Maternal Protein Restriction Impairs Offspring Growth and Neuromuscular Development: Evidence from a Controlled Murine Model

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Abstract. Maternal nutrition during gestation is a critical determinant of offspring developmental trajectories, particularly in relation to early neuromuscular function and subsequent physical performance capacity. Protein deficiency, a prevalent form of chronic undernutrition in developing contexts, has been associated with intrauterine growth restriction and long-term impairments in musculoskeletal and metabolic systems [1], [2]. This study aimed to investigate the impact of maternal low-protein intake on early physical development using a controlled murine experimental model. A total of ten adult female mice were randomly allocated to either a low-protein diet group (LP; n = 5) or a standard diet group (SD; n = 5) throughout gestation. Maternal body weight was assessed pre- and post-pregnancy, while reproductive outcomes, including litter size and offspring birth weight, were recorded immediately after delivery. Statistical analysis was performed using the non-parametric Mann–Whitney U-test with a significance threshold set at $p < 0.05$. The findings demonstrated no statistically significant difference in maternal pre-gestational body weight between groups ($p = 0.511$), indicating baseline homogeneity. However, a significant reduction in post-gestational maternal weight was observed in the LP group ($p = 0.034$), suggesting increased metabolic strain under protein restriction. Although litter size was lower in the LP group, the difference did not reach statistical significance ($p = 0.091$). Notably, offspring birth weight was significantly reduced in the LP group ($p < 0.001$), reflecting impaired fetal growth. These results provide empirical evidence that maternal protein deficiency negatively affects early growth parameters, which are strongly associated with delayed neuromuscular maturation and reduced functional movement capacity [3], [4]. From a sport science perspective, suboptimal early development may predispose individuals to diminished physical fitness, lower muscle mass accretion, and reduced exercise performance in later life stages. In conclusion, adequate maternal protein intake during pregnancy is essential to support optimal fetal growth and to establish a foundation for neuromuscular efficiency and long-term physical performance potential.

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These findings reinforce the importance of maternal nutritional interventions as a preventive strategy to enhance population-level physical capacity and athletic development.

Keywords: Maternal nutrition; Protein deficiency; Fetal growth; Birth weight; Neuromuscular development; Developmental origins of health and disease (DOHaD); Murine model; Physical performance capacity; Early-life programming; Sport science.

1 Introduction

Maternal nutrition during pregnancy constitutes a fundamental determinant of fetal growth trajectories and long-term developmental outcomes. Insufficient intake of essential macronutrients, particularly protein, has been consistently associated with impaired intrauterine development and an elevated risk of growth retardation, including stunting during early childhood [1], [2]. Stunting remains a persistent global health challenge, disproportionately affecting low- and middle-income countries, where maternal undernutrition continues to compromise pregnancy outcomes and child development indicators. Beyond somatic growth, emerging evidence suggests that prenatal nutritional inadequacies may also disrupt early neuromuscular development, thereby influencing movement capacity and functional performance in later life stages.

Protein is a critical substrate for fetal tissue synthesis, skeletal muscle formation, and metabolic regulation. Maternal protein restriction during gestation has been shown to interfere with fetal programming processes, resulting in reduced birth weight and suboptimal development of organ systems, including musculoskeletal structures [3], [4]. These developmental alterations may persist postnatally, affecting motor coordination, muscle strength, and overall physical capacity. Within the domain of sport science, early biological constraints are increasingly recognized as influential determinants of motor competence, which is a strong predictor of sustained participation in physical activity and athletic performance across the lifespan [5].

Recent developments in developmental physiology and exercise science emphasize the integrative role of prenatal conditions in shaping movement behavior. Motor development is not solely dependent on environmental stimulation or pedagogical interventions; rather, it is also biologically embedded through early-life processes that influence neuromuscular readiness and motor unit recruitment efficiency [6]. Children experiencing suboptimal fetal growth are more likely to exhibit delayed acquisition of fundamental motor skills, reduced coordination efficiency, and lower engagement in structured physical activity, which may ultimately limit their sport performance potential [7]. This evidence underscores the importance of incorporating prenatal nutritional variables into sport science frameworks to better understand the origins of movement competence.

