Animal 16 (2022) 100587

Contents lists available at ScienceDirect

Animal
The international journal of animal biosciences

Association between the prion protein genotype and animal performance traits in a large multibreed sheep population

N. McHugh [a,*], A.C. O'Brien [a], T. Pabiou [b], K. McDermott [b], D.P. Berry [a]

[a] Teagasc, Animal & Grassland Research and Innovation Centre, Moorepark, Fermoy P61 P302, Co. Cork, Ireland
[b] Sheep Ireland, Highfield House, Shinagh, Bandon P72 X050, Co. Cork, Ireland

ARTICLE INFO

Article history:
Received 27 April 2022
Revised 10 June 2022
Accepted 13 June 2022

Keywords:
Halotype
Scrapie
Selection
Sheep
PrP protein

ABSTRACT

Genetic susceptibility to scrapie, a fatal disease of sheep and goats, is modulated by polymorphisms in the prion protein (***PrP***). Neither the frequency of the *PrP* genotypes nor their association with animal performance has been investigated in a large multibreed Irish sheep population. Scrapie genotypes were available on 16 416 animals; the breeds represented included purebred Belclare (733), Charollais (333), Suffolk (739), Texel (1 857), Vendeen (191), and crossbreds (12 563). Performance data on lambing, lamb and ewe performance as well as health traits were available. The association between alternative approaches of describing the *PrP* genotype (i.e. 15 individually called *PrP* genotypes, five genotype classes representing susceptibility to scrapie, or number of ARR haplotypes) and animal performance were quantified using animal linear mixed models. All 15 of the possible scrapie genotypes were detected, although the frequency differed by breed. The frequency of the five *PrP* haplotypes in the entire population were 0.70 (ARR), 0.15 (ARQ), 0.11 (ARH), 0.02 (AHQ) and 0.01 (VRQ); the most susceptible haplotype (VRQ) was only detected in purebred Texels and crossbreds. No association was detected between the *PrP* genotype of either the animal or dam and any of the lambing traits (i.e. lambing difficulty score, perinatal mortality and birth weight). With the exception of ultrasound muscle depth, no association between the *PrP* genotype and any of the lamb performance traits (i.e. lamb BW and carcass) was observed. Lambs carrying the category four *PrP* genotype (i.e. ARR/VRQ) had 1.20 (SE = 0.45) mm, 1.38 (SE = 0.12) mm, 1.47 (*S* = 0.25) mm shallower ultrasound muscle depth relative to lambs of the less susceptible scrapie categories of 1, 2, 3, respectively ($P < 0.05$). Nonetheless, no association between *PrP* genotype and lamb carcass conformation, the ultimate end goal of producers, was detected. Ewe litter size, body condition score or lameness did not differ by *PrP* genotype of the ewe ($P > 0.05$). For ewe mature BW, ARH/VRQ ewes differed from most other ewe *PrP* genotypes and were, on average, 3.79 (SE = 1.66) kg heavier than ARR/ARR genotype ewes. Lamb dag score differed by dam *PrP* genotype ($P < 0.05$), although the differences were small. Results from this study show that scrapie is segregating within the Irish sheep population, but the *PrP* genotype was not associated with most traits investigated and, where associations were detected, the biological significance was minimal. This suggests minimal impact of selection on *PrP* genotype on performance, at least for the traits investigated in the present study.

Implications

The frequency of each prion protein genotype across a large multibreed sheep population demonstrates that the prion protein genotype is segregating within the population. The most susceptible haplotype (VRQ) was only detected in the Texel and crossbred population, albeit at a low frequency (0.01). The lack of any real biologically significant association between the prion protein genotype and a whole series of animal performance traits suggests minimal impact of selection for prion protein genotype on performance, at least for the traits investigated in the present study.

Introduction

Scrapie, a fatal disease of sheep and goats, is a transmissible spongiform encephalopathy (**TSE**). Scrapie is distinct from other TSEs such as bovine spongiform encephalopathy in cattle or Creutzfeldt-Jacob in humans, as it is naturally transmissible in the wild between sheep and goats. Genetic susceptibility to scrapie in sheep is modulated by polymorphisms in the prion protein (***PrP***) gene all residing on three codons (Belt et al., 1995). The resulting

* Corresponding author.
E-mail address: noirin.mchugh@teagasc.ie (N. McHugh).

https://doi.org/10.1016/j.animal.2022.100587
1751-7311/

PrP genotype has been shown to be associated with an animal's susceptibility to scrapie, with the ARR haplotype associated with resistance, while the ARQ, ARH, VRQ haplotypes are associated with a reduced level of resistance (Hunter et al., 1994; Dawson et al., 1998).

