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HOST PERFORMANCE AS A TARGET OF MANIPULATION BY PARASITES: A META-ANALYSIS

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ABSTRACT: The mechanisms underlying parasite-altered host behavior and fitness remain largely unanswered. The purpose of this review is to provide a perspective that has not been fully incorporated into the debate on how parasites manipulate their hosts. We argue that performance capacity is an important target of parasitic manipulation, and we aim to integrate the study of performance with that of parasitic manipulations of host behavior and fitness. We performed a meta-analysis from the published literature of 101 measures of the effect of parasites on host performance capacity to address the following questions. (1) Do parasites exert an important effect on host performance capacity? (2) Is that effect routinely to decrease or enhance performance capacity? And, (3) what factors explain variation in the effect sizes that have been quantified? Although negligible–small effect sizes were detected in 40/101 measures, host performance capacity was overall affected by parasitic infection, with a negative direction and medium–large magnitude in 58/101 measures and an increase in performance capacity in 3/101 measures. Host age, type of host performance, the host tissue infected by the parasite, and whether the study was experimental or based on natural infections each explained a significant amount of the variation in effect size. The significance of each factor is briefly discussed in light of the potential adaptive character of host manipulations by parasites.

Parasites are fascinating organisms, and the repulsion they trigger in many people typically changes into an intense attraction that is well exploited in popular culture including movie monsters, e.g., Alien and Slither, popular literature (Nagami, 2001; Zimmer, 2001; Coustau and Hertel, 2008), and science news (Welsh, 2012; Bennington-Castro, 2013) which vividly picture parasites as body snatchers and zombie-engineers. However, this spookiness subverts the subtleties and exquisiteness involved in parasitism, which makes it one of the most successful modes of life (Poulin and Morand, 2000; Combes, 2001). Our fascination is a mere reflection of the parasites' complexity, diversity, and key role in both population and ecosystem dynamics (Sukhdeo and Hernandez, 2005; Kuris et al., 2008; Thompson et al., 2013).

For years, people have observed that parasites could modify the phenotype of their hosts, and the term "manipulation" was coined to group all these modifications together whether they were behavioral, morphological, and/or ecological (Poulin and Thomas, 1999; Moore, 2002; Thomas et al., 2005; Moore, 2013). In an attempt to connect the dots and explain the ways parasites evolve to complete extraordinary life cycles, Combes (1991) coined the term 'favorization.' Although, the adaptive nature of host manipulation, in particular the case of trophic favorization, remains the object of debate and requires prudence (Poulin, 1995; Webster et al., 2000; Cézilly et al., 2010; Perrot-Minnot et al., 2012), the fact that such manipulations are extended phenotypes of the parasite's genes is well acknowledged (Combes, 2001; Beani, 2006; Poulin, 2010; Thomas et al., 2012). Not all parasites manipulate their hosts (Poulin, 2010), some do (Moore, 2002; Hughes et al., 2012), some 'cheat' (the 'hitchhikers' and the 'lucky ones') by taking advantage of manipulative co-infections (Thomas et al., 1998; Lafferty et al., 2000; Mouritsen, 2001; Leung and Poulin, 2007), and for numerous others we simply do not know where they stand in this mosaic of interactions. However, when manipulation occurs, the classic idea is that parasites negatively impact their hosts' fitness, e.g., decreased reproductive output, impeded mating, or reduced growth to the benefit of their own fitness (Robar et al., 2010). However, host manipulation by parasites is multidimensional and complex (Thomas et al., 2010; Ponton et al., 2011; Cézilly et al., 2013), and parasites are now known to target suites of interrelated traits (Biron and Loxdale, 2013; Poulin, 2013). Thus, although there are numerous examples of apparently straightforward negative outcomes of manipulations for the host (e.g., Hurd, 2001; Barber et al., 2004; Shirakashi et al., 2008), the constant arms race and tradeoffs in host–parasite relationships, as well as the molecular "cross-talk" between hosts and parasites, may lead to more subtle and intriguing situations. For instance, a host's longevity and/or size may be increased (Hurd et al., 2001; Ziuganov, 2005; Hartikainen et al., 2013), and some parasites switch how they manipulate their host such that they can be both beneficial and detrimental to the same host at different times during their development in that host (Parker et al., 2008; Hammerschmidt et al., 2009; Dianne et al., 2011; Weinreich et al., 2013). Although the profound evolutionary implications of manipulative parasites are not yet fully understood (Thomas et al., 2005), host phenotype manipulation by parasites, in particular behavioral manipulation, is not uncommon and occurs in multiple host and parasite taxa (Moore, 2002, 2012; Hughes et al., 2012; Lafferty and Shaw, 2013). The ecological consequences of host manipulation are well appreciated, if not fully determined (Poulin and Thomas, 1999; Lafferty and Kuris, 2012), and as stated by Poulin and Levri (2012), "having manipulated hosts in an ecosystem is not unlike having 2 related host species present in a community, sharing many traits but differing sharply with respect to others."

