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Developmental Programming, Evolution, and Animal Welfare: A Case for Evolutionary Veterinary Science

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ABSTRACT

The conditions animals experience during the early developmental stages of their lives can have critical ongoing effects on their future health, welfare, and proper development. In this paper we draw on evolutionary theory to improve our understanding of the processes of developmental programming, particularly Predictive Adaptive Responses (PAR) that serve to match offspring phenotype with predicted future environmental conditions. When these predictions fail, a mismatch occurs between offspring phenotype and the environment, which can have long-lasting health and welfare effects. Examples include metabolic diseases resulting from maternal nutrition and behavioral changes from maternal stress. An understanding of these processes and their evolutionary origins will help in identifying and providing appropriate developmental conditions to optimize offspring welfare. This serves as an example of the benefits of using evolutionary thinking within veterinary science and we suggest that in the same way that evolutionary medicine has helped our understanding of human health, the implementation of evolutionary veterinary science (EvoVetSci) could be a useful way forward for research in animal health and welfare.

KEYWORDS

Developmental programming; animal nutrition; predictive adaptive response; animal health; animal welfare; evolutionary medicine; maternal nutrition

Introduction

The phenomenon of developmental programming – the effects of the early developmental environment on the eventual phenotype of an organism – is gaining increasing attention within the medical and veterinary sciences. The conditions under which a young animal develops – such as prenatal or early postnatal exposure to nutritional state, chemicals and hormones, and maternal stress – can alter its anatomy, physiology, and behavior (Sutton et al., 2016). Exposure to stressors during critical developmental periods in early life will have lasting effects not seen from the same exposure even a few weeks later (Gross & Siegel, 1980). It can also have transgenerational effects, altering phenotypes in not only the young animals, but their own future offspring (Zimmer, Larriva, Boogert, & Spencer, 2017). The primary mechanisms through which fetal development are affected are structural changes in developing organs, accelerated cellular aging, and epigenetic effects such as DNA methylation, which alter the patterns of gene expression (Sutton et al., 2016). These changes can then have ongoing effects on an animal's health and welfare, as will be discussed in some of the examples throughout the paper.

Originally championed by the English physician and epidemiologist David J.P. Barker and colleagues, developmental programming (also sometimes known as the Barker hypothesis) was intended to explain the link between events occurring during the fetal gestation period and the prevalence of diseases in later life (Barker, 1998). This work contributed to the formation of a new research program known as as the developmental origins of health and disease (DOHaD) (Barker et al., 2013). More generally, developmental programming research includes any work relating the

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conditions of fetal gestation to offspring phenotype, such as Barker's earlier doctoral work also observing developmental effects on intelligence (Barker, 1966). The aim of this research has been to elucidate the importance of an organism's early developmental stages for their functioning in later life. Most of this work has focussed on the links between maternal nutrition and offspring health, such as Barker's later work establishing a strong link between the weight of newborns and one-year old children and their eventual risk for heart disease (Barker, Osmond, Winter, Margetts, & Simmonds, 1989) – though this is only one of many possible conditions that can affect fetal development.

Naturally, the DOHaD research program has historically been focused on *human* health (Gluckman, Hanson, & Spencer, 2005; Hales & Barker, 1992, 2001). This is in part a response to the nature of research funding, and the origins of the field in Barker's work on humans. Thus, once we move away from the human animal, far less is known about the effects of developmental programming in other animals (Khanal & Nielsen, 2017). What is known has largely come about as a side-effect of DOHaD research for human medicine, as much of this research is conducted on animal models: for example, sheep are the standard model for human pregnancy, and have been for decades. Work on the effects of maternal stress and early maternal separation have similarly used primate, rodent, and avian models (Goerlich, Nätt, Elfwing, Macdonald, & Jensen, 2012; Murthy & Gould, 2018; Van der Horst & Van der Veer, 2008; Zimmer et al., 2017). Thus, where work on animals has been performed, it has not often been with an eye toward understanding the important conditions for these animals *themselves*. Where developmental programming is considered, it is rarely through an evolutionary lens (e.g. Sinclair et al., 2016). We will discuss some of this animal work in more detail in Section 3.

This neglect is highly unfortunate, for two reasons. *Firstly*, as we will discuss in Section 2, there is substantial evidence that many of the phenomena of developmental programming are adaptive developmental responses of organisms for coping with harsh environments. This piece of evolutionary reasoning naturally applies not only to humans, but equally to nonhuman animals (Bateson et al., 2004; Gluckman & Hanson, 2004; Gluckman, Hanson, & Beedle, 2007; Gluckman et al., 2005; Griffiths & Matthewson, 2018; Matthewson & Griffiths, 2017; Veit, 2021a, 2021b). *Secondly*, an improved understanding of developmental programming can be used to shape research programs aimed at substantially improving not only the productivity of animal farming practices, but also more generally the health and welfare of animals in captivity. An understanding of developmental programming effects can aid in identifying and providing suitable maternal environments to ensure better developmental conditions for offspring.

Within animal welfare science, it has remained a contested issue as to what exactly animal welfare consists in, despite the fact that different conceptions of animal welfare can alter how it is studied and what the best actions are for improving it (Broom, 2011; Browning, 2019; Dawkins, 2009, 2021). However, most currently used concepts take welfare to contain one or more of the following: physical functioning, preference satisfaction, subjective experiencing, and natural living (Green & Mellor, 2011; Veit & Browning, 2020). Developmental programming will have impacts on welfare particularly within the domains of physical functioning and subjective experiencing, as we will see later on in the paper. The health impacts of developmental programming can result in both poor physical functioning and the negative affects that are typically linked with the presence of disease and illness, such as pain, nausea and discomfort (Fraser & Duncan, 1998; Veit & Browning, 2021). Thus, even under a conception of animal welfare that makes health only an instrumental rather than constitutive part of welfare, such as a purely feelings-based account (e.g. Browning, 2020; Duncan, 2002), developmental programming will remain as much of an animal welfare concern as it is a health or a production concern. Developmental programming can also have effects on stress responses – again, with associated changes in physical functioning and subjective experience, as well as performance of of natural or abnormal behaviors. Despite this, welfare issues are rarely raised in discussions on developmental programming, with the growing literature instead focussing primarily on mechanistic understanding (e.g. Beauclercq et al., 2019; Ericsson & Jensen, 2016; Foury et al., 2020; Lay Jr and Wilson 2002) and improved productivity (e.g. Du, Ford, & Zhu, 2017; Greenwood, Clayton, & Bell, 2017; Hynd, Weaver, Edwards, Heberle, & Bowling, 2016).