Since the outbreak of BSE in the 1990s, and its potential threat to human health, breeding programmes were implemented in many EU countries with the aim of increasing the frequency of the resistant *PrP* haplotypes in sheep and goat populations. Such a scheme was introduced in Ireland in the year 2002, but the scheme ceased prior to the complete eradication of the most susceptible *PrP* genotypes, however, the frequency of the *PrP* genotypes in a large multibreed national population remains relatively unknown.

Although the relationship between *PrP* genotype and animal performance has been investigated previously, such studies have tended to be based on a limited number of traits or were estimated using relatively small datasets; moreover, these studies tended to focus on a specific trait or breed (De Vries et al., 2005; Sawalha et al., 2007; Sweeney et al., 2007) or when national eradication programmes were in operation (Moore et al., 2009), the latter impacting the genotype frequency. The objective of the current study, therefore, was first to establish the frequency of the *PrP* genotypes in a large multibreed sheep population and secondly, to quantify the association, if any, between the *PrP* genotype and a suite of animal performance traits. Results from this study would be useful in ascertaining whether a new national scrapie monitoring scheme is required and the impact of introducing a scrapie eradication scheme on animal performance and, ultimately farm profitability.

Material and methods

Data

Scrapie genotypes were available on 16 418 unique lambs and sheep from 252 flocks born between the years 2004 and 2019, inclusive. Performance data on a range of animal-specific events, including date of birth, lambing data, lamb BW records, ewe performance parameters on ewe BW, body condition score (**BCS**) and litter size, were also available. All data originated from the Irish national sheep database hosted by Sheep Ireland (https://www.sheep.ie).

PrP genotypes

The *PrP* genotype of each animal was generated from one of two commercially available single nucleotide polymorphism (**SNP**) medium density genotype panels, namely the Illumina OvineSNP50 v2 Beadchip or the Axiom™ Ovine Genotyping 50 K Array. The SNPs on both panels focused on the polymorphic codons 136 (A/V), 154 (R/H) and 171 (Q/R/H) to identify five main scrapie haplotypes ARR, ARH, ARQ, AHQ and VRQ. The calling of the scrapie genotypes from both panels were validated against the gold standard scrapie genotyping from ISO-accredited laboratories based on Sanger sequencing. In brief, 28 animals diverse for scrapie genotypes based on the gold standard scrapie genotype were sent blindly to an accredited genotyping laboratory for genotyping on the SNP panel; the samples were also re-tested in the same laboratory for scrapie genotyping using Sanger sequencing. One hundred percent concordance was obtained between the called scrapie genotypes from the SNP panel and those from the Sanger sequencing in the approved laboratory.

Of the dataset of 16 416 animals in the present study, a total of 15 *PrP* genotypes were called using one of the two validated SNP-based platforms (Table 1). The purebred status of each animal recorded as purebred in the national sheep database was verified using principal component analysis of the SNP data. The resultant *PrP* genotypes were also grouped into the five main genotype categories reflective of their perceived resistance to scrapie and representative of the reporting strategy commonly used to breeders (Table 1). The frequency of the five *PrP* haplotype was calculated for the entire population but also within each breed separately. In addition, the number of ARR haplotypes carried per animal was also calculated for subsequent use in the association analyses; animals were defined as having two copies (i.e. ARR/ARR), one copy (ARR/XXX) or 0 copy (XXX/XXX) based on the number of ARR haplotypes carried by each animal, where XXX represents any genotype other than ARR.

Lambing performance

Three lambing traits were considered in the present study: lambing difficulty score, lamb perinatal mortality and lamb birth weight. Lambing difficulty score is recorded in Ireland by producers for each lambing event on a scale of 1–4 as: 1 = no lambing assistance /unobserved, 2 = voluntary assistance, 3 = slight assistance and 4 = severe assistance (including caesarean). Lamb mortality is recorded by producers based on whether the lamb was alive (mortality = 0) or dead (mortality = 1) within 24 h of birth; genotype information was also available on 314 stillborn lambs. Lamb birth weight is recorded by producers using a weighing scale within 24 h of birth; only lambs with a recorded BW at birth between 2 and 9 kg were retained for analysis. For all lambing traits, contemporary groups were defined as flock-by-week of lambing (McHugh et al., 2017); only contemporary groups with at least five lambs were retained.