Controlled experimental models, particularly murine studies, provide a robust methodological approach for examining the causal relationship between maternal diet and offspring development. Such models enable precise manipulation of dietary variables and facilitate the observation of physiological adaptations under standardized conditions, thereby offering valuable insights into developmental programming mechanisms [8]. Investigating the effects of maternal low-protein intake within this experimental framework allows for a more detailed exploration of how early nutritional constraints influence growth outcomes and neuromuscular development.

Accordingly, this study aims to examine the impact of maternal protein restriction on offspring growth parameters, with particular emphasis on birth weight and early developmental indicators relevant to movement capacity. By integrating perspectives from nutritional science and sport physiology, this research contributes to a growing body of literature that positions early-life biological conditions as foundational determinants of motor competence and long-term physical performance. The findings are expected to inform both preventive health strategies and sport development models, particularly in populations at risk of maternal undernutrition.

2 Method

2.1 Experimental Design

This study employed a laboratory-based experimental design using a controlled murine model to investigate the effects of maternal protein restriction on offspring growth and early developmental indicators. An experimental approach was selected to enable precise manipulation of dietary intake and systematic observation of physiological responses under standardized conditions. Animal models are extensively used in developmental and nutritional research due to their biological comparability, short reproductive cycles, and high reproducibility in studying early-life programming mechanisms [1], [2].

2.2 Subjects and Ethical Considerations

The study involved ten healthy adult female mice (Mus musculus), aged 8–10 weeks, with a body mass ranging from 20 to 25 g. All animals were housed under controlled laboratory conditions, including a 12-hour light/dark cycle, ambient temperature maintained at 22 ± 2°C, and unrestricted access to water and assigned diets. Experimental procedures were conducted in accordance with internationally recognized guidelines for the care and use of laboratory animals and were approved by the institutional animal ethics committee. Compliance with ethical standards is critical to ensure both animal welfare and the reliability of experimental outcomes [9].

2.3 Dietary Intervention Protocol

Subjects were randomly allocated into two experimental groups: a low-protein diet group (LPD; n = 5) and a normal-protein diet group (NPD; n = 5). The LPD group received a diet containing approximately 8–10% protein, while the NPD group was provided with a standard diet containing 18–20% protein, consistent with established nutritional intervention protocols in rodent studies [4]. The dietary treatment was initiated prior to mating and maintained throughout the gestation period to simulate chronic maternal protein deficiency during pregnancy. This protocol was designed to capture the critical window of fetal programming, during which nutrient availability significantly influences organogenesis and musculoskeletal development [10].

2.4 Outcome Measures and Data Collection

Maternal body weight was recorded at baseline (pre-gestation) and immediately after parturition to assess physiological changes associated with pregnancy and dietary treatment. Following delivery, reproductive outcomes were documented, including litter size (number of pups per dam). Each offspring's birth weight was measured using a calibrated digital precision scale with an accuracy of 0.01 g. Birth weight was selected as the primary indicator of early growth status, given its strong association with neuromuscular maturation, muscle fiber development, and subsequent physical performance potential [5], [6].

2.5 Statistical Analysis

Data analysis was performed using non-parametric statistical methods due to the limited sample size and potential non-normal distribution of variables. The Mann–Whitney U-test was employed to compare differences between the LPD and NPD groups because of the limited sample size and distribution characteristics of the data, consistent with recommendations in statistical methodology literature [11]. Statistical significance was established at $p < 0.05$. All analyses were conducted using validated statistical software to ensure accuracy, reproducibility, and methodological transparency [7].

3 Results and Discussion

3.1 Maternal and Offspring Outcomes

The experimental results indicate that maternal protein restriction significantly affects maternal physiological adaptation during gestation and subsequently influences offspring growth outcomes. As summarized in Table 1, no statistically significant difference was observed in pre-gestational maternal body weight between the low-protein diet (LPD) and normal diet (ND) groups ($p = 0.511$), confirming baseline comparability. However, a significant reduction in post-gestational maternal body weight was identified in the LPD group ($p = 0.034$), suggesting increased metabolic burden and insufficient nutrient reserves during pregnancy.

