Received: 16 October 2017 | Accepted: 20 March 2018

DOI: 10.1111/jbg.12325

ORIGINAL ARTICLE

WILEY Journal of Animal Breeding and Genetics

Detection of selection signatures for agonistic behaviour in cattle

P.G. Eusebi[1] | **O. Cortés**[1] | **C. Carleos**[2] | **S. Dunner**[1] | **J. Cañon**[1]

[1]Departamento de Producción Animal, Facultad de Veterinaria, Universidad Complutense de Madrid, Madrid, Spain

[2]Departamento de Estadística e Investigación Operativa, Universidad de Oviedo, Oviedo, Spain

Correspondence
P.G. Eusebi, Departamento de Producción Animal, Facultad de Veterinaria, Universidad Complutense, Madrid, Spain.
Email: paulinaeusebi@gmail.com

Funding information
CONACYT; CONARGEN from the Mexican government; Genetics Laboratory of the Animal Production Department at the Universidad Complutense of Madrid

Summary

The identification of genomic regions including signatures of selection produced by domestication and its subsequent artificial selection processes allows the understanding of the evolution of bovine breeds. Although several studies describe the genomic variability among meat or milk production cattle breeds, there are limited studies orientated towards bovine behavioural features. This study is focused on mapping genomic signatures of selection which may provide insights of differentiation between neutral and selected polymorphisms. Their effects are studied in the Lidia cattle traditionally selected for agonistic behaviour compared with Spanish breeds showing tamed behaviour. Two different approaches, BayeScan and SelEstim, were applied using genotypic 50K SNP BeadChip data. Both procedures detected two genomic regions bearing genes previously related to behavioural traits. The frequencies of the selected allele in these two regions in Lidia breed were opposite to those found in the tamed breeds. In these genomic regions, several putative genes associated with enriched metabolic pathways related to the behavioural development were identified, as neurochondrin gene (NCDN) or glutamate ionotropic receptor kainate type subunit 3 (*GRIK3*) both located at BTA3 or leucine-rich repeat and Ig domain containing 2 (LINGO2) and phospholipase A2-activating protein (PLAA) at BTA8.

KEYWORDS
aggressive behaviour, Lidia breed, selective sweep, Spanish cattle

1 | INTRODUCTION

Since their domestication (~10,000 years ago), cattle populations have been subjected to natural and artificial selection processes (Ajmone-Marsan, Garcia, & Lenstra, 2010). Currently, most domesticated bovine breeds are specialized in milk and meat traits, and on a smaller scale in other economic traits of interest, such as leather or draft among others (Felius et al., 2014).

An early prerequisite of the domestication process in all the farm animals was probably to reduce their fear to humans (Belyaev, Plyusnina, & Trut, 1985). Thus, as a consequence of domestication, humans have modified the wild nature and social behaviour of bovines.

Different studies have analysed genomic changes produced by the long-term selection in most commercial bovine breeds (Pritchard, Pickrell, & Coop, 2010; Randhawa, 2016). As a consequence, several strong genomic signatures or hard sweeps belonging to traditional selected morphological traits (muscular hypertrophy, coat colour, presence/absence horns) have been reported (Druet, Pérez-Pardal, Charlier, & Gautier, 2013; González-Rodríguez et al., 2017). But so far, studies of selection signatures focused on behavioural features are limited. The Lidia bovine breed has been selected for centuries for its agonistic–aggressive behaviour by means of a series of traits registered by the breeders on a categorical scale that classifies their aggression and fighting capacity (Silva, Gonzalo, &

Cañón, 2006). Furthermore, these traits have evidenced significant heritability values, which make them suitable to genetic selection (Menéndez-Buxadera, Cortés, & Cañon, 2017; Silva et al., 2006). Unlike other bovine breeds in which aggression is an undesirable trait, it is likely that the aggressiveness selection process in the Lidia bovine breed has left detectable genomic signatures (Akey, Zhang, Zhang, Jin, & Shriver, 2002).

The detection of selective sweeps in quantitative traits still presents some limitations because many of the characters of interest, such as behavioural traits, are polygenic. In this case, the response to selection would be generated by modest allele frequency shifts at many loci, detection of which can be difficult to accomplish (Pritchard et al., 2010).

The imputation of genotypes using high-density genotyping platforms has favoured the identification of genomic selection signatures using demographic models, selections models or a combination of both (Ma et al., 2015). Under selection pressure, a new genetic variant at the genomic level may show one or more of the following features: extreme allele frequencies, excess of homozygotes, high frequency of long haplotypes and/or a higher genetic differentiation among populations (Qanbari & Simianer, 2014; Randhawa, 2016).

