



SYMPOSIUM

Does Animal Behavior Underlie Covariation Between Hosts' Exposure to Infectious Agents and Susceptibility to Infection? Implications for Disease Dynamics

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Synopsis Animal behavior is unique in influencing both components of the process of transmission of disease: exposure to infectious agents, and susceptibility to infection once exposed. To date, the influence of behavior on exposure versus susceptibility has largely been considered separately. Here, we ask whether these two key mechanisms act in concert in natural populations, whereby individuals who are most exposed to infectious agents or have the most contact with conspecifics are also the most susceptible or infectious. We propose three mechanisms that can generate covariation between these two key elements of the transmission of disease within and among hosts, and we provide empirical examples of each. We then use a mathematical model to examine the effect of this covariation on the dynamics of disease at the population level. First, we show that the empirical mechanisms generating covariation between behavioral and physiological components of disease transmission are widespread and include endocrine mediators of behavior, mate choice, group size, sickness behaviors, and behavioral avoidance of infectious conspecifics. The diversity of these empirical mechanisms underscores the potential importance and breadth of covariation in the disease process. Second, we show mathematically that the variability in hosts' exposure to infectious agents and susceptibility or infectiousness, and how tightly they are coupled, strongly influences the ability of a disease to invade a host population. Overall, we propose that covariation between behavioral and physiological components of transmission is likely widespread in natural populations, and can have important consequences for the dynamics of disease at the population level as well as for our understanding of sexual selection, social behavior, and animal communication.

Introduction

A role for animal behavior in the transmission of parasites and pathogens has long been appreciated (Alexander 1974; Dobson 1988; Moore 2002). On the one hand, studies of animal behavior and parasitism have focused on how behaviors such as sociality, rank, and mate choice might alter hosts' exposure or contact rates in ways that influence transmission (e.g., Moller et al. 1993; Cote and Poulin 1995; Able 1996; Loehle 1997; Altizer et al.

2003; Ezenwa 2004). A largely separate literature has explored mechanisms whereby behavior might alter a host's physiology in ways that can influence its susceptibility to parasites or pathogens (e.g., Cohen et al. 1997; Barnard et al. 1998; Creel 2001; de Groot et al. 2001; Sapolsky 2005). Interestingly, there has been little discussion of the potential for these two processes to act in concert. Behaviors that influence a host's exposure to parasites might also simultaneously increase or decrease physiological

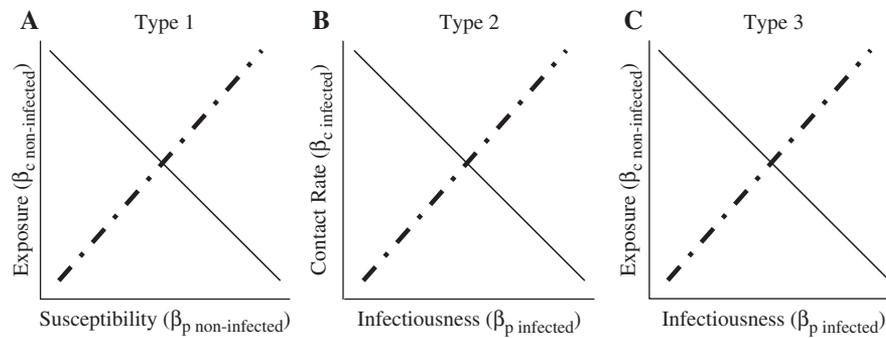


Fig. 1 Three proposed mechanisms that result in positive (dashed line) or negative (solid line) covariation between the behavioral (β_c) and physiological (β_p) components of the transmission of disease. **(A)** Type 1 covariation, whereby exposure and susceptibility covary within non-infected hosts. **(B)** Type 2 covariation, whereby infectiousness and contact with susceptible conspecifics covary within infected hosts, and **(C)** Type 3 covariation, whereby infectiousness of infected hosts covaries with the degree of exposure of uninfected hosts. The key distinction between Type 2 and Type 3 is whether the differences in behavior relevant to contact are driven by the infected (Type 2) or uninfected (Type 3) conspecific.

susceptibility, creating important positive or negative covariation between exposure to parasites and susceptibility to them. In addition, changes in animal behavior in response to infection may further create covariation by altering the degree of contact between the most infectious individuals and new hosts. Here, we propose that for many host–pathogen systems, animal behavior serves as a key link between the two primary steps generating new infections in a host population: exposure of the host to a parasite or pathogen, and the host’s susceptibility once exposed.

