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What is the relationship between level of infection and 'sickness behaviour' in cattle?

Ollie Szyszka*, Ilias Kyriazakis

School of Agriculture Food and Rural Development, Newcastle University, Newcastle upon Tyne, NE1 7RU, UK

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ABSTRACT

We hypothesised that a range of parasite doses that cause subclinical disease would lead to similar behavioural changes in cattle. This was tested by infecting bull calves with one of four different doses of the gastrointestinal parasite *Ostertagia ostertagi*: 0 (control), 75,000 (L), 150,000 (M) or 300,000 (H) larvae, whilst measuring aspects of their behaviour, usually encompassed by the term 'sickness behaviour'. For parasitised bulls faecal egg counts and serum pepsinogen levels were elevated from Day (D) 20, the latter being affected linearly by dose. The different doses had different effects on animal fitness: body weight gain (BWG) was reduced for treatments M and H from D23, with M animals showing a recovery after D30, whereas H bulls continued to have lower BWG. Behaviours were only affected for H animals. Average lying episode duration increased by 25% and lying and standing episode frequency decreased by 22% from around D29 when compared to uninfected controls. The number of steps taken by H animals decreased by 34% relative to the controls from D34–46. There was no significant effect on any parameters of feeding behaviour. The results suggest that, for a wide range of parasite doses, general posture, activity and feeding behaviour may be unaffected despite some effects on host fitness. However, higher doses which may lead to clinical disease result in effects that are possibly directly related to pathogen dose. The practical applications of detecting health challenges through behaviour may therefore depend on the level of infection and their pathophysiological consequences.

1. Introduction

It is now well established that health challenges, such as infection with a pathogen or stimulation of the immune response, may lead to changes in animal behaviour (Hart, 1990; Larson and Dunn, 2001; Weary et al., 2009; Szyszka et al., 2012). Such behavioural changes may have diagnostic value, as these can precede any clinical signs of the condition (Quimby et al., 2001; Huzzey et al., 2007; González et al., 2008; Kyriazakis and Tolkamp, 2010).

The question whether the onset and extent of the behavioural changes are related to the size of the health challenge, such as the infectious dose of a pathogen, remains largely unanswered. There is little information about the relationship between pathogen dose and change in behaviours. The few exceptions are studies, mainly in rodents, suggesting a negative relationship between challenge dose and social exploration (Edwards, 1988; Bluthé et al., 1996), anxiety (Bassi et al., 2012) or activity (Johnson and von Borell, 1994; Skinner et al., 2009). There is also indirect evidence of a possible relationship between pathogen dose and the different dimensions of feeding behaviour (González et al., 2008). In all these experiments, however, infection either occurred naturally, or only a narrow range of infective doses was used. As a consequence, these do not allow conclusions about the form of the relationship.

* Corresponding author. Tel.: +44 (0)191 2227402; fax: +44 (0)191 2226720.
E-mail address: ollie.szyszka2@newcastle.ac.uk (O. Szyszka).

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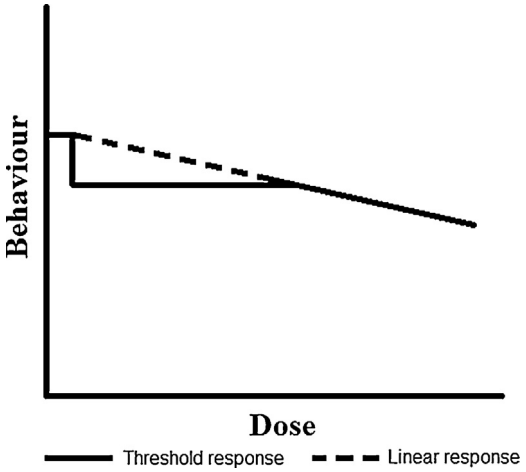

Fig. 1. Two potential relationships between a pathogen infective dose and the effect on host behaviour. Both assume that no effects will be observed at very low doses. The solid line suggests that a range of intermediate infective doses will have similar effects on behaviour initially. Only at higher infective doses does the relationship between the two become dose dependent. The dotted line suggests that increasing pathogen doses lead to increasing effects on behaviour. At high levels of infection the two models relationships coincide. Although a decrease in behaviour is represented here, an increase is also possible depending on the type of behaviour.

