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COMMENT

The Bruce effect should be defined by function, not mechanism: comments on 'How to escape male infanticide: mechanisms for avoiding or terminating pregnancy in mammals'

Matthew N. ZIPPLE* *Department of Biology, Duke University, Durham, NC 27708, USA. Email: matthew.zipple@duke.edu*
Eila K. ROBERTS *Department of Integrative Biology, Michigan State University, East Lansing, MI 48824, USA. Email: eroberts@msu.edu*
Susan C. ALBERTS *Department of Biology, Duke University, Durham, NC 27708, USA and Department of Evolutionary Anthropology, Duke University, Durham, NC 27708, USA. Email: alberts@duke.edu*
Jacinta C. BEEHNER *Departments of Psychology and Anthropology, University of Michigan, Ann Arbor, MI 48109, USA. Email: jbeehner@umich.edu*

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*Correspondence

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ABSTRACT

Bartoš et al. (2021; *Mammal Review* 51: 143–153; https://doi.org/10.1111/mam.12219) reviewed the mechanisms involved in the 'Bruce effect' – a phenomenon originally documented in inseminated female house mice *Mus musculus*, who block pregnancy following exposure to a novel (non-sire) male. They argue that the term 'Bruce effect' should be applied in cases that are mechanistically equivalent to this original observation in mice. We argue that the Bruce effect should be defined instead by its function: a phenomenon by which inseminated or pregnant females benefit by blocking or terminating pregnancy following exposure to a non-sire male. Only functional definitions of phenomena allow for the articulation and testing of evolutionary hypotheses.

INTRODUCTION

In a recently published review, Bartoš et al. (2021) discussed the mechanisms involved in the Bruce effect, a phenomenon originally described by Hilda Bruce, who, more than 50 years ago, observed that exposing recently inseminated females to non-sire males can block pregnancy (Bruce 1959). In their review, Bartoš and colleagues suggest a very specific definition for the Bruce effect; it should be reserved to describe only cases where two conditions are met: 1) a female has physical contact with a male or his secretions; and 2) prenatal loss occurs before implantation. Since Bruce's original publication, many studies in mammalian taxa have demonstrated the general phenomenon of male-mediated prenatal loss, in which the loss does not meet these two criteria, but is nonetheless functionally equivalent to Bruce's original observation. Some include cases where direct contact is not necessary to induce pregnancy loss; some include cases where pregnancy loss occurs post-implantation. Bartoš and colleagues argue that these cases should not be referred to as the Bruce effect. We disagree.

We recently proposed a much broader definition for the term 'Bruce effect' that remains agnostic to the mechanism involved, focusing instead on the function (Zipple et al. 2019). We argue that the Bruce effect comprises all cases where females spontaneously and adaptively abort, following their exposure to a novel male (Zipple et al. 2019). Although we agree with Bartoš and colleagues that the imprecise use of language has hindered progress in this area of research, we disagree about the appropriate solution to this problem. Below, we describe three ways in which the arguments that we put forth in our 2019 article agree with those of Bartoš and colleagues, before describing our most salient points of disagreement.

POINTS OF AGREEMENT

First, despite Bartoš and colleagues' claim to the contrary (see Table 1 of Bartoš et al. 2021), we agree that the term 'Bruce effect' should not be used to refer to all cases where an abortion occurs following exposure to a non-sire male. We agree that a consistent, precise terminology is needed when referring to phenomena surrounding pregnancy loss. Absent such consistent terminology, it is impossible to construct and test hypotheses surrounding the mechanisms and evolution of these phenomena (Zipple et al. 2019, p. 116).

Second, we agree that the mechanisms involved in pre- and post-implantation fetal loss are necessarily very different (Zipple et al. 2019, p. 123). The various mechanisms that cause the Bruce effect in house mice all rely on a functioning vomeronasal system to absorb and process chemosensory information (Brennan & Keverne 2015, deCatanzaro 2015). Use of this chemosensory system has been ruled out for many of the taxa in which post-implantation failure has been identified: geladas *Theropithecus gelada* do not have a functioning vomeronasal system (Bhatnagar & Smith 2007), and the domestic horses and dogs that experienced post-implantation failure did not have physical contact with the males that induced the failure (Bartoš et al. 2011, 2016).

