival for reproductive stock when animals were reared under controlled environment, i.e. for cows (Short and Lawlor, 1992), sows (Serenius and Stalder, 2004) and rabbit does (Theilgaard *et al*., 2006). However, it is when animals suffer discrete but not infrequent and even cyclical suboptimal environments (i.e. resources limitation, heat stress, immunological challenge) that the greater susceptibility of high producing animals to these stressing conditions appears (Schinkel *et al*., 1999; De Greef *et al*., 2001; Yalcin *et al*., 2001; Windig *et al*., 2005).

Knap (2005) defined the concept of robustness in a farm animal as ‘the ability to combine a high production potential with resilience to stressors, allowing for unproblematic expression of a high production potential in a wide variety of environmental conditions. From the results discussed above, it could be hypothesised that perhaps selection in rabbits for only reproductive criteria could have affected the ability of the animals to maintain their reproductive level under stressing environments, while the inclusion of longevity criteria in the constitution of the line could have helped increase their robustness.

With this aim, Savietto (2013) has recently evaluated how selection for litter size at weaning (line V) or the foundation for reproductive longevity criteria (LP line) could have affected the ability of animals to confront restricted resources conditions, by the use of a low-energy diet, during their first two reproductive cycles. The results of this work show how, when resources were limited, LP females compensated the lower dietary energy with a higher daily feed intake even at the first lactation, while daily energy intake of V females was significantly lower than that observed under non-limiting conditions. So, LP females were able to maintain their milk yield, litter growth and body condition unaffected, as well as the litter size at the second kindling, while V36 females reduced their milk yield trying to maintain their body condition and next litter size. During the second lactation, LP females had a lower milk yield than that observed under non-limiting conditions but without any negative effect on their body condition or on the litter performance at third birth, while V36 females in restricted conditions presented a continuous worsening of their main performance traits (milk yield and body condition), with the size of their litters at the third kindling clearly being affected (–1.8 and –2.6 total and alive kits born, respectively; $P<0.05$).

For a better picture of environment sensitivity, the response graphs in Figure 6 represent the effect of genotype (V or LP) on dietary energy intake, body reserves and kits born alive depending on the dietary energy (normal or restricted). As can be seen, the response to environment restriction of females coming from a line founded for reproductive longevity criteria was flatter than those obtained for females selected for litter size at weaning in all the traits controlled, highlighting their differences in robustness. Under non-limiting conditions, females selected for reproduction show their superiority in prolificacy, but when environment quality decreases these animals show greater reduction in their ability to obtain resources, maintenance of body reserves and reproductive performance.

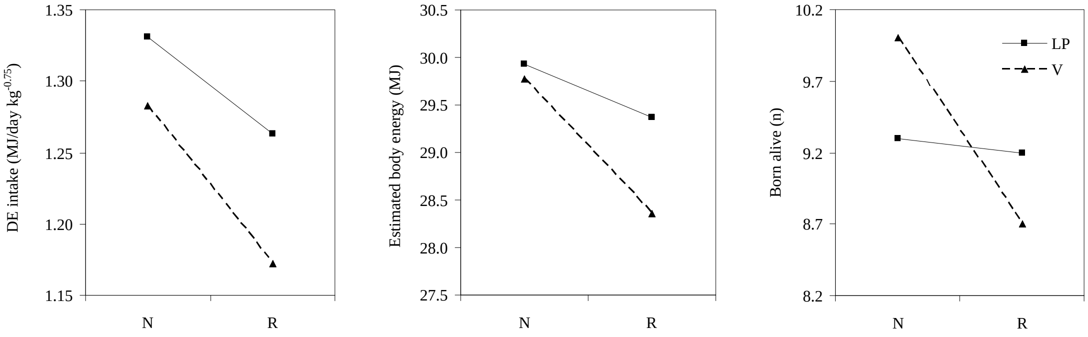

Figure 6 – Effect of genetic type (■ LP and ▲ V) on average estimated body energy, digestible energy (DE) intake and number of kits born alive (second and third kindling) according to dietary environment [normal (N) *vs.* restricted (R)]

In other species, signs of reduced robustness have also been observed in highly productive stocks (Rauw *et al.*, 1998; Knap and Rauw, 2009; Siegel *et al.*, 2009; Veerkamp *et al.*, 2009), supported by the resource allocation theory (Beilharz, 1998; Glazier, 2009) – the energetic resources of an individual are limited and their allocation across metabolic functions is optimised towards the best adaptation of the individual to its environment (fitness). Therefore, when we genetically select for reproduction traits, resources could logically be redirected towards these reproduction traits at the expense of other traits (such as robustness traits), which leads to genotype×environment interaction. However, resource allocation theory also considers the possible development by the animals of nutrient partitioning strategies, which allow them to obtain additional resources for optimised reproduction without a robustness penalty, or to optimise the allocation of resources through time to ensure their fitness success.