The topic has yet received very little attention within animal welfare science itself and in this paper we want to connect two strands of research - developmental programming and evolutionary medicine – to at least partially remedy this omission. We also aim to shift more attention in the veterinary sciences more generally toward the study of the evolutionary functions of fetal and developmental programming. The paper is structured as follows. In Section 2, we take an evolutionary lens to developmental programming and show how this benefits our understanding of animal development. In Section 3 we provide some examples to show how this understanding can be used for shaping research programs and positive welfare implementations. In Section 4 we finish by discussing evolutionary medicine and the potential benefits of extending this approach into evolutionary veterinary science (sometimes abbreviated as EvoVetSci).

Early development and evolution: Predictive adaptive response

The developmental origins of health and disease provide a fruitful case study for an evolutionary approach to health and welfare sciences, as they naturally lend themselves to a close connection with evolutionary medicine. Indeed, some of the phenomena observed in developmental programming have been hypothesized as a predictive adaptive response (PAR) of organisms toward an uncertain and unstable environment (Bateson et al., 2004; Gluckman & Hanson, 2004; Gluckman et al., 2007, 2005; Griffiths & Matthewson, 2018; Matthewson & Griffiths, 2017). An often-quoted example of this developmental evolutionary reasoning is found in Bateson et al. (2004) who argue that the “ill effects of being small, which in the short term include high death rates and childhood illness, are usually treated as yet another inevitable consequence of adversity. However, a functional and evolutionary approach derived from the rest of biology suggests that the pregnant woman in poor nutritional condition may unwittingly signal to her unborn baby that it is about to enter a harsh world. If so, this ‘weather forecast’ from the mother’s body may result in her baby being born with characteristics, such as small body and a modified metabolism, that help it to cope with a shortage of food” (p. 420). The weather forecast analogy is a useful one, as it suggests a sort of rational gambling process during the early stage of development; one based on imperfect acquisition of information about the future. The conditions within the mother’s body provide an estimate of the likely conditions of the environment the offspring will inhabit and it then “bets” on the best developmental strategy for thriving within this predicted environment.

One excellent example of this type of gamble is the case of *Daphnia cucullata* (colloquially known as water fleas) (discussed in Matthewson & Griffiths, 2017). These fascinating planktonic crustaceans measure only a few millimeters and yet have evolved an ingenious developmental programming mechanism. These organisms typically live in an environment of high predation and can grow spikes on their tail and a helmet-like defense that helps them against predators. The production of this “defense phenotype” is costly, so it makes evolutionary sense to only grow them when they are necessary. Offspring *Daphnia*, however, do not have the luxury of waiting until they are born to “decide” whether or not to invest in production of defenses. Extraordinarily, the very same chemical sensors that help mothers to detect predators and decide whether to invest into their own defenses, help to inform the unborn offspring as to whether they should be born with or without defenses (Agrawal, Laforsch, & Tollrian, 1999).

Naturally, though, such bets can go wrong – sometimes drastically so: a developmental switch can misfire, and the organisms can end up with a *heuristic failure* (Matthewson & Griffiths, 2017). The information juvenile *Daphnia* receive during their development is never perfect, as it relies on the information available to the mother. Particularly when the environment undergoes rapid changes between the generations, this information will be misleading. If, for instance, their environment undergoes a sudden explosive growth of predators then the mothers, having themselves faced a low risk of predation, will have passed along incorrect information regarding the environment the offspring will face. The newly born offspring will lack defenses to face the new predators – a highly undesirable outcome. Similarly, *Daphnia* can be born fully armed into an environment that is predator-free, simply because their mother experienced a high number of predators during her life. Akin to a fully armed knight during a period of peace, these *Daphnia* pay an unnecessary cost and would have been better off if they hadn't entered this developmental trajectory. Though they would have higher fitness than unarmed relatives in high-predation environments, in this case something has gone wrong for them. Thus, even when their evolved developmental switch has discharged just "the function for which it was designed, in just the type of environment that selected for that predictive mechanism" there can still be a mismatch as the "best choice, given that information, may still turn out to be the wrong option" (Matthewson & Griffiths, 2017, p. 456).

The purpose of this extended example has been to demonstrate that an evolved mechanism can nonetheless fail to be adaptive under some circumstances, particularly when the rearing environment does not match that predicted by the developmental environment. This can be seen in other cases, such as that of human children who lack the ideal number of active sudoriferous (sweat) glands as a result of having been born into a cold climate and then relocated to a warmer one. A fetus will make predictive adaptive responses based on signals from the maternal developmental environment, and use these to "bet" on the best developmental pathway for the expected environment. Though these predictions may fail, it is still necessary for offspring to make them in order to attempt to be prepared for the environment they are most likely to face. Although the process will sometimes misfire, the heuristic itself can still be adaptive if it often enough gets the prediction right.

The concept of PAR has also been applied to the famous Dutch famine of 1944–45 during which German troops blocked the provision of food to the West of the Netherlands. Longitudinal studies found that children of those women who were pregnant during the famine – receiving only 400–800 calories per day at its peak – had a highly significant increase in health problems including metabolic diseases such as obesity, diabetes and cardiovascular disease (Painter, Roseboom, & Bleker, 2005; Roseboom, de Rooij, & Painter, 2006; Roseboom et al., 2001). These findings were surprising given that the children were born after the food embargo ended and thus themselves had access to (good) nutrition throughout their life. However, within the framework of evolutionary medicine, these results could be readily explained as an example of PAR (Gluckman, Beedle, & Hanson, 2009; Low, Gluckman, & Hanson, 2012).

Similarly to *Daphnia*, a human fetus is faced with important developmental decisions. From an evolutionary perspective, the developing fetus is faced with a decision based on uncertainty – i.e. imperfect information. What is the predictive adaptive response in such a setting? Again, this is nicely described by Matthewson and Griffiths: "if it ["]appears["] to a human fetus that its mother is not receiving adequate nutrition, its metabolism develops to be suited for future nutritional hardship" (Matthewson & Griffiths, 2017, p. 457). Since the environment of these children in fact ended up being one of nutritional abundance, their diseases are a natural result of a heuristic failure, since they "would have been better off if they had not prepared for famine" (Matthewson & Griffiths, 2017, p. 458). These surprising negative health impacts can easily be explained within the framework of evolutionary medicine: they are inevitable developmental trade-offs every organism has to engage in during their life-history – neither humans nor *Daphnia* are unique in this regard. The signals a fetus receives will determine its developmental trajectory, and in cases where these signals inaccurately represent the future environment, we will see a mismatch that will impact health and welfare. As seen, animals could invest in unnecessary costly phenotypes, or be susceptible to metabolic diseases.