Several selection signature detection methods are based on allele frequencies differences among populations that may simply be identified in the extreme tails of the F_{ST} estimates distribution. Theoretically, loci under selection pressure or balancing selection are expected to evidence high and low levels of differentiation among populations, respectively. Foll (2012) extended this approach and directly estimated the probability that each locus is subject to selection using a Bayesian method that evidenced their robustness under different demographic scenarios. However, one criticism of this kind of methodologies is that they do not quantify the intensity of selection. Recently Vitalis, Gautie, Dawson, and Beaumont (2013) developed a Bayesian method which allows distinguishing between selected and nearly neutral polymorphisms and estimated the intensity of selection under a genetic model that assumes the subdivision of a population into subpopulations that may exchange migrants.

In this study, information provided by a panel of SNPs was used to analyse three groups of the Lidia bovine breed traditionally selected for agonistic-related traits, and two non-specialized tamed Spanish breeds (Asturiana de los Valles and Morenas Gallegas) as a reference to locate genomic regions associated with agonistic traits. A marginal second objective was to identify putative candidate genes mapping within these genomic regions in order to understand the evolutionary mechanisms of the Lidia breed.

2 | MATERIAL

A total of 213 (48 from Mexico and 165 from Spain) Lidia bovine breed individuals were genotyped using the Bovine 50K SNP BeadChip (http://www.illumina.com). According to Silva et al. (2006) who evidenced differences among the three main behaviour characteristics that are traditionally scored in the Lidia breed (aggressiveness, ferocity and mobility), 100 samples belonging to those Spanish lineages with higher agonist behaviour (SPA+) and 65 with the lower ones (SPA−) were selected to be genotyped. Those lineages with the higher and lower behaviour scores also evidenced the higher genetic differentiation among the Lidia breed lineages (Supplementary Table 1) (Eusebi et al., 2017; Cañón et al., 2008). In addition, animals from Asturiana de los Valles and from Morenas Gallegas bovine breeds were genotyped as reference group in which agonist behaviour is not desirable: 60 unrelated (based on genealogical information) Asturiana de los Valles breed individuals (35 genotyped with the 50k BeadChip and 25 with the 777k BeadChip) and 30 individuals from the Morenas Gallegas breed genotyped with the 50k BeadChip.

The SNPs in common between the 50K and 777K chips were identified (Nicolazzi et al., 2015). Then, the data sets of the five groups were combined using PLINK v. 1.07 (Purcell et al., 2007), and the following SNP edits were applied including the removal of individuals with a call rate <80%, non-autosomal SNPs and SNPs with minor allele frequency <0.01. After edits, 38,577 SNPs on 303 individuals remained.

3 | METHODS

SelEstim procedure proposed by Vitalis et al. (2013) is a hierarchical Bayesian method whose model is a diffusion approximation for the distribution of allele frequency in a population subdivided into a number of groups that exchange migrants with a rate equal to m. This procedure provides two parameters of differentiation between groups: σ is an average effect of selection and is a hyperparameter that summarizes the strength of dispersion among groups at each specific locus, and the Kullback–Leibler divergence (KLD) which is a non-symmetric measure of difference between two probability distributions calculating the distance of the posterior distribution of σ of the centring distribution. The KLD parameter represents the neutral demographic history of the groups, and KLD values are strongly correlated with F_{ST} estimates. Also, an estimate of the migration rate among the breeds is provided, this parameter is scaled by the effective size (i.e., $M_j = 4N_j m_j$) where M_j is the scaled migration parameter in the jth

population, N is the number of diploid individuals and receives immigrants for the whole population at a rate m.

A first computation is performed on the whole data set to estimate the posterior distribution of the parameters, obtaining a "pseudo-observed" data set; in order to provide a criterion to discriminate between neutral and selected markers, the calibration computation was then performed to achieve the thresholds (0.95, 0.99, 0.995 and 0.9999) quantiles of a "centring" KLD empirical distribution computed from the pseudo-observed data set.

3.1 | Identification of genomic regions with selection signatures

Assuming that behavioural traits are polygenic, low influence of many loci is expected. Hence, a slide window of ~10 MB that contains each of the SNP with KLD higher than 99.99% was selected to identify *genomic regions with selection signatures*. Furthermore, the previously defined SNPs with KLD higher than 95% in the 10 Mb windows were counted and used to define regions of genomic selection signatures. Gene annotation was performed by exploiting the knowledge on UMD3.1 locations of genes from the NCBI (ftp://ftp.ncbi.nih.gov/genomes/Bos_taurus/mapview/seq_gene.md.gz), and as annotation of the bovine genome is still incomplete, BioMart from Ensembl Archive release 90 (www.ensembl.org/biomart) was used to determine the orthologous human gene ID for each gene detected.