It is clear that parasites manipulate their hosts; however, *how* parasites manipulate their hosts at a mechanistic level, i.e., what is the target of the parasitic manipulation, remains a fundamental question and, as such, the physiological mechanisms underlying changes in host phenotype are the object of continuous research (Lefevre et al., 2009; Ludin et al., 2011; Biron and Loxdale, 2013; Hughes, 2013; Perrot-Minnot and Cézilly, 2013; van Houte et al., 2013; Pennisi, 2014). Despite major recent advances, in particular in studies of how brain-controlling/hijacking parasites alter host behavior (Prandovsky et al., 2011; Adamo, 2013; Flegr, 2013; Helluy, 2013), the mechanisms underlying parasite-altered host behavior and fitness remain largely unanswered for most parasites (Thomas et al., 2005; Hughes et al., 2012; Adamo and Webster, 2013; Hughes, 2013). The purpose of this review is to provide

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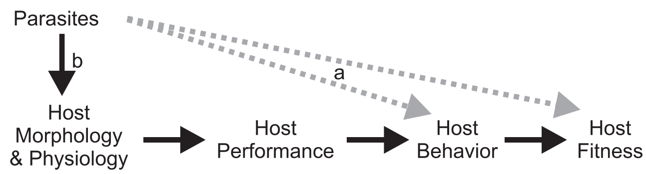

FIGURE 1. Theory predicts and data support the idea that variation in morphology/physiology predicts variation in performance capacity and that variation in performance capacity ultimately determines behavior and differential fitness between individuals (Arnold, 1983; Garland and Losos, 1994). (**a**) Dashed gray arrows showing the classic observation that parasites have an impact on host behavior or fitness. (**b**) The alternative hypothesis that parasites have a direct effect on host morphology and/or physiology, which then alters host performance, which then cascades into changes in host behavior and host fitness.

another perspective that has not yet been fully incorporated into the debate about the target of host manipulation by parasites.

We argue that whole-organism performance capacity is an important target of parasitic manipulation. Whole organism performance capacity is a physical quantity (e.g., distance, speed, frequency, time) that measures how well an organism *can* execute a given behavior or ecologically relevant task (Arnold, 1983; Garland and Losos, 1994; Irschick and Henningsen, 2009), e.g., how fast a fish can swim or how far a grasshopper can jump. Performance capacity has been intensely studied for the last several decades, and it is now widely accepted that performance capacity is a key trait (and maybe *the* key trait) that is targeted by selection (Arnold, 1983; Garland and Losos, 1994; Husak et al., 2006; Irschick and Le Galliard, 2008; Irschick et al., 2008). Performance is related to morphology, physiology, behavior, and fitness (Fig. 1). It is determined, i.e., constrained, by underlying morphological and physiological systems (Fig. 1). For example, the ability of a fish to swim rapidly is determined by its available muscle mass, muscle cell physiology, stored energy, and body/fin shape (Langerhans, 2009). In turn, performance constrains the behaviors in which the organism can engage (Garland and Losos, 1994). For example, a male lizard that cannot bite as hard is less likely to win fights and secure mates (Lappin and Husak, 2005). Thus, parasites that directly alter host morphology or physiology could influence host performance capacity because morphology and physiology constrains/predicts performance. Additionally, because performance constrains behavior and because behavior is a key predictor of fitness, parasites could exert their effect on host fitness and behavior via the filter of performance capacity (Fig. 1). We suggest that a hypothesis for how parasites impact host fitness is that parasites have a direct effect on host morphology and physiology and that this results in a change in performance capacity and then behavior and, ultimately, host fitness (Fig. 1).

Thinking of all of the ways that parasites induce changes in host morphology, physiology, and behavior quickly makes one wonder how often performance is impacted by parasites, especially given that so much research has shown performance as a key linkage between these traits. However, the literature of the effects of parasites on host performance capacity is limited to several examples, and no synthesis is yet available. Thus, the goal of this review paper is to use meta-analysis of the published literature on the effect of parasites on host performance capacity to address the following questions. Do parasites exert an important effect on host performance capacity? Is that effect routinely to decrease or enhance performance capacity? And, what factors explain variation in the effect sizes that have thus far been quantified?

DATA COMPILATION FOR META-ANALYSIS

We compiled published studies of the effect of parasitism on performance capacity. We searched the following databases: Web of Science, Google Scholar, and Zoological Records using the following terms: parasit* and performan* and swim* or flight or run*or stamin* or locomot* or speed*, and various taxonomic terms, e.g., amphib*, fish*, insect*, etc., and we back-tracked the literature prior to 1980. We purposely decided against including studies on parasitoids because the use of the key word parasitoid* mostly yielded papers about the performance of the parasitoids themselves. We also purposely did not include any studies on performance when used in the sense of fitness, e.g., reproductive output or growth/weight gain. This search yielded 76 papers. Several studies recorded multiple types of performance capacity and multiple aspects of the same type of performance. In these cases, we kept each record of a type of performance, e.g., endurance vs. speed, but only 1 aspect of the same type of performance, e.g., if endurance was measured as time and distance, we only kept 1 measurement, chosen randomly. We only included studies that examined parasite presence/absence on performance; measures of the effect of parasite load or density on performance were not included in our meta-analysis (11 studies). We then calculated the effect size (Hedges' g) for the effect of parasite presence/absence on each performance measurement using a spreadsheet function following Gurevitch and Hedges (2001) or using the compute.es (Del Re, 2013) package in R v.3.0.1 (R Core Development Team, 2013). These different techniques were required, as published studies were heterogeneous in how they reported results, i.e., means, standard deviations, and samples sizes vs. *t*-test or *F*-test. Sixteen studies were not usable for the meta-analysis because they did not report enough statistical information to compute an effect size. After removing studies for the reasons stated above, the final dataset consisted of 49 studies (Table I) and 101 measures of effect size. In addition to the effect size, we recorded the following factors that were hypothesized to predict effect size from each study (Table II): (1) host taxon (to class, except Crustacea which is a subphylum), (2) host type (intermediate, definitive, paratenic), (3) host age (juvenile, adult, all ages, or none reported), (4) type of host activity (swimming, running, etc.), (5) type of host performance (speed, endurance, etc.), (6) parasite taxon (various taxonomic levels based on typical classification: digenean, acanthocephalan, etc.; see Table I), (7) type of parasite (endoparasite, mesoparasite, ectoparasite), (8) location of stage of parasite studied (external vs. internal), (9) specific location of parasite on/in the host (skin/gills, blood, viscera, etc.), (10) type of tissue the stage of the parasite studied infects or directly alters (epithelial, connective, etc.), (11) stage of the parasite when it infects the host (developed [adults, trophozoites, etc.] vs. developing [metacercariae, juveniles, etc.]), (12) parasite's type of life cycle (simple, complex, and other for non-defined life cycles such as fungus), (13) mode of transmission of the parasite at the stage it was studied (e.g., trophically via a predator or via a vector, or by direct contact), and (14) type of infection in study (experimental vs. natural).