In some cases where effects occur during the later stages of development, it could be argued that the observed effects are better understood as "making the best of a bad start" with insufficient available nutrients, rather than an adaptive life-history strategy such as a predictive adaptive response (Jones, 2005). These two propositions will not always be easy to distinguish, as for almost any proposal of predictive adaptive response, there is an available alternative explanation postulating the effect as merely an outcome of a lack of resources at some stage in the normal developmental process. However, we need not draw a hard distinction between ontogeny and evolutionary history – rather than looking at whether we need an evolutionary *or* developmental explanation we can see that each raise different questions that nevertheless inform each other (see Tinbergen, 1963). Depending on where in the developmental trajectory an effect is observed may influence how much it is explained by a predictive adaptive response as opposed to the mere optimization of trade-offs arising from a lack of available nutrients. In some cases, rather than resulting from a developing animal making a prediction about its future environment and the best strategy to succeed within it, the animal is instead acting under scarcity and investing the limited available nutrients in the most important structures and processes. Importantly, this does not imply that such developmental programming isn't adaptive: after all, the developing organism is still trying to maximize its benefits. It merely suggests that not all developmental programming is an adaptive response toward a potentially bad environment. It is thus not an argument against an evolutionary understanding of developmental programming, but rather one for the addition of more strands of understanding within the research program.

What we need is a move toward an evolutionary approach to understanding processes such as these. This can come in the form of evolutionary veterinary medicine, which encompasses an understanding of these developmental programming pathways that allows us to predict and offset their effects, and can also help shape our research programs. In the next section, we illustrate the evidence for adaptive developmental programming in domestic animals and thus the importance of evolutionary theorizing in the veterinary sciences, with positive welfare implications.

Developmental programming in domestic animals

We have shown how taking an evolutionary approach toward developmental programming can help us to better understand its causes and effects. In this section, we will take a closer look at the evidence for developmental programming in domestic animals, and how an evolutionary understanding could then be used to promote improved animal welfare in practice through aiding in identifying and implementing appropriate interventions. Here it is not our intention to give a comprehensive survey of the literature, but rather to point to a couple of examples that illustrate how an evolutionary approach to understanding developmental programming may help guide research and management.

The evidence for developmental programming is strongest in those animals most commonly used by humans. These mainly include model organisms used in research, such as the rodent models that have been extensively studied to understand the impact of inadequate nutrition in humans (Khanal & Nielsen, 2017). The study of developmental programming in sheep (and ruminants in general) has also been common as they serve as an excellent model organism for humans. Though pigs are often used (Nissen, Nebel, Oksbjerg, & Bertram, 2011; Oksbjerg et al., 2013), sheep are now typically preferred as their gestation period is more similar to that of humans (Bloomfield et al., 2003; Ford et al., 2007; Gopalakrishnan et al., 2004; Kenyon & Blair, 2014; Khanal et al., 2014; Khanal & Nielsen, 2017; Muhlhausler, Duffield, & McMillen, 2007; Nielsen et al., 2013).

There are two primary areas within which work on developmental programming has been focussed. The first is nutrition. Nutrient insufficiency during any stage of the early developmental process has consistently been shown to impact the health of farm animals during adulthood (Armitage, Khan, Taylor, Nathanielsz, & Poston, 2004; Bloomfield et al., 2003; Du et al., 2010; Fernandez-Twinn & Ozanne, 2006; Noya et al., 2019a; Noya, et al., 2019b; Symonds, Stephenson, Gardner, & Budge, 2006; Todd, Oliver, Jaquiery, Bloomfield, & Harding, 2009; Zhu et al., 2006). While high nutrient availability during pregnancy can signal to the offspring that it will be born into an environment of abundance, low nutrient availability will signal the opposite (Kenyon & Blair, 2014). They will thus develop accordingly, as a PAR to produce the metabolic phenotype that best matches the predicted environment. As discussed in the previous section, when a mismatch occurs – such as nutrient deprivation for the mother during gestation, but abundant feed supplied to the infant – this can result in the development of metabolic problems such as obesity, insulin resistance, and heart disease (Berends & Ozanne, 2012; Canani et al., 2011; Chen, Magliano, & Zimmet, 2012; Kenyon & Blair, 2014; Pinney & Simmons, 2010). Those born with a low birth weight, for instance, tend to have a significant tendency toward developing obesity and cardiovascular problems in later life. From an evolutionary perspective, it makes sense that such developmental changes in metabolisms were designed as an adaptive response for nutritionally poor environments (Hales & Ozanne, 2003). Conversely, abundance of nutrients during pregnancy has also been shown to impact health negatively – causing obesity in offspring (Parlee & MacDougald, 2014; Shankar et al., 2008). Nutritionally imbalanced diets (such as high fat diets) have also been shown to cause developmental changes and hence deserve further investigation for optimal nutrition (Lunesu et al., 2020; Parlee & MacDougald, 2014). Both effects can be of concern to animal husbandry: overfeeding could have as many negative effects as underfeeding, suggesting a delicate balance to maximize yield, health, and welfare. As well as simply affecting productivity, these conditions impact the health and welfare of the animals. Paying attention to providing matching nutritive conditions to both mother and offspring can help prevent this failure of predictive response. As an example, animal managers could take this into account by identifying their preferred diet for production animals and ensuring that the maternal diet corresponds in terms of level of abundance and nutrient availability, to best utilize the offspring PAR.

There are currently conflicting views on the most crucial periods of development for nutrition. Increasing evidence points to the importance of the time around conception for adequate maternal nutrition in guiding fetal development (Fleming et al., 2018). However, particularly for animals that give birth to multiple offspring, nutrient requirements will drastically increase during late gestation (Bell, 1995; Drackley, 1999; Rattray, Garrett, East, & Hinman, 1974; Reynolds, Aikman, Lupoli, Humphries, & Beever, 2003), and this is probably also a crucial time-frame for developmental programming (Khanal & Nielsen, 2017). There are also lasting effects of nutritional deprivation in the early life period, such as for newly-hatched chicks – not just the growth effects of the lack of nutrients itself, but ongoing epigenetic changes impacting metabolism (Kang, Madkour, & Kuenzel, 2017). The critical periods are likely to be related to the life history of the species – precocial animals will be more likely to undergo critical development pre-natally, while altricial species will be more impacted by early postnatal experience (Zimmer et al., 2017).