The rate at which new infections are generated in a host population depends on the number of infectious individuals in the population (I), and the rate, β , at which these infectious individuals transmit infection to susceptible hosts. β can be decomposed into two components that reflect the primary steps of the transmission process (Dobson 1995): (1) a behavioral component, β_c , reflecting the rate at which infectious individuals contact susceptible hosts and (2) a physiological component, β_p or the transmission efficiency, reflecting the probability that encounters between susceptible and infectious individuals will result in new infection. Importantly, β_p depends on both the infectiousness of the infecting host, and the susceptibility of the host receiving infection; β_p is thus a function of susceptibility of the two hosts interacting during the transmission of pathogens. Positive or negative covariation between these behavioral (β_c) and physiological (β_p) components of disease transmission may strongly influence the dynamics of pathogen invasion and spread in a host population, with positive covariation potentially boosting the transmission of disease, and negative covariation slowing down the spread of infection.

There are at least three distinct ways in which animal behavior can lead to positive or negative covariation between behavioral (β_c) and physiological (β_p) components of disease transmission (Fig. 1). First, hosts that are most susceptible to infection may be more, or less, likely to be exposed to parasites or pathogens, resulting in positive or negative covariation, respectively (Fig. 1A; Type 1 covariation). Second, covariation may result once an individual is infected via infection-induced changes in behavior, whereby individuals shedding a parasite or pathogen at the highest rate are more or less likely to come into contact with susceptible individuals, generating positive or negative covariation, respectively (Fig. 1B; Type 2 covariation). Third, among-individual covariation may result if susceptible individuals (e.g., choosy females) actively avoid coming into contact with the most infectious conspecifics (e.g., low quality males), resulting in negative covariation (Fig. 1C; Type 3 covariation). In other cases, susceptible individuals may preferentially contact the most infectious conspecifics, resulting in positive among-individual covariation. Here, we review empirical examples of the three proposed mechanisms (Types 1–3) by which covariation between behavioral and physiological components of disease transmission can be generated in natural populations. Our examples are not meant to be exhaustive, but instead are intended to selectively illustrate the diverse and widespread ways in which animal behavior, via its dual effects on both hosts’ activity and susceptibility, may either enhance or impair the transmission of parasites and pathogens. We then use a simple theoretical approach to explore potential population-level consequences of positive or negative covariation on parasite and pathogen invasion.

Mechanisms generating covariation between behavioral and physiological components of disease transmission

Type 1: Covariation of contact rate and susceptibility within non-infected hosts

Covariation between a host's exposure to parasites and pathogens and susceptibility to infection once exposed is likely widespread. This type of covariation (Type 1) can result from aspects of the hosts' reproductive or social behavior and individual personality, particularly in cases in which endocrine mediators (e.g., testosterone or glucocorticoids) mediate bi-directional interactions between behavior and physiological status. As one example, the androgen testosterone, a key mediator of male mating behavior in vertebrates, is known to increase behaviors relevant to parasite exposure such as spatial or locomotory activity and contact rates of males (e.g., Chandler et al. 1994; Gear et al. 2009). Testosterone is also an important modulator of physiological susceptibility to parasites and pathogens, leading to immunosuppression or immunocompensation across a range of vertebrate taxa (Peters 2000; Owen-Ashley et al. 2004; Roberts et al. 2004; Blas et al. 2006; Ruiz et al. 2010). If immunological and behavioral effects of testosterone on transmission co-occur (either positively or negatively) (Fig. 2A), testosterone may serve as a potential link between contact rate and susceptibility in vertebrates (e.g., Hughes and Randolph 2001). Indeed, several recent studies have identified vertebrate males as key hosts for infectious parasites and pathogens (Perkins et al. 2003; Ferrari et al. 2004; but see Clay et al. 2009). Studies documenting elevated rates of parasitism in dominant males further suggest a role for testosterone in driving covariation between behavior (e.g., dominance and mating success) and susceptibility to parasites across a variety of systems (e.g., Halvorsen 1986; Ezenwa 2004; Mougeot et al. 2006; Negro et al. 2010). For example, territorial male Grant's gazelles (*Nanger granti*) have higher rates of infection by nematodes than do nonterritorial males and females (Ezenwa 2004), and endogenous testosterone levels are associated both with males' territorial behavior and with suppression of immunity, strongly suggesting testosterone-mediated alterations in incidence of exposure to parasites and susceptibility to them, respectively (V. Ezenwa, unpublished data). Similarly, male red grouse (*Lagopus scoticus*) treated experimentally with testosterone implants at the onset of the breeding season showed increased success in pairing and breeding, but accumulated more parasites, suggesting positive