Finally, we agree that male-mediated prenatal loss is likely to be much more widespread than currently appreciated (indeed, more widespread than sexually-selected infanticide), and that the primary roadblock to detecting these phenomena is the difficulty in observing prenatal loss in wild populations (Zipple et al. 2019, p. 116 & 122). We are optimistic that examples of male-mediated prenatal loss from throughout the mammalian taxonomy will emerge if researchers employ methods to detect prenatal loss specifically, following exposure of inseminated or pregnant females to non-sire males.

POINT OF DISAGREEMENT

The primary disagreement that we have with Bartoš and colleagues is that we believe the term 'Bruce effect' should be defined by function, not mechanism. Our view is that observations from different taxa that have identical functional outcomes should be referred to by the same term, an opinion in which we are not alone (Eccard et al. 2017).

The rationale for our argument rests on two main points. First, natural selection acts on functional outcomes, even if the mechanisms involved in achieving that outcome can vary. Second, we need functional definitions to test hypotheses about the evolution of closely related, but mechanistically distinct, phenomena that appear in different taxa. As an example, consider the wide range of signal modalities – acoustic, chemical, vibratory, and visual – by which individuals of different species assess the quality of a potential mate or competitor. The diverse proximate mechanisms involved in each of these signalling modalities have been studied in distantly related taxa, but such inquiries are united by hypotheses about how reliable signalling evolves and is maintained (Searcy & Nowicki 2005). Restricting the term 'assessment signal' to only a subset of these functionally equivalent signal modalities would prevent universal theories of signal evolution from ever being articulated or tested. Thus, to evolutionary biologists, phenomena are defined not by the mechanisms that produce them, but rather by the fitness implications that result from them.

We classify observations of male-mediated prenatal loss into two functionally defined categories: foeticide and the Bruce effect. First, we define foeticide as "when males harass pregnant females with threats and aggression to the extent that females terminate pregnancies" (Zipple et al. 2019). The functional result of this physical harassment for the female is a lost foetus, lost time investment, and (in some instances) physical injury or death for the female. The functional result for the male is that the female will resume oestrous cycling and become fertile during a period when she otherwise would be unavailable to him. Thus, foeticide (or embryocide, if prenatal loss occurs before implantation) is a male adaptation that yields benefits for males and imposes costs on females.

We define the Bruce effect as "when females terminate pregnancies after some form of sensory exposure (olfactory, visual, auditory, or tactile) to nonsire males. Importantly, although nonsire males may exhibit aggression toward females, aggression from males is not necessary to elicit the Bruce effect" (Zipple et al. 2019). The functional outcome of the Bruce effect for males is the same as that presented by foeticide, but it is quite different for females. Rather than simply losing a foetus or embryo and perhaps being injured or even killed in the process (as occurs following foeticide), females that exhibit the Bruce effect do so as a cost-mitigating strategy to avoid future infanticide by the male (Zipple 2020), or perhaps to attain some other benefit (e.g. Schwagmeyer 1979). Thus, the Bruce effect is a female–male co-adaptation that provides relative benefits to females, while foeticide is a male adaptation that is exclusively costly to females.

In contrast to our functional definition, a mechanistic definition focuses on a set of arbitrary neuroendocrine boundaries that underlie related observations. Bartoš and colleagues choose two mechanistic requirements for an observation to be considered the 'Bruce effect': 1) the immediate trigger involves physical contact with the non-sire male (despite evidence from Bruce's early work that physical contact is not strictly necessary to induce pregnancy block in house mice; see 'Situation B' in Bruce 1960); and 2) the prenatal loss occurs before implantation.