The second research area is in the effects of stress – both maternal stress during fetal development and the stress effects arising from maternal separation in early life. Maternal exposure to stressors can alter a range of systems in the offspring, including neuroendocrine, physiological and behavioral (Zimmer et al., 2017). For example, exposure of Japanese quail to stressors both pre-natally (while still in the egg) and during the immediate post-natal period, affected behavior such that the stress-exposed offspring showed shorter latencies in entering a novel environment (Zimmer et al., 2017). Early social deprivation can also have long lasting effects on brain and behavior – social deprivation in newly-hatched chicks causes changes in stress response to handling and learning ability; effects which were also transmitted to their offspring in the next generation (Goerlich et al., 2012). These effects appear to be modulated through changes in gene expression in the brain, and programming of the hypothalamic–pituitary–adrenal (HPA) axis that regulates physiological stress responses.

In these cases, the effects actually seemed to be positive – the birds showed a higher coping ability in stressful situations. This emphasizes the importance of the research – for animals likely to be exposed to stressful situations in their future, controlled exposure to early-life stressors may be crucial for development of an appropriate stress response. It also demonstrates the benefits of evolutionary thinking: the altered functioning of the HPA axis and gene expression within the brain could be seen as PARs – where the prediction of a future stressful environment requires activation of the developmental pathways for appropriate coping responses. Hence, production of animals that are better at coping with novel or stressful environments. Again, these effects are likely to be highly species-specific. For example, the famous maternal deprivation studies conducted on rhesus macaques by Harry Harlow and his team (reviewed in Van der Horst & Van der

Veer, 2008), demonstrated ongoing negative behavioral and mood effects; as did the human cases their experiments were serving as models for. For altricial species, such as primates or rats (Murthy & Gould, 2018), there is the potential for a difference in degree or even in kind of the effects of lost maternal care as compared to more precocial species. This underscores the importance of understanding the life history and selective environment of the species of interest – the important maternal and rearing conditions for chickens are not likely to mimic those for cows, for instance.

Lack of developmental preparation for stressful environments is likely to leave animals with over-reactive stress responses, with the consequent negative affects and physiological effects leading to poor welfare outcomes. Given that many agricultural environments contain such stressors, ensuring a controlled amount of maternal stress exposure may thus help the offspring in coping with their future environment. We emphasize here the importance of *controlled* stressors, as it is likely that both over- and under-exposure can create negative outcomes (Daskalakis, Bagot, Parker, Vinkers, & de Kloet, 2013). What is most important from the point of view of PAR is to ensure that there is not a significant mismatch between the conditions of early development and the conditions the offspring will eventually face. This can be implemented both through exposure to environmental challenges (including positive challenges such as diverse and enriched environments) as well as reduction of occurrence of potential traumatic events for offspring, such as maternal separation.

One potential additional benefit of an evolutionary approach to developmental programming, is to place the possible biomarkers for PARs within the context of a well-established literature in the biological sciences. For example, birth weight has historically been used to identify possible cases of developmental programming (Khanal & Nielsen, 2017). This is partially owing to Barker's early research on the weight of human infants (Barker, 2002), but the primary reason is simply that no better indicators have so far been established. However, this marker is problematic, since birth weight alone is considered to be a poor indicator, providing "little information about body composition, adiposity and potentially altered body functions" (Khanal & Nielsen, 2017, p. 3). Worse, such an approach can lead us substantially astray since a lack of nutrients in the first trimester of pregnancy can often be accommodated through a later "catch-up" in growth (Chadio et al., 2007; Gopalakrishnan et al., 2004; Khanal & Nielsen, 2017) and thus birth weight will fail to identify these cases of early deprivation.[1] Substantial evidence of low-weight births due to malnutrition does not undermine this picture. While low birth weight may be indicative of a negative impact of developmental programming on health, normal or high birth weight cannot be used to infer its absence. Indeed, some have blamed the catch-up growth itself as the cause of disease in later life (Metcalfe & Monaghan, 2001). Birth weight is thus an imperfect indicator, but taking a Darwinian view can help place it within its context. The developmental process, like all biological processes, is one that includes trade-offs.

We have provided here a few examples of how evolutionary thinking about developmental programming could have implications in welfare science and management. The goal of this paper, however, was not to give specific recommendations on how to apply current insights from developmental programming to livestock management. Firstly, this has been attempted elsewhere (e.g. Kenyon & Blair, 2014; Khanal & Nielsen, 2017), and secondly, the evidence is still too scarce to allow for anything but rough guidelines. Instead, we have given some broad examples of how this understanding may benefit animal welfare and help guide informative research programs. This is precisely why we want to propagate the use of an evolutionary lens to understand these phenomena, to help enhance and direct research programs. Thinking about these findings in terms of predictive adaptive responses may help to reveal problems *and* solutions that are otherwise masked. In particular, given that it is through a mismatch between the predictions and the actual environment that problems arise, we should expect these problems to be common within domestic environments where the usual signals may be greatly decoupled from the present environment. An understanding of the selective environments under which they evolved will assist in determining the optimal developmental conditions for ongoing animal health and welfare. It can also help in identifying potential factors in the developmental environment that could be important targets for future investigation.

Conclusion: Toward evolutionary veterinary science

Throughout this paper, we have demonstrated how taking an evolutionary approach to investigating and understanding developmental programming will help guide research and can be used to benefit the health and welfare of animals. We take this as an example of the more general benefits of integrating an evolutionary perspective into veterinary science, in the same way as a similar approach has been gaining popularity within human medicine. Even prominent textbooks on evolution now dedicate entire chapters to evolutionary medicine (Bergstrom & Dugatkin, 2018), despite the relative novelty of the field. Historically, medical practice had relatively little contact with the evolutionary sciences: medical education didn't require courses in evolutionary biology and evolutionary principles were only rarely applied in medical reasoning. Due to this perceived lack of engagement, the physician Randolph M. Nesse and evolutionary biologist George C. Williams aimed to introduce what they called *Evolutionary Medicine*, applying evolutionary insights to the medical sciences (Nesse & Williams, 1998, 2012; Williams & Nesse, 1991).

The proponents of evolutionary medicine have often used the title of the famous essay by the Russian-American geneticist Theodosius Dobzhansky "Nothing in biology makes sense except in the light of evolution" (Dobzhansky, 1973) – to defend and motivate their approach. This is the Darwinian dictum that biology is a historical science: *the* science of shared ancestry. The diverse phenomena within the biological sciences can only be properly understood by considering them as the result of evolutionary processes. This is not the adaptationist stance that every biological process must be understood as an adaptation, but rather that one cannot understand organismal design without an understanding of the various evolutionary tradeoffs organisms have been designed to solve. This has been especially important in the study of the pathologies arising from modern civilization, that are likely to have been caused through an evolutionary mismatch between our new environments and the environments humans have been designed *for*.