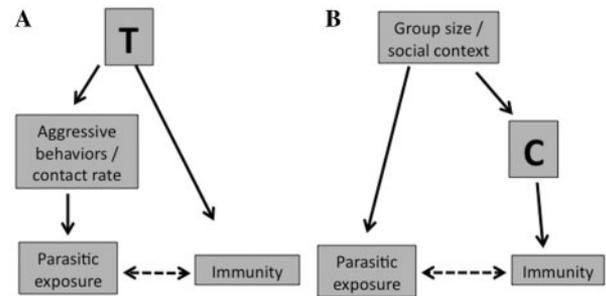


Fig. 2 A conceptual model of Type 1 covariation whereby positive covariation results between host's exposure and susceptibility within uninfected hosts. Causal links (solid arrows) between hormones, behavior, and immunity result in correlations (dashed arrows) between exposure and immunity. **(A)** Testosterone (T) affects aggressive and mating behaviors, which may result in increased exposure to parasites. Testosterone also acts as an immunosuppressor, potentially causing high susceptibility in individuals with the highest rates of contact. **(B)** Social context affects stress levels mediated by corticosterone (C) as well as the extent of exposure to parasites (e.g., via group size). Corticosterone also acts as an immunosuppressor, potentially increasing susceptibility in individuals with the highest or lowest rates of exposure (variable by study system).

covariation between rates of conspecific contact and parasite load (Mougeot et al. 2006). Further studies in the red grouse system using innovative experiments to separate out the physiological and behavioral effects of testosterone provided definitive evidence for a physiological effect of testosterone on susceptibility to parasites in males (Mougeot et al. 2005). Future work focusing on interactions between immunological and behavioral effects of testosterone would shed considerable light on the degree to which testosterone has dual effects on both behavior and susceptibility, and under what contexts.

Group-living or sociality is another important means by which positive covariation between hosts' exposure and susceptibility to pathogens or parasites may be generated. Positive covariation can arise if group-living increases an individual's exposure to parasites, while at the same time altering patterns of susceptibility (Fig. 2B). In terms of the first criterion, basic epidemiological models predict that group-living and increasing group size should enhance transmission of parasites by increasing contact between susceptible and infected individuals and/or with the parasite's infective stages (Anderson and May 1991). Furthermore, substantial empirical evidence has accrued linking size of the social group to increased intensity or prevalence of parasites, particularly for directly transmitted parasites (e.g., Brown and Brown 1986; Moore et al.

1988; Cote and Poulin 1995; Brown et al. 2001; Ezenwa 2004). Increasing group size may also increase stress among individual members of the group for a variety of reasons, including greater intra-group competition for food or mates, and increased levels of aggression in larger social groups (e.g., Saino et al. 2003; Pride 2005; Selva et al. 2011). For example, social groups larger than optimal size were associated with higher glucocorticoid levels in female ring-tailed lemurs (*Lemur catta*), particularly under conditions of food scarcity; while glucocorticoids increased linearly with group size in male lemurs during the premating period, when both food and male–male competition were likely most intense (Pride 2005). Moreover, since chronic elevation of glucocorticoid “stress” hormones have been linked to immunosuppression across a variety of vertebrate taxa (reviewed by Apanius 1998), animals in larger groups may not only be more exposed to parasites as a consequence of higher contact rates in such groups, but also may be more susceptible to infection as a result of stress-mediated immunosuppression. Interestingly, the degree of social stress experienced by different members of a group may vary considerably depending on individual social status. In some circumstances, subordinate individuals may show chronic elevation of glucocorticoids, whereas in others, dominants may experience an increase in social stress (Creel 2001). As such, positive covariation in exposure to parasites or in susceptibility to them that is associated with group size may be strongest for particular classes of individuals, and the most affected social class may vary depending on the social system of the species in question.

Group-living may also generate negative covariation between exposure and susceptibility under some conditions. This may be particularly relevant in social insect systems where “social immunity” can effectively reduce individual susceptibility to infection despite potential increases in parasite exposure due to group-living (Rosengaus et al. 1998; Traniello et al. 2002). These group-level defenses in social insects may be an adaptive response to high levels of parasite exposure in large groups (Cremer et al. 2007). More generally, group-living may lead to negative covariation between parasite exposure and susceptibility in any highly social society where strong antiparasite defense mechanisms have evolved.