BayeScan software (Foll, 2012) was also used to detect signatures of selection, with the difference that this methodology detects divergence selection from Bayesian binomial frameworks identifying loci under selection when they show F_{ST} coefficients that are significantly different to that expected under neutrality.

With BayeScan, F_{ST} coefficients are split into a population-specific component (β), common to all loci and a locus-specific component (α) shared by all the populations using a logistic regression. Allele frequencies are assumed to follow a Dirichlet distribution. Selection is detected when α is significantly different to zero; *that is,* the locus-specific component is necessary to explain the observed pattern of diversity. When $\alpha > 0$ it is assumed that directional selection is acting on the locus under analysis, while $\alpha < 0$ suggests balancing or purifying selection (Foll, 2012).

3.2 | Identification of genomic regions with selection signatures

The standard PLINK files were converted to BayeScan format with the PGDSpider v 2.0.7.3 software (Lischer & Excoffier, 2012) and used the same parameters set with SelEstim to perform the analyses. A first filter was applied to the results, setting a significance threshold of 5% false discovery rate (Randhawa et al., 2016), and then, selecting the SNPs with alpha (α) values higher than 1, as it indicates strong evidence of diversifying selection according to Jeffrey's interpretation (Foll, 2012).

4 | RESULTS

4.1 | SelEstim

A total number of 19,287 SNPs had KLD estimates over the 50% quantile: 3,857 (90%), 1,918 (95%), 386 (99%), 194 (99.5%) and 5 (99.99%). The genomic regions of positive selection containing at least one SNP in the last percentile and the remaining in the 95% are described in Table 1. The migration rates (M_j) ranged from 20.92 in the Asturiana de los Valles breed to 2.52 in the Mexican Lidia group (Table 2).

4.2 | BayeScan

A total of 249 outlier loci displayed strong signals of positive selection, $\alpha > 1$ and q value 5% (Table S2). A q-value of 5% means that it is expected that 5% of the outlier markers (those with a q-value >5%) are false positives (Foll, 2012) and therefore were discarded.

Positional coincidences with SelEstim and BayeScan were identified in chromosomes 3 and 8 (Table 3, Figure S1). Furthermore, these selective sweeps with genomic signals of positive selection were analysed more thoroughly to identify candidate genes that could have been modified by selection.

4.3 | Selection signature at BTA3

The pattern of the average values of selected alleles (κ_{ij}) shown in Figure 1 evidenced that most of the polymorphisms are positively selected in the bovine populations. However, all the groups show an outlier allele at nucleotide

TABLE 1 Putative selective sweeps identified with SelEstim

Selective sweeps	Chr	N SNP	Mb Start	Mb End	Higher KLD
1	3	9	109.49	119.08	1.92
2	8	8	14.89	27.98	1.92
3	11	11	15.07	24.92	2.55
4	13	5	26.52	31.82	1.98
5	18	12	47.83	54.86	2.22

Chr, chromosome; N SNP, number of SNPs included in the genomic region with KLD over 95% and at least one SNP over 99.99%; Mb, Mega base pairs, and the higher value of the Kullback–Leibler Divergence (KLD) of the SNPs included in the selective sweep.

TABLE 2 Estimate of the migration (M_j) parameters for the five groups, mean values and standard deviations (Std. Dev.)

Groups	Mean	Std. Dev.
Asturiana de los Valles	20.92	0.24
Morenas Gallegas	9.14	0.09
Lidia Mexico	2.52	0.02
Lidia Spain(+)	12.81	0.13
Lidia Spain(−)	4.68	0.04

TABLE 3 Genomic concordance of the selective sweeps identified with BayeScan and SelEstim approaches

	SelEstim				BayeScan	
Chr	N SNPS	Mb Start	Mb End	Higher KLD	Mb	Higher α
3	9	109.49	119.08	1.92	116.8	1.02
8	8	14.89	27.98	1.92	19.9	1.16
					22.3	1.28

Chr, chromosome; N SNP, number of markers; Mb, mega base pairs.

BTA3:110,766,510 with the highest KLD value (Table 1). At this locus, the intensity of selection (σ) estimated, which allows for the identification of the strongest selection coefficients, had the same selection direction in the Lidia breed subpopulations and the opposite in the tamed Morenas Gallegas bovine breed. This genomic region contains several genes related to different pathways, such as the serotonergic and dopaminergic signalling pathways, which contribute to the process of differentiation in a selection oriented for behavioural-related traits.

This SNP with the highest KDL value is located proximate to the Neurochondrin gene (*NCDN*) (BTA3: 110,784,499-110,793,283). This gene is highly expressed in the central nervous system (Table S3) and works as a negative regulator of the Ca_2+/calmodulin-dependent protein kinase II (*CaMKII*), a key enzyme present in the early stages of memory formation and involved also in the hippocampal synaptic plasticity (Dateki et al., 2005). This gene is highly associated with the serotonergic signalling pathway in modulating the acquisition and consolidation of memory.