TABLE I. References to studies used in the meta-analysis classified according to the type of performance tested in the original studies and host and parasite taxa.

Type of performance	Host taxon	Parasite taxon	References
Acceleration	Insecta	Chelicerates	McLachlan et al., 2008
	Teleost	Cestodes	Blake et al., 2006
		Digeneans	Blake et al., 2006
		Nematodes	Umberger et al., 2013
Distance	Amphibia	Digeneans	Goodman and Johnson, 2011
		Fungi	Chatfield et al., 2013
Duration	Amphibia	Monogeneans	Pfennig and Tinsley, 2002
Efficacy	Teleost	Monogeneans	Shirakashi et al., 2008
		Nematodes	Umberger et al., 2013
Endurance	Amphibia	Digeneans	Goodman and Johnson, 2011
		Nematodes	Kelehear et al., 2009; Marr et al., 2010
	Crustacea	Digeneans	Kunz and Pung, 2004
	Insecta	Apicomplexans	Schiefer et al., 1977; Bradley and Altizer, 2005
		Nematodes	Hockmeyer et al., 1975; Villacide and Corley, 2008
	Mammalia	Digeneans	Schwanz, 2006
	Squamata	Acanthocephalans	Daniels, 1985
		Apicomplexans	Schall et al., 1982; Schall, 1990; Clobert et al., 2000
		Chelicerates	Main and Bull, 2000
	Teleost	Amoebozoans	Powell et al., 2008
		Ciliophorans	Munderle et al., 2004
		Crustaceans	Wagner et al., 2003; Östlund-Nilsson et al., 2005; Grutter et al., 2011; Binning et al., 2013
		Digeneans	Klein et al., 1969
		Kinetoplastids	Kumaraguru et al., 1995
		Molluscs	Taeubert and Geist, 2013
		Monogeneans	Shirakashi et al., 2008
		Myxozoans	Moles and Heifetz, 1998; Ryce et al., 2001; Wagner et al., 2005; DuBey et al., 2007; Fetherman et al., 2011
		Nematodes	Munderle et al., 2004; Palstra et al., 2007
		Opisthokonta	Kocan et al., 2006
Frequency	Amphibia	Monogeneans	Pfennig and Tinsley, 2002
Maneuvering	Insecta	Chelicerates	McLachlan et al., 2008
Power	Insecta	Apicomplexans	Marden and Cobb, 2004
Repeat endurance	Teleost	Myxozoans	Wagner et al., 2005
Speed	Amphibia	Digeneans	Goodman and Johnson, 2011
		Nematodes	Goodman and Johnson, 2011; Pizzatto and Shine, 2011a, 2011b, 2012; Chatfield et al., 2013
	Crustacea	Acanthocephalans	Medoc and Bessel, 2008
		Cestodes	Wedekind and Milinski, 1996
		Digeneans	Kunz and Pung, 2004
	Insecta	Apicomplexans	Schiefer et al., 1977; Bradley and Altizer, 2005
		Chelicerates	McLachlan et al., 2008
		Kinetoplastids	Roberts, 1981
		Nematodes	Villacide and Corley, 2008
	Mammalia	Digeneans	Schwanz, 2006
		Insects	Devevey et al., 2010
	Squamata	Apicomplexans	Schall et al., 1982; Oppliger et al., 1996
		Chelicerates	Main and Bull, 2000; Ekner-Grzyb et al., 2013
	Teleost	Cestodes	Barber et al., 2004; Blake et al., 2006
		Crustaceans	Nendick et al., 2011
		Digeneans	Blake et al., 2006; Santos et al., 2011
		Nematodes	Umberger et al., 2013
		Teleosts	Brunnschweiler, 2006

STATISTICAL ANALYSES

All analyses were done in R version 3.0.1 (R Core Development Team, 2013). We interpreted effect sizes according to Cohen (1988). We tested for bias in our data set using the function regtest, constructing a funnel plot, and estimating 'missing' data using the trim and fill method in the R package metafor (Viechtbauer, 2010). Our goals were to (1) summarize general findings for effect sizes in the literature, and (2) test for the effect of each factor on effect sizes. To achieve these goals we used

TABLE II. Hypotheses for the impact of each factor studied on the change in host performance due to parasitism. A > denotes a larger negative effect size (i.e., more reduced performance due to parasite). Some hypotheses are based on findings or remarks of previous authors (see references) but do not systematically reflect their conclusions (i.e., more than one reference for a factor may indicate conflicting evidence).

No.	Factor	Hypotheses	References
1	Host taxon	Vertebrate taxa > invertebrate taxa	Poulin, 1994; Lafferty and Shaw, 2013
2	Host type	Intermediate/paratenic > definitive	Perrot-Minnot and Cézilly, 2009
3	Host age	juvenile > adult	Herrel and Gibb, 2006
4	Host activity	No difference expected	
5	Host performance	No differences expected	
6	Parasite taxon	Nematodes and cestodes > acanthocephalans	Poulin, 1994; Lafferty and Shaw, 2013
7	Parasite type	Endoparasite > ectoparasite/mesoparasite	Lafferty and Shaw, 2013
8	General parasite location	Internal > external	Lafferty and Shaw, 2013
9	Specific parasite location	Skin/gills and soma and blood > viscera	Chubb et al., 2010; Lafferty and Shaw, 2013
10	Parasite tissue	Muscle, neural, connective > epithelial, body cavity	Chubb et al., 2010; Lafferty and Shaw, 2013
11	Parasite stage	Developing > developed	Hammerschmidt et al., 2009; Chubb et al., 2010
12	Parasite cycle	Complex > simple	Perrot-Minnot and Cézilly, 2009
13	Parasite transmission	Trophic > vector/dispersal/contact	Holmes and Zohar, 1990
14	Type of infection	Experimental > natural	