Although the mean litter size in the LPD group was lower than that of the ND group, the difference did not reach statistical significance ($p = 0.091$). This finding suggests that maternal protein restriction may not markedly impair reproductive capacity in terms of offspring quantity, but rather exerts a more pronounced effect on fetal growth quality. Similar patterns have been reported in developmental nutrition studies, where nutrient limitation primarily affects fetal growth parameters rather than fertility outcomes [1], [2].

Table 1. Maternal Body Weight and Reproductive Outcomes

Variable	Low-Protein Diet (n=5)	Normal Diet (n=5)	p-value
Weight before pregnancy (g)	26.8 ± 0.83	26.4 ± 1.14	0.511
Weight after pregnancy (g)	25.6 ± 1.14	28.0 ± 1.58	0.034*
Offspring number	6.2 ± 1.3	8.2 ± 1.92	0.091

*Significant at $p < 0.05$

3.2 Offspring Growth and Implications for Motor Development

A principal finding of this study is the significant reduction in offspring birth weight in the LPD group ($p < 0.001$), as presented in Table 2. Birth weight is widely regarded as a sensitive indicator of intrauterine growth and an important predictor of subsequent neuromuscular development [12].

From a physiological perspective, Reduced birth weight is indicative of impaired myogenesis and may adversely affect skeletal muscle development and subsequent physical performance capacity [13]. These structural limitations may hinder the development of fundamental motor skills such as locomotion, postural control, and object manipulation. Within sport science, such impairments are directly linked to reduced motor competence, which is a critical determinant of long-term participation in physical activity and athletic performance [4].

Table 2. Offspring Body Weight

Variable	Low-Protein Diet	Normal Diet	p-value
Birth weight (g)	1.14 ± 0.83	2.60 ± 0.46	< 0.001*

*Significant at $p < 0.05$

3.3 Sport Science Interpretation: Developmental Programming of Movement Capacity

The present findings support the theoretical framework of the Developmental Origins of Health and Disease (DOHaD), which explains how prenatal environmental conditions influence long-term physiological outcomes [14]. Maternal protein deficiency during gestation has been shown to influence skeletal muscle morphology, including reduced muscle fiber density and compromised metabolic efficiency [5], [6].

These alterations may translate into diminished physical performance capacity, lower aerobic fitness, and decreased engagement in physical activity during later developmental stages. Empirical evidence from both animal and human studies demonstrates that individuals with restricted fetal growth are more likely to experience delayed motor milestones and reduced physical activity levels [7].

Furthermore, the observed reduction in maternal post-pregnancy body weight reflects increased metabolic stress, which may limit placental nutrient transfer and exacerbate fetal growth restriction. This mechanism aligns with existing evidence on nutrient partitioning and fetal programming, where maternal nutritional status directly influences offspring physiological outcomes [8].

From a sport pedagogy perspective, these findings highlight the necessity of considering prenatal biological factors in the development of motor competence and physical literacy frameworks. Early-life deficits may require compensatory interventions, including targeted motor skill training and adaptive physical education strategies to optimize developmental outcomes.