The glutamate ionotropic receptor kainate type subunit 3 (*GRIK3*) gene is located close to the *NCDN* gene and has been identified previously by Qanbari and Simianer (2014) as candidate gene for signatures of selection in cattle. The *GRIK3* gene is highly expressed in the central nervous system and is included in a QTL described in the reward-related processes underlying learning and memory

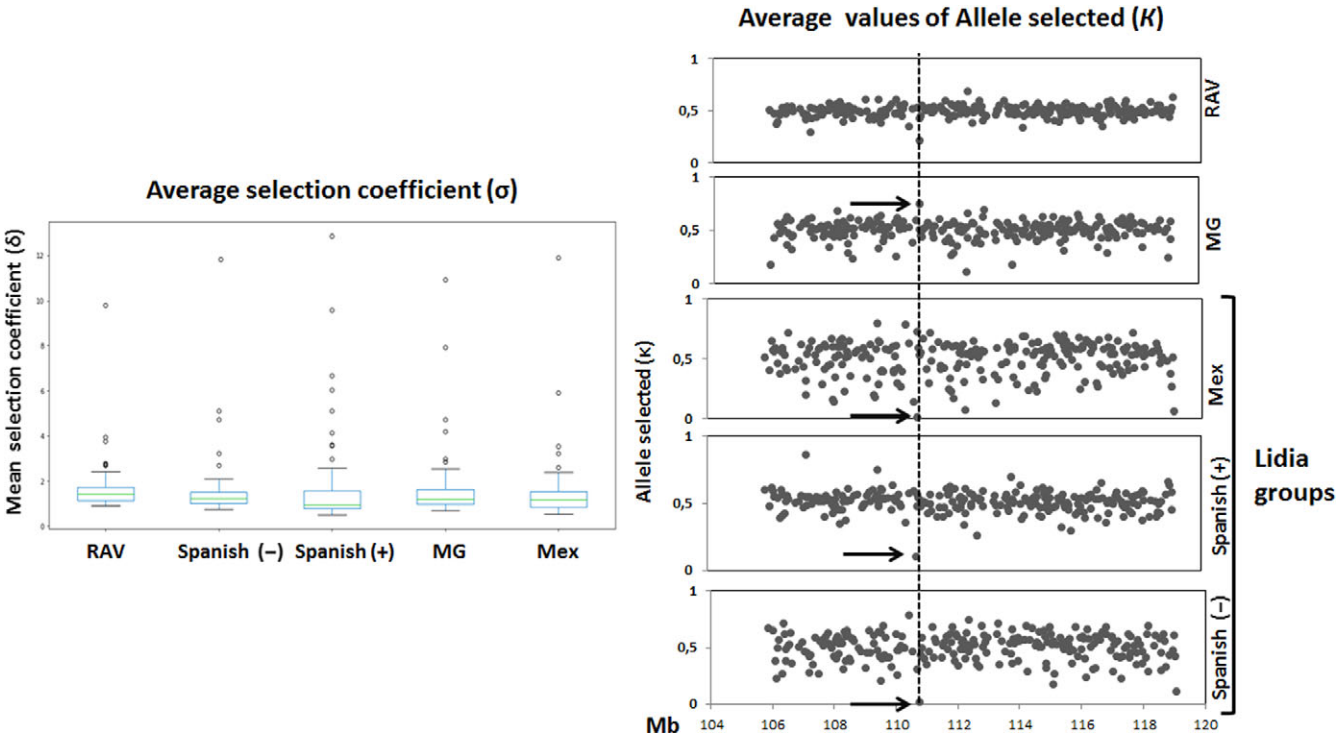

FIGURE 1 Plot of the putative selective sweep localized in BTA3 between 106 and 119 Mb. The left boxplot is the mean selection coefficient (σ) per group and in right boxplot the mean values of the allele selected (κ_{ij}) for each group, where RAV = Asturiana de los Valles, MG = Morenas Gallegas, Mex = Lidia from Mexico, Spanish(−) = Spanish Lidia less aggressive group and Spanish(+) = Spanish Lidia more aggressive group. [Colour figure can be viewed at wileyonlinelibrary.com]

(Minelli, Scassellati, Bonvicin, Perez, & Gennarelli, 2009). Furthermore, the disc large-associated protein 3 (*DLGAP3*) gene located within the same region is also associated with learning processes (Kähne et al., 2016).