mixed-model meta-analysis in metafor (Viechtbauer, 2010), with Hedges' g as the response, studies weighted by the inverse of their variance, factors as fixed effects, and host phylogeny, parasite taxonomy (species nested in factor 6, see above), and study identification as random effects. Two of the 14 factors we tested were collinear with other factors (specific parasite location was collinear with the tissue infected by the parasite, and parasite stage was collinear with host type) which prevented model fitting. Thus, we removed the specific location of the parasite and host type before proceeding. We compiled a host phylogeny based on published studies (Lavrov et al., 2004; Steppan et al., 2004; Ishiwata et al., 2011; Weigmann et al., 2011; von Reumont et al., 2012; Wainwright et al., 2012; Near, Dornburg et al., 2013; Near, Eytan et al., 2013; Pyron et al., 2013) in Mesquite 2.75 (Maddison and Maddison, 2011). To account for multiple measurements per species we included a soft polytomy, with branches of zero length emanating from each species to the individuals within that species. This was necessary, as different measurements within each species corresponded to different levels of the factors studied. We then set all other branch lengths to 1 and then ultrametrized the tree. To compute the phylogenetic correlation matrix we used the branch length transformation (Pagel's lambda) that achieved the maximum likelihood fit using the function corPagel from the ape package (Paradis et al., 2004). Several of the factors had missing data or levels with only 1 or 2 observations; thus, we recoded these levels as 'other' within each factor prior to fitting the model. When a factor had a significant impact on effect size, we tested for differences across factor levels using pairwise *t*-tests whose *P*-values were corrected using the Benjamini-Hochberg method (Benjamini and Hochberg, 1995). We checked the residuals using Lilliefors normality test in the package nortest (Gross and Ligges, 2012) and they were normally distributed ($D = 0.081$, $P = 0.08$). Homogenous residual variance was tested using Fligner-Killeen tests, which revealed slight heteroskedasticity for parasite taxon (F-K median $\chi^2 = 18.5$, df = 9, $P = 0.03$) and parasite transmission (F-K median $\chi^2 = 9.1$, df = 3, $P = 0.03$). Although linear models are generally robust to slight violation of their assumptions, we interpret the results from these factors with caution.

MAGNITUDE AND DIRECTION OF EFFECT SIZE

Host performance capacity was generally reduced due to parasitism, with a negative direction and medium–large magnitude (mean effect size ± 95% confidence interval = –0.666 ± 0.155; Fig. 2). The majority (57%, 58/101 measures) were medium–large negative effect sizes with a large decrease in performance (effect size $\leq$ –0.8) detected in 40 measures and a medium decrease (–0.8 < effect size $\leq$ –0.5) detected in 18 measures (Fig. 2). Increases in performance capacity due to parasitism were rare (3%, 3/101 measures), with a large increase in performance (effect size $\geq$ 0.8) detected in 1 measure and a medium increase (0.5 $\leq$ effect size < 0.8) detected in 2 measures (Fig. 2). These studies included an increase in swimming performance in a rodent, *Microtus arvalis* (see Devevey et al., 2010), an amphipod, *Gammarus roeseli* (see Medoc and Beisel, 2008), and in diving performance in a lizard, *Sphenomorphus quoyii* (see Daniels, 1985). Negligible–small effect sizes were detected in 40 studies (40%, 40/101 measures).

BIAS IN REPORTED EFFECT SIZES

Effect sizes were significantly related to their standard errors (Egger's regression test, $z = -3.8$, $P = 0.0001$), which indicates that reported effect sizes may be biased. The funnel plot and the trim and fill method revealed that there were 15 missing effect size measures all greater than 0 (Fig. 2). Seven of these missing effect sizes were greater than 0.8 (large effect size) and 2 others were greater than 0.5 (medium effect size). This analysis suggests that the reported effect sizes are biased because of a lack of published reports of medium–large magnitude increases in host performance due to parasitic infection.

FACTORS THAT EXPLAIN VARIATION IN EFFECT SIZE

Many of the factors tested did not explain variation in effect size (Table III; Fig. 3) including host taxon, host activity, parasite taxon, type of parasite, general location of parasite, stage when the parasite infects its host, the parasite's type of life cycle, and the way the parasite is transmitted. Host age, type of host performance, the type of tissue the stage of parasite studied