Lamb performance

Lamb BW recorded preweaning, at weaning and postweaning were also available; data editing was undertaken as described by McGovern et al. (2020) for an Irish sheep population. In brief, preweaning weight was defined as the BW taken between 20 and 65 days of age; only records of lambs weighing between 12 and 32 kg were retained. Weaning weight was defined as the BW recorded between 66 and 120 days of age; only BW records between 20 and 55 kg were retained. Postweaning weight was defined as BW measured between 121 and 180 days of age; only lambs with BW records between 25 and 65 kg were considered. Muscle and fat depth were also measured on a subset of animals when weighing the animal postweaning; only muscle depth measurements between 20 and 35 mm and fat depth measures between 1 and 15 mm were retained. For all BW and ultrasound observations, each lamb was allocated to a contemporary group of flock-date of weighing or measurement (McGovern et al., 2020). For both BW and ultrasound, only records from contemporary groups with at least five records were retained.

Lamb carcass

Carcass data including date of slaughter, carcass weight, carcass conformation and carcass fat were also available on a subset of 4 256 lambs slaughtered between 95 and 365 days of age. For all carcass traits, lambs were allocated to two contemporary groups; the first contemporary group was defined as flock-week of birth and the second contemporary group was defined as abattoir-date of slaughter; only contemporary groups with at least five records were retained.

Ewe performance

Ewe BCS was evaluated by producers on a one (emaciated) to five (over fat) point scale (Jefferies, 1961) in increments of one unit as described by O'Brien et al. (2017). Ewe BW was defined as the weight of a female who had at least one recorded lambing event;

Table 1
Number of animal records (n), mean (μ; SD in parenthesis), number of sheep flocks, number of contemporary groups (CG), number of sires and dams for each trait.

Trait Group	Trait	n	μ (SD)	No. Flocks	No. CG	No. Sires	No. Dams
Lambing							
	Lambing Difficulty Score (1–4)[1]	10 069	1.71 (0.92)	50	279	526	5 111
	Perinatal Mortality (%)	9 098	3.47 (18.31)	48	253	493	4 752
	Birth Weight (kg)	10 223	4.82 (1.10)	50	284	531	5 200
Lamb Performance							
	Preweaning weight (kg)	9 128	19.96 (3.90)	55	188	554	5 311
	Weaning weight (kg)	9 519	33.72 (5.76)	57	201	549	5 455
	Postweaning weight (kg)	6 098	42.19 (6.70)	49	176	462	3 844
	Muscle depth (mm)	2 757	29.57 (3.73)	45	126	342	2 133
	Fat depth (mm)	2 776	5.95 (1.72)	45	125	341	2 140
Lamb Carcass							
	Carcass weight (kg)	4 256	20.74 (1.74)	11	74	192	2 575
	Carcass conformation (1–5)[2]	4 256	3.37 (0.49)	11	74	192	2 575
	Carcass fat (1–5)[2]	4 256	2.58 (0.55)	11	74	192	2 575
	Age at slaughter (day)	4 256	199.96 (59.77)	11	74	192	2 575
Ewe Performance							
	Body condition score (1–5)[3]	2 404	3.45 (0.93)	20	36	230	861
	Mature weight (kg)	28 790	68.98 (14.01)	70	565	708	4 795
	Litter Size (1–4)	8 148	1.87 (0.73)	51	407	523	3 024
Health							
	Dag score (1–5)[4]	19 896	3.59 (0.87)	60	272	644	4 506
	Ewe lameness (%)	6 118	8.83 (28.37)	23	93	354	1 557
	Lamb lameness (%)	10 589	7.79 (26.80)	21	69	277	3 005

[1] Score 1 (no assistance) to 4 (significant assistance).
[2] Score 1 (poor conformation/low fat cover) to 5 (excellent conformation/high fat cover).
[3] Score 1 (emaciated) to 5 (over fat).
[4] Score 1 (faecal soiling and dags covering the breech area) to 5 (no faecal soiling).

only recorded ewe BW between 45 and 120 kg were retained (McHugh et al., 2019). Ewe litter size was defined as the number of lambs born per litter for each lambing event; only ewe litter sizes between one (singles) and four (quadruplets) were considered. For ewe BCS and BW, contemporary group was defined as flock-by-date of scoring or weighing (O'Brien et al., 2017). For ewe litter size, contemporary group was defined as flock-by-week of lambing. For all ewe performance traits, only contemporary groups with at least five records were retained for analysis.

Health

Dag score for lambs and ewes was assessed by trained technicians on a five-point scale (1 = no faecal soiling to 5 = faecal soiling and dags covering the breech area and extending down the hind legs towards the pasterns) described by O'Brien et al. (2017). Lameness was assessed by trained technicians as lame (lame = 1) or not (lame = 0; O'Brien et al., 2017); in the present study, lameness in ewes and lambs was treated as a separate trait (O'Brien et al., 2017). For the health traits (i.e. dag score, ewe lameness and lamb lameness), contemporary group was defined as flock-by-date of health recording (O'Brien et al., 2017). For the binary traits of ewe and lamb lameness, only contemporary groups with at least one recorded incidence of lameness were retained for analysis. Across all health traits, only contemporary groups with at least five records were retained for analysis.