Besides, thyroid hormone receptor-associated protein 3 (*THRAP3*) and splicing factor proline- and glutamine-rich (*SFPQ*) genes, also located within the frame of this genomic region, are linked to the circadian cycle. Other genes are associated with processes implicated in domestication-related changes like sensory perception (*GJB4, SAG* and *TRPM8*), brain development and neurobehavioural functioning *(POU3F1)*, muscle contraction (*FHL3*) and pigmentation (*NCDN*) (Xing, Ling, Chen, & Gu, 2006) (Table S3).

4.4 | Selection signature at BTA8

The pattern of the average values of the selected alleles (κ_{ij}) revealed opposite direction of selection intensity (σ) in the Lidia breed subpopulations compared with Asturiana de los Valles and Morenas Gallegas tamed breeds (Figure 2). Also it should be noted that the SNP with the strongest intensity of selection is present in the Lidia with higher agonist behaviour (SPA+) group. Several genes are located in this genomic region; however, the leucine-rich repeat and Ig domain containing 2 (*LINGO2)* and phospholipase A2-activating protein (*PLAA*) genes are related with extreme neurobehavioural phenotypes and psychiatric disorders and probably with behaviour characteristics (Table S3).

5 | DISCUSSION

In the present study, two Bayesian approaches that are able to detect both recent and old selection events, BayeScan and SelEstim, were applied to identify genomewide signatures of selection in three bovine breeds traditionally selected for opposite behaviour characteristics.

Additionally, SelEstim procedure also estimates intensity and direction of the selection at each locus for each population and the migration rate (M_i) reflecting the relative admixture of each group with respect to all the groups. The relative genetic proximity of the Asturiana de los Valles breed respect to the rest of cattle populations analysed (Table 2) is noteworthy. A similar result for the Asturiana de los Valles breed was also obtained by González-Rodríguez et al. (2017) using seven Spanish bovine beef breeds, suggesting that this breed has been used as terminal sire line and crossbred individuals are