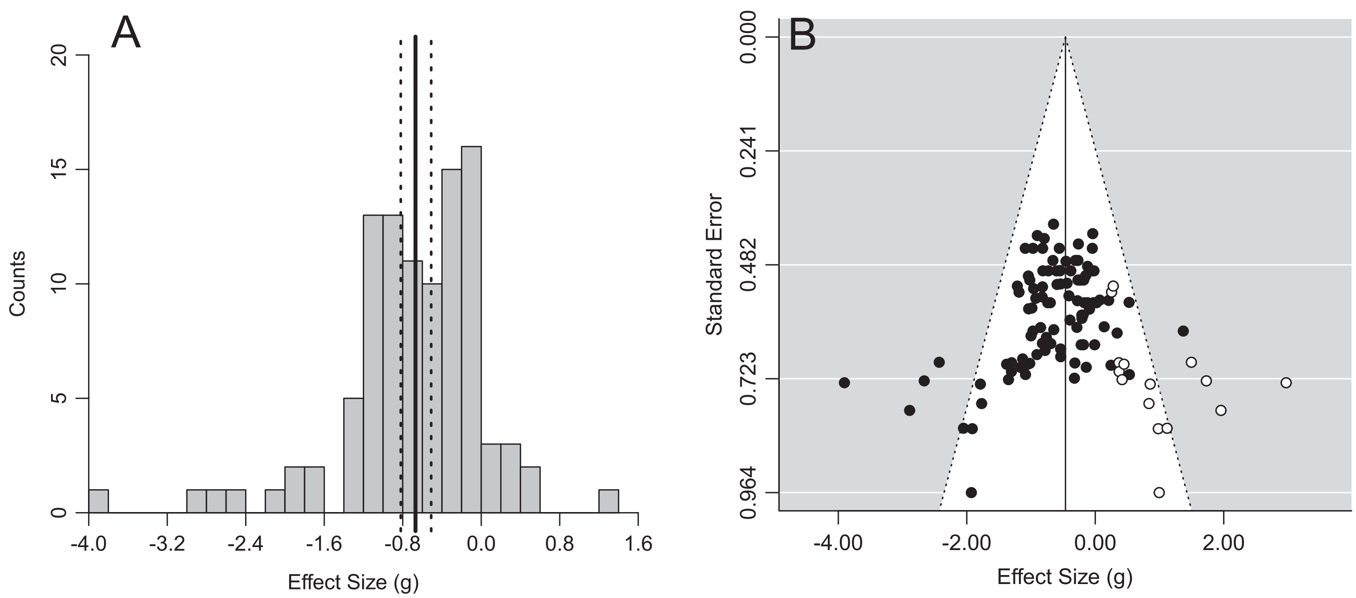

FIGURE 2. (**A**) Frequency histogram of effect sizes from published studies of the effect of parasitism on host performance capacity. Effects sizes less than 0 indicate a decrease in performance due to parasitism; values greater than 0 indicate an increase in performance due to parasitism. Solid vertical line is the mean effect size; dashed vertical lines are the 95% confidence intervals. (**B**) Funnel plot of effect sizes vs. standard error of the effect size. Dotted lines indicate the 95% pseudo-confidence intervals. Black dots are the measured effects from the literature. White dots are those estimated to be 'missing studies' based on the trim and fill method.

infects, and the type of infection in the study each explained a significant amount of the variation in effect size (Table III; Fig. 3). Studies that did not report host age or included all ages had significantly greater decreases in performance than did known adult or juvenile hosts ($P = 0.03$), and juvenile hosts had marginally greater decreases in performance than did adult hosts ($P = 0.09$). Endurance had marginally greater decreases in performance than did speed ($P = 0.09$), whereas all other host performance comparisons showed similar effect sizes ($P > 0.10$). Connective tissue had greater decreases in performance than did all 'other' tissues (which included studies with no data). Finally, experimental infections resulted in greater negative effects on host performance than did naturally occurring infections. Year of publication was not correlated with effect size ($r = -0.04$, $P = 0.69$). However, more-recent publications show greater variance in effect sizes than did the older studies (Fig. 4).

GENERAL PATTERNS IN HOW PARASITES INFLUENCE PERFORMANCE

The majority of studies analyzed show that the presence of parasites reduces host performance capacity and that the effect of parasites is most often in the medium–large category (Fig. 2). This result agrees with the general idea that parasites harm or live at the expense of their hosts, even if not grossly pathogenic, and that they impact their host at the individual, population, and ecosystem levels (see review by Combes, 2001). Additionally, via a recent meta-analysis, Robar et al. (2010) showed that parasitized individuals have an ~2.6× higher mortality than do non-parasitized individuals. Therefore, our result suggests that the mechanism by which parasites reduce host fitness and, thus, by which they can impact the host population, could often be due to the reduction of host performance capacity even though rarely studied, per se. For instance, parasitized animals show different migratory patterns compared to uninfected ones (Sjöberg et al., 2009) or cannot reach, or are delayed in reaching, their spawning grounds (Palstra et al., 2007; Kocan et al., 2009) or breeding grounds (Møller et al., 2004; Lopez et al., 2013). Among these examples, only Palstra et al. (2007) and Kocan et al. (2009) demonstrate that a reduction in performance is what constrains the host's ability to engage in effective (swimming) behavior. Other reasons, often invoked by authors to explain an alteration of behavior that reduces infected hosts' fitness include poor body condition, increased metabolism, or depressed immune function (Yorinks and Atkinson, 2000; Madelaire et al., 2013) or changes in host morphology such as alteration of feathers (Marzal et al., 2013; Pap et al., 2013) or lateralization (Roche et al., 2013) due to parasitic infection. Here, we emphasize that these changes in physiology and morphology likely underpin changes in performance capacity, and yet most studies have not identified how performance changes and whether it constrains behavior.

Some parasite-induced behavioral alterations may benefit the host (see examples in Combes, 2001 and Moore, 2012). We found 3 cases of medium–large increases in host performance capacity due to parasitism (Fig. 2). Two of them involve acanthocephalans, many of which are known to manipulate their intermediate hosts (Poulin, 1995; Moore, 2002). Daniels (1985) reported increased diving time in a lizard due to infection by an acanthocephalan, and Medoc and Beisel (2008) reported increased swimming speed in an amphipod also infected by an acanthocephalan. In these 2 cases, it was reasoned by the authors that the increase in host performance capacity might make the host less likely to be eaten by the 'wrong' predators (birds for the skink, a benthic invertebrate for the amphipod) and more likely to be eaten by the definitive host (a snake for the skink and a bird for the amphipod). Thus, these may be examples of predation suppression (sensu Hammerschmidt et al., 2009), which is a