Information was also available on dam parity number (or ewe parity for traits of the ewe herself), as well as animal breed composition and both heterosis and recombination loss coefficients of each animal and its dam. Ewe or dam parity was categorised as 1, 2, 3, 4, 5, 6 or $\geq$ 7. Age of the ewe or dam at first lambing was categorised as lambing either: 1) between 8 and 18 months of age, or 2) between $\geq$ 18 and 28 months of age as per McHugh et al. (2016). Animals were grouped into distinct classes based on their breed proportion as: purebred Belclare, Charollais, Suffolk, Texel and Vendeen; all other animals were considered as crossbred. Heterosis and recombination loss coefficients were calculated for each animal (and dam) as $1-\sum_{i=1}^{n} sire_i \cdot dam_i$ and $1-\sum_{i=1}^{n}\frac{sire_i^2+dam_i^2}{2}$, respectively, where $sire_i$ and dam_i are the proportion of breed i in the sire and dam, respectively. The numbers of records available for each trait are shown in Table 1.

Association analyses

All associations were undertaken using animal linear mixed models in ASReml (Gilmour et al., 2009), with a direct genetic and, where appropriate, a maternal genetic and a dam permanent environmental effect included as random effects in all models. Relationships among animals were accounted for using the numerator relationship matrix; the number of animals in the pedigree differed per trait but varied from 15 690 (ewe lameness) to 30 338 (weaning weight). In all models, the association between the three alternative approaches to depicting the *PrP* genotype (i.e. the 15 called *PrP* genotypes, the five genotype categories, or the number of ARR haplotypes) were separately investigated; where a maternal effect was suspected, both the genotype of the lamb and the dam were both included in the statistical model. Furthermore, in all models whether the association between the *PrP* genotype and the dependent variable differed by breed class of both the animals (and dam for lamb traits) was investigated; animal (and dam for lamb traits) breed class was either Belclare, Charollais, Suffolk, Texel, Vendeen or crossbred.

Lamb traits

Irrespective of which of lamb traits (lambing, BW, carcass or health traits) was under investigation, fixed effects included in all models were *PrP* genotype of both the lamb and dam, lamb birth type (single, twin, triplet or quadruplet), sex of the lamb (male or female), contemporary group, parity of the dam (1, 2, 3, 4, 5, 6, or $\geq$ 7), age at first lambing of the dam (8 and 18 months of age or $\geq$ 18 and 28 months of age), and the heterosis and recombination loss coefficients of both the lamb and the dam. For all lamb BW, carcass and health traits, the rearing type of the lamb (single, twin or triplet) and the age of the lamb when recorded for BW and health or when slaughtered were also included in the model. A

maternal genetic and dam permanent environmental effect was considered alongside a direct genetic effect as random effects in all lamb trait models.

Ewe traits

A repeatability model was used to test the association between the *PrP* genotype and each of the three ewe traits (i.e. ewe BW, ewe BCS and ewe litter size). Across all models, the fixed effects were the *PrP* genotype of the ewe, contemporary group, parity of the ewe (1, 2, 3, 4, 5, 6, or $\geq$ 7), age at first lambing of the ewe (8 and 18 months of age or $\geq$ 18 and 28 months of age), and the heterosis and recombination loss coefficients of the ewe. For ewe BW, BCS and health data, the previous litter size and rearing litter size as well as the days since lambing were also included as fixed effects. For ewe litter size, the dam age in months relative to the median age within parity was also tested as a fixed effect.

Results and discussion

All 15 of the possible scrapie genotypes were detected in the population (Table 2). Across all breeds, the frequency of the five *PrP* haplotypes was 0.70 (ARR), 0.15 (ARQ), 0.11 (ARH), 0.02 (AHQ) and 0.01 (VRQ), although they differed ($P < 0.05$) by breed (Table 2). The frequency of the ARR haplotype ranged from 0.59 (Texel) to 0.88 (Suffolk), while the frequency of the AHQ haplotype ranged from 0.00 (Charollais, Suffolk and Vendeen) to 0.03 (Texel and Crossbreds). The VRQ haplotype was only detected in the Texel and crossbred population, albeit at a low frequency (0.01). The frequency of the five *PrP* haplotypes reported in the present study differs considerably to the frequencies previously reported in 366 Irish Belclare ewes (Sweeney et al., 2007) as well as in other populations (Sawalha et al., 2007; L'Homme et al., 2008; Moore et al., 2009), with a greater frequency of the favourable ARR haplotype and considerably fewer of the unfavourable VRQ haplotype in the sample population used in the present study. Although the Irish national scrapie eradication program ended in 2009, results from the present study clearly demonstrate that Irish sheep producers, especially seed stock breeders, have continued to select animals for the favourable haplotypes (i.e. ARR). Sharing of sheep germplasm is common between Ireland and other European countries, especially the UK (Fitzmaurice et al., 2022); one of the main criteria dictating whether importation or exportation of breeding sheep to and from Ireland is allowed is that, unless animals originate from a scrapie-monitored flock, animals must have an ARR/ARR scrapie genotype; this may also help explain the high frequency of the favourable ARR haplotype in certain breeds.