Such a definition leads to at least three undesirable outcomes. First, the definition of Bartoš and colleagues requires us to be either too liberal or too restrictive in how we classify observations of prenatal loss. For example, their definition requires that we either assign the Bruce effect to numerous species of rodents, even though we have not precisely isolated the mechanism they use (too liberal), or that we restrict all use of the term until we conduct experiments that demonstrate they use the same mechanism as observed in the taxon that Bruce, herself, observed – house mice (too restrictive). At best, this definition assumes that the mechanisms involved in many species are equivalent, even where the endocrinological mechanisms are unknown. At worst, this definition means that the term remains forever off-limits for wild taxa where invasive experiments are not possible.

Second, this definition requires that different terms are used to describe the same functional outcome, even in a single species. For example, several species of rodents display male-mediated prenatal loss both before and after implantation (reviewed in Zipple et al. 2019, Bartoš et al. 2021). The definition advocated by Bartoš and colleagues would require researchers to use the term Bruce effect for loss *before implantation yet use a different term* (such as 'pregnancy termination') to refer to loss *after* implantation. Their definition necessitates this distinction despite identical functional outcomes. We believe this will only increase confusion in our science.

Third, Bartoš and colleagues' definition inevitably results in functionally distinct phenomena being grouped together. For example, embryocide would fall under their definition of the Bruce effect because it occurs before implantation and involves physical contact with males. Yet, embryocide (included in our definition of foeticide) imposes a net cost to females (where, by contrast, the Bruce effect yields a net benefit). The same is true for foeticide. Bartoš and colleagues treat foeticide as equivalent to adaptive male-mediated prenatal loss occurring after implantation. For example, pregnant female yellow baboons *Papio cynocephalus* terminate their pregnancies after being attacked by males that have recently immigrated into their groups (a clear net cost for females; Pereira 1983, Zipple et al. 2017). In contrast, pregnancy termination in geladas occurs without any apparent physical aggression from males, and females that terminate following male takeover have greater reproductive success than females that lose their offspring to infanticide (so that termination is an adaptive, cost-mitigating strategy for females; Roberts et al. 2012). Yet, despite both these mechanistic and functional differences, the framework put forward by Bartoš and colleagues groups foeticide and adaptive male-mediated loss occurring after implantation together.

In sum, the definition of the Bruce effect put forward by Bartoš and colleagues is simultaneously too restrictive in some applications and too broad in others. More generally, taking a mechanistic approach to defining phenomena fails to uncover the role of natural selection in producing these phenomena and can lead to an incorrect interpretation of the evolutionary dynamics involved. For example, a researcher that focuses only on mechanisms and does not consider the functional significance of these phenomena may conclude that non-sire males use the Bruce effect to 'hijack' the reproductive system of females and induce pregnancy block or failure. Yet, with an understanding of the role of selection in the evolution of communication systems, we can dismiss this interpretation: communication systems break down quickly if the receiver does not benefit from the signal (Searcy & Nowicki 2005). Thus, a functional understanding leads us to assign agency to the pregnant female instead, who terminates her pregnancy as a cost-cutting effort to limit future costs of infanticide.

Choosing to focus on function, rather than mechanism, allows researchers to identify equivalent evolutionary outcomes in distantly related taxa that would otherwise be missed. For example, in addition to the Bruce effect, rodents also display the Vandenbergh effect, a phenomenon first described in house mice in which immature females respond to chemical cues by accelerating their sexual maturation following exposure to a novel male (Vandenbergh 1967). Just as multiple primate species have evolved the Bruce effect without relying on chemical cues (Roberts et al. 2012, Amann et al. 2017), geladas also exhibit the Vandenbergh effect and rely on social and visual cues, rather than chemical cues to do so (Lu et al. 2021). Thus, in the case of both the Bruce and Vandenbergh effects, selection has resulted in convergent functional evolution in rodents and primates, even though the mechanisms involved are different. A functional view of the world allows these evolutionary parallels to be identified and hypotheses about the selective processes involved in this evolution to be tested. A view of the world that focuses exclusively on mechanism allows for neither.

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