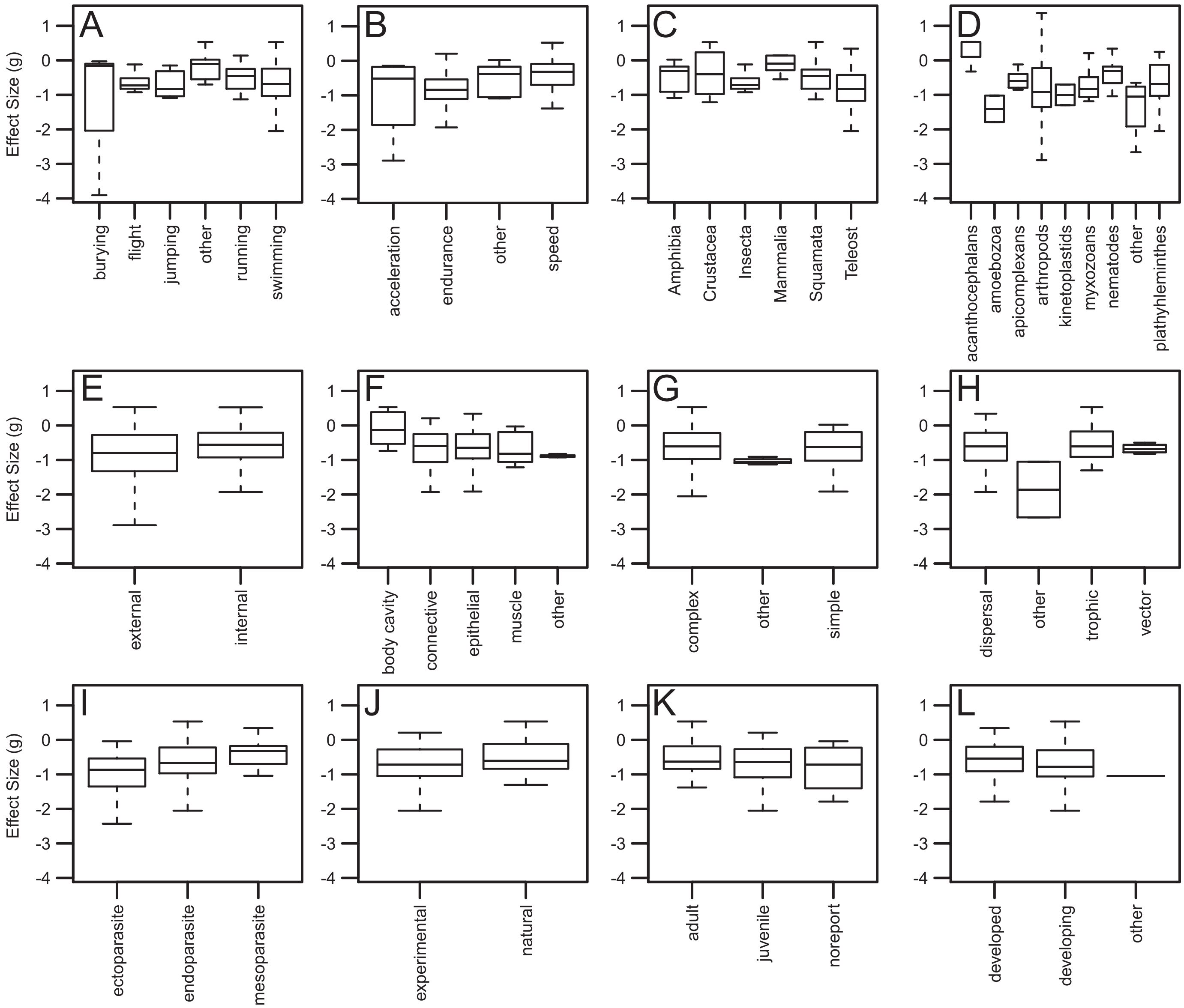

FIGURE 3. Effect sizes in change of host performance according to various factors. For each level, black bar is the median, box is the interquartile range, and whiskers are 1.5 times the interquartile range. (**A**) Host activity. (**B**) Host performance. (**C**) Host taxa. (**D**) Host age. (**E**) Location of the parasite on/in the host. (**F**) Type of tissue the parasite infects. (**G**) Parasite's type of life cycle (**H**) Parasite's mode of transmission. (**I**) Type of parasite. (**J**) Type of infection. (**K**) Host age. (**L**) Parasite's stage when it infects.

general phenomenon where parasites enhance the abilities of their host to protect it until transmission is optimal. While examples of predation suppression with respect to host behavior and host fitness are amassing (Koella et al., 2002; Hammerschmidt et al., 2009), examples of changes in performance capacity are, however, generally lacking (Chubb et al., 2010), with the caveat that some studies indeed measure performance but under the confusing term of 'activity' (see below). The third example of performance enhancement is for fleas infesting adult female voles (Devevey et al., 2010) and for which a performance increase is difficult to interpret in the light of either manipulation to favor parasite transmission or a beneficial value to the host, particularly because such performance enhancement is not observed in male voles or in either sex of voles infected as juveniles. For all 3 of these examples, we again emphasize the need for exploration of the mechanism linking parasite to performance, i.e., morphology and physiology (Fig. 1).