Individual personalities, or suites of behaviors that are consistent across time and contexts (Stamps and Groothuis 2010), may result in strong within-individual covariation between exposure and susceptibility (Barber and Dingemanse 2010). A dichotomy used in some systems is the shy versus bold personality,

whereby shy individuals avoid taking risks while bold individuals are more proactive and less averse to risk (Sih et al. 2004). Other axes of personality or behavioral syndromes include coping reactivity, exploratory behavior, and aggressiveness; these measures are often correlated such that reactive or exploratory individuals are also more aggressive (Verbeek et al. 1996; Verbeek et al. 1999; Rodel et al. 2006; Kinnally et al. 2008). These consistent suites of behaviors may influence exposure to trophically-transmitted parasites (via foraging risk and exploratory behavior) as well as to directly transmitted pathogens (via aggressiveness or contact rate) (Pontier et al. 1998; Barber and Dingemanse 2010). In one of the few studies to explicitly examine the role of personality on ectoparasite load, more exploratory chipmunks had higher burdens of ticks, although this effect was mediated in large part by the sizes of their territories (Boyer et al. 2010). Relationships between boldness and exposure to pathogens are likely not always straightforward and need to be empirically documented across a range of systems. For example, in three-spined sticklebacks, bold individuals had fewer social interactions than did shy fish, but the distribution of those interactions differed, with shy individuals interacting with only a few individuals repeatedly (Pike et al. 2008). These results suggest that personality may underlie differences in exposure to pathogens among individuals, but the direction and extent of these relationships likely varies among systems.

Because personalities and behavioral syndromes interact bidirectionally with the neuroendocrine system in vertebrates (Koolhaas et al. 2010), they can simultaneously influence hosts’ behaviors relevant to exposure and aspects of physiology important to susceptibility (Koolhaas et al. 1999). For example, proactive and reactive vertebrates, including studies on mice, rats, pigs, and hens, show consistent differences in HPA axis activity and reactivity, sympathetic and parasympathetic nervous system reactivity, and testosterone (reviewed in Koolhaas et al. 1999). Effects of behavioral syndromes on parameters of immunity and susceptibility to disease are less well elucidated but have been documented in mice, cats, pigs, rats, and humans (Kavelaars et al. 1999; reviewed in Koolhaas et al. 1999; Natoli et al. 2005; Capitanio 2008; Koolhaas 2008). Reactive coping pigs have stronger humoral immune responses to keyhole limpet hemocyanin (KLH) but exhibit lower cellular immunity as measured via lymphocyte proliferation assays (Hessing et al. 1995), suggesting that in some systems behavioral syndromes may be immunomodulatory. To date, studies of behavioral

syndromes and disease outcome have been limited to autoimmune diseases, inflammatory diseases, or tumor development (reviewed in Koolhaas 2008), with no studies explicitly examining how behavioral syndromes influence hosts' response to infectious agents. However, studies of other factors such as maternal separation that cause significant neuroendocrine changes and disrupt the hypothalamic–pituitary–adrenal (HPA) axis in a manner similar to behavioral syndromes have found striking effects on susceptibility to influenza viral infection in mice (Avitsur et al. 2006).

Personalities or behavioral syndromes have the potential to result in either positive or negative covariation between physiological and behavioral components of susceptibility (Fig. 1A). In some cases, bold or proactive individuals may both have higher exposure to parasites and pathogens and may have greater reactivity of the sympathetic branch of the automatic nervous system, associated with susceptibility to pathogens (Koolhaas et al. 1999), leading to positive covariation. In contrast, Kortet et al. (2010) used an evolutionary model to predict that bolder individuals should have more efficient immune systems (i.e., lower susceptibility) in the face of strong parasite-mediated selection, such that bold individuals can afford to risk higher exposure to parasitism through their behavior. Although Kortet et al. (2010) focused on intake of food as the risky behavior of bold individuals, their conceptual model readily applies to parasites and pathogens transmitted via direct contact or by other environmental sources, and suggests that strong negative covariation in physiological and behavioral components of transmission may result when fitness costs of parasites are high. Overall, further study is needed in order to determine to what extent, and under what contexts, personalities or behavioral syndromes mediate patterns of covariation between hosts' exposure and susceptibility to parasites and pathogens.