Evolutionary medicine is the simple recognition that responses to pathology are evolved biological phenomena like any other. Thus, understanding the evolution of disease processes and responses can help shed new light on human medicine and treatment options. Though many medical practitioners have often shied away from evolutionary considerations – deeming them unimportant or too speculative for questions of interest to medicine – the field of evolutionary medicine has grown substantially. It can now largely be considered a success, since many medical schools have started to teach evolutionary medicine and evolutionary biologists have taken a greater interest in medicine, offering fruitful cross-fertilization (Day & Stearns, 2009; Ganten & Nesse, 2012; Gluckman et al., 2009; Grunspan, Moeller, Nesse, & Brownell, 2019; Nesse et al., 2010; Nesse & Stearns, 2008; Stearns, 2005; Stearns & Ebert, 2001; Stearns & Koella, 2008; Stearns, Nesse, Govindaraju, & Ellison, 2010; Swynghedauw, 2008; Trevathan, Smith, & McKenna, 2008; Varki, 2012; Wjst, 2013). The field now has its own conferences, journals, and professorships, and is on a steady path toward becoming an integral part of human medicine.

Unfortunately, only little effort has been undertaken to include veterinary practitioners in the *evolutionary medicine* movement. This is surprising, since the very idea of *evolutionary* medicine naturally lends itself to a more unified view of medicine and veterinary science. Indeed, much could be gained – both in terms of treatment and research – from a comparative approach to human and animal diseases that takes the evolutionary lens seriously (Stearns, 2012; Varki, Strobert, Dick, Benirschke, & Varki, 2011). However, there have so far been few mentions or uses of such an approach, and these have not received much uptake. Some exceptions include Böhmer and Böhmer (2017), who apply an evolutionary veterinary science approach to investigating dental problems in domestic rabbits and Natterson-Horowitz and Bowers (2012) who examine in depth how an understanding of the shared evolutionary history of humans and other animals can lead to useful cross-fertilization between medicine and veterinary science. Perhaps most notably, an early paper by LeGrand and Brown (2002) emphasized the usefulness of taking a Darwinian lens in veterinary science – highlighting its insights into virulence, host defense, genetic conflicts, and evolutionary mismatch. Unfortunately, their paper has so far received scant attention. In contrast, the goal of our paper was more humble, targeting only an evolutionary approach to developmental programming, as opposed to these four much broader areas. Our strategy was to highlight the potential benefits of taking an evolutionary perspective to developmental programming, and how this can serve as an example for the EvoVetSci approach more generally.

To conclude, we have used the example of developmental programming to show how the tools of evolutionary biology could improve our understanding of veterinary science by supplementing its mechanistic "how" questions with the historical "why" questions of evolutionary biology. Where developmental programming has so far been considered within veterinary medicine and animal welfare science, it is far more often through the former lens than the latter. As LeGrand and Brown argued early on, veterinarians could become better practitioners, researchers, and educators through the use of evolutionary theorizing (LeGrand & Brown, 2002). This is especially important since veterinary science lacks the long-term epidemiological studies that are common in human medicine. Ultimately, such a merger of ways of biological thinking could greatly benefit and unify our understanding of developmental processes relevant to maintaining animal health and welfare. Taking an evolutionary approach allows us to shape our research programs, identifying potential questions to ask and possible solutions to existing problems. To use a phrase the animal welfare scientist Marian Dawkins (1998) once used (albeit in a different context): "[a]nimal welfare, in other words, needs a dose of Darwinian medicine (Nesse & Williams, 1995)" (p. 305).

Note

1. Though there is evidence that an individual's full size as an adult, despite catch-up growth, is still smaller than they would have otherwise been (Schinckel & Short, 1961).

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References

Agrawal, A. A., Laforsch, C., & Tollrian, R. (1999). Transgenerational induction of defences in animals and plants. *Nature*, *401*(6748), 60–63.

Armitage, J. A., Khan, I. Y., Taylor, P. D., Nathanielsz, P. W., & Poston, L. (2004). Developmental programming of the metabolic syndrome by maternal nutritional imbalance: How strong is the evidence from experimental models in mammals? *The Journal of Physiology*, *561*(2), 355–377.

Barker, D. J., Osmond, C., Winter, P., Margetts, B., & Simmonds, S. J. (1989). Weight in infancy and death from ischaemic heart disease. *The Lancet*, *334*(8663), 577–580.

Barker, D. J. (1998). In utero programming of chronic disease. *Clinical Science*, *95*(2), 115–128.

Barker, D. J. (2002). Fetal programming of coronary heart disease. *Trends in Endocrinology & Metabolism*, *13*(9), 364–368.

Barker, D. (1966). *Prenatal influences and subnormal intelligence* [Ph. D. thesis]. University of Birmingham.

Barker, J., Barker, M., Fall, C., Osmond, C., Cooper, C., Keilty, S., … Edwards, S. (2013). David J P Barker. *BMJ*, *347*. doi:10.1136/bmj.f7358

Bateson, P., Barker, D., Clutton-Brock, T., Deb, D., D'Udine, B., Foley, R. A., … Lahr, M. M., (2004). Developmental plasticity and human health. *Nature*, *430*(6998), 419–421.

Beauclercq, S., Lef`evre, A., Montigny, F., Collin, A., Tesseraud, S., Leterrier, C., … Guilloteau, L. A. (2019). A multiplatform metabolomic approach to characterize fecal signatures of negative postnatal events in chicks: A pilot study. *Journal of Animal Science and Biotechnology*, *10*(1), 1–12.

Bell, A. W. (1995). Regulation of organic nutrient metabolism during transition from late pregnancy to early lactation. *Journal of Animal Science*, *73*(9), 2804–2819.

Berends, L., & Ozanne, S. (2012). Early determinants of type-2 diabetes. *Best Practice & Research Clinical Endocrinology & Metabolism*, *26*(5), 569–580.

Bergstrom, C. T., & Dugatkin, L. (2018). *Evolution* (*2nd* ed.). New York: W W Norton & Company.

Bloomfield, F. H., Oliver, M. H., Giannoulias, C. D., Gluckman, P. D., Harding, J. E., & Challis, J. R. (2003). Brief undernutrition in late-gestation sheep programs the hypothalamic-pituitary-adrenal axis in adult offspring. *Endocrinology*, *144*(7), 2933–2940.

Böhmer, C., & Bo¨hmer, E. (2017). Shape variation in the craniomandibular system and prevalence of dental problems in domestic rabbits: A case study in evolutionary veterinary science. *Veterinary Sciences*, *4*(1), 5.

Broom, D. M. (2011). A history of animal welfare science. *Acta biotheoretica*, *59*(2), 121–137.

