THE UNIVERSITY of EDINBURGH

Edinburgh Research Explorer

Phenotypic and genetic characterisation of disease subtypes of equine recurrent exertional rhabdomyolysis

Citation for published version:
Lindsay, V, Massey, C, Li, YT, Clark, E, Piercy, RJ & Psifidi, A 2023, Phenotypic and genetic characterisation of disease subtypes of equine recurrent exertional rhabdomyolysis. in *Proceedings of the British Society of Animal Science: (BSAS 2023).* 2 edn, vol. 14, 077, Elsevier B.V., pp. 340-341, British Society of Animal Science, Birmingham, 28/03/23. https://doi.org/10.1016/j.anscip.2023.01.454

Digital Object Identifier (DOI):
10.1016/j.anscip.2023.01.454

Link:
Link to publication record in Edinburgh Research Explorer

Document Version:
Peer reviewed version

Published In:
Proceedings of the British Society of Animal Science

General rights
Copyright for the publications made accessible via the Edinburgh Research Explorer is retained by the author(s) and / or other copyright owners and it is a condition of accessing these publications that users recognise and abide by the legal requirements associated with these rights.

Take down policy
The University of Edinburgh has made every reasonable effort to ensure that Edinburgh Research Explorer content complies with UK legislation. If you believe that the public display of this file breaches copyright please contact openaccess@ed.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.

OPEN ACCESS

Download date: 24. Feb. 2024

Phenotypic and genetic characterisation of disease subtypes of equine recurrent exertional rhabdomyolysis

V. Lindsay a,b,, C. Massey a, Y.T. Li a, E.L. Clark c, R.J. Piercy d, A. Psifidi a,c

a Royal Veterinary College, London, United Kingdom

b University of Edinburgh, Edinburgh, United Kingdom

c Roslin Institute, University of Edinburgh, Edinburgh, United Kingdom

d Royal Veterinary College, Edinburgh, United Kingdom

Presenting author.

Victoria Lindsay. E-mail: vlindsay@ed.ac.uk

Application

Identification of clinical subtypes of RER improves our ability to study the genetic basis and aetiopathogenesis of the disease, as well as seek potential treatments. This improves the welfare of the animals as well as having an impact on the huge financial losses suffered by the racing industry due to RER.

Introduction

Equine recurrent exertional rhabdomyolysis (RER) is a myopathy characterised by exercise-induced episodes of myofibre necrosis. RER is clinically heterogenous, with variation between clinical signs and severity of those signs between individuals and between episodes, with severe cases resulting in recumbency, kidney failure and even death. RER is a moderately heritable disease ($h2 = 0.34–0.49$) (Norton et al.,2016), but causal genetic variants have not yet been identified. Previous studies in another exertional myopathy, polysaccharide storage myopathy, identified disease subtypes with differing genetic basis (McCue et al., 2008, 2009). We aimed to identify possible disease sub-types within the RER syndrome.

Materials and methods

We applied principal components analysis, k-means clustering and hierarchical clustering methods to 209 RER horses retrospectively from the Royal Veterinary College's Comparative Neuromuscular Diseases Laboratory diagnostic biopsy service, to identify clusters of cases based on clinical history and histological records. We then tested variables for association with clusters using Chi-square testing.

A support vector machine algorithm was trained successfully to differentiate between classic and non-classic RER cases, and this algorithm was applied to a dataset of 127 Warmblood horses (WB) and Connemara ponies (CP) (CP: 16 cases, 17 controls; WB: 50 cases, 44 controls).

Genome-wide association studies (GWAS) were carried out within and across breed and disease subtype.

Using 69 samples of equine semimembranosus muscle from Arabian, Thoroughbred and WB horses (24 classic RER, 12 non-classic RER, 26 negative controls, and 7 with myofibrillar abnormalities), we carried out a blinded histological study comparing features identified by a specialist between disease groups from a standard panel of myopathy staining and immunohistochemistry, including for

desmin. We selected features with $p < 0.1$ on a univariate contingency table or two-way ANOVA for inclusion in a binary (between the subtypes) or multinomial logistic regression model.

Results

Consistently, horses grouped into 'classic' and 'non-classic' RER subtypes: cases with no particular defining features, versus cases associated with gait abnormalities ($p < 0.001$), muscle pain ($p < 0.001$), weakness ($p = 0.001$), ataxia ($p = 0.001$), and reluctance to move ($p = 0.001$).

GWAS identified different patterns of genetic associations between breeds and between the disease subtypes. No convincing histological differences were identified between the disease subtypes, supporting our clustering analysis, and indicating that any histological differences between disease subtypes are not captured by current staining panels.

Conclusions

Overall, RER is a complex disease, likely consisting of multiple disease subtypes with possible distinct genetic associations.

Acknowledgments

This work was funded by the RVC Mellon Fund for Equine Research. We also wish to thank the referring vets and owners for submitting

samples.

References

McCue, M.E., Valberg, S.J., Miller, M.B., Wade, C., DiMauro, S., Akman, H.O., Mickelson, J.R., 2008. Genomics 91 (5), 458–466.

McCue, M.E., Armién, A.G., Lucio, M., Mickelson, J.R., Valberg, S.J., 2009. Vet. Pathol. 46 (6), 1281–1291.

Norton, E.M., Mickelson, J.R., Binns, M.M., Blott, S.C., Caputo, P., Isgren, C.M., McCoy, A.M., Moore, A., Piercy, R.J., Swinburne, J.E., Audin, M., McCue, M.E., 2016. J. Heredity 107

(6), 537–543.

doi: 10.1016/j.anscip.2023.01.454

078

Microbiological etiology of infectious infertility in Arabic mares

B. Qasemi-Panahi , M. Khodaei, G. Moghaddam, A. Rafat

Department of Animal Science, Faculty of Agriculture, University of Tabriz, Tabriz, Islamic Republic of Iran

Presenting author.

Babak Qasemi-Panahi. E-mail: babakpanahi98@gmail.com