Type 2: Covariation between contact rate and infectiousness within infected hosts

The second form of covariation may result from infection-induced changes in behavior that influence contact rates of infected hosts, which may be strongest for the most infectious individuals. Differences in behavior between infected and uninfected individuals are frequently reported (reviewed by Moore 1984), but relatively few studies have explicitly examined how infection alters the rate of contact between infectious and susceptible conspecifics. This is particularly surprising given the importance of this contact rate for population-level dynamics of disease

(Lloyd-Smith et al. 2004). Interestingly, in the milkweed leaf beetle, males parasitized by the subelytral mite *Chrysomelobia labidomerae* were more likely to contact unparasitized male conspecifics and each contact tended to be longer in duration (Abbot and Dill 2001). Because the parasite of interest is transmitted during copulation, these changes in behavior are unlikely to have direct effects on transmission in this case. However, the authors interpret the behavioral changes as higher investment in reproduction by parasitized males (e.g., terminal investment, thought to result when host survival probability is reduced due to parasite infection, senescence, etc). Evidence for terminal investment or fecundity compensation in response to parasite infection or pseudo-parasite infection (e.g., vaccine or immune antigen injection) has been documented in invertebrates (Chadwick and Little 2005) and several groups of vertebrates (e.g., Bonneaud et al. 2004; Weil et al. 2006). Furthermore, sexually-transmitted pathogens of animals are more likely than “ordinary infectious diseases” to induce sterility (Lockhart et al. 1996), potentially resulting in increased mating attempts and resulting transmission by infected, sterile individuals. If stronger investment in reproduction and/or an increased number of mating attempts is a more widespread phenomenon in infected males or females, these changes in behavior may lead to positive covariation between contact rate and the level of infectiousness within infected hosts (Fig. 1B, dashed line). However, many other studies have found the opposite result, whereby infected males invest relatively less in reproductive behaviors (e.g., in guppies, inter-male contests and courtship; Kolluru et al. 2009), which would result in negative covariation (Fig. 1B, solid line). The extent to which infection results in increases or decreases in hosts' reproductive activity, thereby altering contact rates, likely depends on the life history of the host and on the biology of the host–parasite interaction.

Many vertebrates express “sickness behaviors,” a constellation of behavioral changes that occur early in infection as part of the inflammatory response. Intriguingly, sickness behaviors are a component of the innate immune response (Adelman and Martin 2009), thus potentially linking behavioral changes in infected hosts with the strength of one component of susceptibility (the acute phase response). As such, the expression of sickness behaviors may be dependent on the level of infectiousness of the host, resulting in positive or negative covariation within infected hosts (Fig. 1B). In house finches, behavioral changes associated with *Mycoplasma gallisepticum* infection (Kollias et al. 2004) persist throughout the infectious

period (D. Hawley et al., unpublished data), and include reductions in movement, sociality, and aggression in males (Hawley et al. 2007; Bouwman and Hawley 2010). These behavioral changes may lead to negative covariation between host infectiousness and contact rate, in that the most infectious hosts are least likely to encounter healthy conspecifics.

An understudied characteristic of the acute phase response in vertebrates is the decrease in testosterone levels that follows infection or the injection of immune antigens (Spratt et al. 1993; Muehlenbein et al. 2005; Boonekamp et al. 2008). If testosterone is predictive of contact rates, changes in testosterone may be the proximate cue that underlies positive or negative covariation within infected individuals. This mechanism of covariation assumes that the decrease in testosterone depends on the level of infectiousness of the host. In humans, males admitted to critical-care units had decreased levels of testosterone that varied with the severity of illness (Spratt et al. 1993). To our knowledge, no study to date has examined whether nonhuman vertebrates alter their testosterone levels when infected with an ecologically-relevant pathogen, or whether changes in testosterone vary with the degree of infectiousness. However, reductions in aggression by infectious males, which are consistent with changes in testosterone, have been detected in red grouse (Fox and Hudson 2001), house finches (Bouwman and Hawley 2010), and mice (Gourbal et al. 2002). Reductions in aggression by infected males may generally lead to negative covariation between contact rate and infectiousness in that males that are most infectious will be least likely to contact susceptible conspecifics (Fig. 1B, solid line). However, in some systems, reductions in aggression of infected individuals may lead to increases in rates of contact with conspecifics (Bouwman and Hawley 2010), and hence to positive covariation between contact rate and infectiousness (Fig. 1B, dashed line).

Type 3: Covariation among hosts: Correlations between conspecific behavior and infectiousness of infected hosts.