Across the entire population investigated in the present study, 16 416 animals, 38% of the animals had at least one parent with a known *PrP* genotype, with a further 28% of animals having a known *PrP* genotype for both parents; of these, only three pairs of animals (i.e. 0.03%) displayed Mendelian inconsistency. Of all the performance traits investigated in the present study, no additive effect of the *PrP* genotype of the ewe and the lamb was detected; therefore, the genotypes of the lamb and ewe are hereafter discussed independently.

Previous studies have documented how the relationship between the *PrP* genotype and animal performance differed by breed (De Vries et al., 2004; Hanrahan et al., 2008; Moore et al., 2009), although such studies generally focused on a limited number of breeds. With the exception of lamb carcass conformation and fat, ewe BW and lamb lameness in the present study (Supplementary Table S1 to S4), no interaction between breed and the *PrP* genotype existed. Nonetheless, for all four performance traits where an interaction between breed and the *PrP* genotype was detected, the interaction was significant for only one of the three approaches to depicting the *PrP* genotype. Moreover the approach to depicting the *PrP* genotype that was significant varied between the four traits; for lamb carcass fat score and ewe BW only the interaction between breed and the 15 called *PrP* genotypes was significant, whereas for lamb carcass conformation score and lamb lameness, the only breed interaction was detected when *PrP* was defined using the five genotype categories. With the exception of ewe BW, the association between the trait and the *PrP* genotype did not persist when across breed associations were investigated. It is quite likely, therefore, that the detected interactions may actually be a Type I error attributable to multiple testing.

No association was observed between the *PrP* genotype of either the animal or the dam no matter how defined (i.e. the 15 called *PrP* genotypes, the five genotype categories, or the number of ARR haplotypes) and any of the lambing traits investigated in the present study ($P > 0.05$; Table 3). Few studies have investigated the association between scrapie genotype and lambing traits, although no association between scrapie genotype and perinatal lamb survival has been reported previously (Sawalha et al., 2007; Hanrahan et al., 2008). Contrasting results have been documented on the association between scrapie genotype and postnatal lamb survival (>24 h after birth). Sawalha et al. (2007) reported that Scottish Blackface lambs carrying the ARQ haplotype had greater postnatal lamb survival than lambs carrying either the ARR or AHQ haplotypes. In contrast, Gubbins et al. (2009) found no association between the *PrP* genotype and lamb survival except in the Charollais breed but concluded that this association was a little

Table 2
Number of records (n) and percentage of purebred Belclare, Charollais, Suffolk, Texel and Vendeen, as well as crossbred animals with each prion protein (*PrP*) genotype along with the associated five-class *PrP* genotype category.

PrP category	*PrP* genotype	Belclare	Charollais	Suffolk	Texel	Vendeen	Crossbred
N		733	333	739	1 857	191	12 563
1	ARR/ARR	69.58	81.08	85.93	44.7	79.58	62.64
2	ARR/AHQ	1.50	–	0.27	2.53	–	2.74
	ARR/ARH	5.87	0.60	0.14	26.28	–	11.44
	ARR/ARQ	17.87	17.12	13.25	14.54	19.9	17.15
3	AHQ/AHQ	–	–	–	0.05	–	0.03
	AHQ/ARH	0.14	–	–	0.81	–	0.30
	AHQ/ARQ	0.14	–	–	0.48	–	0.31
	ARH/ARH	0.68	–	–	4.41	–	0.56
	ARH/ARQ	1.50	–	–	4.09	–	1.69
	ARQ/ARQ	1.91	0.60	0.41	1.35	0.52	1.21
4	ARR/VRQ	0.68	0.60	–	0.54	–	1.50
5	AHQ/VRQ	–	–	–	–	–	0.01
	ARH/VRQ	–	–	–	0.22	–	0.20
	ARQ/VRQ	0.13	–	–	–	–	0.21
	VRQ/VRQ	–	–	–	–	–	0.01

Table 3
The significance (*P-value)* of the association between the animal (ani) and dam prion protein (*PrP)* genotype and each animal performance trait in a sheep population where *PrP* genotype was defined as either: the 15 called *PrP* genotypes (Genotype), the five genotype categories (Category), or the number of ARR haplotypes (Haplotype).