Browning, H. (2020). *If I could talk to the animals: Measuring subjective animal welfare* [Ph. D. thesis]. Australian National University. doi:10.25911/5f1572fb1b5be.

Browning, H. (2019). The natural behavior debate: Two conceptions of animal welfare. *Journal of Applied Animal Welfare Science*, 1–13. doi:10.1080/10888705.2019.1672552

Canani, R. B., Di Costanzo, M., Leone, L., Bedogni, G., Brambilla, P., Cianfarani, S., … Agostoni, C. (2011). Epigenetic mechanisms elicited by nutrition in early life. *Nutrition Research Reviews*, *24*(2), 198–205.

Chadio, S., Kotsampasi, B., Papadomichelakis, G., Deligeorgis, S., Kalogiannis, D., Menegatos, I., & Zervas, G. (2007). Impact of maternal undernutrition on the hypothalamic–pituitary–adrenal axis responsiveness in sheep at different ages postnatal. *Journal of Endocrinology*, *192*(3), 495–503.

Chen, L., Magliano, D. J., & Zimmet, P. Z. (2012). The worldwide epidemiology of type 2 diabetes mellitus—present and future perspectives. *Nature Reviews Endocrinology*, *8*(4), 228–236.

Daskalakis, N. P., Bagot, R. C., Parker, K. J., Vinkers, C. H., & de Kloet, E. R. (2013). The three-hit concept of vulnerability and resilience: Toward understanding adaptation to early-life adversity outcome. *Psychoneuroendocrinology*, *38*(9), 1858–1873.

Dawkins, M. S. (1998). Evolution and animal welfare. *The Quarterly Review of Biology*, *73*(3), 305–328.

Dawkins, M. S. (2009). Concepts of distress, suffering and their operational interpretation. *Ethology of Nonhuman Animals Paper*, *5*, https://www.wellbeingintlstudiesrepository.org/acwp_ena/5

Dawkins, M. S. (2021). *The science of animal welfare: understanding what animals want*. Oxford: Oxford University Press.

Day, T., & Stearns, S. C. (2009). Editorial: Evolutionary medicine special issue. *Evolutionary Applications*, *2*(1), 7.

Dobzhansky, T. (1973). Nothing in biology makes sense except in the light of evolution. *The American Biology Teacher*, *35*(3), 125–129.

Drackley, J. K. (1999). Biology of dairy cows during the transition period: The final frontier? *Journal of Dairy Science*, *82*(11), 2259–2273.

Du, M., Ford, S. P., & Zhu, M.-J. (2017). Optimizing livestock production efficiency through maternal nutritional management and fetal developmental programming. *Animal Frontiers*, *7*(3), 5–11.

Du, M., Tong, J., Zhao, J., Underwood, K., Zhu, M., Ford, S., & Nathanielsz, P. (2010). Fetal programming of skeletal muscle development in ruminant animals. *Journal of Animal Science*, *88*(suppl 13), E51–E60.

Duncan, I. J. (2002, December). Poultry welfare: Science or subjectivity? *British Poultry Science*, *43*(5), 643–652.

Ericsson, M., & Jensen, P. (2016). Domestication and ontogeny effects on the stress response in young chickens (Gallus gallus). *Scientific Reports*, *6*(1), 1–7.

Fernandez-Twinn, D., & Ozanne, S. (2006). Mechanisms by which poor early growth programs type-2 diabetes, obesity and the metabolic syndrome. *Physiology & Behavior*, *88*(3), 234–243.

Fleming, T. P., Watkins, A. J., Velazquez, M. A., Mathers, J. C., Prentice, A. M., Stephenson, J., … Godfrey, K. M. (2018, May). Origins of lifetime health around the time of conception: Causes and consequences. *The Lancet*, *391* (10132), 1842–1852.

Ford, S., Hess, B., Schwope, M., Nijland, M., Gilbert, J., Vonnahme, K., … Nathanielsz, P. (2007). Maternal undernutrition during early to mid-gestation in the ewe results in altered growth, adiposity, and glucose tolerance in male offspring. *Journal of Animal Science*, *85*(5), 1285–1294.

Foury, A., Collin, A., Helbling, J.-C., Leterrier, C., Moisan, M.-P., & Guilloteau, L. A. (2020). Spontaneous intake of essential oils after a negative postnatal experience has long-term effects on blood transcriptome in chickens. *Scientific Reports*, *10*(1), 1–14.

Fraser, D., & Duncan, I. J. (1998). 'Pleasures','pains' and animal welfare: Toward a natural history of affect. *Animal Welfare*, *7*(4), 383–396.

Ganten, D., & Nesse, R. (2012). The evolution of evolutionary molecular medicine. *Journal of Molecular Medicine*, *90* (5), 467–470.

Gluckman, P. D., Hanson, M. A., & Beedle, A. S. (2007). Early life events and their consequences for later disease: A life history and evolutionary perspective. *American Journal of Human Biology*, *19*(1), 1–19.

Gluckman, P. D., Hanson, M. A., & Spencer, H. G. (2005). Predictive adaptive responses and human evolution. *Trends in Ecology & Evolution*, *20*(10), 527–533.

Gluckman, P. D., & Hanson, M. A. (2004). Living with the past: Evolution, development, and patterns of disease. *Science*, *305*(5691), 1733–1736.

Gluckman, P., Beedle, A., & Hanson, M. (2009). *Principles of evolutionary medicine*. Oxford: Oxford University Press.

Goerlich, V. C., Nätt, D., Elfwing, M., Macdonald, B., & Jensen, P. (2012). Transgenerational effects of early experience on behavioral, hormonal and gene expression responses to acute stress in the precocial chicken. *Hormones and Behavior*, *61*(5), 711–718.

Gopalakrishnan, G., Gardner, D., Rhind, S., Rae, M., Kyle, C., Brooks, A., … Stephenson, T., (2004). Programming of adult cardiovascular function after early maternal undernutrition in sheep. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, *287*(1), R12–R20.

Green, T. C., & Mellor, D. J. (2011, November). Extending ideas about animal welfare assessment to include 'quality of life' and related concepts. *New Zealand Veterinary Journal*, *59*(6), 263–271.

Greenwood, P., Clayton, E., & Bell, A. (2017). Developmental programming and beef production. *Animal Frontiers*, *7* (3), 38–47.

Griffiths, P. E., & Matthewson, J. (2018). Evolution, dysfunction, and disease: A reappraisal. *The British Journal for the Philosophy of Science*, *69*(2), 301–327.