The third type of covariation may arise when traits related to behavioral and physiological components of transmission covary among interacting individuals. For example, if susceptible individuals actively avoid coming into contact with infectious individuals this would lead to negative covariation between the number of behavioral contacts experienced by an infected host and its level of infectiousness (i.e., the most infectious individuals will have the fewest

contacts as a function of both their own physiological status and the behavioral responses of conspecifics to that status; Fig. 1C, solid line). Alternatively, if noninfected individuals that are the most susceptible to infection are unable to avoid contacts with infectious conspecifics (e.g., animals of low social status), then this might generate positive covariation (Fig. 1C, dashed line) whereby the majority of a highly susceptible individual's contacts are with the most infectious conspecifics.

Negative covariation in the context described above can come about only if individuals can discern the infection or immune status of conspecifics. Avoidance of infected conspecifics has been documented in species ranging from social lobsters to amphibians and rodents (Kiesecker et al. 1999; Kavaliers et al. 2004; Behringer et al. 2006), indicating that in many systems animals can detect infected or infectious conspecifics, mainly via chemical or olfactory cues. In fact, female mice can discriminate between the urine odors of males infected with parasites ranging from the nematode *Heligmosmoides polygyrus*, to the mouse louse, *Polyplax serrata* and even influenza virus, and this behavior is typically observed in the context of mate selection (reviewed by Kavaliers et al. 2005). As a consequence, infection or infectiousness in males may be correlated with the lowest rates of contact with females. Interestingly, the mating preferences of female mice in relation to infection of males have also been shown to depend on previous experience, whereby females that have been previously exposed to infection may display the highest level of aversion to mating (Kavaliers et al. 2005). In this case, increased susceptibility of the female (due to potential previous exposure) may negatively covary with future contacts.

More generally, and even in the absence of discrimination of infected and uninfected conspecifics by the host species, mate choice can generate negative covariation between contact and infectiousness if the number of matings a male acquires and his degree of resistance to pathogens (which should influence both susceptibility and infectiousness) are negatively correlated. Hamilton and Zuk (1982) proposed that the intensity of a male's secondary sexual ornaments should be associated with his level of resistance to parasites, and that females may choose males based on the extravagance of these secondary sexual traits. If females do choose mates based on the magnitude of such sexual traits, then the least colorful and least resistant males (i.e., the most susceptible or infectious) should also have the lowest rates of mating contact, and vice versa, generating strong negative covariation. Given considerable evidence

demonstrating that females across many taxa choose males based on the intensity or size of male secondary sexual traits, and corresponding evidence linking male sexual traits to resistance to pathogens (Moller 1990; Zuk et al. 1990, 1992; Houde and Torio 1992; Andersson 1994; Thompson et al. 1997), sexual selection via female choice may be a key behavioral process generating negative covariation in the components of transmission of pathogens. Furthermore, this negative covariation would likely be strongest in highly skewed polygynous mating systems in which only a few of the males perform the majority of the matings, since those males should be least likely to carry infectious parasites and pathogens. Indeed, the type of mating system and the nature of mate choice among hosts may strongly determine the extent of Type 3 covariation.

Attraction to infected conspecifics, which would generate positive covariation between noninfected hosts and infected hosts, has also been detected in some systems. Uninfected *Rana cascadae* tadpoles were more likely to associate with conspecifics infected with *Batrachochytrium dendrobatidis* than with uninfected conspecifics (Han et al. 2008). Although the mechanisms remain unknown, the authors speculate that uninfected tadpoles may be seeking infected conspecifics as prey. In house finches, uninfected individuals were most likely to feed in the vicinity of an infected, same-sex conspecific (Bouwman and Hawley 2010). In this case, uninfected individuals prefer to feed in the vicinity of the least aggressive conspecific. Because infected male house finches significantly reduce their aggression, uninfected individuals preferred to feed in their vicinity for ~75% of the time (Bouwman and Hawley 2010). A key remaining question in order for covariation to result is whether behavioral attraction to infectious conspecifics is strongest for the most susceptible hosts (e.g., those of low social status who benefit most strongly from consuming infected conspecifics or seeking out low-aggressive flockmates). Overall, further studies are needed documenting behavioral responses of healthy hosts to infectious conspecifics, and the extent to which these responses vary with hosts' immune status.