Trait Group	Trait	Genotype		Category		Haplotype	
		Ani	Dam	Ani	Dam	Ani	Dam
Lambing							
	Lambing Difficulty Score (1–4)[1]	0.909	0.671	0.991	0.708	0.914	0.818
	Perinatal Mortality (%)	0.952	0.830	0.391	0.204	0.330	0.080
	Birth Weight (kg)	0.496	0.391	0.927	0.627	0.852	0.492
Lamb Performance							
	Preweaning (kg)	0.991	0.100	0.982	0.106	0.999	0.060
	Weaning (kg)	0.516	0.104	0.264	0.175	0.376	0.117
	Postweaning (kg)	0.207	0.162	0.794	0.514	0.677	0.260
	Muscle depth (mm)	0.120	0.382	0.040	0.487	0.756	0.190
	Fat depth (mm)	0.806	0.835	0.494	0.988	0.763	0.965
Lamb Carcass							
	Carcass weight (kg)	0.520	0.812	0.585	0.332	0.262	0.170
	Carcass conformation (1–5)[2]	0.219	0.839	0.107	0.677	0.317	0.435
	Carcass fat (1–5)[2]	0.115	0.355	0.117	0.134	0.06	0.260
	Age at slaughter (d)	0.883	0.49	0.499	0.557	0.589	0.344
Ewe Performance							
	Body condition score (1–5)[3]	0.367		0.390		0.459	
	Mature weight (kg)	0.001		0.0009		0.015	
	Litter Size (1–4)	0.984		0.648		0.638	
Health							
	Dag score (1–5)[4]	0.257	0.019	0.446	0.069	0.257	0.019
	Ewe lameness (%)	0.733		0.823		0.733	
	Lamb lameness (%)	0.878	0.149	0.549	0.061	0.549	0.060

[1] Score 1 (no assistance) to 4 (significant assistance).
[2] Score 1 (poor conformation/low fat cover) to 5 (excellent conformation/high fat cover).
[3] Score 1 (emaciated) to 5 (over fat).
[4] Score 1 (faecal soiling and dags covering the breech area) to 5 (no faecal soiling).

consequence; postnatal lamb survival phenotypes were unavailable in the present study.

For lamb performance traits, ultrasound muscle depth differed by the genotype category of the lamb ($P < 0.05$); lambs of category four *PrP* genotype (i.e. ARR\VRH) had on average 1.20 (SE = 0.45) mm, 1.38 (SE = 0.12) mm, 1.47 (SE = 0.25) mm less ultrasound muscle depth relative to lambs of categories 1, 2, 3, respectively ($P < 0.05$). Hanrahan et al. (2008) detected an association between lamb ultrasound muscle depth and scrapie genotype of the sire, albeit the association differed by breed investigated. In addition, when carcass conformation, the ultimate end goal of producers, was the dependent variable in the statistical model, no association with any of the *PrP* genotype definitions was detected either in the present study or by others (Hanrahan et al., 2008); the partial correlation between ultrasound muscle depth and conformation (after adjusting for breed) was 0.11 in the present study. No association was observed between any of the other lamb performance or lamb carcass traits with the different *PrP* genotype definitions ($P > 0.05$; Table 3). Similarly, no association between *PrP* genotype and lamb lameness was detected ($P > 0.05$).

Ewe litter size, ewe BCS or ewe lameness did not differ by *PrP* genotype of the ewe ($P > 0.05$). When the *PrP* genotype of the ewe was defined based on the 15 individually called *PrP* genotypes or the five genotype categories, an association between the ewe *PrP* genotype and ewe BW was observed ($P < 0.05$). Ewes with a *PrP* genotype of ARH/VRQ differed from most other *PrP* genotypes and were on average 3.79 (SE = 1.66) kg heavier than ARR/ARR genotype ewes ($P < 0.05$); ewe BW for all other *PrP* genotypes did not differ from each other ($P > 0.05$). Relative to ewes with a *PrP* genotype category 1 (i.e. ARR/ARR), heavier ewe BW was associated with category 2 (+0.44 kg), 4 (+1.67 kg) and 5 (+3.87 kg; $P < 0.05$). No previous study has investigated the association between ewe BW and *PrP* genotype. Nonetheless, *PrP* genotype differences in ewe BW in the present study were biologically small representing just 0.64–5.49% of the mean mature ewe BW of the entire population. In addition, a large proportion of the ewes in the most susceptible genotype categories (i.e. 4 and 5) and most especially in the ARH/VRQ genotype were of Texel origin, either as purebreds or in the case of the crossbred ewes, had a high proportion of Texel bloodlines. McHugh et al. (2019) have shown that relative to some of the other breeds commonly used in Ireland, the Texels have a heavier mature ewe BW although the inclusion of breed of the ewe in the model should have accounted for these breed effects in the present study. No association was observed between the number of ARR haplotypes and ewe BW ($P > 0.05$).