These results highlight the improvement in robustness characteristics when rabbits are selected or founded for reproductive longevity criteria. These criteria would provide the animals with additional tools for more appropriate management of the available resources under conditions of high productive effort (Theilgaard *et al.*, 2009) and/or nutritional challenge. Therefore, while animals selected for reproduction clearly seem to be more sensitive to the nutritional challenge, robust females were able to maintain most of their reproduction traits unaffected, which could help confer their reproductive longevous character.

Another component in the definition of the female's lifespan is her susceptibility to the common diseases that could appear on the rabbit farms. Possible changes in resource allocation as a consequence of genetic selection or reproductive management should lead the female to situations where body condition could be withdrawn from the adequate level, increasing the susceptibility of animals to occasional immunological challenges. For example, the greatest drop in body reserves takes place at the end of gestation, which is the time of greater elimination of commercial does on the farm (Rosell and de la Fuente, 2009) and the lowest B lymphocyte counts in blood (Ferrian *et al.*, 2012), and an excessive falloff of the reserves at parturition conditions the success of mating during the following lactation (Quevedo, 2005; Savietto, 2013). These results would reflect the importance of not moving too far from the appropriate body status to ensure reproduction and reduce the risk of elimination. Thus, Guerrero *et al.* (2010) and Ferrian *et al.* (2012) observed a positive correlation between the body status of the rabbit does and the population of B lymphocytes (from +0.40 to +0.82) and that there is a positive correlation between the lymphocyte populations of the does and their litters (e.g. T CD5+: +0.35). Moreover, there is a maternal effect on the definition of the digestive microbiota of the kits (Abecia *et al.*, 2007) and a litter (and/or maternal) effect on the rate of digestive disorders in growing rabbits (Quevedo *et al.*, 2003; Carabaño *et al.*, 2006).

In other species, there is evidence that susceptibility to immune challenges may be different depending on the genetic diversity (Rauw *et al.*, 1998; Siegel and Honaker, 2009). There, it is possible that this "more robust" type of animals may also have a greater capacity to withstand immune challenges, and that the introduction of this type of animals could improve the general health conditions on the farm. In rabbit does, Ferrian *et al.* (2012) recently reported how selection for litter size over 20 generations could have reduced the average counts of total and B lymphocytes in blood (–17 and –36%, respectively; $P<0.05$), mainly due to the decrease of these populations in the blood of more selected females from the first to the second parturition. In addition, this work also reported an increase in the lymphocyte counts (total and T CD5+) of "more robust" females under heat compared to normal conditions when lymphocyte populations showed the lowest value (second parturition), while "less robust" females counts remained invariable. Other recent works (Savietto *et al.*, 2011; Ferrian, 2012) would show indications in favour of the theory about a possible improvement of the immune system modulation in robust animals (lower susceptibility to challenge with LPS, or lower mortality of their kits during the fattening period), although further research efforts should be made in the future to confirm this matter.

CONCLUSIONS

The present review has provided enough evidence about how nutrient partitioning between the different metabolic functions throughout rabbit female life is genetically driven. Consequently, resource allocation in the rabbit female takes place to ensure their genetic selection success at all times. Therefore, if rabbit females have been selected by a reproduction criterion, such as viable litters produced in a lifetime, nutrient partitioning is defined as the optimal trade-off between the maternal investment addressed to the current and the future litter, to maximise the number of viable litters produce in a lifetime. On the other hand, the constitution of a line through high selection intensity in its foundation by reproductive longevity has led to rabbit females characterised by a higher robustness. Particular nutrient partitioning in these robust females enables them to better cope with the possible reproductive, environmental and immunological challenges that they may meet in the course of their productive life, which could explain their greater life expectancy on the farm.

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