Population-level consequences of covariation between contact rate and susceptibility

Historically, variation among individuals in susceptibility or in contact rate has been largely ignored by studies of disease at the population level. However, empirical studies suggest that individual variation in

contributions to the transmission of disease is the rule rather than the exception. The 80/20 rule, which posits that 80% of parasites or pathogens are transmitted by only 20% of individuals (Woolhouse et al. 1997), appears to apply to a range of systems (Ferrari et al. 2004), and may often be even more extreme (Bansal et al. 2007). Individuals who contribute disproportionately to the transmission of pathogens are often referred to as key hosts or superspreaders (Lloyd-Smith et al. 2005). The population-level consequences of key hosts are striking: models reveal that individual variation can result in more severe outbreaks of pathogens (Bansal et al. 2007; Lloyd-Smith et al. 2005). Two variables have been proposed to largely characterize key hosts: (1) more frequent *contacts* with susceptible conspecifics or (2) a higher likelihood of transmission to a susceptible host given a contact (due to some aspect of the key host's physiological susceptibility). Although interest in the former has revealed behavioral predictors of superspreaders (e.g., Temime et al. 2009), few studies have considered whether these two characteristics may covary among individuals, and if so, what the consequences of this covariation are for population-level spread of disease.

To explore the potential consequences of covariation in hosts' susceptibility and behavior on the dynamics of disease, we consider the basic reproductive number, R_0 , of the pathogen. R_0 is the number of secondary infections a single index case is expected to generate in a naïve host population, and can be calculated as the *per capita* rate at which new infections arise ($\beta_c \beta_p$), divided by the rate at which individuals are lost from the infectious class, $(\alpha + \mu + \gamma)$, where μ represents the background mortality rate, α is the disease-induced mortality rate, and γ the recovery rate. Thus, $R_0 = \beta_c \beta_p / (\alpha + \mu + \gamma)$. R_0 can be interpreted as an index of the pathogen's invasive ability, with invasion only possible if $R_0 > 1$, and the spread of the disease more rapid with increasing R_0 . Heterogeneities in the contact rate and transmission efficiency of the host will change R_0 according to the moment expansion, a Taylor expansion about the mean (derivation in Supplementary Data)

$$R_0 \approx \bar{\beta}_c \bar{\beta}_p / (\alpha + \mu + \gamma) (1 + cv(\beta_c)cv(\beta_p)Corr[\beta_c \beta_p]),$$

where $\bar{\beta}_c$ and $\bar{\beta}_p$ are the mean contact rate between infectious and susceptible hosts and the mean efficiency of transmission, respectively; $Corr[\beta_c \beta_p]$ is the correlation coefficient between host's contact rate and transmission efficiency, and $cv(\beta_c)$, $cv(\beta_p)$ are the coefficients of variation for β_c and β_p . The correlation coefficient $Corr[\beta_c \beta_p]$ can vary between -1 and $+1$, resulting in reduced R_0 for negative

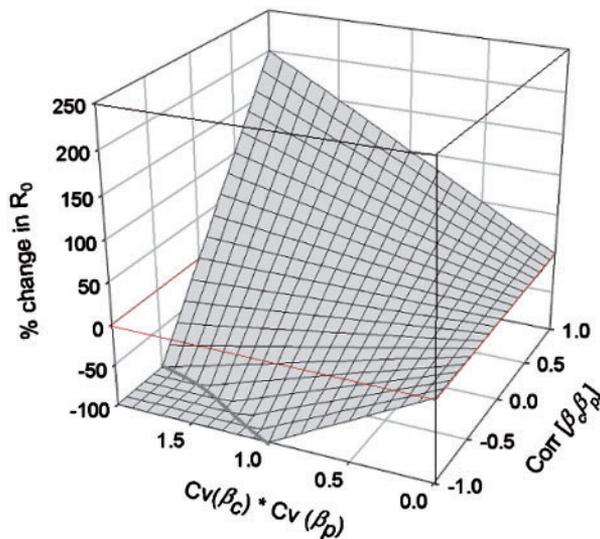


Fig. 3 Effect of covariation between contact rate (β_c) and transmission efficiency (β_p) on the pathogen's basic reproductive number, R_0 . The x-axis shows the extent of covariation between rate of contact and efficiency of transmission, expressed as the correlation coefficient of β_c and β_p , $\text{Corr}[\beta_c, \beta_p]$. The y-axis shows the combined variability in rate of contact and efficiency of transmission, expressed as the product of their coefficients of variation, $\text{Cv}(\beta_c)\text{Cv}(\beta_p)$. For positive covariation between β_c and β_p , increases in R_0 are proportional to variability in rate of contact and efficiency of transmission; for negative covariation, R_0 decreases linearly with variability in β_c and β_p . The tighter β_c and β_p are correlated, the greater the response in R_0 , as evidenced by steeper slopes of R_0 on $\text{Cv}(\beta_c)\text{Cv}(\beta_p)$.

covariation and increased R_0 when contact rate and transmission efficiency covary positively.