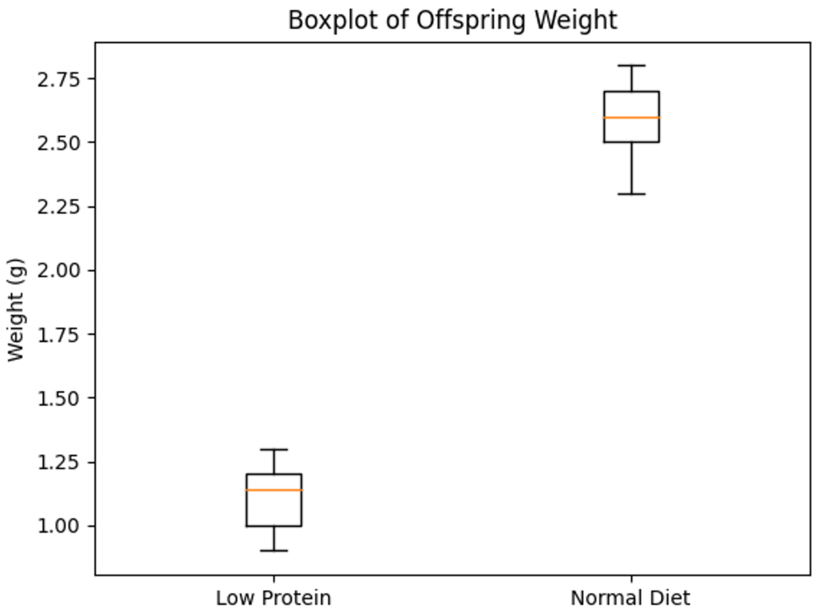

Fig. 1. Boxplot diagram comparing offspring weight between low protein mother diet and normal maternal diet

3.4 Discussion

This study demonstrates that maternal protein intake is a critical determinant of offspring growth, particularly in parameters closely associated with neuromuscular development and movement capacity. While reproductive output was not significantly affected, the substantial reduction in birth weight underscores the sensitivity of fetal growth processes to maternal nutritional status.

In the context of sport science, these findings reinforce the concept that physical performance potential is partially established during prenatal development Motor competence is not solely shaped by environmental exposure but also follows developmental trajectories linking early movement proficiency and later physical activity participation [15]. Consequently, efforts to enhance physical activity participation and sport performance should adopt a life-course perspective that includes prenatal nutritional factors as foundational determinants.

Moreover, low birth weight may serve as an early biomarker for identifying individuals at risk of delayed motor development and reduced physical capacity. This has practical implications for educators and practitioners in physical education, who may need to implement differentiated and developmentally appropriate strategies to support motor skill acquisition.

Despite these contributions, several limitations should be acknowledged. The relatively small sample size may restrict the generalizability of the findings, and the absence of direct functional assessments (e.g., grip strength, locomotor performance, or endurance capacity) limits the ability to establish a direct causal relationship between prenatal nutrition and motor performance. Future research should adopt longitudinal designs and incorporate comprehensive motor function assessments to better elucidate the relationship between early nutritional conditions and long-term physical performance outcomes.

4 Conclusion

This study provides empirical evidence that maternal protein intake during pregnancy is a critical determinant of offspring growth and early physical development. While no significant difference was observed in pre-gestational maternal body weight between groups, maternal protein restriction resulted in a significant reduction in post-gestational body weight, indicating impaired metabolic adaptation during pregnancy. More importantly, offspring from the low-protein diet group exhibited significantly lower birth weight, reflecting compromised intrauterine growth and suboptimal developmental conditions.

From a sport science perspective, reduced birth weight constitutes an early biological constraint that may negatively influence neuromuscular maturation, muscle development, and movement efficiency. These early-life limitations are closely associated with delayed acquisition of fundamental motor skills and altered developmental trajectories in growth and physical activity behavior [16]. The findings therefore reinforce the concept that physical capacity is not solely shaped by postnatal training or environmental exposure but is also biologically programmed during prenatal development.

Furthermore, although reproductive output in terms of litter size was not significantly affected, the substantial decline in offspring growth quality highlights the sensitivity of fetal development to maternal nutritional status. This distinction between quantity and quality of offspring outcomes underscores the importance of adequate nutrient availability during critical periods of fetal programming [3].

In conclusion, sufficient maternal protein intake is essential not only for supporting optimal fetal growth but also for establishing the physiological and neuromuscular foundations necessary for future movement competence and physical performance. These findings have important implications for both public health and sport science, suggesting that maternal nutrition should be integrated into long-term strategies aimed at enhancing physical development, promoting active lifestyles, and improving athletic potential across the lifespan. Future research should incorporate longitudinal designs and direct assessments of motor performance to further elucidate the relationship between prenatal nutrition and functional movement outcomes.

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