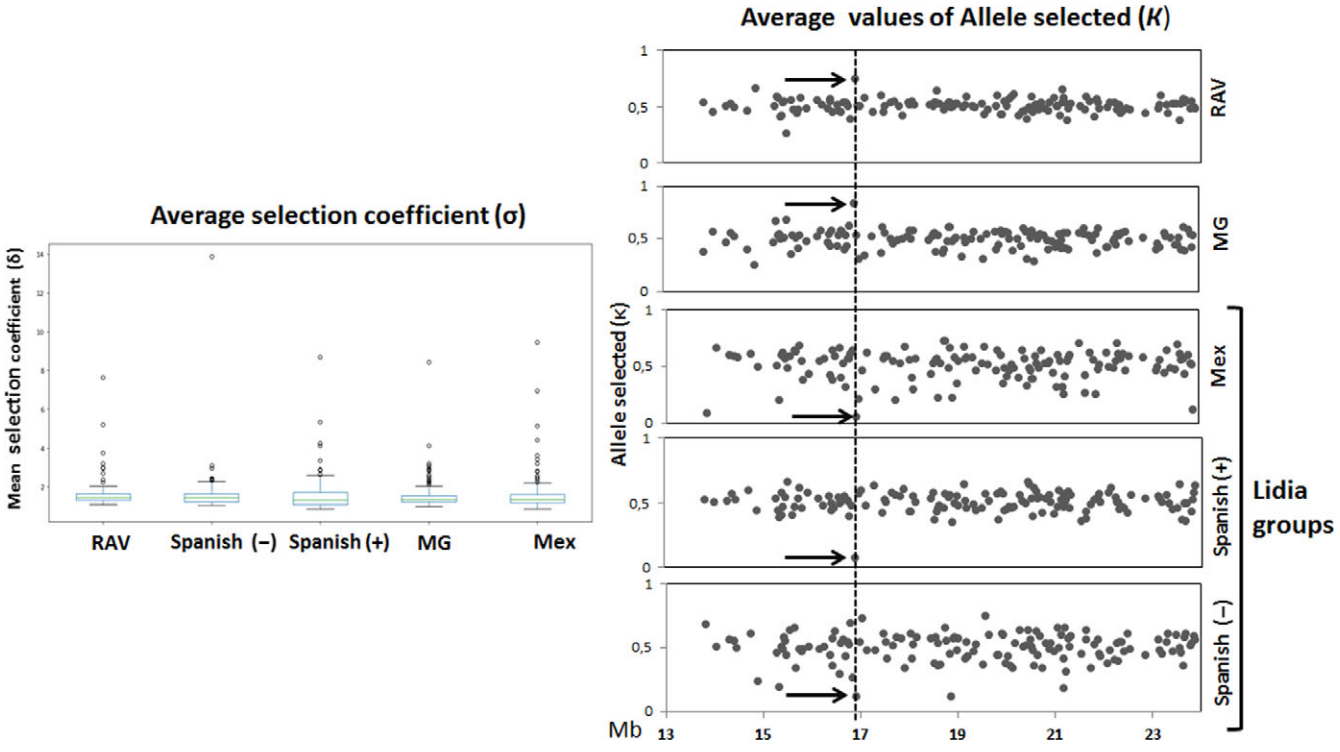

FIGURE 2 Plot of the putative selective sweep localized in BTA8 between the 13 and 24 Mb. The left boxplot is the mean selection coefficient (σ) per group and in right boxplot the mean values of the allele selected (κ_{ij}) for each group, where AST = Asturiana de los Valles, MG = Morenas Gallegas, Mex = Lidia from Mexico, Spanish(−) = Spanish Lidia less aggressive group and Spanish(+) = Spanish Lidia more aggressive group. [Colour figure can be viewed at wileyonlinelibrary.com]

introduced into the receptor populations. However, it is difficult to embrace this argument in our case taking into account the presence of the Lidia breed, which is extremely isolated and with low effective population sizes (Cortés, Sevane, Baro, & Cañón, 2014).

A curious appreciation is the need to decrease the threshold of KLD to 90% to identify genomic regions under selection that are known to be under positive selection, such as the one bearing MSTN or myostatin gene (Supplementary Table 4). This threshold identified 3,857 SNPs, so this large amount of polymorphisms may be related to polygenic selection or adaptation processes (Pritchard et al., 2010), involving several genes or polymorphisms with minor effects. However, when the most restrictive threshold (99.99%) was applied, the number of selected polymorphisms was reduced to only five (Table 1).

The difficulty to detect selective sweeps with statistical significance in polygenic traits, in which many loci shift their frequency moderately (Pritchard et al., 2010), could explain that only two genomic regions were shared with both methodologies. Other reasons may be the limitations of the 50K chip and the sample size of the analysis.

Furthermore, a high rate of false positives is expected due to the divergence in allelic frequencies between breeds (and groups within the Lidia breed and Morenas Gallegas) as a consequence of the genetic drift and founder effects; this is particularly important during the development of the cattle breeds (Petersen et al., 2013). These factors can bias the footprints left in the genome by selection and hamper the identification of selective sweeps.

The results of the present study suggest that the methods employed are able to detect signals of selection generated by recent selection events within populations. Furthermore, the absence of regions with strong signals of selection may be hidden considering that (i) artificial selection processes do not always leave relevant signatures of selection; (ii) the polygenic nature of the behavioural traits (Pritchard et al., 2010) and (iii) the limitations of the bovine genomic resources of the SNP BeadChip already mentioned. However, both methodologies detected genomic signatures of selection in BTA3 and BTA8 regions, where genes whose higher expression is detected mainly in the prefrontal cortex of the brain, where the reactions of violence and social aggression take place (Lotze, Veit, Anders, & Birbaumer, 2007) (Table S3).

Besides, the candidate genes *NCDN, GRIK3, DLGAP3*, *THRAP3* and *SFPQ* located in the selective sweep at chromosome 3 are involved in the serotonergic signalling pathway involved with the development of personality and behavioural traits (Minelli et al., 2009) and also in the development of different aggressive behaviour manifestations, such as fear-induced aggression (Popova, Naumenko, Plyusnina, & Kulikov, 2005), intermale aggression (Kulikov, Osipova, Naumenko, & Popova, 2005), predatory aggression (Nikulina & Popova, 1988) and maternal aggression (da Veiga, Miczek, Lucion, & de Almeida,2011). However, the candidate gene approach has mainly been conducted using rats, albeit with limited success. Studies involving putative behavioural genes such like those involved on serotonergic, catecholaminergic and glutamatergic pathways have failed to find variants of significance, mainly because of a small number of study subjects and a lack of functional assays (Spady & Ostrander, 2008).

In conclusion, the present study identifies two genomic regions associated with agonistic-related traits in cattle. The direction of selection of both regions differed between the aggressive Lidia breed and the tamed Asturiana de los Valles and Morenas Gallegas breeds that were used for comparative purposes. These findings corroborate that intensive targeted selection for different goal traits has left detectable imprints in the genome.

ACKNOWLEDGEMENTS

The authors gratefully acknowledge to the Breeders of the ANCTL, to the Federación de razas autóctonas gallegas-BOAGA and to the Asociación Española de criadores de ganado vacuno selecto de la raza Asturiana de los Valles—ASEAVA for providing the animal material. This work has been funded by grants of CONACYT and CONARGEN from the Mexican government and by the Genetics Laboratory of the Animal Production Department at the Universidad Complutense of Madrid. This work has been carried out within the framework of the PhD program of Animal Production of the Universitat Autònoma de Barcelona.

CONFLICT OF INTEREST

All authors declare that they have no conflict of interest.