Gross, W., & Siegel, P. (1980). Effects of early environmental stresses on chicken body weight, antibody response to RBC antigens, feed efficiency, and response to fasting. *Avian Diseases*, *24*(3), 569–579.

Grunspan, D. Z., Moeller, K. T., Nesse, R. M., & Brownell, S. E. (2019). The state of evolutionary medicine in undergraduate education. *Evolution, Medicine, and Public Health*, *2019*(1), 82–92.

Hales, C. N., & Barker, D. J. (1992). Type 2 (non-insulin-dependent) diabetes mellitus: The thrifty phenotype hypothesis. *Diabetologia*, *35*(7), 595–601.

Hales, C. N., & Barker, D. J. (2001). The thrifty phenotype hypothesis: Type 2 diabetes. *British Medical Bulletin*, *60*(1), 5–20.

Hales, C., & Ozanne, S. (2003). The dangerous road of catch-up growth. *The Journal of Physiology*, *547*(1), 5–10.

Hynd, P. I., Weaver, S., Edwards, N. M., Heberle, N. D., & Bowling, M. (2016). Developmental programming: A new frontier for the poultry industry? *Animal Production Science*, *56*(8), 1233.

Jones, J. H. (2005). Fetal programming: Adaptive life-history tactics or making the best of a bad start? *American Journal of Human Biology*, *17*(1), 22–33.

Kang, S. W., Madkour, M., & Kuenzel, W. J. (2017). Tissue-specific expression of DNA methyltransferases involved in early-life nutritional stress of chicken, Gallus gallus. *Frontiers in Genetics*, *8*, 204.

Kenyon, P., & Blair, H. (2014). Foetal programming in sheep – Effects on production. *Small Ruminant Research*, *118* (1–3), 16–30.

Khanal, P., Husted, S. V., Axel, A. M. D., Johnsen, L., Pedersen, K. L., Mortensen, M. S., … Nielsen, M. O. (2014). Late gestation over-and undernutrition predispose for visceral adiposity in response to a post-natal obesogenic diet, but with differential impacts on glucose–insulin adaptations during fasting in lambs. *Acta Physiologica*, *210*(1), 110–126.

Khanal, P., & Nielsen, M. O. (2017). Impacts of prenatal nutrition on animal production and performance: A focus on growth and metabolic and endocrine function in sheep. *Journal of Animal Science and Biotechnology*, *8*(1), 75.

Lay, D., Jr, & Wilson, M. (2002). Development of the chicken as a model for prenatal stress. *Journal of Animal Science*, *80*(7), 1954–1961.

LeGrand, E. K., & Brown, C. C. (2002). Darwinian medicine: Applications of evolutionary biology for veterinarians. *The Canadian Veterinary Journal*, *43*(7), 556.
Low, F. M., Gluckman, P. D., & Hanson, M. A. (2012). Developmental plasticity, epigenetics and human health. *Evolutionary Biology*, *39*(4), 650–665.
Lunesu, M., Ledda, A., Correddu, F., Fancello, F., Marzano, A., Mossa, F., … Atzori, A. (2020). Prenatal exposure to different diets influences programming of glucose and insulin metabolism in dairy ewes. *Journal of Dairy Science*, *103*(10), 8853–8863.
Matthewson, J., & Griffiths, P. E. (2017). Biological criteria of disease: Four ways of going wrong. *Journal of Medicine and Philosophy*, *42*(4), 447–466.
Metcalfe, N. B., & Monaghan, P. (2001). Compensation for a bad start: Grow now, pay later? *Trends in Ecology & Evolution*, *16*(5), 254–260.
Muhlhausler, B. S., Duffield, J., & McMillen, I. (2007). Increased maternal nutrition increases leptin expression in perirenal and subcutaneous adipose tissue in the postnatal lamb. *Endocrinology*, *148*(12), 6157–6163.
Murthy, S., & Gould, E. (2018). Early life stress in rodents: Animal models of illness or resilience? *Frontiers in Behavioral Neuroscience*, *12*, 157.
Natterson-Horowitz, B., & Bowers, K. (2012). *Zoobiquity: What animals can teach us about health and the science of healing*. New York: Vintage.
Nesse, R. M., Bergstrom, C. T., Ellison, P. T., Flier, J. S., Gluckman, P., Govindaraju, D. R., … Schwartz, M. D., (2010). Making evolutionary biology a basic science for medicine. *Proceedings of the National Academy of Sciences*, *107* (suppl 1), 1800–1807.
Nesse, R. M., & Stearns, S. C. (2008). The great opportunity: Evolutionary applications to medicine and public health. *Evolutionary Applications*, *1*(1), 28–48.
Nesse, R. M., & Williams, G. C. (1995). *Evolution and healing: The new science of darwinian medicine*. London: Weidenfeld & Nicolson.
Nesse, R. M., & Williams, G. C. (1998). Evolution and the origins of disease. *Scientific American*, *279*(5), 86–93.
Nesse, R. M., & Williams, G. C. (2012). *Why we get sick: The new science of darwinian medicine*. New York: Vintage.
Nielsen, M. O., Kongsted, A. H., Thygesen, M., Strathe, A. B., Caddy, S., Quistorff, B., … Chwalibog, A., (2013). Late gestation undernutrition can predispose for visceral adiposity by altering fat distribution patterns and increasing the preference for a high-fat diet in early postnatal life. *British Journal of Nutrition*, *109*(11), 2098–2110.
Nissen, P. M., Nebel, C., Oksbjerg, N., & Bertram, H. C. (2011). Metabolomics reveals relationship between plasma inositols and birth weight: Possible markers for fetal programming of type 2 diabetes. *Journal of Biomedicine and Biotechnology*, *2011*, 1–8.
Noya, A., Casasús, I., Ferrer, J., & Sanz, A. (2019b). Effects of developmental programming caused by maternal nutrient intake on postnatal performance of beef heifers and their calves. *Animals*, *9*(12), 1072.
Noya, A., Casasús, I., Ferrer, J., & Sanz, A. (2019b). Long-term effects of maternal subnutrition in early pregnancy on cow-calf performance, immunological and physiological profiles during the next lactation. *Animals*, *9*(11), 936.
Oksbjerg, N., Nissen, P. M., Therkildsen, M., Møller, H. S., Larsen, L. B., Andersen, M., & Young, J. F. (2013). Meat science and muscle biology symposium: In utero nutrition related to fetal development, postnatal performance, and meat quality of pork. *Journal of Animal Science*, *91*(3), 1443–1453.
Painter, R. C., Roseboom, T. J., & Bleker, O. P. (2005). Prenatal exposure to the Dutch famine and disease in later life: An overview. *Reproductive Toxicology*, *20*(3), 345–352.
Parlee, S. D., & MacDougald, O. A. (2014). Maternal nutrition and risk of obesity in offspring: The Trojan horse of developmental plasticity. *Biochimica Et Biophysica Acta (Bba)-molecular Basis of Disease*, *1842*(3), 495–506.
Pinney, S. E., & Simmons, R. A. (2010). Epigenetic mechanisms in the development of type 2 diabetes. *Trends in Endocrinology & Metabolism*, *21*(4), 223–229.
Rattray, P., Garrett, W., East, N., & Hinman, N. (1974). Growth, development and composition of the ovine conceptus and mammary gland during pregnancy. *Journal of Animal Science*, *38*(3), 613–626.
Reynolds, C., Aikman, P., Lupoli, B., Humphries, D., & Beever, D. (2003). Splanchnic metabolism of dairy cows during the transition from late gestation through early lactation. *Journal of Dairy Science*, *86*(4), 1201–1217.
Roseboom, T. J., Van Der Meulen, J. H., Ravelli, A. C., Osmond, C., Barker, D. J., & Bleker, O. P. (2001). Effects of prenatal exposure to the Dutch famine on adult disease in later life: An overview. *Twin Research and Human Genetics*, *4*(5), 293–298.
Roseboom, T., de Rooij, S., & Painter, R. (2006). The Dutch famine and its long-term consequences for adult health. *Early Human Development*, *82*(8), 485–491.
Schinckel, P., & Short, B. (1961). Influence of nutritional level during prenatal and early post-natal life on adult fleece and body characters. *Australian Journal of Agricultural Research*, *12*(1), 176–202.
Shankar, K., Harrell, A., Liu, X., Gilchrist, J. M., Ronis, M. J., & Badger, T. M. (2008). Maternal obesity at conception programs obesity in the offspring. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*, *294*(2), R528–R538.