Knowledge of such relationships has both theoretical and diagnostic value, as it would allow targeted interventions and will therefore enhance animal health and welfare.

There are at least two possible forms of the relationship, shown on Fig. 1. The first is that above a certain dose the change in behaviour is of the same magnitude for a wide range of doses that may lead to (subclinical) diseases. Only at high pathogen doses that may lead to clinical disease, further changes in behaviour become apparent and may be linearly related. This expectation comes from the studies on pathogen-induced anorexia; these have demonstrated that over a wide range of infective doses with macro- or micro-parasites the reduction in food intake is very similar for a variety of animals and pathogens (as summarised by Kyriazakis et al., 1998; Sandberg et al., 2006; Kyriazakis, 2010). The second possible form is that increasing pathogen doses lead to increasing changes in behaviour. These two relationships will have different (intervention) consequences when using behaviour as a predictor of the level of infection. The objective of this study was to investigate the relationship between the infective dose of a macroparasite, *Ostertagia ostertagi*, and a number of behaviours in growing cattle. *O. ostertagi* is the most significant parasite affecting cattle in temperate climates (Anderson, 1988; Rinaldi and Geldof, 2012). As the selected range of macroparasite doses was expected to lead to subclinical infections (Szyszka et al., 2012, 2013), we hypothesised that the relationship would be of the first form, i.e. that the effects on the behaviours would be of similar magnitude across all doses. The behaviours focused upon in this study and considered representative of 'sickness behaviour' were chosen on the basis that they had previously been found to change as a consequence of an *O. ostertagi* infection (Szyszka et al., 2012, 2013). They consisted of activity, general posture and feeding behaviour. The behavioural changes were expected to occur as a consequence of the pathophysiological consequences (abomasal damage) induced by the parasite.

2. Materials and methods

The experiment took place at the facilities of Newcastle University after approval of the experimental protocols by the Animal Experiments Committee and under license according to the UK Animals (Scientific Procedures) Act for regulated procedures.

2.1. Animals and housing

The animals selected for the study were 24 Holstein-Friesian bull calves aged between 5 and 6 months, with an average weight of 210 ± 30 kg and obtained from a single source. All animals were housed in a single, straw-bedded pen, measuring 116 m^2. Both food and water were available *ad libitum*. The food offered was a total mixed ration, consistent throughout the experiment, containing 31.3% barley, 18.5% sugar beet pellets, 16% soya bean meal, 13.4% crushed barley, 9.8% distillers maize, 7.4% molasses and 3.8% chopped barley straw. The nutrient composition of the food was 13.01 MJ Metabolisable Energy and 197 g Crude Protein per kg dry matter as estimated from AFRC (1993) feed tables. The animals had not received any prior challenge with parasites and were treated with 2 ml of the anti-inflammatory dexamethasone (Rapidexon, Eurovet, Cambridge, UK), 8 ml of the antibiotic florfenicol (Nuflor, Shering-Plough, Milton Keynes, UK) and 7.5 mg/kg body weight (BW) of the anthelmintic albendazole (Albenil, Virbac, Woolpit, UK) two weeks before the experiment started, to prevent interference from other potential health challenges.

2.2. Experimental design

The experiment was considered to start when the animals first received a parasite challenge (designated as Day 0). Prior to being challenged (Day −8) animals were fitted with a pedometer (Icetag, IceRobotics, South Queensferry, UK) on their right front leg; the pedometer was secured with a Velcro strap. Video recordings of their behaviour started at the same time in order to provide background data before the start of the experiment.

The animals were randomly assigned, whilst balancing for BW, to one of four treatments ($n = 6$ per treatment). The first three treatment groups, High (H), Medium (M) and Low (L) received a total dose of 300,000, 150,000 or 75,000 L3 *O. ostertagi* larvae respectively, which were administered on three occasions by gavage on Days 0, 7 and 14 of the experiment in three equal amounts. Dose H had been used in previous experiments (Szyszka et al., 2013) and had led to significant changes in the behaviour of bulls during the course of the infection seen as an increase in average lying duration and reductions in lying episode frequency, activity and meal frequency. The parasitism induced by all doses was expected to be subclinical (Szyszka et al., 2012, 2013). Animals remained infected for the duration of the experiment (up to Day 55). The fourth treatment group acted as an unchallenged control (C). Animals on this