From this formulation, it is clear that covariation between behavioral and immunological traits may strongly influence the pathogen's R_0 (Fig. 3). The more variability there is among individuals in their contact patterns and in susceptibility or infectiousness, the greater is the potential for covariation in these traits to increase or decrease R_0 ; also, the tighter the correlation between contact rate and susceptibility, the greater is the effect on R_0 . Importantly, if transmission efficiency and contact rate are tightly coupled, even moderate variability in β_c and β_p can substantially increase or reduce R_0 . For example, if the coefficients of variation for β_c and β_p are both 0.5, their covariation can lead to an increment or decrement in R_0 of up to 25%. In populations in which susceptibility and contact behavior are highly variable and tightly coupled, the majority of the pathogen's R_0 may be attributable to the effect of covariation in susceptibility and rate of contact; in other words, superspreading individuals with high contact rates and susceptibility may be responsible

for the bulk of transmission of disease. In contrast, if β_c and β_p have distributions with coefficients of variation that are >1 , strong negative correlations between efficiency of transmission and rate of contact could result in the virtual disappearance of a disease from a population. Overall, the extent and direction of covariation between behavioral and physiological components of the transmission rate may well make the difference between invasion of a disease or its fade-out.

Conclusions

The mechanisms that can result in covariation between behavioral and physiological components of disease transmission appear to be widespread, and therefore are likely important mediators of the costs and benefits of mating systems, group-living, and discrimination of the disease status of conspecifics. Although the costs of parasites and pathogens have long been considered in the study of sexual selection and sociality, the influence of these behaviors on exposure to infectious agents versus susceptibility to disease have largely been considered separately. Our results suggest that it is important to consider them simultaneously, as the two components acting in concert can have important implications for the process of invasion by disease.

We see several exciting areas for future research on this topic. First, just how variable are rates of contact and susceptibility to disease among individuals; and is covariation the rule or the exception? To our knowledge, the coefficient of variation for these parameters has not been quantified for any system and it is intriguing to speculate whether there may be systematic differences among host–pathogen systems in behavioral and immunological variability and their linkage. Macroparasite populations are generally highly aggregated among hosts, owing to variability among hosts in susceptibility and exposure to infectious stages (Shaw et al. 1998). The heavily parasitized individuals contribute the bulk of infectious stages, strongly driving the dynamics of populations of macroparasites (Anderson and May 1978). The extent to which covariation in susceptibility and exposure among hosts contributes to variability in the aggregation of macroparasites across study systems has not been investigated. Highly aggregated distributions of macroparasites may be indicative of tight covariation between hosts' susceptibility and exposure, and could thus represent an accessible screening criterion for identifying study systems most suitable for investigating the behavioral and physiological linkages discussed here.

Second, to what extent are patterns of covariation influenced by environmental context? As one example, ambient temperature can influence changes in behavior of infected individuals (Sutherland et al. 2007), thereby potentially altering the strength of Type 2 covariation across varying ambient temperatures. Third, from the perspective of the management of diseases, it is critical to understand whether superspreaders, or individuals that contribute disproportionately to transmission, are characterized largely by behavioral components of transmission, physiological components, or both acting in concert. Finally, the relative influence of genotype versus phenotype on patterns of covariation may be crucial in terms of determining whether covariation between behavioral and physiological components of disease transmission can act as a set of coevolving traits, as has been proposed for personality. In one of the few studies to explicitly examine genetic covariation between hosts' susceptibility to disease and their exposure to infection, sheep that were genetically resistant to gastrointestinal helminths were also more effective in avoiding foraging in parasite-rich areas of the habitat (Hutchings et al. 2007). However, because these sheep were selectively bred lines, it is unclear what the genetic mechanism of resistance was, and whether behavior might have contributed to traits under selection.

In summary, we propose that covariation between physiological and behavioral components of susceptibility is likely widespread, but significantly more empirical study is needed in order to determine whether aspects of the hosts' life history and social and mating systems predict the extent and direction of covariation. Using a simple modeling framework, we show that the implications of behaviorally-mediated covariation can be substantial (e.g., tipping the balance between invasion and fade-out of a disease), and depend on both the amount of variability in rates of contact and in efficiency of transmission among individuals, and how tightly these are coupled. Consequently, linking the multifactorial effects of animal behavior on transmission of parasites to the dynamics of disease at the population-level represents an important and exciting research frontier at the nexus of animal behavior, disease ecology, and ecological immunology.

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Supplementary Data

Supplementary Data are available at *ICB* online.

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