ORCID

P.G. Eusebi http://orcid.org/0000-0002-0682-038X
O. Cortés http://orcid.org/0000-0001-7685-3980
S. Dunner http://orcid.org/0000-0001-8637-2208
J. Cañon http://orcid.org/0000-0003-1137-0958

REFERENCES

Ajmone-Marsan, P., Garcia, J. F., & Lenstra, J. A. (2010). On the origin of cattle: How aurochs became cattle and colonized the world. *Evolutionary Anthropology*, *19*(4), 148–157. https://doi.org/10.1002/evan.20267

Akey, J. M., Zhang, G., Zhang, K., Jin, L., & Shriver, M. D. (2002). Interrogating a high-density SNP map for signatures of natural selection. *Genome Research*, *12*(12), 1805–1814. https://doi.org/10.1101/gr.631202

Belyaev, D. K., Plyusnina, I. Z., & Trut, L. N. (1985). Domestication in the silver fox (Vulpes fulvus Desm): Changes in physiological boundaries of the sensitive period of primary socialization. *Applied Animal Behaviour Science*, *13*, 359–370. https://doi.org/10.1016/0168-1591(85)90015-2

Cañón, J., Tupac-Yupanqui, I., García-Atance, M. A., Cortés, O., García, D., Fernández, J., & Dunner, S. (2008). Genetic variation within the Lidia bovine breed. *Animal Genetics*, *39*(4), 439–445. https://doi.org/10.1111/j.1365-2052.2008.01738.x

Cortés, O., Sevane, N., Baro, J. A., & Cañón, J. (2014). Pedigree analysis of a highly fragmented population, the Lidia cattle breed. *Livestock Science*, *167*, 1–8. https://doi.org/10.1016/j.livsci.2014.05.011

Dateki, M., Horii, T., Kasuya, Y., Mochizuk, R., Nagao, Y., Ishida, J., … Fukamizu, A. (2005). Neurochondrin negatively regulates CaMKII phosphorylation, and nervous system-specific gene disruption results in epileptic seizure. *Journal of Biological Chemistry*, *280*(21), 20503–20508. https://doi.org/10.1074/jbc.M414033200

Druet, T., Pérez-Pardal, L., Charlier, C., & Gautier, M. (2013). Identification of large selective sweeps associated with major genes in cattle. *Animal Genetics*, *44*(6), 758–762. https://doi.org/10.1111/age.12073

Eusebi, P. G., Cortés, O., Dunner, S., & Cañón, J. (2017). Genomic diversity and population structure of Mexican and Spanish bovine Lidia breed. *Animal Genetics*, *48*(6), 682–685. https://doi.org/10.1111/age.12618

Felius, M., Beerling, M. L., Buchanan, D. S., Theunissen, B., Koolmees, P. A., & Lenstra, J. A. (2014). On the history of cattle genetic resources. *Diversity*, *6*(4), 705–750. https://doi.org/10.3390/d6040705

Foll, M. (2012). BayeScan v2. 1 user manual. *Ecology*, *20*, 1450–1462.

González-Rodríguez, A., Munilla, S., Mouresan, E. F., Cañas-Álvarez, J. J., Baro, J. A., Molina, A., & Varona, L. (2017). Genomic differentiation between Asturiana de los Valles, Avileña-Negra Ibérica, Bruna dels Pirineus, Morucha, Pirenaica, Retinta and Rubia Gallega cattle breeds. *Animal*, *11*, 1667–1679. https://doi.org/10.1017/S1751731117000398

Kähne, T., Richter, S., Kolodziej, A., Smalla, K. H., Pielo, R., Engler, A., … Naumann, M. (2016). Proteome rearrangements after auditory learning: High-resolution profiling of synapse-enriched protein fractions from mouse brain. *Journal of Neurochemistry*, *138*(1), 124–138. https://doi.org/10.1111/jnc.13636

Kulikov, A. V., Osipova, D. V., Naumenko, V. S., & Popova, N. K. (2005). Association between Tph2 gene polymorphism, brain tryptophan hydroxylase activity and aggressiveness in mouse strains. *Genes, Brain, and Behavior*, *4*, 482–485. https://doi.org/10.1111/j.1601-183X.2005.00145.x

Lischer, H. E. L., & Excoffier, L. (2012). PGDSpider: An automated data conversion tool for connecting population genetics and genomics programs. *Bioinformatics*, *28*, 298–299. https://doi.org/10.1093/bioinformatics/btr642

Lotze, M., Veit, R., Anders, S., & Birbaumer, N. (2007). Evidence for a different role of the ventral and dorsal medial prefrontal cortex for social reactive aggression: An interactive fMRI study. *NeuroImage*, *34*(1), 470–478. https://doi.org/10.1016/j.neuroimage.2006.09.028