Sinclair, K. D., Rutherford, K., Wallace, J., Brameld, J., Stöger, R., Alberio, R., … Adam, C., (2016). Epigenetics and developmental programming of welfare and production traits in farm animals. *Reproduction, Fertility and Development*, *28*(10), 1443–1478.

Stearns, S. C., & Ebert, D. (2001). Evolution in health and disease: Work in progress. *The Quarterly Review of Biology*, *76*(4), 417–432.

Stearns, S. C., & Koella, J. C. (2008). *Evolution in health and disease*. Oxford: Oxford University Press.

Stearns, S. C., Nesse, R. M., Govindaraju, D. R., & Ellison, P. T. (2010). Evolutionary perspectives on health and medicine. *Proceedings of the National Academy of Sciences*, *107*(suppl 1), 1691–1695.

Stearns, S. C. (2005). Issues in evolutionary medicine. *American Journal of Human Biology: The Official Journal of the Human Biology Association*, *17*(2), 131–140.

Stearns, S. C. (2012). Evolutionary medicine: Its scope, interest and potential. *Proceedings of the Royal Society B: Biological Sciences*, *279*(1746), 4305–4321.

Sutton, E. F., Gilmore, L. A., Dunger, D. B., Heijmans, B. T., Hivert, M.-F., Ling, C., … Szyf, M., (2016). Developmental programming: State-of-the-science and future directions–Summary from a Pennington Biomedical symposium. *Obesity*, *24*(5), 1018–1026.

Swynghedauw, B. (2008). Nothing in medicine makes sense except in the light of evolution: A review. Pontarotti, Pierre. In *Evolutionary biology from concept to application*, (pp. 197–207). London: Springer.

Symonds, M. E., Stephenson, T., Gardner, D. S., & Budge, H. (2006). Long-term effects of nutritional programming of the embryo and fetus: Mechanisms and critical windows. *Reproduction, Fertility and Development*, *19*(1), 53–63.

Tinbergen, N. (1963). On aims and methods of ethology. *Zeitschrift fu¨r tierpsychologie*, *20*(4), 410–433.

Todd, S. E., Oliver, M. H., Jaquiery, A. L., Bloomfield, F. H., & Harding, J. E. (2009). Periconceptional undernutrition of ewes impairs glucose tolerance in their adult offspring. *Pediatric Research*, *65*(4), 409–413.

Trevathan, W., Smith, E. O., & McKenna, J. J. (2008). *Evolutionary medicine and health: New perspectives*. Oxford: Oxford University Press.

Van der Horst, F. C., & Van der Veer, R. (2008). Loneliness in infancy: Harry Harlow, John Bowlby and issues of separation. *Integrative Psychological and Behavioral Science*, *42*(4), 325–335.

Varki, A. (2012). Nothing in medicine makes sense, except in the light of evolution. *Journal of Molecular Medicine*, *90* (5), 481–494.

Varki, N. M., Strobert, E., Dick, E. J., Jr, Benirschke, K., & Varki, A. (2011). Biomedical differences between human and nonhuman hominids: Potential roles for uniquely human aspects of sialic acid biology. *Annual Review of Pathology: Mechanisms of Disease*, *6*(1), 365–393.

Veit W. (2021b). Experimental philosophy of medicine and the concepts of health and disease. Theor Med Bioeth, 10.1007/s11017-021-09550-3

Veit, W., & Browning, H. (2020, November). Perspectival pluralism for animal welfare. *European Journal for Philosophy of Science*, *11*(9), https://doi.org/10.1007/s13194-020-00322-9

Veit, W., & Browning, H. (2021). Phenomenology applied to animal health and suffering. In S. Ferrarello (Ed.), *Phenomenology of bioethics: Technoethics and lived-experience*(73–88). London: Springer. doi:10.1007/978-3-030-65613-3_6

Veit, W. (2021a). Biological normativity: A new hope for naturalism? *Medicine, Health Care and Philosophy*, 1–11. doi:10.1007/s11019-020-09993-w

Williams, G. C., & Nesse, R. M. (1991). The dawn of darwinian medicine. *The Quarterly Review of Biology*, *66*(1), 1–22.

Wjst, M. (2013). Evolutionäre medizin. *DMW-Deutsche Medizinische Wochenschrift*, *138*(51/52), 2663–2665.

Zhu, M. J., Ford, S. P., Means, W. J., Hess, B. W., Nathanielsz, P. W., & Du, M. (2006). Maternal nutrient restriction affects properties of skeletal muscle in offspring. *The Journal of Physiology*, *575*(1), 241–250.

Zimmer, C., Larriva, M., Boogert, N. J., & Spencer, K. A. (2017). Transgenerational transmission of a stress-coping phenotype programmed by early-life stress in the Japanese quail. *Scientific Reports*, *7*(1), 1–19.