GESTATIONAL IMMATURITY HAS A BILATERAL DYSREGULATORY EFFECT ON THE HPA AXIS IN ADULT HORSES

Jane Clothier[1,2], Geoff Hinch[2], Wendy Brown[2], and Alison Small[1]

[1] CSIRO Agriculture, FD McMaster Laboratory, New England Highway, Armidale, NSW, Australia, [2] School of Environmental and Rural Sciences, University of New England, NSW, Australia

AGRICULTURE FLAGSHIP
www.csiro.au

This study tested the hypothesis that adult horses with a history of prematurity or dysmaturity at birth would present adrenocortical dysregulation, and would therefore have an abnormal (blunted or elevated) cortisol response to a low dose ACTH stimulation.

INTRODUCTION

It is known that impaired foetal growth in mammals can lead to prematurity and/or low birthweight, resulting in an adaptation of the immature Hypothalamic Pituitary Adrenal (HPA) axis and a hypo- or hyper-responsiveness to later stressors. In the equine, foetal stressors, including undernutrition, placentitis, and hypoxia, and/or environmental stresses affecting the dam, have been associated with transient adrenal dysregulation. However, research to date has been limited.

Methods

- Horses (n=22), aged 3 to 22 yo, maintained in paddocks in Northern NSW, Australia. Breeds included Arabians, Warmbloods, Warmblood-Thoroughbreds, Shires, Standardbreds, and crosses thereof.
- Case horses (n=10) had a history of prematurity (296-310 d gestation) or dysmaturity (small for gestational age, 321-376 d gestation). Positive controls (n=7) and negative controls (n=5) were matched by family group, breed and location.

Fig 1: 4yo Arabian gelding, born prematurely at 305 d gestation.

- Cases and positive controls received 0.1 µg/kg BW of synthetic ACTH (Tetracosactrin 250 mg/mL, Synacthen®), administered intramuscularly. Saliva samples were collected from all horses at baseline and 30 min intervals to 2.5 h post-stimulus. Samples were assayed for salivary cortisol concentration (SCC) using a salivary cortisol enzyme immuno-assay kit (Salimetrics®).
- SCC values were measured (peak; deltaAUC: integrated area under the curve), and Cases' values compared against Positive Controls' distribution. Cases fell into 2 groups: supressed and elevated cortisol responses and were reallocated to low and high responder groups.
- Relationships between gestational status and SCC were assessed using one-way ANOVA in a statistical computing program (R Studio).

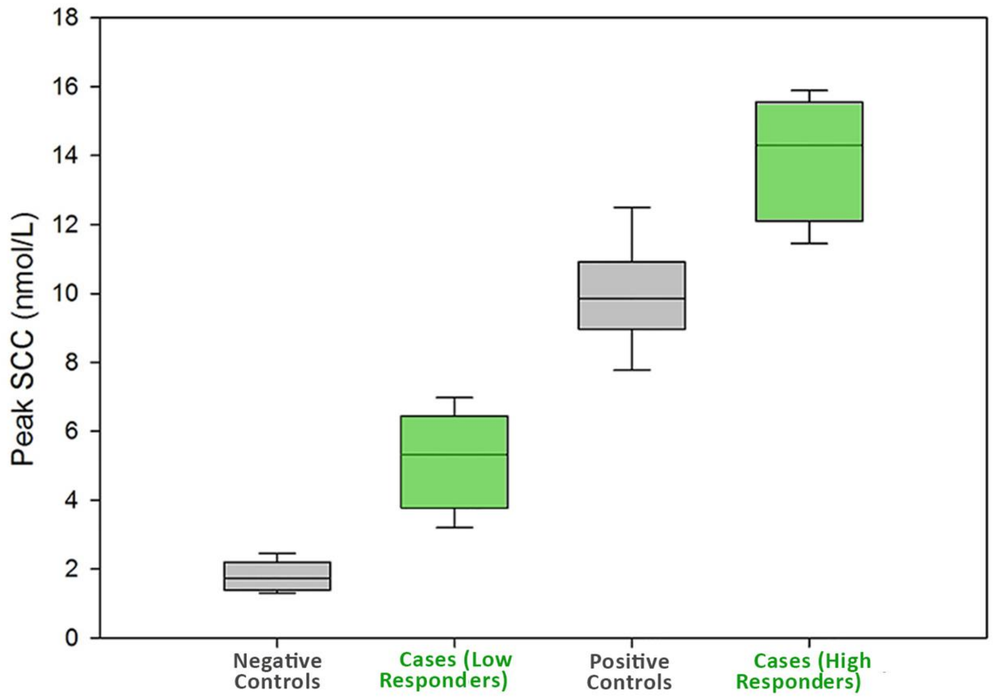

Fig 2: Means for SCC following ACTH stimulation.

Results

Data were normally distributed; values are presented as means ± S.E. All basal values were within normal published ranges. Peak and AUC values (corrected for baseline) for case horses were significantly different (ANOVA $p<0.001$) to positive controls, with either higher (H-cases) or lower (L-cases) SCC values, outside the 95% CI of the reference population. There was no significant effect of breed, age, sex, test month, or location on results.

Group	Basal SCC and Range (nmol/L)	DeltaAUC SCC and Range (nmol/L)
L-cases (n=6)	1.54 ± 0.42 (0.63 - 3.42)	7.03 ± 2.39 (-0.01 - 16.91) *
H-cases (n=5)	1.12 ± 0.13 (0.8 - 1.35)	30.88 ± 0.82 (28.51 - 32.36) *
P-controls (n=7)	1.33 ± 0.30 (0.55 - 2.59)	20.6 ± 2.20 (12.57 - 24.68) *
N-controls (n=5)	1.53 ± 0.55 (0.47 - 3.5)	-0.68 ± 1.76 (-6.12 – 2.7) *

* Means differ significantly (P < 0.001)

Table 1: Basal and post-stimulation SCC for all horses. Data are mean ± SE.

Conclusion

Results suggest that premature and dysmature birth results in persisting adrenocortical dysregulation, with affected adults presenting an elevated or blunted response to a low-dose ACTH stimulation.

FOR FURTHER INFORMATION
Jane Clothier
e jane.clothier@csiro.au

All procedures were approved by the CSIRO Armidale Animal Ethics Committee under the NSW Animal Research Act, 1985 (Animal Research Authority ARA 16/03) and the University of New England Animal Ethics Committee (Authority no. AEC15-061).