Ma, Y., Ding, X., Qanbari, S., Weigend, S., Zhang, Q., & Simianer, H. (2015). Properties of different selection signature statistics and a new strategy for combining them. *Heredity*, *115*(5), 426. https://doi.org/10.1038/hdy.2015.42

Menéndez-Buxadera, A., Cortés, O., & Cañon, J. (2017). Genetic (co) variance and plasticity of behavioural traits in Lidia bovine breed. *Italian Journal of Animal Science*, *16*, 208–216. https://doi.org/10.1080/1828051X.2017.1279035

Minelli, A., Scassellati, C., Bonvicin, C., Perez, J., & Gennarelli, M. (2009). An association of GRIK3 Ser310Ala functional polymorphism with personality traits. *Neuropsychobiology*, *59*(1), 28–33. https://doi.org/10.1159/000202827

Nicolazzi, E. L., Caprera, A., Nazzicari, N., Cozzi, P., Strozzi, F., Lawley, C., … Evans, G. (2015). SNPchiMp v. 3: Integrating and standardizing single nucleotide polymorphism data for livestock species. *BMC Genomics*, *16*(1), 1.

Nikulina, E. M., & Popova, N. K. (1988). Predatory aggression in the mink (*Mustela vison*): Roles of serotonin and food satiation. *Aggressive Behavior*, *14*, 77–84. https://doi.org/10.1002/(ISSN)1098-2337

Petersen, J. L., Mickelson, J. R., Rendahl, A. K., Valberg, S. J., Andersson, L. S., Axelsson, J., … Brama, P. (2013). Genome-wide analysis reveals selection for important traits in domestic horse breeds. *PLoS genetics*, *9*(1), e1003211. https://doi.org/10.1371/journal.pgen.1003211

Popova, N. K., Naumenko, V. S., Plyusnina, I. Z., & Kulikov, A. V. (2005). Reduction in 5-HT1A receptor density, 5-HT1A mRNA expression, and functional correlates for 5-HT1A receptors in genetically defined aggressive rats. *Journal of Neuroscience Research*, *80*, 286–292. https://doi.org/10.1002/(ISSN)1097-4547

Pritchard, J. K., Pickrell, J. K., & Coop, G. (2010). The genetics of human adaptation: Hard sweeps, soft sweeps, and polygenic adaptation. *Current Biology*, *20*(4), R208–R215. https://doi.org/10.1016/j.cub.2009.11.055

Purcell, S., Neale, B., Todd-Brown, K., Thomas, L., Ferreira, M. A. R., Bender, D., … Sham, P. C. (2007). PLINK: A tool set for whole-genome association and population-based linkage analyses. *The American Journal of Human Genetics*, *81*(3), 559–575. https://doi.org/10.1086/519795

Qanbari, S., & Simianer, H. (2014). Mapping signatures of positive selection in the genome of livestock. *Livestock Science*, *166*, 133–143. https://doi.org/10.1016/j.livsci.2014.05.003

Randhawa, I. A., Khatkar, M. S., Thomson, P. C., Raadsma, H. W. (2016). A meta-assembly of selection signatures in cattle. *PLoS One*, *11*(4), e0153013.

Silva, B., Gonzalo, A., & Cañón, J. (2006). Genetic parameters of aggressiveness, ferocity and mobility in the fighting bull breed. *Animal Research*, *55*(1), 65–70. https://doi.org/10.1051/animres:2005046

Spady, T. C., & Ostrander, E. A. (2008). Canine behavioral genetics: Pointing out the phenotypes and herding up the genes. *American Journal of Human Genetics*, *82*(1), 10–18. https://doi.org/10.1016/j.ajhg.2007.12.001

da Veiga, C. P., Miczek, K. A., Lucion, A. B., & de Almeida, R. M. (2011). Social instigation and aggression in postpartum female rats: Role of 5-Ht1A and 5-Ht1B receptors in the dorsal raphe nucleus and prefrontal cortex. *Psychopharmacology (Berl)*, *213*, 475–487. https://doi.org/10.1007/s00213-010-2083-5

Vitalis, R., Gautie, M., Dawson, K. J., & Beaumont, M. A. (2013). Detecting and measuring selection from gene frequency data. *Genetics*, *196*, 799–817.

Xing, H., Ling, J., Chen, M., & Gu, J. G. (2006). Chemical and cold sensitivity of two distinct populations of TRPM8-expressing somatosensory neurons. *Journal of Neurophysiology*, *95*(2), 1221–1230. https://doi.org/10.1152/jn.01035.2005

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: Eusebi PG, Cortés O, Carleos C, Dunner S, Cañón J. Detection of selection signatures for agonistic behaviour in cattle. *J Anim Breed Genet*. 2018;135:170–177. https://doi.org/10.1111/jbg.12325