Every meta-analysis must confront publication bias, which can skew results and interpretations. That most published studies show a medium–large negative effect size suggests that the literature may be biased towards studies reporting 'significant' results in the expected direction, i.e., parasites reducing host performance. This notion was confirmed by a significant linear trend in the funnel plot and by the trim-and-fill method that suggests that studies with medium–large positive effect sizes representing increases in host performance capacity due to parasitism were 'missing' from our data set (Fig. 2B). This suggests either that studies that have demonstrated increases in

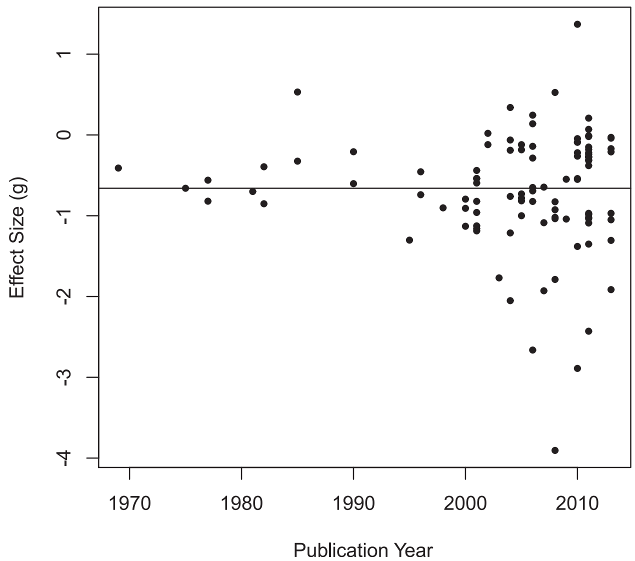

FIGURE 4. Bivariate plot of effect size vs. year of publication. Solid line is the mean effect size (–0.66).

host performance capacity due to parasites have not been published or that, on the contrary, cases of parasites increasing host performance capacity are indeed rare. The former explanation is not unreasonable given the difficulty in shifting paradigms (see also Poulin [2000] for additional arguments about publication bias). However, the fact that variance in effect sizes is increasing with publication year, and that new studies are rapidly accumulating (39 of the 101 measures were collected since 2010 [Fig. 4]), suggests that performance enhancement by parasites is on the cusp of being more broadly recognized. Also encouraging is that 35% of the published studies show no, or negligible, size effect, suggesting that non-significant results are regularly reported and that the potential lack of such reports is not a source of bias.

Another issue is that we chose not to use the term 'behavior' in our search criteria, whereas parasitologists appear to often treat the terms "behavior," "activity," and "performance" similarly. Consequently, although parasitologists have been heavily invested in testing how parasites change host behavior, there are undoubtedly studies where 'behavior' was reportedly tested but 'performance' was actually measured, and these studies may have been missed by our search criteria. To address the scope of this issue, we reviewed all papers cited in a meta-analysis of parasite-induced changes in host behavior which explicitly included activity (Poulin, 1994). Of the 21 studies examined, 3 clearly measured performance (Townson, 1970; Benton and Pritchard, 1990; Carmichael and Moore, 1991), although none of these 3 papers actually called the measurement 'performance.' Therefore, it is important to emphasize the definitions of performance and behavior within the classic framework of the ecomorphological or performance paradigm. Performance is defined as the capacity for an organism to do an ecologically relevant task or execute a behavior (Arnold, 1983; Garland and Losos, 1994). In other words, performance defines what an organism *can do* and behavior is what an organism actually *does* (Reilly and Wainwright, 1994). It would be most useful for these definitions and this framework to be fully incorporated into the study of behavioral manipulations by parasites to help differentiate change in behavior from performance and change in the underlying mechanisms of performance.

PARASITE-RELATED FACTORS THAT EXPLAIN VARIATION IN EFFECT SIZE

We examined 8 factors related to parasite biology that could be expected to influence the magnitude of change in host performance due to parasitism (Table II). Among these factors, only the tissue that the parasite infects (or directly alters) explained a significant amount of the variation in effect sizes (Table III). Post hoc tests differentiated connective tissue from all others as being the habitat of parasites showing larger effect size on their host performance (Table III; Fig. 3). Although Lafferty and Shaw (2013) also found that site of infection often defined the parasites' capacities to manipulate their hosts, they noted that, in contradiction to our findings, manipulative parasites more-commonly inhabited the central nervous system, the body cavity, or the muscles of their hosts. However and significantly, measurements included in our results also took into account the tissues altered by the parasites, most of which altered blood either by living in it (Schall, 1990; Oppliger et al., 1996) or feeding on it (Main and Bull, 2000; Devevey et al., 2010; Ekner-Grzyb et al., 2013). Because parasites are well recognized to affect both their host metabolism and immune function, which can be considered physiological targets for some manipulative parasites, these results support our hypothesis that by having a direct effect on host physiology, parasites induce a change in their performance capacity. It is also possible that infections by *Myxobolus* spp., which were reported as inducing skeletal deformities (Ryce et al., 2001; DuBey et al. 2007; Fetherman et al., 2011) and that we thus tagged as altering the connective tissue, may have biased our findings because these parasites also likely affect the hosts' muscular and nervous systems. However, such a complication is inherent to studying parasitism and will require an extremely large data set to be overcome.

Although previous meta-analyses suggested that acanthocephalans are less likely to influence host activity than are other helminthes (Poulin, 1994; Lafferty and Shaw, 2013), and that trophic transmission has a smaller effect on host activity than do other modes of transmission (Poulin, 1994), we found little statistical support for either of these (Table III). However, it should be noted that 2 of the 3 studies of acanthocephalans had increased host performance (see above) and, thus, there could be a difference due to infection by this parasite taxon that is known to be almost entirely comprised of manipulators. In fact, overall we found that very few aspects of the parasite's biology explained variation in effect size, even though there are valid hypotheses for why these factors should explain changes in performance (Table II). Additionally, several of these factors explain parasite-induced host mortality (Robar et al., 2010). The reason for the lack of significant factors in the present study is unclear. One issue that slices across many factors is wildly uneven sampling in factor levels and factor levels with uneven taxa sampling, e.g., all acanthocephalans have complex life cycles. In addition, parasite–host interactions are typically specialized, and it may be the specialized nature of these interactions that prevents these

TABLE III. Results of the mixed model meta-analysis for the impact of each factor on variation in effect size. Post hoc groupings were determined by *t*-tests corrected for multiple comparisons using the Benjamini-Hochberg method (Benjamini and Hochberg, 1995); only significant differences between levels within a factor are reported (A > denotes a larger negative effect size). Comparisons not listed are not significantly different.