Few studies have investigated the association between *PrP* genotype and sheep health traits, with most studies tending to focus on mastitis or somatic cell count (De Vries et al., 2004; Ligious et al., 2005) while the present study was on meat sheep. In the present study, an association existed between lamb dag score and dam *PrP* genotype when defined using the five *PrP* genotype categories and the number of ARR haplotypes. Relative to lambs born to dams of *PrP* genotype category 2, a 0.11 (SE = 0.04) lower (i.e. dirtier) dag score was associated with lambs born to dams of *PrP* genotype category 3 ($P < 0.05$). Lambs born to dams with no copy of the ARR haplotype had, on average, a 0.10 (SE = 0.02) unit lower dag score compared to animals born to dams with 1 copy of the ARR haplotype. A maternal influence on lamb dag score has been observed previously, with O'Brien et al. (2017) reporting a significant maternal heritability for lamb dag score in Irish sheep. However, the small differences in dag score observed between the dam *PrP* genotypes would lead the authors to question whether the association between dam *PrP* genotype and lamb dag score is of actual biological consequence. Dag score did not differ by any of the genotype definitions of the lamb or the 15 called *PrP* genotypes of the dam ($P > 0.05$).

Conclusion

Results from the present study failed to detect any association between the *PrP* genotype of either the lamb or dam with 15 of the 18 performance traits investigated. Where associations were detected between the *PrP* genotype and animal performance (lamb ultrasound muscle depth, lamb dag score and ewe BW), the effects were biologically small, suggesting that selection for the *PrP* genotype will have little to no consequence on animal performance. The prevalence of the five *PrP* haplotypes highlights that some of the unfavourable haplotypes are still segregating within the Irish sheep population, albeit at low frequencies; this is especially true for some breeds (i.e. Texel). Although cognisance of the genetic merit or genetic diversity should be considered if participants cull animals with undesirable scrapie haplotypes, the removal of such animals from the breeding population is not expected to impact animal performance, at least for the traits investigated in the present study. Routine genotyping of seed stock is now available for all breeders in Ireland and approximately 6 000 seed stock animals are genotyped annually; this enables the development of a mating decision support tool for breeders that not only matches potential sire-dam pairings based on the expectant genetic merit or inbreeding but also on the expectant resultant *PrP* genotype of the offspring.

Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.animal.2022.100587.

Ethics approval

Not applicable.

Data and model availability statement

The data/models were not deposited in an official repository. The data/models that support the study findings are available from the authors upon request.

Author ORCIDs

McHugh, N. https://orcid.org/0000-0002-3105-8796.
Berry, D.P. https://orcid.org/0000-0003-4349-1447.

Author contributions

McHugh, N.: Conceptualization, Methodology, Writing - Original Draft, **Pabiou, T.**: Validation, Writing- Reviewing, **McDermott, K.**: Conceptualization, Resources, **Berry, D.P.**: Conceptualization, Methodology, Writing- Reviewing and Editing.

Declaration of interest

None.

Acknowledgements

None.

Financial support statement

Funding from the Irish Department of Agriculture, Food and Marine Research Stimulus Fund MultiRepro (14/S/849).

References

Belt, P.B., Muileman, I.H., Schreuder, B.E., Bos-de Ruijter, J., Gielkens, A.L., Smits, M. A., 1995. Identification of five allelic variants of the sheep PrP gene and their association with natural scrapie. Journal of General Virology 76, 509–517. https://doi.org/10.1099/0022-1317-76-3-509.

Dawson, M., Hoinville, L.J., Hosie, B.D., Hunter, N., 1998. Guidance on the use of *PrP* genotyping as an aid to the control of clinical scrapie. Veterinary Record 142, 623–625.

De Vries, F., Hamann, H., Drogenmuller, C., Ganter, M., Distl, O., 2004. Analysis of associations between the prion protein genotypes and reproductive traits in meat sheep breeds. Animal Science 79, 397–404. https://doi.org/10.1017/S1357729800090263.

De Vries, F., Hamann, H., Drogenmuller, C., Ganter, M., Distl, O., 2005. Analysis of associations between the prion protein genotypes and production traits in East Friesian milk sheep. Journal of Dairy Science 88, 392–398. https://doi.org/10.3168/jds.S0022-0302(05)72699-0.

Fitzmaurice, S., Conington, J., McDermott, K., McHugh, N., Banos, G., 2022. Across-country genetic evaluation of meat sheep from Ireland and the UK. Journal of Animal Breeding and Genetics 139, 342–350. https://doi.org/10.1111/jbg.12668.

Gilmour, A.R., Gogel, B.J., Cullis, B.R., Thompson, R., 2009. ASReml User Guide Release 3.0 [www.vsni.co.uk]. VSN International Ltd, Hemel Hempstead, HP1 1ES, UK.

Gubbins, S., Cook, C.J., Hyder, K., Boulton, K., Davis, C., Thomas, E., Haresign, W., Bishop, S.C., Villanueva, B., Eglin, R.D., 2009. Associations between lamb survival and prion protein genotype: analysis of data for ten sheep breeds in Great Britain. BMC Veterinary Research 5, 3. https://doi.org/10.1186/1746-6148-5-3.

Hanrahan, J.P., Casey, K.C., Sweeney, T., 2008. Evidence for a breed specific association between PrP genotype and ultrasonic muscle depth but not for survivability, growth or carcass traits in sheep. Livestock Science 117, 249–254. https://doi.org/10.1016/j.livsci.2007.12.015.

Hunter, N., Goldmann, W., Smith, G., Hope, J., 1994. The association of codon 136 *PrP* variants with the occurrence of natural scrapie. Archives of Virology 137, 171–177. https://doi.org/10.1007/bf01311184.

Jefferies, B.C., 1961. Body condition scoring and its use in management. Tasmanian Journal of Agriculture 32, 19–21.

L'Homme, Y., Leboeuf, A., Cameron, J., 2008. *PrP* genotype frequencies of Quebec sheep breeds determined by real-time PCR and molecular beacons. Canadian Journal of Veterinary Research 72, 320–324.

Ligios, C., Sigurdson, C.J., Santucciu, C., Carcassola, G., Manco, G., Basagni, M., Maestrale, C., Cancedda G, M., Madau, L., Aguzzi, A., 2005. PrPSc in mammary glands of sheep affected by scrapie and mastitis. NatureMedicine 11, 1137–1138. https://doi.org/10.1038/nm1105-1137.

McGovern, F.M., McHugh, N., Fitzmaurice, S., Pabiou, T., McDermott, K., Wall, E., Fetherstone, N., 2020. Phenotypic factors associated with lamb live weight and carcass composition measurements in an Irish multi-breed sheep population. Translational Animal Science 4, 1–9. https://doi.org/10.1093/tas/txaa206.

McHugh, N., Berry, D.P., Pabiou, T., 2016. Risk factors associated with lambing traits. Animal 10, 89–95. https://doi.org/10.1017/S1751731115001664.

McHugh, N., Pabiou, T., Wall, E., McDermott, K., Berry, D.P., 2017. Impact of alternative definitions of contemporary groups on genetic evaluations of traits recording at lambing. Journal of Animal Science 95, 1926–1938. https://doi.org/10.2527/jas2016.1344.

McHugh, N., McGovern, F., Creighton, P., Pabiou, T., McDermott, K., Wall, E., Berry, D. P., 2019. Mean difference in live-weight per incremental difference in body condition score estimated in multiple sheep breeds and crossbreds. Animal 13, 549–553. https://doi.org/10.1017/S1751731118002148.

Moore, R.C., Boulton, K., Bishop, S.C., 2009. Associations of *PrP* genotype with lamb production traits in three commercial breeds of British lowland sheep. Animal 3, 1688–1695. https://doi.org/10.1017/S175173110099067X.

O'Brien, A.C., McHugh, N., Wall, E., Pabiou, T., McDermott, K., Randles, S., Fair, S., Berry, D.P., 2017. Genetic parameters for lameness, mastitis and dagginess in a multi-breed sheep population. Animal 11, 911–919. https://doi.org/10.1017/S1751731116002445.

Sawalha, R.M., Brotherstone, S., Conington, J., Villanueva, B., 2007. Lambs with scrapie susceptible genotypes have higher postnatal survival. PLoS ONE 11,. https://doi.org/10.1371/journal.pone.0001236 e1236.

Sweeney, T., Hanrahan, J.P., O'Doherty, E., 2007. Is there a relationship between prion protein genotype and ovulation rate and litter size in sheep. Animal Reproduction Science 101, 153–157. https://doi.org/10.1016/j.anireprosci.2006.12.004.