No.	Factor	Q_m	P	df	Post hoc comparisons
1	Host taxon	6.6	0.26	5	
2	Host type*				
3	Host age	8.5	0.01	2	No report > juvenile/adult ($P = 0.03$), juvenile > adult ($P = 0.09$)
4	Host activity	5.0	0.41	5	
5	Host performance	8.6	0.04	3	Endurance > speed ($P = 0.09$)
6	Parasite taxon	11.3	0.19	8	
7	Parasite type	2.9	0.24	2	
8	General parasite location	0.1	0.96	1	
9	Specific parasite location†				
10	Tissue altered	10.3	0.04	4	Connective > others ($P = 0.04$)
11	Parasite stage	1.4	0.49	2	
12	Parasite cycle	1.1	0.59	2	
13	Parasite transmission	0.8	0.86	3	
14	Type of infection	5.0	0.03	1	Experimental > natural

* Collinear with factor 11.
† Collinear with factor 10.

simplistic factors from explaining variation in how parasites influence host performance capacity.

HOST-RELATED FACTORS THAT EXPLAIN VARIATION IN EFFECT SIZE

Host age explained a significant amount of variation in effect size, and post hoc testing provided marginal support for the hypothesis that parasites should have a greater effect on juveniles when compared to adults (Tables II, III). Juveniles in general are thought to be under strong selection for performance capacity because they often must compete with adults, which have greater absolute abilities because of their larger size (Herrel and Gibb, 2006). This leads to performance compensation in juveniles (Herrel and Gibb, 2006) and to a juvenile's greater use of its physiological maximum performance capacity, particularly in nature (Irschick, 2000). That is, if a parasite infects a juvenile and adult of the same species, one would expect a greater effect on the juvenile because its morphological and physiological systems are already working near their maximum physical capacity and, thus, any alteration induced by a parasite would come at a relative greater performance cost to the juvenile. We identified 3 cases where the juvenile and adult data are available for the same host, infected by the same parasite, and involved in the same type of performance, i.e., *Anguilla anguilla* infected by *Anguillicoloides crassus* (see Münderle et al., 2004; Palstra et al., 2007), *Tiliqua rugosa* infected by *Aponomma hydrosauri* (see Main and Bull, 2000), and *Gasterosteus aculeatus* infected by *Schistocephalus solidus* (see Barber et al., 2004; Blake et al., 2006). The effect size for juveniles was more negative in 2 of these 3 examples and very large in *G. aculeatus*, suggesting that the pattern seen across studies is mirrored in this subset. Future studies that explicitly examine how parasites influence performance across both host and parasite ontogenies would be useful.

We did not expect the type of performance to explain variation in effect size, and yet we found that endurance was more affected than speed (Table III; Fig. 3). Endurance is dependent upon the host's metabolic capacity, and several studies have demonstrated altered host metabolism due to parasitism (Robar et al., 2011), which can result in a reduction in endurance (Binning et al., 2013).

Finally, experimental infections had larger negative effect sizes than did natural infections (Table III; Fig. 3), suggesting (not surprisingly) that experimental approaches are more powerful. Yet, these experimental approaches are done by investigating the effect of a single parasite species and often with both the host and parasite raised for some time under laboratory conditions. Although this approach is scientifically sound and powerful for detecting causal relationships, it ignores the fact that most hosts are infected by several species of parasites, and the interaction between these parasites can be as important as the isolated effect of each species. Future experimental approaches that examine how multiple infections impact host performance capacity (Ferguson et al., 2012) under more-realistic conditions (mesocosms, field experiments) would likely yield a better understanding of how much parasites influence host performance capacity in nature.

THE EFFECT OF STUDY YEAR

Publication year was not correlated with effect size (Fig. 4). This finding is different from a previous meta-analysis of the effect of parasite on host behavior which showed that effect sizes were negatively related to publication year. This suggests that the publication history of parasites' impact on host performance capacity has not been unduly influenced by biases due to trends or prior expectations, as is apparent in the literature on parasites' effects on host behavior (Poulin, 2000). Although there is no trend, the amount of variation in reported effect sizes has increased with publication year. This may be due to the accumulation of studies that have examined a greater diversity of host–parasite interactions, which could be expected to result in more variable effect sizes. As noted above, the increase in variation with time may suggest that more positive effect sizes will soon be discovered, as after ~2000 there are many more reports of effect sizes greater than 0.

CONCLUSION AND PROSPECTUS

Parasites exert important impacts on host performance capacity. In some cases the mechanistic underpinnings of changes in host performance, i.e., alteration of morphology or/and physiology (Fig. 1), are well understood; for example, a non-functional swimbladder in eels infected by nematodes (Palstra et al., 2007), a reduction in tracheal gas exchange in honey bees by mites (Harrison et al., 2001), or deformities of rainbow trout due to infection by myxozoans (Fetherman et al., 2011). However, in most cases they are not, and some possible mechanism can only be hypothesized (Goater et al., 1993; Bradley and Altizer, 2005). Although the mechanistic link between parasites and performance may be difficult to separate from other factors affecting host behavior, it nevertheless could involve a broad range of factors from simple morphological alterations to more-complex hormonal/biochemical changes in the host (Lafferty and Shaw, 2013). Importantly, parasites may impact host evolution via performance alteration. As such, an integrative understanding of parasites, host morphology/physiology, and host performance would greatly refine our understanding of how parasites alter host fitness and whether or not such an impact may have an adaptive value not only for the parasite but for the host as well (Harrison et al., 2001; Ebert, 2005).

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